Human Research Application (Version 1.10)

1.0 General Information

***Please enter the full title of your study:**

Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.

***Enter an ACRONYM, protocol nickname, or sponsor's protocol #. This field should contain the name colloquially used to refer to the study. It will assist in identifying the study easily. (Velos users: 20 character maximum.)**

HOPE
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add Department(s)

2.1 List the PI's academic appointment department as the primary department here (for the Department of Medicine at Einstein/Montefiore, the Division must be identified). IN ADDITION: ** For studies conducted at NBHN, an NBHN department must be listed here. **For studies managed by the Office of Clinical Trials, OCT must be listed here. ** For studies conducted at the CRC, CRC must be listed here. **For Quality Improvement studies conducted at MMC, Network Performance Group must be listed here. For drug studies: list either the Einstein-Montefiore Pharmacy or the NBHN Pharmacy here. :**

Primary Dept?	Department Name
◉	**E-MMC** - Surgery

3.0 Assign Key Personnel access to the project

3.1 *Please add a Principal Investigator for the study:

Azzi, Yorg A

3.2 Identify all other Key Personnel (individuals who contribute in a substantive way to the scientific development or execution of the project, or the consent process) here. Individuals from external institutions covered by their own IRB approval need not be listed here.

A) Additional Investigators

Ajaimy, Maria
Co-Investigator
Akalin, Enver
Co-Investigator
Bellemare, Sarah
Co-Investigator
Fortune, Brett, M.D.

Co-Investigator
Goldstein, Daniel
Co-Investigator
Graham, Jay A
Co-Investigator
Hemmige, Vagish
Co-Investigator
Hemmige, Vagish
Co-Principal Investigator
Kinkhabwala, Milan
Co-Investigator
Minamoto, Grace Y, M.D.
Co-Investigator
Muggia, Victoria A
Co-Investigator
Patel, Snehal R
Co-Investigator
Puius, Yoram
Co-Investigator
Pynadath, Cindy
Co-Investigator

B) Research Support Staff

Gjelaj, Christiana
Nurse
Mejia, Paola
Research Associate
Nucci, Cecilia
Nurse
Raees, Harith
Research Associate
Saeed, Omar
Participating Clinician
Wokonko, Olachi
Nurse

3.3 *Please add a Study Contact:

Azzi, Yorg A
Mejia, Paola
Raees, Harith

In this section, list the PI and all individuals who should receive communications (e.g. notification of approval, issues requiring revisions, etc.). Note that this section is not considered "Key Personnel" - anyone listed here who is involved in the conduct of the project must be named in one of the sections above.

3.4 If the PI is an Einstein faculty member, Montefiore physician or if the study will consent participants at any Montefiore facility, please identify the Regulatory Coordinator for this protocol. (PIs must designate here the individual that will be allowed access to their study in the Velos Clinical Research Management System and will be RESPONSIBLE for: (1) Entering /verifying all of the study information in Velos; Assigning access roles/rights in Velos and Epic for all study personnel ; (3) Activating a study after IRB approval. This person must be trained in the Velos system. Note that this section is not considered "Key Personnel" - anyone listed here who is involved in the conduct of the project must be named in one of the

sections above. If you have questions about Velos, please view the Velos Information Portal (https://ephpublic.montefiore.org/Velos_CTMS) or contact veloshelp@montefiore.org.)

4.0 iRIS Resources

4.1 The Einstein IRB requires that you use the latest version of the application. If a "Convert to the New Form Version" button appears above, click on it to update to the newest version. You will then need to click "Save and Continue" to recreate the saved answers to your application.The version you are using is: March 2021

4.2 For guidance on using iRIS, please consult the following resources:

- **our FAQ (Frequently Asked Questions) at the link here.**
- **download the Researcher Handbook from the Help Menu (orange and white question mark on the upper right of your screen).**

For IRB Staff only: The application is enabled for the Final Rule.
The response to this question should be "Yes" after 12/25/2018.

(•) Yes ( ) No

4.3 Would you like to go to void the application? (for IRB Administrators only)

( ) Yes (•) No

Selecting "Yes" to this question will send an incomplete application to the IRB.

5.0 Type of Application

5.1 Please note: These questions were re-ordered in July 2015.

5.2 Select the payroll or primary appointment for the PI:

( ) Einstein
(•) Montefiore
( ) PAGNY/JMC/HHC
( ) YU
( ) Burke
( ) White Plains Hospital
( ) Montefiore New Rochelle
( ) Montefiore Mount Vernon
( ) Montefiore Nyack
( ) Montefiore St. Luke's Cornwall
( ) Other

5.3 Does this project involve any staff or resources from White Plains Hospital?

( ) Yes (•) No

5.4 Does this project involve any staff or resources from the Burke Rehabilitation Hospital?

○ Yes ◉ No

If yes, review is required by Dr. Mooyeon Oh-Park and Valerie Vermiglio-Kohn. Routing instructions will appear on the last page of your Submission Form.

5.5 Is this protocol investigator- or student-initiated?

Investigator Initiated Studies: Studies initiated, developed, designed and managed by a qualified individual who assumes sole responsibility for the conduct and management of the study.

◉ Yes ○ No

5.6 Was the Principal Investigator a major author/initiator of this study?

◉ Yes ○ No

5.7 Is this project being conducted by a student/resident/fellow as part of their academic curriculum?

○ Yes ◉ No

5.8 Are there any sources of support (e.g. funds, supplies, drugs, devices or equipment) or sponsors? This includes departmental funds.

Sponsor: The company, institution, government agency or individual that holds the IND/IDE and/or is responsible for initiation, management and financing the study.

○ Yes ◉ No

Does this study receive funding from the NIH (either directly or through a subcontract)?

○ Yes ◉ No

5.9 Is this project grant funded?

○ Yes ◉ No

5.10 Do you anticipate having a grant awarded to this project or obtaining support (e.g. funds, supplies, drugs, devices or equipment) from an outside source in the future?

○ Yes ◉ No

When this funding or support is received, update the IRB application with an amendment.

5.11 Is this a multicenter study? A multicenter study is conducted according to *a single protocol* but at *more than one site*, and therefore, carried out by *more than one principal investigator*.

○ Yes ◉ No

5.12 Is this a cancer related project being conducted at/by Einstein/Montefiore/White Plains Hospital?

○ Yes ◉ No

5.13 Does this project involve the Montefiore Office of Clinical Trials in any way (e.g. management of clinical trial agreements, subject compensation, MTAs, DUAs, etc.)?

○ Yes ◉ No

5.14 Select all that apply:

☐ The study involves Epic orders (medications, tests or services)
☐ Research visits will be scheduled in Epic
☐ The study involves a drug or device
☐ The CRC will draw blood for this study
☐ Blood will be processed at a Montefiore facility

For questions about research studies in Epic, please contact Jason Hussey JHUSSEY@montefiore.org.

5.15 Is this a migration of a study previously approved by the Burke IRB?

○ Yes ◉ No

5.16 Is this a migration of a study previously approved by the White Plains Hospital IRB?

○ Yes ◉ No

5.17 Is this a migrated study that was originally approved by the Einstein or Montefiore IRBs outside of iRIS? (If the IRB number at the top of the screen is in the format YYYY-NNNN (e.g. 2014-2222), answer "No.")

○ Yes ◉ No

For studies previously approved by the Burke IRB you should answer "No" to this question.

5.18 Do you consider your submission to be a quality improvement (QI) project?

○ Yes ◉ No

5.19 Is this application for the non-emergency use of a Humanitarian Use Device (HUD)?

○ Yes ◉ No

5.20 Is this application for the emergency use of an investigational drug or device, or emergency use of a Humanitarian Use Device (HUD)?

○ Yes ◉ No

5.21 Is this a treatment use of an investigational drug or device?

- *Do not select "Yes" without discussing this with a member of the Einstein IRB staff. You may reach out to irb@einsteinmed.org.*
- *Note: For a Humanitarian Use Device (HUD) the response to this question should be "No".*
- *Note: For an Emergency Use the response to this question should be "No".*
- *For guidance refer to the policies on **Treatment Use of an Investigational Drug** and **Treatment Use of an Investigational Device**.*

○ Yes ◉ No

5.22 Primary Purpose

Make a single selection. If you are not sure of the response, please consult the PI.

- ○ Treatment Study: Testing new treatments, new drug combinations, or new approaches to surgery or therapy
- ○ Prevention Study: Examining ways to improve prevention or recurrence of disease through, for example, medicines, vitamins, vaccines, minerals, and lifestyle changes
- ○ Diagnostic Study: Finding improved testing techniques and procedures for diagnosing diseases and conditions
- ○ Screening Study: Testing the best method of identifying certain diseases or health conditions
- ◉ Supportive care/Quality of Life Study: Investigating procedures to improve comfort and quality of life for patients with a chronic condition
- ○ Health Services Research Study: Evaluating the delivery, process, management, organization, or financing of health care
- ○ Basic Science: Examining how an intervention works
- ○ Epidemiological Study: Identifying patterns, causes and control of disorders in groups of people
- ○ Emergency Use/Treatment Use (Expanded Access)/Humanitarian Use Device (HUD)

5.23 Clinical Research Category

Select one:

- ◉ Interventional
- ○ Observational
- ○ Ancillary/Correlative
- ○ None of the Above - Not Clinical Research

Select "None of the Above" for Emergency Use, Treatment Use (Expanded Access) and Humanitarian Use Device (HUD).

5.24 Is this a protocol registration? The IRB responsible for the research is not the Einstein IRB (e.g. BRANY, NCI CIRB, and other approved external IRBs).

○ Yes ◉ No

5.25 Please select all that apply:

This section is designed to help identify studies subject to the European Union's General Data Protection Regulation (EUGDPR).

- ☑ We are the lead site for research activities taking place at EU sites, such as acting as a prime recipient of an NIH grant which flows through sub-awards to EU sites.
- ☐ This study involves mobile applications that target enrollment in the European Economic Area (EEA).
- ☐ This is an industry-sponsored study for a company located in the European Economic Area (EEA), with personal data of US residents being sent to and/or processed in the EEA.
- ☐ None of the above.

5.26 Will human specimens be utilized under this study?

Human tissue includes fresh tissue (in saline), fixed tissue (in formalin), tissue processed and embedded in paraffin blocks, frozen tissue, tissue on histology slides (unstained, H&E stained, etc.).
Human tissue also includes body fluids (e.g., blood, serum, plasma, urine, CSF, etc.)

This includes the main study, substudies and optional procedures.

◉ Yes ○ No

5.27 Will you be contracting with an external vendor or service to collect, manage or store your research data?

○ Yes ◉ No

The vendor must be listed as an External Site on the Protocol Sites page.

5.28 Will you be conducting this project as part of your affiliation with Einstein, MMC, or an affiliated institution?

Do not select "No" without discussing this with a member of the Einstein IRB staff. You may reach out to irb@einsteinmed.org.

◉ Yes ○ No

5.29 Is this a COVID19 related project being conducted at/by Einstein/Montefiore/White Plains Hospital?

○ Yes ◉ No

6.0 Clinical Trials and ClinicalTrials.gov

6.1 There are numerous definitions of clinical trials. Please check "Yes" for any that apply.

*Note that the trial does not need to be under the jurisdiction of the **NIH** or **FDA** in order to meet their definitions of clinical trial. If you mark "Yes" to either NIH or ICMJE in most cases you will need to mark "Yes" to **both**.*
*Note: Studies that meet the FDA definition of clinical trial and NIH-funded studies that meet the NIH definition of clinical trial are required to be registered on clinicaltrials.gov. (See IRB **guidelines**.)*

6.2 Is this an FDA Clinical Trial?

*Note that Expanded Access and Compassionate Use protocols are not generally considered to be clinical trials under these definitions. Please consult this **document** and contact clinicaltrials.gov@einsteinmed.org for further guidance.*

A. This is a trial of one or more drugs and/or biologics.

○ Yes ◉ No

B. This is a trial of one or more devices.

○ Yes ◉ No

This is an ***interventional clinical trial*** (with one or more arms) of FDA-regulated drugs, biological products, or devices according to the following definition:

FDA defines an ***interventional clinical trial*** to mean that human participants are assigned prospectively to an intervention or interventions according to a protocol to evaluate the effect of the intervention(s) on biomedical or health related outcomes.

○ Yes ◉ No

6.3 Does this study meet the definition of an ICMJE Clinical Trial?

The ICMJE defines a clinical trial as any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention and a health outcome. Health-related interventions are those used to modify a biomedical or health-related outcome; examples include drugs, surgical procedures, devices, behavioural treatments, educational programs, dietary interventions, quality improvement interventions, and process-of-care changes. Health outcomes are any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. The ICMJE does not define the timing of first patient enrollment, but best practice dictates registration by the time of first patient consent.

Note: The ICMJE requires, and recommends that all medical journal editors require registration of clinical trials in clinicaltrials.gov at or before the time of first patient enrollment as a condition of consideration for publication. If this study meets the definition of an ICMJE clinical trial and you plan to publish, the answer below should be marked "Yes".

○ Yes ◉ No

6.4 Is this study funded by the NIH and meets the definition of a NIH Clinical Trial as described below?

NIH defines a clinical trial as a research study in which **one or more** human subjects are prospectively assigned to one or more interventions (as defined below) to evaluate the effects of those interventions on health-related biomedical and/or behavioral outcomes.

Intervention: Any manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs /small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

Guidance on the NIH Clinical Trial definition may be found here: https://grants.nih.gov/policy/clinical-trials /definition.htm.

○ Yes ◉ No

6.5 Is this an OHRP Clinical Trial?

OHRP defines a clinical trial as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Intervention: Intervention includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

○ Yes ◉ No

6.6 Regardless of your answers above, is this study already registered with clinicaltrials.gov?

IMPORTANT NOTE: If this is an investigator-initiated clinical trial and it does not meet the NIH or FDA or OHRP clinical trials registration requirements, you are strongly advised to consider registering your trial to comply with the following additional requirements:

- International Committee of Medical Journal Editors (ICMJE) for publication purposes. See **http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues /clinical-trial-registration.html**
- Center for Medicare & Medicaid for research billing claims for qualifying clinical trials. See CMS Q&A **https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development /Downloads/Mandatory-Clinical-Trial-Identifier-Number-QsAs.pdf**
- Many sponsors are now requiring registration and results reporting. **https://www.who.int /news-room/detail/18-05-2017-major-research-funders-and-international-ngos-to-implement-who-standards-on-reporting-clinical-trial-results**

○ Yes ◉ No

If "Yes," what is this NCT # of this study?

7.0 Protocol Sites and Collaborators

7.1 Sites and collaborators under the jurisdiction of the Einstein IRB

Select all AFFILIATED site(s) and collaborators at which ANY of the following activities will occur:

- Protocol dictated procedure or research assessment (including sample collection, interviews, evaluations, tests, or other interventions)
- Data storage/data analysis
- Consenting subjects
- Recruiting subjects
- Administering an emergency use drug or implanting/using an emergency use device
- Using/implanting a Humanitarian Use Device (HUD)

- Quality improvement, quality assurance, program evaluation activities

If you select CRC as a site:
* It must be listed as a Department in Section 2.0 (Setup Department Access).
*CRC approval is required. To apply for CRC approval submit your protocol **here**. The CRC will then forward their approval to the IRB. You may apply for IRB approval and CRC approval simultaneously.
*For studies in which the study drug is being stored at CRC the approval of Director, Clinical Research Center (CRC) must be obtained via the signature routing page during the submission of the application (or amendment). The name of the Director can be found **here**.

If you select an NBHN site, the NBHN Department must also be listed as a Department in Section 2.0 (Setup Department Access).

Einstein	Montefiore	NBHN	Yeshiva University
☐ Laboratory/Office ☐ CRC East ☐ CRC West ☐ MRRC ☐ CERC (Einstein) - only prior to 4/1/2018 ☐ DOSA (Einstein) - only prior to 4/1/2018 ☐ SVTN (Einstein) - only prior to 4/1/2018 ☐ Off-site rental space - only prior to 4/1/2018	☑ Moses Division ☐ CHAM ☐ Wakefield (North) Division ☐ Weiler Division ☐ Westchester Square Division ☐ Hutchinson Division ☐ Montefiore Medical Group (MMG) ☐ CERC ☐ DOSA ☐ SVTN ☐ Radiation Oncology @ St. Barnabas ☐ Burke Rehabilitation Hospital ☐ White Plains Hospital (requires WPH PI or co-I) ☐ Montefiore New Rochelle (EXPANDED ACCESS ONLY) ☐ Montefiore Mount Vernon (EXPANDED ACCESS ONLY) ☐ Off-site clinics and faculty practice locations ☐ Advanced Oncology Associates ☐ Nyack (EXPANDED ACCESS ONLY) ☐ St. Luke's Cornwall (EXPANDED ACCESS ONLY)	☐ Jacobi Medical Center ☐ North Central Bronx Hospital ☐ Child Health Center at Glebe Ave - only prior to 4/1/2018 ☐ Health Center at Gunhill - only prior to 4/1/2018 ☐ Health Center at Tremont - only prior to 4/1/2018	☐ Azrieli School of Education ☐ Cardozo School of Law ☐ Center for Public Health Sciences ☐ Ferkauf Graduate School of Psychology ☐ Wurzweiler School of Social Work ☐ Stern College ☐ Syms School of Business ☐ Katz School ☐ Yeshiva College ☐ Marsha Stern Talmudical Academy ☐ Samuel H. Wang High School for Girls

***The Einstein IRB only reviews Expanded Access protocols for Montefiore Mount Vernon, Montefiore New Rochelle, Montefiore Nyack and Montefiore St. Luke's Cornwall at this time. Please contact the IRB at irb@einsteinmed.org if you have questions.*

7.2 Will the study participant have or be assigned a Montefiore MRN in order to have study related procedures performed at an MMC site?

○ Yes ◉ No

Answer "No" for retrospective chart reviews ONLY.
Answer "Yes" if blood draws will be done at the CRC.

7.3 External sites and collaborators

List all UNAFFILIATED/EXTERNAL sites and collaborators at which ANY of the following activities will occur:

- Data coordinating center
- Sending or receiving data or specimens
- Protocol dictated procedure or research assessment (including sample collection, interviews, evaluations, tests, or other interventions)
- Data storage/data analysis
- Consenting subjects
- Quality improvement, quality assurance, program evaluation activities

For multi-center trials: enter each participating site only if the YU/MMC/JMC/NCB PI is the national /international coordinator for this study OR if the site is sending specimens/data to or receiving specimens from YU/MMC/JMC/NCB.

Name of Site	Responsible IRB	Site Characteristics	Site Activities
No records have been added			

**Before selecting Not Engaged, IIA (Individual Investigator Agreement) or IAA (IRB Authorization Agreement), please consult with the Einstein IRB Office.*

For studies submitted approved prior to January 1, 2018: If IIA or IAA or "Not Applicable (site not engaged in research)" is selected for any site, provide the following information:
1. A list of research activities that will be done at each site
2. Who will be conducting each activity and his/her institutional affiliation

8.0 CITI Education Check Information

8.1 PRINT THESE INSTRUCTIONS SINCE YOU WILL NEED TO NAVIGATE AWAY FROM THIS FORM. Click "Print Friendly" and select "HTML Form" and click OK.

8.2 Instructions for checking the education status for key personnel:

1. **Open iRIS in a second browser such as IE, Chrome or Firefox.**
2. **Click on Study Assistant > My Studies**
3. **Click on the notepad icon next to your study to open the study.**
4. **Next to Navigation in the blue field above, click on "study mgmt."**
5. **Click on the Study Management tab (on the upper left, a little bit underneath the red IRB number).**
6. **Click on Study Summary/Profile.**

7. **Click on the head icon next to each study personnel (except those listed ONLY as study contacts). The CITI status is under Education History. The following courses qualify for the education check: Basic Course and Refresher Course and any course name with "Human" in the beginning. Effective January 1, 2015, Good Clinical Practice (GCP) training is required of all KP for studies involving drugs and/or devices. Effective January 1, 2017, GCP training is required for all KP on NIH-sponsored, NIH-defined clinical trials. For more information on GCP courses click here.**
8. **If the Education History only has expired courses, the Key Personnel will NOT pass the CITI check on iRIS. As a result, the IRB application will not be received by the IRB.**

8.3 I understand that if any Key Personnel do NOT pass the CITI education check, the IRB application will NOT reach the IRB.

☑ I have checked the CITI status of all Key Personnel on this study.

8.4 I understand that if any Key Personnel do NOT pass the CITI education check, the IRB application will need to be re-approved by the Department Chair.

☑ I have checked the CITI status of all Key Personnel on this study.

9.0 Conflict of Interest Disclosure Requirements

9.1 NOTE: THIS SUBMISSION WILL BE DENIED AND SENT BACK TO THE RESEARCHERS IF ANY INVESTIGATORS DO NOT HAVE CURRENT COI DISCLOSURES ON FILE (SEE #1 BELOW FOR DETAILS).

9.2 In order to ensure prompt review by the COI committee, you must complete the following steps:

9.3 1. Verify that the Principal Investigator and Additional Investigators (individuals listed in section 3.2. a) have current (filed within the past 6 months) COI disclosures on file. You may email coi@einsteinmed.org your list of key personnel to very they have current disclosures. Individuals listed as "Research Support Staff" do not need to have COI disclosures on file.

9.4 2. The IRB recommends that you send the following information by e-mail to all investigators who do not have a current COI disclosure on file:

9.5 ***PI Name: Protocol Title: Conflict of Interest (COI) disclosure forms are accessible via the COI web system. You have to be registered as a user – in the COI web system - in order to complete a Conflict of Interest disclosure form. The COI web system requires MMCAD* username credentials for access. Please go directly to the COI web system log-in screen; at this link https://einstein.coiriskmanager.com you will be prompted to enter your MMCAD credentials*. If the screen is blank after you've entered your credentials and logged in, contact COI at*** **coi@einsteinmed.org** ***for access. Once reaching the main COI log-in page: 1- If you have completed a COI disclosure form in the past and the system does not recognize the MMCAD credentials you are using, please send an e-mail to*** **coi@einsteinmed.org** ***stating you need your log-in credentials updated in the COI web system. *For those without MMCAD credentials, please contact*** **coi@einsteinmed.org** ***and include in the e-mail your full name, department, office/lab number, e-mail address, the purpose of your request (IRB submission, grant application, academic appointment, etc.) and MMCAD username (if known). PLEASE DO NOT REQUEST NEW MMCAD CREDENTIALS IF YOU HAVE ALREADY BEEN PROVIDED THEM.***

9.6 I understand that if any individuals listed as Investigators do NOT have a Conflict of Interest disclosure on file, the IRB application will NOT reach the IRB.

☑ I have checked that the Principal Investigator and all Additional Investigators (individuals listed in section 3.2.a) have current electronic Conflict of Interest disclosures on file.

10.0 General Application Introduction

10.1 Congratulations on completing the preliminary sections of the application! Press "Save and Continue" to proceed to the main sections of the human research application.

(•) Proceed with the IRB application

11.0 Preliminary Questions

11.1 Does this research involve Einstein medical students as collaborators? *These protocols must be approved by the Dean of Students, Christina Chin, via the signature routing pages. See the Researcher Handbook (located in the help menu) for additional information.*

( ) Yes (•) No

11.2 This IRB application is being sent for exemption determination prior to January 1, 2019.

This option may not be selected after January 1, 2019.

( ) Yes (•) No

11.3 We are applying for an exempt determination on or after January 1, 2019.

This option must be selected for new exempt submissions submitted to the IRB after January 1, 2019.

The following categories of research may be eligible for exempt determination and/or limited IRB review:

- Determinations that the institution is not engaged in research
- Research on deidentified specimens or data
- Research conducted in established or commonly accepted educational settings
- Research that only includes interactions involving educational tests, survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) of adults
- Research involving benign behavioral interventions with adult subject if the subjects prospectively agrees to the intervention and information collection.
    - Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing.
    - The research may not involve deception (unless subjects are prospectively informed that they will be misled).
- Secondary research uses of identifiable private information or identifiable biospecimens
- Research and demonstration projects that are conducted or supported by a Federal department or agency
- Taste and food quality evaluation and consumer acceptance studies

( ) Yes (•) No

- *A detailed summary of all the new Exempt Categories is available **here**.*
- *And a decision chart for the new Exempt Categories is available **here**.*
- *More information about Benign Behavioral Research is available **here**.*

11.4 Will an electronic system be used to extract patient data from the Montefiore medical charts for this study?

○ Yes ◉ No

11.5 Does this study involve stem cells and/or fetal tissue?

○ Yes ◉ No

11.6 Is this an NIH supported or conducted Genome-Wide Association Study (GWAS)?

○ Yes ◉ No

11.7 Is this a research study involving Acutely toxic materials (e.g., arsenic, cyanide), Neurotoxic materials (e.g., MPTP), Carcinogens (e.g., ENU, MNU, formaldehyde, azoxymethane), Mutagens /teratogens (e.g., BrdU), Heavy metals (e.g., mercury, cadmium, chromium, silver, lead), Other chemicals that may be toxic to target organs (e.g., streptozotocin, carbon tetrachloride), Chemotherapy agents (e.g., mitoxantrone, 5-FU), Waste anesthetic gases (e.g., isoflurane, halothane), Other regulated chemicals (e.g., EPA P-list or U-listed, OSHA toxic and hazardous substances)? *If you are unsure email ehs@montefiore.org or call 718-920-7600.*

○ Yes ◉ No

12.0 Accrual Information

Local researchers here means researchers under the jurisdiction of the Einstein IRB, including those under an IIA or an IAA.

12.2 Will the ONLY research activity be analysis of specimens or data/medical records obtained without consent by the local researchers? *(Note: This means there will be NO interventions with human subjects during the research study.)*

○ Yes ◉ No

12.4 What is the anticipated total number of participants to be enrolled by the local researchers? *This should include the number of subjects expected to complete the study PLUS however many subjects you anticipate will fail screening, drop out, or otherwise not complete the protocol. **For migrated studies, this refers to the number of participants to be enrolled by the local researchers over the course of the study (from the beginning of the study, not just from today forward).*

200

How many participants do you expect to complete the study?

200

Either of these numbers may be used in the consent document.

12.5 Number of Specimens/Research Records/Medical Records

Will you be accessing specimens, research records and/or medical records without consent (for activities other than recruitment of subjects)?

○ Yes ◉ No

If "Yes":

How many specimens will be studied over the life of the study?

How many research/medical records will be reviewed over the life of the study?

13.0 Human Specimens

13.1 Will your study use human tissues obtained through Montefiore Medical Center?

Human tissue includes fresh tissue (in saline), fixed tissue (in formalin), tissue processed and embedded in paraffin blocks, frozen tissue, tissue on histology slides (unstained, H&E stained, etc.).

○ Yes ◉ No

13.2 Will your study use body fluids (blood/serum/plasma/urine/CSF/other) at Einstein or Montefiore?

Note: All samples provided by Surgical Pathology for research purposes require tracking and approval by the Einstein/Montefiore Biorepository/BARC (Jeff LaFleur). Please enter the request for services into the ICTR portal – choose BIOR. The link for the portal is here: **http://www.einsteinmed.org/centers/ictr/**.

○ Yes ◉ No

13.3 Will any samples be stored within the Einstein/Montefiore Biorepository?

○ Yes ◉ No

Where will you be storing the samples?

No samples will be collected

13.4 Will specimens be collected under another protocol approved by the Einstein IRB?

○ Yes ◉ No

If “Yes,” provide the IRB number(s).

13.5 Will specimens be left over from standard clinical care?

○ Yes ◉ No

If "Yes," answer the following two questions:

Type(s) of specimens:

How and where will the specimens be obtained?

13.6 Will the research team have access to identifiers (or, if the specimens will be coded, will the research team have access to the key to the code)?

○ Yes ◉ No

13.7 Will specimens be received from any unaffiliated or external sites (e.g. blood banks, sponsoring institutions, agencies, etc.)?

○ Yes ◉ No

13.8 Will the specimens be sent to any unaffiliated or external sites (e.g. blood banks, sponsoring institutions, agencies, etc.)?

○ Yes ◉ No

13.9 Will the specimens collected be destroyed once this study is complete?

If "Yes," and if the specimens will be sent to external entities, provide written verification that the specimens will be destroyed at the conclusion of the study.

○ Yes ◉ No

14.0 General Information for the Standard Application

14.1 Brief summary:

Montefiore's research in HIV-positive to HIV-positive transplantation will address questions related to HIV superinfection; incidence and severity of opportunistic infections (including transmission of occult OIs from donor to recipient); immunologic mechanisms contributing to the increased rate of kidney rejection observed in HIV-positive recipients and quality of life for recipients of HIV- positive to HIV-positive transplantation.

14.2 Risks (other than breach of confidentiality):

Risks listed here MUST be consistent with the risks on the consent form.

1-Blood draw may cause discomfort, bleeding or bruising where the needle enters the body
2-Graft Biopsy complication of a biopsy include pain and bleeding
3- Genetic information Montefiore Medical Center follows procedures to prevent people who work with your DNA information from being discoverable

14.3 Benefits:

Benefits listed here MUST be consistent with the benefits on the consent form.

The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV.

14.4 Was this ever submitted to the Einstein IRB under a different IRB number?

○ Yes ◉ No

If "Yes," provide the IRB number:

14.5 Was this ever disapproved by an IRB?

○ Yes ◉ No

If "Yes," specify the reviewing committee and findings related to the disapproval:

15.0 Confidentiality

15.1 May individuals, other than members of the research team, OHRP, FDA, and the Einstein IRB, review the research records and/or medical records? (e.g. Sponsors, Collaborators, etc.)

(•) Yes ( ) No

If "Yes," specify below who may have access:

Patient's physician other than the research team for the patient's safety

15.2 Specify how confidentiality will be ensured (e.g. will the records be kept in a secured manner; who will have access to the records; will the records be identifiable or coded; will computer records be password protected, etc.):

The records will be kept in a secured manner; only research team will have access to the records; the records will be identifiable or coded; computer records will be password protected
All paper charts will be kept in a secured room and inside a secured cabinet. All Data will be coded by assigned subject number.

Will you be storing research data without a code?

( ) Yes (•) No

If "Yes," provide an explanation:

15.3 Specify when the identifiers will be destroyed (if they will not be destroyed, state so here):

Only clinical data will be recorded in the Electronic Data Capture System. No Identifiers will be shared

15.4 Will the researchers be destroying the samples AND data collected during this study at the end of the study?

( ) Yes (•) No

Describe the plan for storage and distribution of samples and/or data:

We will store patient's specimens and information in a "biobank", which is a library of information and specimens (tissue and blood) from many studies.

This information should also be included in the Protocol. If samples and/or data are being stored in an IRB approved biobank, state so here and provide the IRB# for this bank.

15.5 Will you be applying for or have you received a Certificate of Confidentiality for this study?

( ) Yes (•) No

As of October 1, 2017 a Certificate of Confidentiality became a term and condition for NIH grant awards that commenced or were ongoing after December 1, 2016. Any NIH-sponsored research that collects identifiable data or biospecimens or generates human genomic data automatically receives a Certificate. In addition, any research project that collects personally identifiable, sensitive information and that has been approved by an IRB is eligible for a Certificate. NIH or federal funding is not a prerequisite for a Certificate. A Certificate of Confidentiality helps researchers protect the privacy of human research

participants enrolled in research that collects sensitive information. Sensitive information includes information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information pertaining to illegal conduct; information that, if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant. Researchers may apply for a Certificate through the NIH or Center funding the research. Further information about obtaining a Certificate of Confidentiality is available on the NIH website at: ***http://grants2.nih.gov/grants/policy/coc/index. htm***
Einstein provides guidance on Certificates of Confidentiality ***here****.*

16.0 Informed Consent

16.1 Will protected health information (PHI) be collected or accessed or created under this study?

(•) Yes ( ) No

16.2 Will you be identifying potential subjects for this study by accessing medical/clinical records without consent?

(•) Yes ( ) No

16.3 Will you be obtaining written consent?

(•) Yes ( ) No

16.4 Are you requesting a waiver of signed documentation of consent? (e.g., oral consent, web survey consent, etc.)

Select "Yes" if you are NOT obtaining any signed consent documents. This does NOT refer to the oral presentation of the written consent document.

( ) Yes (•) No

16.5 Are you planning a prospective intervention for or interaction with subjects without their written or oral consent? (For example, an intervention conducted for all patients on a particular day or on a particular floor.) Approval of this option is very limited and consultation with the IRB before requesting this is recommended.

( ) Yes (•) No

Provide the name of the IRB staff member that you consulted with:

16.6 Will you be doing research on decedents?

( ) Yes (•) No

16.7 Will the research involve deception?

( ) Yes (•) No

17.0 Exclusion/Inclusion Criteria

17.1 Population Exclusion

17.2 Is any gender excluded?

○ Yes ◉ No

If "Yes," provide a justification:

17.3 Is any race excluded?

○ Yes ◉ No

If "Yes," provide a justification (including which race(s) and why):

17.4 Is any ethnic group excluded?

○ Yes ◉ No

If "Yes," provide a justification (including which ethnic group(s) and why):

17.5 Are pregnant women excluded?

*Please note: The inclusion of pregnant women in research studies is limited. Please see our policy **here**. Note that unless you are **specifically** studying this population you should mark "yes" below (pregnant women are excluded).*

◉ Yes ○ No

If "**No**," provide a justification:

17.6 Are non-pregnant women excluded?

○ Yes ◉ No

If "Yes," provide a justification:

17.7 Are minors excluded?

*Please note: The inclusion of children in research studies is limited. Please see our policy **here**. Note that unless you are **specifically** studying this population you should mark "yes" below (minors are excluded).*

◉ Yes ○ No

If "Yes," provide a justification:

Our team follows up only adult transplant recipients.

If minors are **included** provide the age range below:

Minimum age:

Maximum age:

17.8 Are monolingual Spanish speaking subjects excluded?

○ Yes ◉ No

If "Yes," provide a justification:

17.9 Are other non-English speaking subjects excluded?

◉ Yes ○ No

If "Yes," provide a justification:

We do not expect to enroll a significant number of subjects who speak a common language other than English or Spanish

17.10 Are subjects with HIV excluded from participation in this study?

○ Yes ◉ No

A. If "Yes," does the research study include testing of HIV status?

○ Yes ○ No

B. If "Yes" to A above (HIV testing), are you only studying HIV infected people who already know their HIV status?

○ Yes ○ No

17.11 Population Inclusion

17.12 Are subjects being enrolled in the study while they are experiencing significant pain? (See the Subjects in Significant Pain policy.)

○ Yes ◉ No

If "Yes," how will consent be obtained?

17.13 Are subjects who have an altered mental status (e.g. patients who are under the influence of sedatives or narcotics, etc.) included?

◉ Yes ○ No

If "Yes," how will consent be obtained?

Patients with altered mental status as a result of their end organ disease (i.e. end stage liver disease or heart disease) who are consenting to the actual transplant surgery by proxy will also consent to the potential receipt of HIV-positive organs by proxy.

17.14 Are adult subjects who may not be capable of giving informed consent (e.g. intellectual disability, dementia, acute psychiatric disorders) included?

Please check all that apply:

☐ This is a research protocol specifically intended to study individuals with diminished capacity (e.g.

Alzheimer's disease; mental retardation; delirium).

☐ This is a research protocol conducted in an environment (e.g. nursing home, ICU, ER) or on a population group (e.g. schizophrenic patients, intoxicated patients) in which it can be reasonably anticipated that some potential subjects will have diminished capacity, either permanently or at some time during the study.

☐ Included at the request of the IRB.

☑ None of the above.

If "Included at the the request of the IRB" was selected above, state the name of the staff or Board member you spoke with:

17.15 Is this a research protocol specifically intended to study individuals who are at risk of having capacity diminish during the course of the study (e.g., a longitudinal study enrolling subjects at the early stages of Alzheimer's disease)?

○ Yes ◉ No

17.16 Are women in labor included?

○ Yes ◉ No

17.17 Are YU students the target population under study?

○ Yes ◉ No

17.18 Are YU/MMC/JMC/NCB employees the target population under study?

○ Yes ◉ No

18.0 Waiver of Informed Consent/HIPAA Authorization to Review Records for Recruitment Purposes

18.1 Confirm that all of the following are true:

The review of medical/clinical records involves no more than minimal risk to the subjects.

The waiver of consent/authorization does not adversely affect the rights and welfare of the subjects.

The review of medical/clinical records could not practicably be carried out without the requested waiver.

The plan to protect confidentiality (including protection of identifiers from improper use and a plan to destroy identifiers, where appropriate) is described in the confidentiality section of the application.

If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

The PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

The research team will be accessing records that contain health information that may also include some or all of the 18 HIPAA identifiers.

18.2 Are all of the preceding statements true?

(•) Yes ( ) No

19.0 Informed Consent Process

19.1 ***Informed consent is a process that takes place between the potential subject and the researcher /research team, before, during and sometimes after, the study. Participants are required to receive a full explanation of the research protocol and all the required elements of informed consent. They are to be provided the opportunity to ask questions and have their questions answered by a knowledgeable member of the research team. Non-English speaking subjects are required to have a translator present during the consent process. The consent process is subject to monitoring.***

19.2 When and where will the informed consent process take place?

Prior to Transplant and it will be in Montefiore Medical Center/Moses division

19.3 Does this study involve research activities for which maintaining privacy would be a concern or expectation for subjects or potential subjects? (e.g., studies on illegal activities, sexual activity or any stigmatized behavior or disease)

( ) Yes (•) No

If "Yes", describe how subjects and potential subjects privacy is maintained during the recruitment process as well as throughout the study.

19.4 List the names of the Key Personnel who will conduct the informed consent process:

PI: Yorg Azzi, MD.
Victoria Muggia, MD
Grace Minamoto, MD
Yoram Puius, MD
Enver Akalin, MD
Maria Ajaimy, MD
Stuart Greenstein, MD
Jay Graham, MD
Milan Kinkhabwala, MD
Sam Sigal, MD
Snehal Patel, MD
Daniel Goldstein, MD

All personnel who will be consenting subjects must be listing in the "Key Personnel and Project Contacts" section of the Application. See section 3.0 of the Application.

For greater than minimal risk studies at MMC all informed consent discussions must be conducted by a Licensed Independent Practitioner. LIPs at MMC include the following categories of practitioners: Attending Physicians, Doctors of Osteopathy, Doctors of Dental Surgery, Nurse Practitioners, Certified Nurse Midwives, Doctors of Podiatric Medicine and Psychologists. The informed consent discussion is the responsibility of the LIP who will be providing the professional treatment.

19.5 Do you expect to enroll a significant number of subjects who speak a common language other than English or Spanish?

( ) Yes (•) No

If "Yes," which languages?

If "Yes," who will serve as the translator?

20.0 Recruitment

20.1 How and when will subjects be approached for this study? (Provide a brief description of how subjects will be recruited.)

Example #1: Clinicians will ask their patients (who are being treated) whether they are interested in the study. Study team members will then approach the interested patients to obtain consent for the research.

Example #2: Study is advertised, participant contacts researcher, screening take place, person is invited in to initiate the consent process.

Example #3: Dr. Smith will send a letter to his patients informing them of this study. Interested patients will use the contact information in the letter to contact the PI.

Study team members will then approach the interested patients to obtain consent for the research

20.2 Check all of the following recruitment mechanisms that apply:

- [x] Physician referral
- [ ] Radio/TV announcement
- [ ] Newspaper announcement
- [ ] ResearchMatch
- [ ] Internet
- [ ] Bulletin board/e-screen
- [ ] Recruitment letter
- [ ] Mailed flyer
- [ ] Random telephone contact
- [x] Databases
- [ ] Other:

If other, please describe:

NOTE: All public announcements, postings, recruitment letters, and telephone dialogs must be approved by the IRB prior to use. When possible, submit proposed recruitment text with the IRB application. Refer to the Advertisement Guidelines and the Informed Consent Guidelines.

20.3 If you are submitting any recruitment material at this time, upload the materials into the Other Study Documents section of the Initial Review Submission form.

Advertisements should include the following information:

- The name, address and telephone # of the investigator (or contact person) and the institution(s) conducting the research
- Condition under study and/or purpose of the research
- Inclusion/exclusion criteria in summary form
- A brief list of procedures involved
    - Specify what type of care is to be provided and at what cost. If "free" care is offered, the announcement should state whether all patients are entitled to that care or whether certain eligibility conditions must be met, and precisely what care or service will be provided free ofcharge. The announcement may not state a financial equivalent of the "free" care provided (e.g., "$1,000 worth of free medical care").
- Time or other commitment required (number of visits, total duration including follow-up visits, etc.)
- Compensation/Reimbursement. If remuneration is offered, give actual or at least ball park amounts (e.g. up to....)

- Location of research
- A statement indicating the project is research

Other helpful hints:

- Err on the side of underestimating benefits and overestimating risks.
- Do not make claims of safety, equivalence, or superiority.
- Avoid phrases like "new treatment," "new medicine," or "new drug."
- Do not use dollar signs or focus on monetary issues.
- Avoid catch phrases such as exciting, fast, cutting-edge, and free.

21.0 Study Costs and Subject Remuneration

21.1 Will subjects be reimbursed for travel expenses, childcare costs, etc?

○ Yes ◉ No

21.2 Will subjects be paid for their participation in the research?

○ Yes ◉ No

If subjects will be paid, is the payment within Einstein IRB guidelines?

○ Yes ○ No

If the payments are not within the guidelines, provide a justification:

21.3 Tests and procedures

List in the table below all tests/procedures that will be performed for research purposes only (not part of standard clinical care). Also indicate who will be responsible for the costs.
Interventions or procedures ore tests that have no costs should also be listed.
Examples include: blood draw, MRI, questionnaire

Test/Procedure/Drugs/Devices	Billed to:
Biobanking of transplant biopsy specimens	○ Sponsor ○ Subject/Insurer ○ Primary-Insurer/Secondary-Research Study ○ No Cost ◉ Departmental Funds
Transplantation surgery	○ Sponsor ◉ Subject/Insurer ○ Primary-Insurer/Secondary-Research Study ○ No Cost ○ Departmental Funds

22.0 Application Customization

22.1 This study is:

◉ Full Board (Greater than Minimal Risk)
○ Expedited (Minimal Risk)

22.2 Will subjects be audio or video recorded during this study?

○ Yes ◉ No

22.3 Does the study involve the use of a drug or drug combination or the use of a biologic?

○ Yes ◉ No

Note: If this investigation is for a single patient under a Single Patient IND, please contact the IRB at irb@einsteinmed.org with the IRB# for this submission for further guidance.

22.4 Does the study involve the evaluation of a device?

○ Yes ◉ No

Note: If this investigation is for a single patient under a Single Patient IDE, please contact the IRB at irb@einsteinmed.org with the IRB# for this submission for further guidance.

22.5 Does this study involve the use of an application ("app") on a mobile device/phone?

○ Yes ◉ No

If "Yes," answer the following questions:

Does this study involve one or more mobile apps that are an extension of one or more medical devices by connecting to such device(s) for purposes of controlling the device(s) or for use in active patient monitoring or analyzing medical device data?

○ Yes ○ No

Does this study involve one or more mobile apps that transform the mobile platform into a regulated medical device by using attachments, display screens, or sensors or by including functionalities similar to those of currently regulated medical devices?

○ Yes ○ No

Does this study involve one or more mobile apps that become a regulated medical device (software) by performing patient-specific analysis and providing patient-specific diagnosis, or treatment recommendations? These types of mobile medical apps are similar to or perform the same function as those types of software devices that have been previously cleared or approved.

○ Yes ○ No

22.6 Does this study involve the use of a placebo?

○ Yes ◉ No

22.7 Does the study involve the use of Diagnostic Imaging, Nuclear Medicine/Radiopharmaceuticals or Radiation Therapy?

Check all that apply:

- [ ] MRI (magnetic resonance imaging)
- [ ] CT (computed tomography)
- [ ] Echocardiography
- [ ] Vascular Ultrasound
- [ ] General Ultrasound
- [ ] Interventional Radiology
- [ ] Nuclear Medicine / Radiopharmaceuticals
- [ ] Radiation Therapy
- [ ] Plain x-ray
- [ ] Other
- [x] None of the above

22.8 Does this research involve the use of newborn dried blood spots?

( ) Yes (•) No

Note: Between March 16, 2015 and July 19, 2018, research approved by the IRB using newborn dried blood spots may not be conducted without obtaining informed consent.

22.9 Will tests be performed under the current protocol (as opposed to possible future tests) that will yield genetic information?

( ) Yes (•) No

22.10 Does this study involve recombinant gene transfer therapy?

( ) Yes (•) No

22.11 Does the study involve the use of potentially infectious materials (e.g. viral vectors) which are intended to be administered to patients?

( ) Yes (•) No

22.12 Will services from nursing staff be utilized for research-related procedures?

( ) Yes (•) No

23.0 CV for Principal Investigator

23.1 Attach a copy of the Principal Investigator's CV below:

Version	Title	Category	Expiration Date	Document Outcome	Checked Out	View Document
1.0	AzziCV 07272021)	CV or resume		Acknowledged		128.13 KB

24.0 Data Safety Monitoring Plan

24.1 Has the sponsor or other external entity established a monitoring plan (e.g. DSMB)?

○ Yes ◉ No

If "Yes," who has established the monitoring plan?

If "No," describe in detail the Data Safety Monitoring Plan, including all required elements specified in the **policy**:

The Data Safety Monitoring Plan for the study was established by the prior PI, Juan Rocca, in 2016. The current members of the DSMB are as below and last met in August, 2021.
The members of the DSMB are independent of the IRB and independent of the investigators of the study. They will meet every 12 months. The details of these meetings are spelled out in the DSMB charter, which is scanned in IRIS. All required elements of the Einstein/Montefiore DSMB policy are met by the DSMB charter.

24.2 Is there a monitoring board/committee (e.g. DSMB)?

◉ Yes ○ No

If "Yes," specify the composition and credentials of the DSMB members:

1- Rachel Bartash Attending Physician/Division of Infectious Diseases.
2- Beatrice Goilav Pediatric - Nephrology.
3- Nicole Hayde Pediatric - Nephrology

If "Yes," how frequently will the DSMB meet?

They will meet every 12 month

24.3 Is this study blinded?

○ Yes ◉ No

25.0 Pregnancy Testing

25.1 Do the research procedures present any known risks to a potential fetus?

○ Yes ◉ No

25.2 Will there be pregnancy testing as part of the study procedures?

○ Yes ◉ No

If you answered "Yes" to question #2 above, answer the following questions.

Will the pregnancy testing be repeated during the course of the study?

○ Yes ○ No

What is the schedule of pregnancy testing (e.g. at screening only, every month during protocol interventions)?

Additional information about pregnancy testing in research can be found in the Einstein IRB's Non-Pregnant Women Research Policy available **here**.

26.0

Additional Radiation Questions

26.8 **No additional questions required**

27.0 Final Page

27.1 **Contact information**

Provide the email and contact phone number of the **PI** in the event that the IRB has to reach out.

Email address:

yazzi@montefiore.org

Phone number:

646-630-531

Provide the name, email and contact phone number of the **person working on this submission** in the event that the IRB has to reach you. If it is the same as the PI, please note this below.

Name:

Vagish Hemmige

Email address:

vahemmig@montefiore.org

Phone number:

7189202705

27.2 **Required Approvals**

If you have any questions or concerns regarding this list of required approvals, please note them here:

27.4 **Congratulations! The application is complete, but the submission is NOT. To complete the submission you must click "Save and Continue" and proceed as directed.**

If you have any additional comments that you would like to convey to the IRB staff, please enter them here:

ENFÒMASYON PRENSIPAL POU [Pwotokòl rechèch pou grèf ògàn ki soti nan donè ki pozitif pou VIH pou ale jwenn resevè ki pozitif pou VIH selon Dènye Lwa sou Politik Ekite nan domèn Don Ògàn ki lye ak VIH (Final HIV Organ Policy Equity [HOPE] Act).]

N ap mande w pou w chwazi si wi ou non, ou vle pòte w kòm volontè pou yon etid rechèch sou itilizasyon ògàn ki soti nan moun ki gen VIH pou grèf. Paj sa a dedye pou li ba ou enfòmasyon esansyèl pou ede w deside si wi ou non w ap patisipe. Nou enkli enfòmasyon detaye apre paj sa a. Poze ekip rechèch la kesyon. Si w gen kesyon annapre, kowòdone anketè rechèch ki responsab etid la pi ba a.

SOU KISA ETID LA CHITA E KONBYEN TAN L AP DIRE?

Nan etid sa a, n ap bay ògàn ki soti nan moun ki gen VIH pou bay moun tankou w ki bezwen grèf ògàn.

Nan fè etid sa a, nou swete aprann konnen si grèf ògàn ki soti nan donè ki pozitif pou VIH san danje ak efikas pou resevè ki pozitif pou VIH menm jan ak grèf ki soti nan donè ki negatif pou VIH yo. Patisipasyon w nan rechèch sa a ap dire omwen 1 lane apre grèf la, e jiska 3 rive 5 lane.

KI REZON PRENSIPAL KI TA KA FÈ W CHWAZI POU PÒTE W VOLONTÈ POU ETID SILA A?

Avantaj prensipal patisipasyon an se chans ka genyen pou w resevwa yon grèf ògàn. Lis datant pou ògàn nan long. Ògàn ki soti kay donè ki gen VIH yo disponib aktyèlman sèlman atravè etid rechèch yo, e se sèlman pou pasyan ki gen VIH, kidonk patisipasyon w nan etid sa a ka se fason ki pi rapid pou w resevwa yon grèf ògàn. Pou w ka jwenn deskripsyon konplè sou avantaj yo, refere w ak Dokiman Konsantman ki pi ba a.

KI REZON PRENSIPAL KI TA KA FÈ W CHWAZI POU W PA PÒTE W VOLONTÈ POU ETID SILA A?

Ou ka chwazi pou w pa pòte w volontè paske nou pa konnen si ògàn ki soti nan donè ki gen VIH yo ap dire osi lontan ke ògàn ki soti nan donè ki pa gen VIH, oswa si y ap asosye ak plis pwoblèm apre grèf tankou enfeksyon oswa kansè. Pou w ka jwenn deskripsyon konplè sou tretman/pwosedi altènatif yo, refere w ak Dokiman Konsantman ki pi ba a.

ÈSKE W OBLIJE PATISIPE NAN ETID LA?

Si w deside patisipe nan etid la, ou dwe patisipe ladan l paske w vrèman vle pòte w volontè. Ou p ap pèdi okenn sèvis, avantaj oubyen dwa oswa aksè ak swen ke w ta dwe genyen nòmalman si w chwazi pou pa pòte w volontè.

KISA W DWE FÈ SI W GEN KESYON, SIGJESYON OSWA ENKYETID?

Moun ki responsab etid la se Doktè Yorg al-Azzi. Si w gen kesyon, sigjesyon oswa enkyetid konsènan etid sa a oswa si ou vle retire tèt ou nan etid la, kowòdone li yo se: 111 East 210th St, Rosenthal C, 2nd floor, Bronx, NY 10467 (# telefòn: (718) 920-6421).

Si w gen kesyon, sigjesyon oswa enkyetid konsènan dwa w kòm yon volontè nan rechèch sa a, kontakte pèsonèl nan Komite Egzamen Enstitisyonèl Einstein (Einstein Institutional Review Board, IRB) ant lè travay yo ki se 9:00 am ak 5:00 pm Lè Zòn Lès, soti lendi rive vandredi nan 718-430-2253 oswa irb@einsteinmed.edu.

ALBERT EINSTEIN FAKILTE MEDSIN ALBERT EINSTEIN NAN MONTEFIORE MEDICAL CENTER

DOKIMANTASYON POU KONSANTMAN EKLERE AK OTORIZASYON LWA AMERIKEN SOU TRANSFERABILITE AK RESPONSABILITE NAN DOMÈN ASIRANS SANTE (HIPAA)

Si w se ranplasan desidè pou yon adilt ki ta ka patisipe nan etid sa a, n ap egzije yon konsantman nan men w ak apwobasyon (akò) patisipan etid la. Lè mo "ou/oumenm/w (ou/pa w/w)" / "mwen/pa m/m" / "mwen/mwen menm/m" / "mwenm" parèt nan fòmilè konsantman sa a, nou vle di patisipan an; "nou/noumenm/n" vle di doktè etid rechèch la yo ak pèsonèl rechèch la.

Entwodiksyon

N ap mande w pou ou patisipe nan yon etid rechèch ki rele **[Pwotokòl rechèch pou grèf òganki soti nan donè ki pozitif pou VIH pou ale jwenn resevè ki pozitif pou VIH selon Dènye Politik Ekite nan domèb Don Òganki lye ak VIH Lwa (Final HIV Organ Policy Equity [HOPE] Act).]**. Patisipasyon w volontè. Ou gen tout libète w pou chwazi patisipe ou pa. Pa gen okenn pwoblèm si w di "non" kounye a oswa nan nenpòt ki moman apre w fin kòmanse etid la. Si w di "non," desizyon w lan p ap afekte okenn nan dwa oswa avantaj oswa aksè w pou jwenn swen.

Chèchè ki responsab pwojè sa a rele "Anketè Prensipal" la. Non **[**li**]** se Doktè **[**Yorg al-Azzi**]**. Ou ka antre an kontak ak Doktè **[**Azzi**]** nan: **Adrès Biwo: 111 East 210th St, Rosenthal C, 2nd floor, Bronx, NY 10467** **# Telefòn: (718) 920-6421** Pou kesyon sou etid rechèch la, oswa si w kwè ke w gen yon blesi, kontakte Anketè Prensipal la oswa IRB a.	Komite Egzamen Enstitisyonèl (IRB) Fakilte Medsin Albert Einstein ak Montefiore Medical Center a apwouve etid rechèch sa a. # IRB a ekri sou so a lan ki nan kwen anwo adwat la. Si w gen kesyon ki konsène dwa w antanke yon sijè nan rechèch la ou ka kontakte biwo IRB a nan 718-430-2253, pa imèl sou irb@einsteinmed.edu, oswa pa lapòs: Einstein IRB Albert Einstein College of Medicine 1300 Morris Park Ave., Belfer Bldg #1002 Bronx, New York 10461
Pa gen okenn sipò finansye ekstn yo resevwa pou etid sa a.	

Poukisa y ap fè etid sa a?

Objektif etid sa a se pou aprann konnen si grèf òganki soti nan donè ki pozitif pou VIH yo san danje e efikas pou resevè ki pozitif pou VIH menm jan ak grèf ki soti nan donè ki negatif pou VIH yo.

Poukisa y ap mande m pou m patisipe?

Y ap mande w pou w patisipe nan etid sa a paske yo dyagnostike w ak yon maladi òganan faz tèminal e ou gen enfeksyon VIH, e ou kalifye pou grèf òganan. Òganan espesifik oswa òganan ke ou pral resevwa yo se:
_____ Ren
_____ Fwa
_____ Kè

Konbyen moun k ap patisipe nan etid rechèch la?

Ou pral youn pami **200** moun k ap patisipe nan etid sa a

Pandan konbyen tan m ap patisipe nan rechèch sa a?

W ap nan etid sa a pandan omwen yon lane, ak jiska twa oswa senk lane apre grèf ògàn ou an. Pandan tan sa a, nou pral mande w pou w fè omwen 15 vizit etid nan **Montefiore Medical Center**.

Kisa k ap rive si m patisipe nan etid la?

Ou deja sou lis datant lan pou w resevwa yon don ògàn nan kad estanda swen klinik ou a. Patisipasyon w nan etid sa a p ap afekte evalyasyon y ap fè avan chiriji w la, chiriji a ak tout suivi yo.

Si w dakò pou w nan etid sa a, nou pral mande w pou w fè bagay sa yo nan kad objektif rechèch la: Ou pral gen vizit ak doktè etid la oswa yon manm nan ekip etid la omwen 15 fwa jan sa dekri pi ba a.

Depistaj
Apre w fin siyen fòmilè konsantman sa a, y ap evalye w apati yon revizyon dosye medikal ou, medikaman aktyèl yo, rezilta tès sangen, ak lòt tès, epi w ap gen yon egzamen fizik.

Vizit Etid
Si apre depistaj ak grèf ou a, ou anmezi pou kontinye patisipe nan etid sa a, n ap rankontre ak ou nan lè vizit regilye yo pwograme pou apre grèf la:

- Premye mwa: tès sangen de fwa pa semèn (ren) oswa yon fwa pa semèn (fwa) ak vizit klinik yon fwa pa semèn
- 2-3 mwa: tès sangen yon fwa pa semèn ak vizit klinik chak de semèn
- 4-5 mwa: tès sangen chak de semèn ak vizit klinik yon fwa pa mwa
- 6-12 mwa: tès sangen yon fwa pa mwa, tès sangen ak vizit klinik chak de mwa
- Dezyèm ane a: tès sangen chak 2 mwa, tès sangen ak vizit klinik chak 4 mwa
- Twazyèm jiska senkyèm ane a: tès sangen chak 3 mwa ak vizit klinik chak 6 mwa
- Apre 5 ane: tès sangen chak 3 mwa ak vizit klinik chak ane

Nan vizit klinik yo, n ap fè bagay swivan yo:

- Revize medikaman w yo ak sante w
- Fè yon egzamen fizik ki enkli kontwole siy vital ou yo
  - Pran echantiyon san ak echantiyon pipi pou wè ak ki efikasite ògàn yo grefe a ap fonksyone, pou mezire ki kantite medikaman iminosipresè ki nan san w, epi pou wè si w gen sèten enfeksyon
  - Nan jou apre grèf ògàn ou a epi nan semèn 1, 2, 3, 4, 12, 24, 36 ak 48 ki vin apre yo, epi chak 6 mwa apresa, n ap teste san w tou pou n chèche konnen kijan sistèn iminitè ou (ki se yon sistèm defans ki defann kò a kont atak mikwòb tankou viris, bakteri, parazit ak chanpiyon ki ka lakoz enfeksyon) ap fonskyone ak ki kantite VIH ki prezan.

Yo pral fè tou biyopsi sou ògàn grefe a nan moman grèf la ap fèt. Y ap fè sa tou apre grèf la lè doktè w la gen enkyetid sou sante ògàn grefe a (fwa, ren) oswa selon pwotokòl estanda pou apre grèf la (kè). Y ap itilize biyopsi sa yo pou detekte rejè ògàn grefe a e y ap fè yo menm si w pa t patisipe nan etid sa a. Toutfwa, si w patisipe nan etid sa a, y ap konsève yon pati nan tisi a pou rechèch pou teste alavni bagay ki ka chanje nivo antikò nuizib yo oswa pou pèmèt doktè yo detekte blesi nan ògàn nan, si w dakò, sa ka enkli tès pou bagay ke yo poko konnen, men ke yo dekouvri alavni.

Èske y ap fè tès VIH?

Wi, y ap fè tès VIH pandan peryòd rechèch sa a. Enfòmasyon swivan an se enfòmasyon enpòtan sou VIH, tès VIH, ak rezilta tès ou yo:

- VIH bay SIDA e li ka pwopaje atravè aktivite seksyèl, pataj sereng, fanm ansent ka bay fetis yo li, epi atravè nourison k ap tete.
- Gen tretman pou VIH ki ka ede w rete an sante.
- Moun ki gen VIH oswa SIDA dwe adopte pratik pou pwoteje moun ki nan vi yo pou yo pa vin enfekte ak VIH la.
- Fè tès pou VIH se yon aksyon volontè e li ka fèt yon fason anonim nan yon sant tès piblik. Toutfwa, li egzijib pou fè tès la si w ta renmen patisipe nan etid rechèch sa a.
- Lalwa pwoteje konfidansyalite rezilta tès ki lye ak VIH.
- Lalwa entèdi diskriminasyon ki baze sou estati VIH ou epi gen sèvis ki disponib pou trete tout ka diskriminasyon.
- Si apre patisipasyon w nan etid sa a yo dyagnostike w INISYALMAN ak VIH, yo rapòte rezilta yo bay Depatman Sante Eta Nouyòk (New York State Department of Health) nan objektif pou chèche retrase kontak ou yo.
- Si apre patisipasyon w nan etid sa a yo dyagnostike w ak VIH, y ap ba w konsèy sou VIH oswa yon referans pou jwenn konsèy sou VIH.

Tès Jenetik

Etid sa p ap enplike rechèch jenetik oswa tès jenetik.

Bank pou Echantiyon (Itilizasyon Alavni ak Estokaj)

N ap konsève echantiyon ou yo ak enfòmasyon sou ou yo nan yon "bank byolojik", ki se yon bibliyotèk enfòmasyon ak echantiyon (tisi ak san) ki soti nan plizyè etid. Yo pa kapab asosye echantiyon sa yo ak enfòmasyon sa a avèk oumenm. Alavni, chèchè yo ka aplike pou mande pèmisyon pou itilize echantiyon ak enfòmasyon yo pou nouvo etid pou anpeche, dyagnostike, oswa trete maladi, ki enkli rechèch jenetik. Yo ka konsève echantiyon ak enfòmasyon ou yo pandan anpil tan, petèt plis pase 50 lane. Si w dakò pou itilizasyon alavni an, yo ka plase kèk nan enfòmasyon jenetik ak enfòmasyon sante depèsonalize ou yo (ki pa relye ak ou) nan youn oswa plizyè bazdone syantifik. Sa yo ka enkli bazdone ke se gouvènman federal la ki antreteni yo.

Ou ka chwazi pou w pa patisipe nan bank byolojik la epi pou malgresa ou patisipe nan etid prensipal la e sa p ap afekte tretman w nan etablisman sa a.

METE INISYAL OU NAN YOUN (1) NAN OPSYON SA YO
_____ Mwen dakò yo itilize echantiyon m ak enfòmasyon sou mwen pou etid rechèch alavni.
_____ Mwen PA dakò pou yo itilize echantiyon m ak enfòmasyon sou mwen pou etid rechèch alavni.
Y ap konsève enfòmasyon sou mwen yo osi lontan ke règleman ak politik enstitisyonèl yo mande sa, men yo p ap itilize yo pou etid fiti.

Èke y ap peye m paske m ap patisipe nan etid rechèch sa a?

Ou p ap resevwa okenn peman oswa lòt konpansasyon paske w patisipe nan etid sa a.

Kèk nan chèchè yo ka devlope tès, tretman oswa pwodui ki vo lajan. Ou p ap resevwa okenn fòm peman pou echantiyon ak enfòmasyon ou yo oswa pou okenn tès, tretman, pwodui oswa lòt bagay ki gen valè ki ka se rezilta rechèch la.

Èske sa ap koute m yon bagay pou m patisipe nan etid sa a?

Patisipe nan etid sa a p ap enplike okenn chaj adisyonèl pou ou. Oumenm ak/oswa konpayi asirans ou an ap gen pou peye pou tout depans ki fè pati swen medikal regilye ou yo.

Kisa k ap pase si m blese akoz mwen patisipe nan etid sa a?

Si w blese kòm konsekans patisipasyon w nan rechèch sa a, sèlman tretman medikal imedya, ki esansyèl e ki akoutèm selon sa lopital k ap patisipe a detèmine, ap disponib pou blesi a san yo pa chaje w pou li pèsonèlman.

- Yo p ap ofri okenn konpansasyon monetè.
- Lè w siyen dokiman konsantman eklere sa a, ou pa renonse ak okenn nan dwa legal ou genyen yo.
- Si li obligatwa pou w resevwa tretman adisyonèl akoz yon blesi fizik ki lye ak rechèch la, w ap resevwa tretman medikal ki nesesè e y ap voye fakti a bay konpayi asirans ou an oswa ba ou nan kad depans medikal ou yo.

Ki lòt bagay ke m dwe fè?

- Si w pa santi w byen nan nenpòt ki moman, rele doktè w la oswa doktè etid rechèch la touswit.
- Si w panse ou tonbe ansent, kontakte doktè etid rechèch ou a touswit.

Rapò touswit tout malèz, pwoblèm oswa blesi ke w santi pandan dewoulman patisipasyon w nan etid la bay **Dr. Azzi nan 718-952-6421.**

Konfidansyalite

N ap kenbe enfòmasyon ou yo konfidansyèl. N ap kenbe dosye rechèch ou yo konfidansyèl e yo p ap itilize non w nan okenn rapò ekri oswa vèbal. Y ap bay enfòmasyon ou yo yon nimewo kòd e y ap separe li ak non w oswa ak tout lòt enfòmasyon ki ka idantifye w. Y ap kenbe fòmilè ki relye non w ak nimewo kòd la yon fason ki sekirize e se sèlman anketè a ak pèsonèl etid la k ap gen aksè ak fichye a. Y ap konsève tout enfòmasyon yo yon fason ki sekirize e dosye enfòmatik yo ap pwoteje ak modpas. Y ap konsève enfòmasyon etid ak echantiyon ou yodepi yo itil pou rechèch sa a.

Yo ka anrejistre enfòmasyon medikal yo kolekte pandan rechèch la, tankou rezilta tès yo, nan dosye medikal elektwonik Montefiore ou a e y ap disponib pou klinisyen yo ak lòt pèsonèl nan Montefiore k ap ba w swen yo.

Enfòmasyon sou patisipasyon w nan etid sa a ap anrejistre nan Dosye Medikal Eletwonik (Electronic Medical Record, EMR) ou a. Yon fwa yo antre yo nan EMR ou a, enfòmasyon yo pral disponib pou tout founisè w yo ki patisipe nan sistèm EMR la. Objektif anrejistreman sa a se pou founi enfòmasyon rechèch la jwenn ki gen potansyèl pou fè enpak sou swen medikal ou.

Sèl moun ki ka wè dosye rechèch ou yo se:

- ekip rechèch la ak pèsonèl k ap travay ak yo
- òganizasyon ki finanse rechèch la
- òganizasyon ak enstitisyon ki enplike nan rechèch sa a
- gwoup ki revize rechèch la (Einstein IRB, ak Biwo pou Pwoteksyon Rechèch sou Moun [Office for Human Research Protections], ak Administrasyon Aliman ak Medikaman nan peyi Etazini [US Food and Drug Administration])

Moun sa yo, ki resevwa enfòmasyon sante w yo, ka pa oblije pwoteje enfòmasyon sante w selon lwa sou konfidansyalite vi prive yo e yo ka pataje enfòmasyon w yo ak lòt moun san pèmisyon w, si lwa ki reji yo a pèmèt sa. Yo mande tout gwoup sa yo pou yo kenbe enfòmasyon w yo konfidansyèl.

Èske gen kèk ris pou mwen?

Yon ris nan patisipe nan etid sa a se posibilite pou gen yon pèt konfidansyalite oswa pwoteksyon vi prive. Pèt pwoteksyon vi prive vle di lè yo pataje enfòmasyon pèsonèl ou yo ak yon moun ki pa nan ekip etid la e ki pa t sipoze wè oswa konnen enfòmasyon w yo. Ekip etid la prevwa pou pwoteje vi prive w – konsilte seksyon Konfidansyalite a ki pi wo a pou w jwenn detay.

Lè w se yon pasyan ki pozitif pou VIH ki pral sibi yon grèf ògàn, ou ka gen youn oswa plizyè nan ris ki pi ba yo la kèlkeswa etid k ap fèt la, kit ou pral sibi yon grèf ògàn ki soti nan yon donè ki negatif pou VIH ki se yon estanda swen, oswa ke se nan men yon donè ki pozitif pou VIH ki se ka sa a nan etid rechèh sa a. Ris sa yo se:

- Yon posiblite pou entèraksyon ak medikaman yo ka rive, sa ki ka grav anpil e ki ka antrene efè endezirab grav akoz chanjman sanzatann nan konsantrasyon medikaman yo nan san an; sa yo ka enkli: ogmantasyon nan to rejè, ogmantasyon to viris nan san an, epi diminisyon nan kantite selil Tw yo ak posibilite pwogresyon pou genyen SIDA.
- To rejè egi ki pi elve
- Ris elve pou twobo-anboli nan venn (fòmasyon youn oswa plizyè kayo sangen nan venn ou) nan moun ki pozitif pou VIH.
- Si w gen yon ko-enfeksyon ak Viris Epatit B (HBV), Viris Epatit C (HCV) oswa toulède, grèf la ajoute ris adisyonèl, ris pou devlope yon kasinòm Epatoselilè (yon kansè selil nan fwa a) elve
- Ka gen yon posibilite chanjman nan estanda rejim tretman grèf ògàn nan oswa yon chanjman nan dozaj medikamn yo ki ka lakoz posiblite pou rezilta endezirab.
- Ou ka bezwen yon tretman pou tout rès vi w pou enfeksyon opòtinis yo (ki se enfeskyon ki vini pi souvan e ki pi grav lakay moun ke sistèm iminitè yo afebli tankou moun ki pozitif ak HIV yo).

Yon ris adisyonèl, ke w ka genyen nan patisipasyon w nan etid sa a, se transmisyon yon tip viris ki rezistan ak medikaman apati ògàn donè a.

Prelèvman San
Raman, sa rive ke venn kote nou antre zegwi a sansib oswa vin wouj. Dèfwa, yon mak "ble e nwa" inofansif tanporè ka devlope. Trè raman, sa rive ke ou ka endispoze.

Nouvo Dekouvèt
Si nou aprann ke gen nenpòt nouvo dekouvèt enpòtan pandan etid la ki ka enfliyanse desizyon w pou w patisipe, n ap kontakte w epi eksplike w yo.

Ris Enkoni
Nou dekri tout ris ke nou konnen yo. Toutfwa, etandone sa a se yon rechèch, gen yon posibilite ke oumenm oswa anbriyon oswa fetis ou a ka gen yon reyaksyon ke nou poko konnen e ke nou pa atann. Si nou aprann pou lòt ris, n ap fè w konnen kisa yo ye konsa w ap ka deside si wi ou non ou vle kontinye patisipe nan etid la.

Èske gen posibilite avantaj pou mwen?

Ou ka resevwa oswa ou ka pa resevwa avantaj pèsonèl, dirèk lè w patisipe nan etid sa a. Avantaj posib ki genyen lè w patisipe nan etid sa a, pandan yo pèmèt itilizasyon ògàn donè ki sewopozitif, se potansyalite pou ogmante ansanm donè ògàn ki disponib pou ou yo, epi petèt diminye tan atant ou jiska lè grèf la. Patisipasyon w pral jenere nouvo konesans klinik ak yon meyè konpreyansyon sou grèf ògàn ki soti nan moun ki pozitif pou VIH pou ale sou moun ki pozitif pou VIH.

Ki chwa mwen genyen apade patisipe nan etid sa a?

Ou ka refize patisipe nan etid la. Si w deside pa patisipe, founisè swen medikal yo nan etablisman sa a ap toujou ba ou swen estanda ak tretman ki apwopriye pou ou yo.

Èske gen kèk konsekans pou mwen si m deside kanpe patisipasyon m nan etid sa a?

Non. Si w deside patisipe, ou lib pou w kanpe patisipasyon w lan nenpòt lè w vle san w pa bezwen bay rezon. Sa p ap afekte swen ou yo e y ap kontinye trete w nan etablisman sa a. Toutfwa, yo ka te gentan anrejistre kèk nan enfòmasyon yo nan etid la e yo p ap retire yo. Chèchè yo ka kontinye itilize ak pataje enfòmasyon yo te gentan kolekte yo.

Pou w anile (repran) konsantman ak otorizasyon ou, ou dwe kontakte Anketè Prensipal la alekri nan adrès ki nan paj 1 fòmilè sa a. Toutfwa, ou ka rele anvan oswa pale ak Anketè Prensipal la epi l ap sispann kolekte nouvo enfòmasyon ki konsène w. Si w repran konsantman w ak otorizasyon ou te bay, ou p ap otorize pou kontinye patisipe nan etid rechèch sa a.

KONSANTMAN POU PATISIPE

Mwen li fòmilè konsantman an e mwen konprann ke se mwen ki pou deside si wi ou non moun ki gen non li make pi ba a ap patisipe. Mwen gen ase enfòmasyon sou objektif, metòd, ris ak avantaj etid rechèch la genyen pou mwen deside. Mwen konprann ke lè mwen siyen dokiman konsantman eklere sa a, mwen pa renonse ak okenn nan dwa legal li genyen yo. Y ap ban mwen yon kopi fòmilè konsantman sa a ki siyen.

Non patisipan an ekri ak lèt detache	Siyati patisipan an	Dat	Lè
Non Ranplasan an ekri ak lèt detache (lè sa aplikab)	Siyati Ranplasan an (lè sa aplikab)	Dat	Lè
Non moun k ap dirije pwosesis konsantman an, ekri ak lèt detache	Siyati	Dat	Lè

INFORMATIONS CLÉS POUR [Protocole de recherche pour la transplantation d'organes de donneurs séropositifs à des receveurs séropositifs en vertu de la loi définitive sur l'équité en matière de politique de dons d'organes dans le cadre du VIH (Final HIV Organ Policy Equity [HOPE] Act).]

Nous vous demandons de choisir de vous porter volontaire ou non pour une étude de recherche sur l'utilisation d'organes de personnes vivant avec le VIH pour une transplantation. Cette page a été conçue pour vous donner des informations clés susceptibles de vous aider à décider de participer ou non. Nous avons inclus des informations détaillées après cette page. N'hésitez pas à poser des questions à l'équipe de recherche. Si vous avez des questions ultérieurement, utilisez les coordonnées du chercheur responsable de l'étude que vous trouverez ci-dessous.

EN QUOI CONSISTE L'ÉTUDE ET COMBIEN DE TEMPS DURERA-T-ELLE ?

Dans le cadre de cette étude, nous donnons des organes de personnes vivant avec le VIH à des personnes comme vous qui ont besoin de greffes d'organes.

Grâce à cette étude, nous espérons déterminer si la transplantation d'organes de donneurs séropositifs est aussi sûre et efficace chez les receveurs séropositifs que celle d'organes de donneurs séronégatifs. Votre participation à cette recherche durera au moins un an après la greffe, et jusqu'à trois à cinq ans.

QUELLES SONT LES PRINCIPALES RAISONS POUR LESQUELLES VOUS POURRIEZ CHOISIR DE VOUS PORTER VOLONTAIRE POUR CETTE ÉTUDE ?

Le principal avantage de la participation serait la possibilité de recevoir une greffe d'organe. Les listes d'attentes pour les organes sont longues. Les organes de donneurs séropositifs ne sont actuellement disponibles que par le biais d'études de recherche, et uniquement pour les patients séropositifs. La participation à cette étude pourrait donc être votre moyen le plus rapide de recevoir une greffe d'organe. Pour une description complète des avantages, reportez-vous au document de consentement ci-dessous.

QUELLES SONT LES PRINCIPALES RAISONS POUR LESQUELLES VOUS POURRIEZ CHOISIR DE NE PAS VOUS PORTER VOLONTAIRE POUR CETTE ÉTUDE ?

Vous pourriez choisir de ne pas vous porter volontaire, car nous ne savons pas si les organes de donneurs séropositifs dureront aussi longtemps que les organes de donneurs non séropositifs, ou s'ils seront associés à un plus grand nombre de problèmes post-transplantation, tels qu'une infection ou un cancer. Pour une description complète des traitements/procédures alternatifs, reportez-vous au document de consentement ci-dessous.

SUIS-JE OBLIGÉ(E) DE PARTICIPER À CETTE ÉTUDE DE RECHERCHE ?

Si vous décidez de participer à l'étude, cela devrait être parce que vous voulez vraiment vous porter volontaire. Les services, avantages, droits ou accès aux soins dont vous bénéficieriez normalement ne seront nullement affectés si vous choisissez de ne pas vous porter volontaire.

ET SI VOUS AVEZ DES QUESTIONS, DES SUGGESTIONS OU DES PRÉOCCUPATIONS ?

Le responsable de l'étude est Dr Yorg al-Azzi. Si vous avez des questions, des suggestions ou des préoccupations concernant cette étude, ou si vous souhaitez vous retirer de l'étude, ses coordonnées sont : 111 East 210th St, Rosenthal C, 2nd floor, Bronx, NY 10467 (numéro de téléphone : (718) 920-6421).

Si vous avez des questions, des suggestions ou des préoccupations concernant vos droits en tant que volontaire dans le cadre de cette recherche, contactez le personnel du Conseil d'examen institutionnel Einstein (Einstein Institutional Review Board, IRB) entre les heures ouvrables de 9h00 à 17h00 HNE, du lundi au vendredi, au 718-430-2253 ou à irb@einsteinmed.edu.

v. 05/12/2018

FACULTÉ DE MÉDECINE ALBERT EINSTEIN DU MONTEFIORE MEDICAL CENTER

DOCUMENTATION DE CONSENTEMENT ÉCLAIRÉ ET AUTORISATION HIPAA (LOI AMÉRICAINE SUR L'ASSURANCE MALADIE)

Si vous êtes le décideur de substitution d'un adulte susceptible de participer à cette étude, votre consentement et l'assentiment (accord) du participant à l'étude seront requis. Lorsque les mots « vous/votre/vos » / « mon/ma/mes » / « me/moi » / « je » apparaissent dans ce formulaire de consentement, nous entendons « le participant » ; « nous » désigne les médecins de l'étude de recherche et le personnel de recherche.

Introduction

Il vous a été demandé de participer à une étude de recherche intitulée **[Protocole de recherche pour la transplantation d'organes de donneurs séropositifs à receveurs séropositifs en vertu de la loi définitive sur l'équité en matière de politique de dons d'organes dans le cadre du VIH (Final HIV Organ Policy Equity [HOPE] Act)].** Votre participation est volontaire. C'est à vous de décider si vous souhaitez y participer ou non. Vous pouvez dire « non » maintenant ou à tout moment après le démarrage de l'étude. Si vous dites « non », votre décision n'aura aucune incidence sur vos droits et prestations, ou votre accès aux soins.

Le chercheur chargé de ce projet est appelé le « chercheur principal ». [Son] nom est [Dr Yorg al-Azzi]. Vous trouverez ci-dessous les coordonnées du Dr **[**Azzi**]** :
Adresse du cabinet :
111 East 210th St
Rosenthal C, 2nd floor
Bronx, NY 10467
Numéro de téléphone : (718) 920-6421
Pour toute question concernant l'étude de recherche, ou si vous pensez être blessé(e), contactez le chercheur principal ou l'IRB.

Aucun soutien financier externe n'est reçu pour cette étude.

Le Conseil d'examen institutionnel (Institutional Review Board, IRB) de la faculté de médecine Albert Einstein et du Montefiore Medical Center ont approuvé cette étude de recherche. Le numéro de l'IRB figure dans le sceau situé dans le coin supérieur droit. Si vous avez des questions sur vos droits en tant que sujet de recherche, contactez le bureau de l'IRB au numéro 718-430-2253, par courrier électronique à l'adresse irb@einsteinmed.edu, ou par courrier postal à l'adresse :

Einstein IRB
Albert Einstein College of Medicine
1300 Morris Park Ave.
Belfer Bldg #1002
Bronx, New York 10461

Pourquoi cette étude est-elle effectuée ?

L'objectif de cette étude est de déterminer si la transplantation d'organes de donneurs séropositifs est aussi sûre et efficace chez les receveurs séropositifs que celle d'organes de donneurs séronégatifs.

Pourquoi me demande-t-on de participer ?

Il vous est demandé de participer à cette étude parce que vous avez reçu un diagnostic de maladie organique en phase terminale, que vous êtes infecté(e) par le VIH et que vous êtes admissible à une greffe d'organe. Le ou les organes spécifiques que vous recevrez est ou sont :

_____ Rein
_____ Foie
_____ Cœur

Combien de personnes participeront-elles à cette étude de recherche ?

Vous ferez partie d'environ **200 personnes** qui participeront à cette étude.

Combien de temps suis-je censé(e) participer à cette recherche ?

Vous participerez à cette étude pendant au moins un an, et jusqu'à trois ou cinq ans après votre greffe d'organe. Pendant toute cette période, nous vous demanderons d'effectuer au moins 15 visites d'étude auprès du **Montefiore Medical Center**.

Que se passera-t-il si je participe à l'étude ?

Vous êtes déjà sur la liste d'attente pour recevoir un organe donné dans le cadre de vos soins cliniques standard. Votre évaluation préchirurgicale, l'intervention chirurgicale que vous subirez et tous les suivis ne seront pas affectés par votre participation à cette étude.

Si vous acceptez de participer à cette étude, nous vous demanderons d'effectuer les démarches suivantes à des fins de recherche : Vous rencontrerez le médecin de l'étude ou un membre de l'équipe de l'étude au moins 15 fois, comme décrit ci-dessous.

Évaluation
Après avoir signé ce formulaire de consentement, vous serez évalué(e) par l'intermédiaire d'un examen de votre dossier médical, de vos médicaments actuels, des résultats de vos tests sanguins et autres, et d'un examen physique.

Visites dans le cadre de l'étude
Si après votre évaluation et votre greffe, vous êtes en mesure de continuer à participer à cette étude, nous vous rencontrerons lors de vos visites régulières post-transplantation :

- Premier mois : tests sanguins 2 fois par semaine (rein) ou 1 fois par semaine (foie) et visites à la clinique 1 fois par semaine
- 2-3 mois : tests sanguins 1 fois par semaine et visites à la clinique toutes les 2 semaines
- 4-5 mois : tests sanguins toutes les 2 semaines et visites à la clinique 1 fois par mois
- 6-12 mois : tests sanguins 1 fois par mois et visites à la clinique tous les 2 mois
- Deuxième année : tests sanguins tous les 2 mois et visites à la clinique tous les 4 mois
- Troisième à cinquième année : tests sanguins tous les 3 mois et visites à la clinique tous les 6 mois
- Après 5 ans : tests sanguins tous les 3 mois et visites à la clinique tous les ans

Lors des visites à la clinique, nous procèderons aux examens suivants :

- Passer en revue vos médicaments et votre santé
- Effectuer un examen physique, y compris la vérification de vos signes vitaux
  - Prélever des échantillons de sang et d'urine pour savoir dans quelle mesure votre organe greffé fonctionne, pour mesurer la quantité de médicaments immunosuppresseurs dans votre sang, et pour voir si vous avez certaines infections
  - Le jour de votre greffe d'organe, aux semaines 1, 2, 3, 4, 12, 24, 36 et 48 par la suite, et tous les 6 mois ultérieurement, nous analyserons votre sang pour savoir comment votre système immunitaire (qui est un système de défense qui défend le corps contre les attaques de microbes tels que les virus, les bactéries, les parasites et les champignons susceptibles de causer des infections) fonctionne, et la quantité de VIH présente.

Nous effectuerons également des biopsies de l'organe transplanté au moment de la transplantation. Des biopsies seront également effectuées post-transplantation, lorsque votre médecin se préoccupe de la santé de votre organe transplanté (foie, rein) ou si le protocole post-transplantation standard (cœur) l'exige. Ces biopsies sont utilisées pour détecter le rejet éventuel de l'organe transplanté, et seront effectuées même si vous ne participez pas à cette étude. Cependant, si vous participez à cette étude, une partie du tissu sera stockée, à des fins de recherche, pour effectuer de futurs tests liés aux facteurs susceptibles de modifier les niveaux d'anticorps nocifs ou pour permettre à vos médecins de détecter des lésions de l'organe. Si vous êtes d'accord, des tests pourraient également se rapporter à des facteurs qui ne sont pas connus actuellement, mais qui seront découverts à l'avenir.

Des tests de dépistage du VIH seront-ils effectués ?

Oui, le dépistage du VIH sera effectué au cours de cette étude de recherche. Vous trouverez ci-dessous des informations importantes sur le VIH, le dépistage du VIH et les résultats de vos tests :

- Le VIH cause le SIDA et peut être transmis par l'activité sexuelle, le partage d'aiguilles, par les femmes enceintes à leurs fœtus, et par l'allaitement des nourrissons.
- Il existe un traitement contre le VIH qui peut vous aider à rester en bonne santé.
- Les personnes vivant avec le VIH ou le SIDA devraient adopter des pratiques pour protéger les personnes présentes dans leur vie contre toute infection par le VIH.
- Le dépistage du VIH est volontaire et peut être effectué de manière anonyme dans un centre de dépistage public.
- Des tests seront néanmoins nécessaires si vous souhaitez participer à cette étude de recherche.
- La loi protège la confidentialité des résultats des tests liés au VIH.
- La loi interdit toute discrimination fondée sur votre état sérologique ; des services sont disponibles pour lutter contre la discrimination.
- Si, à la suite de votre participation à cette étude, vous recevez INITIALEMENT un diagnostic de VIH, les résultats doivent être communiqués au Département de la santé (Department of Health) de l'État de New York à des fins de traçage de contacts.
- Si, à la suite de votre participation à cette étude, vous recevez un diagnostic de VIH, vous recevrez un suivi psychologique relatif au VIH ou une orientation vers un service de suivi psychologique relatif au VIH.

Test génétique

Cette étude n'impliquera ni recherche génétique ni tests génétiques.

Banque d'échantillons (utilisation future et stockage)

Nous conserverons vos échantillons et les informations vous concernant dans une « biobanque », qui est une bibliothèque d'informations et d'échantillons (tissus et sang) provenant de nombreuses études. Aucun lien ne peut être établi entre ces échantillons et informations et vous. À l'avenir, les chercheurs pourront demander l'autorisation d'utiliser les échantillons et les informations pour de nouvelles études visant à prévenir, diagnostiquer ou traiter des maladies, y compris la recherche génétique. Vos échantillons et informations pourraient être conservés pendant longtemps, possiblement plus de 50 ans. Si vous acceptez leur utilisation future, certaines de vos informations génétiques et médicales désidentifiées (sans lien établi avec vous) pourraient être enregistrées dans une ou plusieurs bases de données scientifiques. Cela peut inclure des bases de données gérées par le gouvernement fédéral.

Vous pouvez choisir de ne pas participer à la biobanque tout en faisant partie de l'étude principale ; cela n'affectera pas votre traitement dans cet établissement.

VEUILLEZ PARAPHER UNE (1) DES OPTIONS SUIVANTES
_____ Je consens à ce que mes échantillons et les informations me concernant soient utilisés dans le cadre de futures études de recherche.
_____ Je NE consens PAS à ce que mes échantillons et les informations me concernant soient utilisés dans le cadre de futures études de recherche. Les informations me concernant seront conservées aussi longtemps que requis par la réglementation et la politique institutionnelle, mais ne seront pas utilisées dans le cadre de futures études.

Serai-je rémunéré(e) pour ma participation à cette étude de recherche ?

Vous ne recevrez aucun paiement ou autre compensation pour votre participation à cette étude.

Certains chercheurs peuvent développer des tests, des traitements ou des produits ayant une valeur pécuniaire. Vous ne recevrez aucun paiement de quelque nature que ce soit pour vos échantillons et informations, ni pour aucun test, traitement, produit ou quoi que ce soit d'autre de valeur pouvant découler de la recherche.

La participation à cette étude me coûtera-t-elle quelque chose ?

Votre participation à cette étude n'entraînera aucuns frais supplémentaires pour vous. Vous et/ou votre compagnie d'assurance devrez payer tous les frais qui font partie de vos soins médicaux réguliers.

Que se passera-t-il si je suis blessé(e) en raison de ma participation à cette étude ?

Si vous êtes blessé(e) à la suite de cette recherche, seul un traitement médical immédiat, essentiel et à court terme, tel que déterminé par l'hôpital participant, sera disponible pour soigner la blessure sans frais à votre charge.

- Aucune compensation monétaire ne sera offerte.
- Vous ne renoncez à aucun de vos droits légaux en signant ce document de consentement éclairé.
  Si un traitement supplémentaire est requis à la suite d'une blessure physique liée à la recherche, le traitement médical nécessaire vous sera fourni et facturé à votre compagnie d'assurance ou vous sera facturé dans le cadre de vos frais médicaux.

Quelles autres démarches dois-je effectuer ?

- Si vous ne vous sentez pas bien à tout moment, appelez immédiatement votre médecin ou le médecin de l'étude de recherche.
- Si vous pensez être enceinte, contactez immédiatement votre médecin de l'étude de recherche.

Signalez immédiatement tout gêne, problème ou blessure que vous ressentez au cours de votre participation à l'étude à **Dr Azzi au 718-952-6421**.

Confidentialité

Nous garderons vos informations confidentielles. Vos dossiers de recherche seront confidentiels et votre nom n'apparaîtra dans aucun des rapports écrits ou verbaux. Un numéro de code sera attribué à vos informations, qui seront séparées de votre nom ou de toute autre information qui pourrait vous identifier. Le formulaire qui relie votre nom au numéro de code sera conservé de manière sécurisée et seuls le chercheur et le personnel de l'étude auront accès au fichier. Toutes les informations seront sécurisées et les dossiers informatiques seront protégés par un mot de passe. Les informations de l'étude vous concernant et les échantillons seront conservés aussi longtemps qu'ils seront utiles pour ce projet.

Les informations médicales recueillies au cours de la recherche, telles que les résultats des tests, pourraient être saisies dans votre dossier médical électronique Montefiore et mises à la disposition des médecins et autres membres du personnel de Montefiore qui vous prodiguent des soins.

Les informations concernant votre participation à cette étude seront saisies dans votre dossier médical électronique (DME). Une fois placées dans votre DME, les informations seront disponibles pour tous vos prestataires participant au système DME. L'objectif de cette saisie est de fournir des informations de recherche susceptibles d'avoir un impact sur vos soins médicaux.

Les seules personnes qui peuvent consulter vos dossiers de recherche sont :

- l'équipe de recherche et le personnel avec qui elle collabore ;
- l'organisation qui a financé la recherche ;
- les organisations et institutions impliquées dans cette recherche ;
- les groupes qui examinent les recherches (l'IRB d'Einstein, le Département de protection pour la recherche humaine [Office for Human Research Protections] et l'Agence des produits alimentaires et médicamenteux [Food and Drug Administration, FDA])

Les personnes recevant vos informations médicales pourraient ne pas être tenues par des lois de protection de la vie privée de les protéger, et pourraient les partager avec d'autres personnes sans votre autorisation, si les lois applicables les y autorisent. Il a été demandé à tous ces groupes de préserver la confidentialité de vos informations.

Ma participation à cette étude présente-t-elle des risques pour moi ?

Un risque lié à la participation à cette étude est la possibilité de perte de confidentialité ou d'atteinte à la vie privée. La perte de confidentialité signifie que vos informations personnelles pourraient être partagées avec une personne qui ne fait pas partie de l'équipe de l'étude et qui n'était pas censée voir ou connaître vos informations. L'équipe de l'étude prévoit de protéger votre vie privée (voyez la section Confidentialité ci-dessus pour plus de détails).

Étant un patient séropositif qui subira une greffe d'organe, vous pourriez courir un ou plusieurs des risques ci-dessous, indépendamment de l'étude, que vous subissiez une greffe d'organe d'un donneur séronégatif, qui est la norme de soins, ou d'un donneur séropositif, comme cela sera le cas dans le cadre de cette recherche d'étude. Les risques en question sont :

- Une interaction médicamenteuse possible pourrait se produire, qui pourrait être grave et entraîner des résultats indésirables graves dus à des changements inattendus des taux de médicaments dans le sang ; ceux-ci pourraient inclure : un taux de rejet accru, une augmentation du taux viral dans le sang et une diminution de votre nombre de lymphocytes T accompagnée d'une progression possible vers le SIDA.

- Taux de rejet aigu plus élevé.
- Risques accrus de thrombo-embolie veineuse (formation d'un ou plusieurs caillots de sang dans vos veines) chez les personnes séropositives.
- Si vous souffrez d'une co-infection par le VHB, le VHC, ou les deux, la transplantation ajoute des risques supplémentaires, le risque de développer un carcinome hépatocellulaire (un cancer des cellulaires du foie) est élevé.
- Des changements dans le schéma thérapeutique standard de la transplantation d'organe, ou des changements dans les doses de médicaments pourraient se produire, ce qui pourrait entraîner un résultat indésirable.
- Vous pourriez avoir besoin d'un traitement à vie pour les infections opportunistes (qui sont des infections plus fréquentes et plus graves chez les personnes dont le système immunitaire est affaibli, comme les séropositifs).

Un risque supplémentaire, que vous pourriez courir en participant à cette étude, est la transmission d'un type de virus résistant aux médicaments à partir de l'organe du donneur.

Prise de sang
Rarement, la veine où nous avons inséré l'aiguille deviendra douloureuse ou rouge. Parfois, un « bleu » inoffensif temporaire peut se développer. Encore plus rarement, un évanouissement peut survenir.

Nouvelles découvertes
Si nous faisons de nouvelles découvertes importantes au cours de l'étude qui pourraient influencer votre décision de participer, nous vous contacterons et vous les expliquerons.

Risques inconnus
Nous avons décrit tous les risques que nous connaissons. Cependant, comme il s'agit de recherche, il est possible que vous ou l'embryon ou le fœtus ayez une réaction que nous ne connaissions pas encore et qui n'était pas prévue. Si nous découvrons d'autres risques, nous vous informerons de leur nature afin que vous puissiez décider si vous souhaitez ou non continuer à participer à l'étude.

L'étude présente-t-elle des avantages possibles pour moi ?

Vous pourriez tirer ou non des avantages personnels directs de votre participation à cette étude. Un avantage possible de votre participation à cette étude qui permet l'utilisation de donneurs d'organes infectés par le VIH est le potentiel d'augmenter le groupe de donneurs d'organes disponibles pour vous, et de raccourcir ainsi potentiellement votre temps d'attente jusqu'à la transplantation. Votre participation générera également de nouvelles connaissances cliniques et une meilleure compréhension de la transplantation d'organes séropositifs à séropositifs.

Quels choix ai-je autres que la participation à cette étude ?

Vous pouvez refuser de participer à l'étude. Même si vous décidez de ne pas y participer, les prestataires de soins médicaux de cet établissement continueront de vous prodiguer les soins et traitements standard appropriés.

Si je décide d'arrêter de participer à cette étude, y aura-t'y des conséquences pour moi ?

Non. Si vous décidez de participer, vous serez libre de vous retirer à tout moment sans avoir à donner de raison. Cela n'affectera pas vos soins et vous continuerez à être traité dans cet établissement. Cependant, certaines de vos informations pourraient avoir été déjà saisies dans l'étude et ne seront pas supprimées. Les chercheurs pourront continuer à utiliser et à partager les informations qu'ils avaient déjà recueillies.

Pour révoquer (reprendre) votre consentement et votre autorisation, vous devrez contacter le chercheur principal par écrit à l'adresse figurant à la page 1 de ce

formulaire. Cela dit, vous pouvez commencer par appeler ou parler au chercheur principal et il cessera de recueillir de nouvelles informations à votre sujet. Si vous retirez votre consentement et votre autorisation, vous ne pourrez plus continuer à participer à cette étude de recherche.

CONSENTEMENT À PARTICIPER

J'ai lu le formulaire de consentement et je comprends qu'il m'incombe de décider si la personne nommée ci-dessous participe ou non. Je suis suffisamment informé(e) sur l'objectif, les méthodes, les risques et les avantages de l'étude de recherche pour prendre une décision. Je comprends que je ne renonce à aucun de ses droits légaux en signant ce document de consentement éclairé. Je recevrai une copie signée de ce formulaire de consentement.

Nom en caractères d'imprimerie du participant	Signature du participant	Date	Heure
Nom en caractère d'imprimerie de la personne de substitution	Signature de la personne de substitution (le cas échéant)	Date	Heure
Nom en caractères d'imprimerie de la personne chargée du processus de consentement	Signature	Date	Heure

INFORMACIÓN BÁSICA SOBRE EL ESTUDIO:

Protocolo de investigación para el trasplante de órganos de personas donantes infectadas por el VIH en receptores infectados por el VIH según la Ley de Equidad de Órganos y VIH (Ley HOPE)

Le invitamos a participar como persona voluntaria en un estudio sobre el uso de los órganos de personas infectadas por el VIH (virus de la inmunodeficiencia humana) para trasplantes. Esta página está diseñada para dar información básica que le ayudará a decidir si participa o no. Hemos incluido más información después de esta página. Pregunte las dudas que tenga al equipo del estudio. Si después tiene preguntas, a continuación, le ofrecemos la información de contacto del investigador responsable del estudio.

¿DE QUÉ SE TRATA EL ESTUDIO Y CUÁNTO DURARÁ?

En este estudio, estamos haciendo trasplantes de órganos de personas infectadas por el VIH a personas como usted que necesitan trasplantes de órganos.

Con en este estudio, esperamos saber si el trasplante de órgano de donantes infectados por el VIH en receptores con el VIH es seguro y eficaz como lo son los trasplantes de donantes no infectados por el VIH. Su participación en esta investigación durará como mínimo un (1) año después del trasplante y le llevará hasta 3 a 5 años.

¿CUÁLES SON LOS MOTIVOS PRINCIPALES POR LOS QUE DECIDIRÍA PARTICIPAR DE MANERA VOLUNTARIA EN ESTE ESTUDIO?

El beneficio principal de participar sería la probabilidad de que reciba un trasplante de órgano. La lista de espera de órganos es larga. Los órganos de donantes infectados por el VIH solo están disponibles actualmente a través de investigaciones, y están a disposición solo para pacientes con el VIH. De manera que su participación en este estudio puede ser la vía más rápida para que reciba un trasplante de órgano. Para tener una descripción detallada de los beneficios, refiérase al siguiente documento de consentimiento.

¿CUÁLES SON LOS MOTIVOS PRINCIPALES POR LOS QUE DECIDIRÍA NO PARTICIPAR DE MANERA VOLUNTARIA EN ESTE ESTUDIO?

Puede decidir no prestarse como persona voluntaria porque no sabemos si los órganos de donantes infectados por el VIH durarán tanto como los órganos de donantes sin el VIH, o si estos órganos estarán relacionados con más problemas después del trasplante como infección o cáncer. Para encontrar una descripción detallada del tratamiento alternativo o procedimientos, refiérase al siguiente documento de consentimiento.

¿TIENE QUE PARTICIPAR EN EL ESTUDIO?

Si decide participar en el estudio, debe ser porque desea hacerlo voluntariamente. No perderá ningún servicio, beneficios ni derechos o acceso a atención médica que, en condiciones normales, recibiría si decide no participar como voluntaria(o).

¿QUÉ PASA SI TIENE PREGUNTAS, SUGERENCIAS O DUDAS?

La persona encargada del estudio es el médico Yorg al-Azzi. Si tiene preguntas, sugerencias o dudas sobre este estudio o si quiere retirarse del mismo, esta es la información de contacto del doctor al-Azzi: 111 East 210th St, Rosenthal C, 2nd floor, Bronx, NY 10467, y su número de teléfono es (718) 920-6421.

Si tiene preguntas, sugerencias o dudas sobre sus derechos como persona voluntaria en este estudio, comuníquese con el personal de la Junta de Revisión Institucional *(Institutional Review Board, IRB*) de Einstein durante el horario de oficina de 9 a. m. a 5 p. m. hora oficial de la costa este de los Estados Unidos (EST), de lunes a viernes al 718-430-2253 o por correo electrónico irb@einsteinmed.edu

ALBERT EINSTEIN COLLEGE OF MEDICINE
MONTEFIORE MEDICAL CENTER

DOCUMENTACIÓN DEL CONSENTIMIENTO INFORMADO Y LA AUTORIZACIÓN PARA USAR Y COMUNICAR SU INFORMACIÓN MÉDICA PROTEGIDA SEGÚN LA LEY HIPAA

Si usted es el representante para tomar las decisiones a nombre de un adulto que puede participar en este estudio, se necesitará contar con su consentimiento y con el asentimiento (conformidad) de la persona participante del estudio. Cuando las palabras «usted(es)» / «su(s)» / «mi(s)» / «a mí» / «yo» aparezcan en este documento de consentimiento, nos referimos al participante; «nosotros» se refiere a los doctores del estudio y al personal investigador.

Introducción

Le invitamos a participar en un estudio llamado **Protocolo de investigación para el trasplante de órganos de personas donantes infectadas por el VIH en receptores infectados por el VIH según la Ley de Equidad de Órganos y VIH (en inglés, *HIV Organ Policy Equity Act*, o *HOPE Act*)**. Su participación es voluntaria; depende de usted si le gustaría participar. Está bien decir que no quiere participar ahora o en cualquier momento después de haber empezado el estudio. Si dice que no quiere participar, tal decisión no afectará ninguno de sus derechos ni beneficios o su acceso a la atención médica.

La persona a cargo de este proyecto es Yorg al-Azzi, M. D. quien es el «investigador principal». Usted se puede contactar con el doctor al-Azzi en: **Dirección del consultorio: 111 East 210th St, Rosenthal C, 2nd floor, Bronx, NY 10467** **Número de teléfono: (718) 920-6421** Si tiene preguntas relacionadas con el estudio, o si cree que tiene una lesión, comuníquese con el investigador principal o con la Junta de Revisión Institucional (*Institutional Review Board*, *IRB*). Este estudio no recibe ninguna ayuda económica externa.	La Junta de Revisión Institucional (IRB) de la Escuela de Medicina Albert Einstein (*Albert Einstein College of Medicine*) y del Centro Médico Montefiore (*Montefiore Medical Center*) ha aprobado este estudio. El número de la IRB está en el sello que se encuentra en la parte superior derecha de este documento. Si tiene alguna pregunta con relación a sus derechos como participante del estudio, puede comunicarse con la oficina de la IRB al teléfono 718-430-2253, por correo electrónico (*email*) a irb@einsteinmed.edu, o por correo regular a la siguiente dirección: Einstein IRB Albert Einstein College of Medicine 1300 Morris Park Ave., Belfer Bldg #1002 Bronx, New York 10461

¿Por qué se está haciendo este estudio?

La meta de este estudio es saber si el trasplante de órganos de donantes infectados por el VIH (virus de la inmunodeficiencia humana) en los receptores infectados por el VIH es tan seguro y eficaz como lo son los trasplantes de donantes de personas que no están infectadas por el VIH.

¿Por qué me invitan a participar?

Le invitamos a participar en este estudio porque le han diagnosticado enfermedad de órgano en etapa terminal (*end-stage organ disease,* por su nombre en inglés) y tiene infección por el VIH, y también reúne los requisitos para recibir un trasplante de órgano. El órgano o los órganos específico(s) que recibirá es/son:

_____ riñón

_____ hígado

_____ corazón

¿Cuántas personas participarán en el estudio?

Usted será una de aproximadamente **200** personas que participarán en este estudio.

¿Por cuánto tiempo participaré en este estudio?

Participará en este estudio por al menos un año, y hasta por tres a cinco años después de su trasplante de órgano. Durante este tiempo, le pediremos que haga como mínimo 15 visitas de estudio al **Montefiore Medical Center**.

¿Qué pasará si participo en el estudio?

Usted ya se encuentra en la lista de espera de órganos para recibir un órgano donado como parte de su atención médica habitual. Ninguna evaluación antes de la cirugía (evaluación prequirúrgica), cirugía ni control se verán afectados por su participación en este estudio.

Si acepta participar en este estudio, le pediremos que haga lo siguiente para fines de investigación: visitará al doctor del estudio o al personal de investigación como mínimo 15 veces tal como se describe abajo.

Selección
Después de firmar este documento de consentimiento, le haremos un examen mediante el análisis de su historia clínica, sus medicamentos actuales, sus resultados de análisis de sangre y de otras pruebas, y le haremos un examen físico.

Visitas de estudio
Si después de la visita de selección y de su trasplante, usted puede continuar participando en este estudio, nos reuniremos con usted en sus visitas después de su trasplante habituales y programas:

- Primer mes: análisis de sangre dos veces por semana (trasplante de riñón) o una vez por semana (trasplante de hígado) y visitas a la clínica una vez por semana.
- Meses 2 a 3: análisis de sangre una vez a la semana, y visitas a la clínica una semana sí y otra semana no.
- Meses 4 a 5: análisis de sangre una semana sí y otra no, y visitas a la clínica una vez al mes.

- Meses 6 a 12: análisis de sangre una vez al mes, y visitas a la clínica un mes sí y otro no.
- Segundo año: análisis de sangre cada 2 meses, análisis de sangre y visitas a la clínica cada 4 meses.
- Del tercer al quinto año: análisis de sangre cada 3 meses, y visitas a la clínica cada 6 meses.
- Después de 5 años: análisis de sangre cada 3 meses, y visitas a la clínica cada año.

En las visitas a la clínica, haremos lo siguiente:

- Una evaluación de sus medicamentos y de su salud.
- Un examen físico que incluye la revisión de sus signos vitales.
  - Obtendremos muestras de sangre y de orina para averiguar qué tan bien está funcionando su trasplante, para determinar cuánto medicamento inmunosupresor está en su sangre, y para saber si tiene ciertas infecciones.
  - El día de su trasplante de órgano y en las semanas 1, 2, 3, 4, 12, 24, 36 y 48 después, y cada 6 meses a partir de ahí, también le haremos análisis de sangre para saber cómo está funcionando su sistema inmunitario (que es un sistema de defensa que defiende al cuerpo de los ataques de los microbios como los virus, las bacterias, los parásitos y los hongos que pueden causar infecciones) y cuánto VIH está presente.

También, le haremos biopsias del órgano trasplantado al momento del trasplante. Además, se harán después del trasplante cuando su médico esté preocupado por la salud de su órgano trasplantado (hígado, riñón) o según el protocolo habitual después del trasplante (corazón). Estas biopsias se usan para detectar un rechazo del órgano trasplantado y se le haría a pesar de que no participara en este estudio. Pero, si participa, una parte del tejido se almacenará para investigaciones con el fin de hacer análisis en el futuro de aspectos que puedan cambiar los niveles de anticuerpos dañinos o que permitan a sus médicos detectar lesión al órgano, si acepta, esto puede incluir pruebas para aspectos que no se conocen en la actualidad, pero que se descubren en el futuro.

¿Habrá pruebas para detectar el VIH?

Sí, la prueba de detección del VIH se hará durante este estudio. Lo que sigue es información importante sobre el VIH, la prueba del VIH y los resultados de su prueba:

- El VIH causa el sida y se puede transmitir a través de las relaciones sexuales, del intercambio de agujas, de la madre al feto y por medio de la lactancia materna.
- Existe tratamiento contra el VIH que puede ayudarle a que se mantenga sana(o).
- Las personas con el VIH o con el sida deben aceptar proteger a las personas en sus vidas de infectarse del VIH.
- Las pruebas del VIH es algo voluntario y se pueden hacer de manera anónima en un centro de pruebas público. Pero, necesita hacerse la prueba si desea participar en este estudio.
- La ley protege la confidencialidad de los resultados de las pruebas relacionadas con el VIH.
- La ley prohíbe la discriminación debido a su estado de VIH y hay servicios disponibles para abordar cualquier discriminación.

- Si, como resultado de su participación en este estudio, se le diagnostica VIH al INICIO, los resultados se deben informar al Departamento de Salud de Nueva York (*New York State Department of Health*) para el rastreo de los contactos.
- Si, como resultado de su participación en este estudio, se le diagnostica el VIH, usted recibirá consejería sobre el VIH o una derivación para consejería sobre el VIH.

Pruebas genéticas

Este estudio no consistirá en hacer investigaciones ni pruebas genéticas.

Banco de muestras (almacenamiento y uso futuros)

Almacenaremos sus muestras y la información sobre usted en un «biobanco», el cual es una colección de información y muestras (tejido y sangre) de muchos estudios. Estas muestras e información no pueden relacionarse con usted. En el futuro, los investigadores pueden solicitar autorización para usar las muestras y la información, y así poder realizar nuevos estudios que tengan como finalidad prevenir, diagnosticar o tratar enfermedades, entre ellos investigaciones genéticas. Sus muestras y su información pueden guardarse por mucho tiempo, posiblemente sobrepase los 50 años. Si usted acepta el uso futuro de tales muestras e información, parte de su información genética y de salud no identificada (que no se relaciona con usted) se puede colocar en una o más bases de datos científicas. Estas pueden consistir en bases de datos administradas por el gobierno federal.

Usted puede decidir no participar en el biobanco, y aun así puede seguir participando en el estudio principal, y esto no afectará su tratamiento en este centro.

ESCRIBA SUS INICIALES (PRIMERA LETRA DE SU NOMBRE Y DE SU APELLIDO) EN UNA (1) DE LAS SIGUIENTES OPCIONES

_____ Doy mi consentimiento para que mis muestras y la información sobre mí se utilicen en estudios en el futuro.

_____ NO doy mi consentimiento para que mis muestras ni la información sobre mí se utilicen en estudios en el futuro. La información sobre mí se guardará durante el tiempo establecido por las normas y las políticas institucionales, pero no se usará para hacer estudios en el futuro.

¿Me pagarán por participar en este estudio?

No recibirá pago ni otra compensación por participar en este estudio.

Algunos investigadores pueden desarrollar pruebas, tratamientos o productos que valgan dinero. Usted no recibirá pago de ninguna clase por sus muestras ni por su información ni por ninguna prueba, tratamiento, producto ni otras cosas de valor que puedan ser el resultado de la investigación.

¿Habrá algún costo para mí por participar en este estudio?

No habrá costos adicionales para usted por participar en el estudio. Usted, su compañía de seguro médico o ambos tendrán que pagar por todos los costos que formen parte de su atención médica habitual.

¿Qué pasará si me lesiono porque participé en este estudio?

Si usted se lesiona como resultado de este estudio, solamente se le proveerá tratamiento médico inmediato, esencial, y a corto plazo para la lesión, libre de costo para usted, según lo determine el hospital participante.

- No se le ofrecerá ninguna indemnización monetaria.
- Usted no renuncia a ninguno de sus derechos legales mediante la firma de este documento de consentimiento informado.
- Si requiere tratamiento adicional como resultado de una lesión física relacionada con el estudio, se le dará el tratamiento médico necesario para usted y se facturará a su compañía de seguro médico o a usted como parte de sus gastos médicos.

¿Qué más tengo que hacer?

- Si no se siente bien en algún momento, llame a su médico o al doctor del estudio de inmediato.
- Si piensa que ha quedado embarazada, comuníquese enseguida con el doctor del estudio.

Informe de inmediato cualquier molestia, dolencia o lesión que presente durante su participación en el estudio al **doctor Azzi** al teléfono **718-952-6421**.

Confidencialidad

Mantendremos su información de manera confidencial. Sus documentos de investigación se mantendrán privados y no se usará su nombre en ningún reporte oral o escrito. Su información tendrá un código numérico de identificación y estará separada de su nombre o cualquier otra información que pueda identificarla(o). El documento que relaciona su nombre con el código numérico se guardará de manera segura y solo el investigador y el personal investigador tendrán acceso al archivo. Toda la información se mantendrá de manera segura y los datos computarizados estarán protegidos con una contraseña. Su información del estudio y sus muestras se guardarán siempre y cuando sean útiles para esta investigación.

La información médica obtenida durante la investigación, como los resultados de pruebas, se puede ingresar a su historia clínica electrónica de Montefiore y estará disponible para los médicos y otro personal de Montefiore que le proporcionan atención médica.

La información sobre su participación en este estudio se ingresará a su historia clínica electrónica (*Electronic Medical Record* o EMR). Una vez que se ingrese a su historia clínica electrónica, la información estará disponible para todos los profesionales de la salud que participan en dicho

sistema. La finalidad de este ingreso de información es proporcionar información de investigación que tenga la posibilidad de afectar su atención médica.

Las únicas personas que pueden tener acceso a sus documentos de investigación son:

- El equipo investigador y el personal que trabaja con ellos,
- la organización qui financia la investigación,
- las organizaciones y las instituciones que participan en esta investigación,
- los grupos que examinan la investigación: la Junta de Revisión Institucional de Einstein (*Einstein IRB*), la Oficina para la Protección de Seres Humanos en Estudios de Investigación (*Office for Human Research Protections*), y la Administración de Alimentos y Medicamentos de los Estados Unidos (*U. S. Food and Drug Administration*).

Estas personas, que reciben su información de salud, pueden que no requieran, por leyes de privacidad, proteger su información y puede ser que comuniquen la misma a otros sin su autorización, si esto es permitido por las leyes que los regulan. A todos estos grupos se les ha pedido que mantengan su información de forma confidencial.

¿Hay riesgos para mí?

Un riesgo de participar en este estudio es la posibilidad de pérdida de confidencialidad o privacidad. Pérdida de privacidad quiere decir comunicar su información personal a alguien que no pertenece al equipo del estudio y que no se supone que vea o sepa su información. El equipo del estudio se propone proteger su privacidad - véase la sección anterior de Confidencialidad por más detalles.

Si es un(a) paciente VIH positivo que recibe un trasplante de órgano, es posible que tenga uno o más de los riesgos que se enumeran a continuación, independientemente del estudio, ya sea que reciba un trasplante de órgano de un donante no infectado por el VIH que es atención médica habitual, o el de un paciente infectado por VIH que es el caso en este estudio. Los riesgos son:

- Puede ocurrir una posible interacción con el medicamento que puede ser muy grave, y puede llevar a resultados graves no deseados de cambios imprevistos en los niveles de los medicamentos en la sangre; estos pueden incluir: un mayor índice de rechazo, un aumento de los niveles del virus en la sangre, y una disminución de su cifra de linfocitos T con una posible evolución a sida.
- Mayor índice de rechazo grave.
- Aumento del riesgo de la tromboembolia venosa (formación de uno o más coágulos de sangre en las venas) en personas infectadas por el VIH.
- Si tiene una coinfección con el virus de la hepatitis B, el virus de la hepatitis C, o ambos, el trasplante agrega riesgos adicionales, el riesgo de presentar carcinoma hepatocelular (cáncer de células del hígado) es alto.
- Puede haber una posibilidad de cambio en el régimen de tratamiento habitual para el trasplante de órgano o de cambio en la(s) dosis de sus medicamentos que puede llevar a un

posible resultado indeseado.

- Puede ser que necesite un tratamiento de por vida contra las infecciones oportunistas (infecciones que suceden con mayor frecuencia y son más graves en personas con sistemas inmunitarios debilitados como en personas infectadas por el VIH).

Un riesgo adicional, que puede tener por participar en este estudio, es una transmisión de la resistencia a medicamentos de un tipo de virus del órgano del donante.

Obtención de muestra de sangre
Raras veces, la vena en la que le introducimos la aguja se enrojece o queda adolorida. A veces, puede aparecer un moretón que es temporal. Muy raras veces, puede ocurrir desmayo.

Nuevos resultados
Si sabemos de algún resultado nuevo e importante durante el estudio que pudiera influir en su decisión de participar en el estudio, nos comunicaremos con usted y se lo explicaremos.

Riesgos desconocidos
Hemos explicado todos los riesgos que sabemos. Sin embargo, como esto es una investigación, existe la posibilidad de que usted o el embrión o feto tenga una reacción que no sepamos todavía y no se espere. Si sabemos de otros riesgos, se lo diremos para que pueda decidir si quiere seguir participando o no en el estudio.

¿Hay posibles beneficios para mí?

Es posible que reciba beneficio directo o personal por participar en este estudio. El posible beneficio de participar en este estudio, y del uso de los órganos de donantes infectados por el VIH, es el beneficio eventual de un aumento del grupo de donantes de órganos disponibles para usted, y la posible reducción del tiempo de espera hasta el trasplante. Su participación generará un nuevo conocimiento clínico y un mejor entendimiento del trasplante de órganos de personas infectadas por el VIH a otras personas con VIH.

¿Qué opciones tengo además de participar en este estudio?

Puede negarse a participar en el estudio. Si decide no participar, los proveedores de atención médica de este centro continuarán prestándole toda la atención médica habitual y el tratamiento indicado para usted.

¿Habrá alguna consecuencia para mí si decido dejar de participar en este estudio?

No. Si decide participar, tiene la libertad de dejar de participar en el estudio en cualquier momento sin tener que dar ninguna explicación. Esto no afectará su atención médica y seguirá recibiendo tratamiento en este centro. Sin embargo, parte de su información puede que ya se haya ingresado en el estudio y eso no se eliminará. Los investigadores del estudio pueden seguir usando y comunicando la información que ya hayan recogido.

Para revocar (retirar) su consentimiento y autorización, debe contactarse con el investigador principal por escrito a la dirección que se encuentra en la página 1 de este documento. Sin embargo, primero debe llamar o hablar con el investigador principal para que deje de recoger nueva información sobre usted. Si usted retira su consentimiento y autorización, no se le permitirá seguir participando en este estudio.

CONSENTIMIENTO PARA PARTICIPAR

He leído el documento de consentimiento y entiendo que depende de mí si quiero o no que la persona que se nombra a continuación participe en el estudio. Sé lo suficiente acerca del propósito, los métodos, los riesgos y los beneficios del estudio como para tomar mi decisión. Entiendo que no renuncio a ninguno de sus derechos legales mediante la firma de este documento de consentimiento informado. Recibiré una copia firmada de este documento de consentimiento.

Nombre y apellido en letra de imprenta del participante	Firma del participante	Fecha	Hora
Nombre y apellido en letra de imprenta del representante legal (cuando corresponda)	Firma del representante legal (cuando corresponda)	Fecha	Hora
Nombre y apellido en letra de imprenta de la persona que realiza el proceso de consentimiento	Firma	Fecha	Hora

KEY INFORMATION FOR [Research protocol for organ transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.]

We are asking you to choose whether or not to volunteer for a research study about the use of organs from people with HIV for transplant. This page is designed to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

In this study, we are giving organs from people with HIV to people like you who need organ transplants.

By doing this study, we hope to learn whether organ transplantation from HIV-positive donors is as safe and effective in HIV-positive recipients as transplants from HIV-negative donors.. Your participation in this research will last at least 1 year post-transplant, and up to 3-5 years.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

The main benefit of participation would be the chance to receive an organ transplant. The waitlist for organs is long. Organs from donors with HIV are only available currently via research studies, and only to patients with HIV, and so participation in this study may be your fastest way to receive an organ transplant. For a complete description of benefits, refer to the Consent Document below.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You may choose not to volunteer because we do not know if organs from donors with HIV will last as long as organs from donors without HIV, or will be associated with more problems post-transplant such as infection or cancer. For a complete description of alternate treatment/procedures, refer to the Consent Document below.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights or access to care you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Yorg al-Azzi, MD. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, his contact information is: 111 East 210th St, Rosenthal C, 2nd floor, Bronx, NY 10467 (telephone #: (718) 920-6421).

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the Einstein Institutional Review Board (IRB) between the business hours of 9am and 5pm EST, Monday-Friday at 718-430-2253 or irb@einsteinmed.edu.

ALBERT EINSTEIN COLLEGE OF MEDICINE
MONTEFIORE MEDICAL CENTER

DOCUMENTATION OF INFORMED CONSENT AND HIPAA AUTHORIZATION

If you are the surrogate decision maker of an adult who may take part in this study, consent from you and the assent (agreement) of the study participant will be required. When the word "you(r)" / "my" / "me" / "I" appears in this consent form, we mean the participant; "we" means the research study doctors and research staff.

Introduction

You are being asked to participate in a research study called **[Research protocol for organ transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.].** Your participation is voluntary. It is up to you whether you would like to participate. It is fine to say "no" now or at any time after you have started the study. If you say "no," your decision will not affect any of your rights or benefits or your access to care.

The researcher in charge of this project is called the "Principal Investigator." **[**His**]** name is [Yorg al-Azzi, MD.]. You can reach Dr. **[**Azzi**]** at:
Office Address: 111 East 210th St, Rosenthal C, 2nd floor, Bronx, NY 10467
Telephone #: (718) 920-6421
For questions about the research study, or if you believe you have an injury, contact the Principal Investigator or the IRB.

The Institutional Review Board (IRB) of the Albert Einstein College of Medicine and Montefiore Medical Center has approved this research study. The IRB # is in the stamp in the upper right hand corner. If you have questions regarding your rights as a research subject you may contact the IRB office at 718-430-2253, by e-mail at irb@einsteinmed.edu, or by mail:

Einstein IRB
Albert Einstein College of Medicine
1300 Morris Park Ave., Belfer Bldg #1002
Bronx, New York 10461

There is no external financial support being received for this study.

Why is this study being done?

The goal of this study is to learn whether organ transplantation from HIV-positive donors is as safe and effective in HIV-positive recipients as transplants from HIV-negative donors.

Why am I being asked to participate?

You are being asked to participate in this study because you are diagnosed with end-stage organ disease and have HIV infection, and qualify for organ transplantation. The specific organ or organs you will receive are:
_____ Kidney
_____ Liver
_____ Heart

How many people will take part in the research study?

You will be one of about **200** people who will be participating in this study

How long will I take part in this research?

You will be in this study for at least one year, and up to three or five years after your organ transplant. During this time, we will ask you to make at least 15 study visits to **Montefiore Medical Center**.

What will happen if I participate in the study?

You are already on the waiting list to receive a donated organ as part of your standard clinical care. Your pre- surgical evaluation, surgery and any follow-up will not be affected by your participation in this study.

If you agree to be in this study, we will ask you to do the following things for research purposes: You will visit with the study doctor or a member of the study team at least 15 times as described below.

Screening
After you sign this consent form, you will be evaluated by a review of your medical record, current medications, blood test results, and other tests, and have a physical exam.

Study Visits
If after screening and your transplant, you are able to continue to take part in this study, we will meet with you at your regularly scheduled post-transplant visits:

- First month: blood tests twice a week (kidney) or once weekly (liver) and clinic visits once a week
- 2-3 months: blood tests once a week and clinic visits every other week
- 4-5 months: blood tests every other week and clinic visits once a month
- 6-12 months: blood tests once a month blood tests and clinic visits every other month
- Second year: blood tests every 2 months, blood tests and clinic visit every 4 months
- Third through fifth year: blood tests every 3 month and clinic visits every 6 months
- After 5 years: blood tests every 3 months and clinic visits every year

At the clinic visits, we will do the following:

• Review your medications and health
• Perform a physical examination including checking your vital signs

- Take blood and urine samples to find out how well your transplanted organ is functioning, to measure how much immunosuppressant medication is in your blood, and to see if you have certain infections
- On the day of your organ transplant and at 1, 2, 3, 4, 12, 24, 36 and 48 weeks afterward, and every 6 months thereafter, we will also test your blood to find out how your immune system (which is a defense system that defends the body against attacks by microbes such as virus, bacteria, parasites, and fungi that can cause infections) is functioning and how much HIV is present.

You will also have biopsies of the transplanted organ performed at the time of transplant. They will also be performed post-transplant when your doctor is concerned about the health of your transplanted organ (liver, kidney) or as per the standard post-transplant protocol (heart). These biopsies are used to detect rejection of the transplanted organ and would be done even if you did not take part in this study. However, if you take part in this study, a portion of the tissue will be stored for research for future testing of things that may change the levels of harmful antibodies or allow your doctors to detect injury to the organ, if you agree, this may include tests for things that are not currently known, but are discovered in the future.

Will there be testing for HIV?

Yes, HIV testing will be done during this research study. The following is important information about HIV, HIV testing, and your test results:

- HIV causes AIDS and can be spread through sexual activity, sharing needles, by pregnant women to their fetuses, and through breastfeeding infants.
- There is treatment for HIV that can help you stay healthy.
- People with HIV or AIDS should adopt practices to protect people in their lives from becoming infected with HIV.
- HIV testing is voluntary and can be done anonymously at a public testing center. However, testing is required if you would like to be in this research study.
- The law protects the confidentiality of HIV related test results.
- The law prohibits discrimination based on your HIV status and services are available to address any discrimination.
- If as a result of participation in this study you are INITIALLY diagnosed with HIV, the results must be reported to the New York State Department of Health for contact tracing purposes.
- If as a result of participation in this study you are diagnosed with HIV, you will be given HIV counseling or a referral for HIV counseling.

Genetic Testing

This study will not involve genetic research or genetic testing.

Specimen Banking (Future Use and Storage)

We will store your specimens and information about you in a "biobank", which is a library of information and specimens (tissue and blood) from many studies. These specimens and information cannot be linked to you. In the future, researchers can apply for permission to use the specimens and information for new studies to prevent, diagnose, or treat disease, including genetic research. Your specimens and information may be kept for a long time, perhaps longer than 50 years. If you agree to the future use, some of your de-identified genetic and health information (not linked to you) may be placed into one or more scientific databases. These may include databases maintained by the federal government.

You can choose not to participate in the biobank and still be part of the main study and this will not affect your treatment at this facility.

INITIAL ONE (1) OF THE FOLLOWING OPTIONS
_____ I consent to have my specimens and information about me used for future research studies.
_____ I do NOT consent to have my specimens and information about me used for future research studies. Information about me will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

Will I be paid for being in this research study?

You will not receive any payment or other compensation for taking part in this study.

Some researchers may develop tests, treatments or products that are worth money. You will not receive payment of any kind for your specimens and information or for any tests, treatments, products or other things of value that may result from the research.

Will it cost me anything to participate in this study?

Taking part in this study will not involve added costs to you. You and/or your insurance company will have to pay for any costs that are part of your regular medical care.

What will happen if I am injured because I took part in this study?

If you are injured as a result of this research, only immediate, essential, short-term medical treatment as determined by the participating hospital, will be available for the injury without charge to you personally.

- No monetary compensation will be offered.
- You are not waiving any of your legal rights by signing this informed consent document.
- If additional treatment is required as a result of a physical injury related to the research, necessary medical treatment will be provided to you and billed to your insurance company or to you as part of your medical expenses.

What else do I have to do?

- If you do not feel well at any time, call your doctor or the research study doctor immediately.
- If you think you have become pregnant, contact your research study doctor immediately.

Immediately report any discomforts, problems or injuries you experience during the course of your participation in the study to **Dr. Azzi at 718-952-6421**.

Confidentiality

We will keep your information confidential. Your research records will be kept confidential and your name will not be used in any written or verbal reports. Your information will be given a code number and separated from your name or any other information that could identify you. The form that links your name to the code number will be kept in a secure manner and only the investigator and study staff will have access to the file. All information will be kept in a secure manner and computer records will be password protected. Your study information and specimens will be kept as long as they are useful for this research.

Medical information collected during the research, such as test results, may be entered into your Montefiore electronic medical record and will be available to clinicians and other staff at Montefiore who provide care to you.

Information about your participation in this study will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, the information will be available to all of your providers who participate in the EMR system. The purpose of this entry is to provide research information that has the potential to impact your medical care.

The only people who can see your research records are:

- the research team and staff who work with them
- the organization that funded the research
- organizations and institutions involved in this research
- groups that review research (the Einstein IRB, and the Office for Human Research Protections, and the US Food and Drug Administration)

These people, who receive your health information, may not be required by privacy laws to protect it and may share your information with others without your permission, if permitted by laws governing them. All of these groups have been asked to keep your information confidential.

Are there any risks to me?

A risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your privacy – see the Confidentiality section above for details.

Being a HIV positive patient who will undergo organ transplantation, you may have one or more of the risks below regardless of the study, whether you will undergo organ transplant from HIV

negative donor which is the standard of care, or from the HIV positive donor which is the case in this study research. These risks are:

- A possible drug interaction may occur which can be quite severe and may lead to serious undesirable outcomes from unexpected changes in blood levels of drugs; these may include: increased rejection rate, increase viral level in the blood, and decrease in your T-cell count with possible progression to AIDS.
- Higher acute rejection rate
- Increased risks of venous thromboembolism (formation of one or more blood clots in your veins) in HIV Positive individuals.
- If you have a co-infection with HBV, HCV or both, transplantation adds additional risks, risk of developing Hepatocellular carcinoma (a liver cell cancer) is high
- There may be a possibility of change in the standard organ transplant treatment regimen or change in the doses of their medications which may lead to a possible undesirable outcome.
- You may need a life-long treatment for opportunistic infections (which are infections that occur more frequently and are more severe in individuals with weakened immune systems like in HIV positive).

An additional risk, that you may have from participation in this study, is a transmission of a medication resistance type of virus from the donor organ.

Blood Draw
Rarely, the vein where we inserted the needle will become sore or red. Sometimes, a temporary harmless “black and blue” may develop. Very rarely, fainting may occur.

New Findings
If we learn any significant new findings during the study that might influence your decision to participate, we will contact you and explain them.

Unknown Risks
We have described all the risks we know. However, because this is research, there a possibility that you or the embryo or fetus will have a reaction that we do not know about yet and is not expected. If we learn about other risks, we will let you know what they are so that you can decide whether or not you want to continue to be in the study.

Are there possible benefits to me?

You may or may not receive personal, direct benefit from taking part in this study. The possible benefit of taking part in this study, allowing the use of organ donors infected with HIV, is the potential for increasing the pool of available organ donors to you, and potentially shortening your wait time until transplantation. Your participation will generate new clinical knowledge and a better understanding of HIV-positive to HIV-positive organ transplantation.

What choices do I have other than participating in this study?

You can refuse to participate in the study. If you decide not to participate, the medical care providers at this facility will still give you the standard care and treatment that is appropriate for you.

Are there any consequences to me if I decide to stop participating in this study?

No. If you decide to take part, you are free to stop participating at any time without giving a reason. This will not affect your care and you will continue to be treated at this facility. However, some of the information may have already been entered into the study and that will not be removed. The researchers may continue to use and share the information they have already collected.

To revoke (take back) your consent and authorization, you must contact the Principal Investigator in writing at the address on page 1 of this form. However, you may first call or speak to the Principal Investigator and he will stop collecting new information about you. If you take back your consent and authorization, you will not be allowed to continue to participate in this research study.

CONSENT TO PARTICIPATE

I have read the consent form and I understand that it is up to me whether or not the individual named below participates. I know enough about the purpose, methods, risks and benefits of the research study to decide. I understand that I am not waiving any of his/her legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Printed name of participant	Signature of participant	Date	Time
Printed Name of Surrogate (when applicable)	Signature of Surrogate (when applicable)	Date	Time
Printed name of the person conducting the consent process	Signature	Date	Time

Protocol Version 1.0

April 11th, 2016

1. Title:

Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.

2. Investigators:

PI: Juan P Rocca[1], MD.

AIs: Victoria Muggia[3], MD; Grace Minamoto[3], MD; Yoram Puius[3] Enver Akalin[2], MD; Michelle Lieberman Lubetzky[2], MD; Maria Ajaimy[2],MD; Layla Kamal[2], MD; Stuart Greenstein[1], MD, Jay Graham[1], MD; Milan Kinkhabwala [1], MD.

[1] Montefiore-Einstein Center for Transplantation, Transplant Surgery, Department of Surgery.

[2] Montefiore-Einstein Center for Transplantation, Transplant nephrology, Department of Medicine.

[3] Montefiore-Einstein Center for Transplantation, Transplant Infectious Diseases, Department of Medicine.

3. Background and purposes:

The advent of effective antiretroviral therapy (ART) in the mid-1990s for treatment of individuals infected with HIV transformed a rapidly fatal disease into a well-controlled chronic illness. Currently, the life expectancy of individuals infected with HIV and receiving ART early in the course of their disease approaches that of individuals without HIV infection (Wada, 2013, 2014). In this era of greater longevity, liver failure, end-stage renal disease, and cardiovascular disease have emerged as important causes of morbidity and mortality in patients with HIV infection (Neuhaus, 2010).

Organ transplantation prolongssurvival and improves quality of life for individuals with end-stage organ disease (Matas, 2014; Kim, 2014). Until recently, however, organ transplantation was unavailable to those infected with HIV due to concerns that pharmacologic immunosuppression to prevent organ rejection would hasten the progression from HIV infection to AIDS, concerns about disease transmission, and reluctance to allocate organs to a population whose outcome was unpredictable (Blumberg, 2009, 2013a, 2013b; Mgbako, 2013; Taege, 2013).

Nevertheless, a few transplant programs accepted HIV-positive patients on their transplant waiting lists and accumulated data showing kidney or liver transplantation could be done safely in these patients (Roland, 2002, 2003a, 2003b, 2003c; Blumberg, 2009; Stock, 2010; Yoon, 2011; Terrault, 2012). Subsequently, a prospective, multicenter clinical trial of kidney and liver transplantation in 275 patients demonstrated that, among HIV-positive kidney and liver transplant recipients, patient and graft survival

rates were acceptable and within the range of outcomes currently achieved among non-infected transplant recipients.

However, the rate of kidney rejection was unexpectedly high, demonstrating that the immune dysregulation resulting from HIV infection, HCV co-infection, and antirejection drugs is complex and incompletely understood. Some of the challenges encountered in that study remain relevant for clinical sites offering organ transplantation to HIV-positive individuals today (e.g., management ofdrug interactions and toxicities when combining complex medical regimens, management of combined morbidities of two or more active diseases, and the need for ongoing collaboration among medical professionals from different specialties) (Frassetto, 2007, 2014; Locke, 2014). Despite the complexities, this study and others (Ragni, 1999; Frassetto, 2009; Huprikar, 2009; Stock,2010; Touzot, 2010; Cooper, 2011;Duclos-Vallee, 2011; Reeves-Daniel,2011; Fox, 2012; Terrault, 2012; Grossi,2012; Gomez, 2013; Harbell, 2013) demonstrate that kidney and liver transplantation are appropriate in HIV- positive individuals with liver or kidney failure, although gaps in knowledge and many research questions remain. There is much less experience with heart (Calabrese, 2003; Bisleri, 2003; Pelletier,2004; Uriel, 2009, 2014; Castel, 2011a,2011b; Durante-Mangoni, 2011 and 2014) and lung (Mehta, 2000; Humbert,2006; Petrosillo, 2006; Bertani, 2009; Kern, 2014a, 2014b) transplantation in HIV-positive recipients, or mechanical circulatory assistance (Brucato, 2004; Fieno, 2009; Mehmood, 2009; Sims, 2011) as a bridge to transplantation, although case reports and small case series suggest acceptable short-term outcomes are possible.

Prior to the passage of the HOPE Act,U.S. law required that all U.S. transplants for HIV-positive recipients utilize organs from HIV-uninfected donors. (See 42 U.S.C. 273(b)(3)(C), 274(b) and 18 U.S.C. 1122, all prior to amendment by the HOPE Act). The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV (hereinafter referred to as ‘‘HIV-positive to HIV-positive transplantation’’) is recognized (Boyarsky, 2011, 2015; Mgbako, 2013; Mascolini, 2014; Kucirka, 2015; Richterman, 2015). It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients (Boyarsky, 2011). The published experience with HIV-positive to HIV- positive SOT at this time comes from Muller et al from the University of Cape Town in South Africa. Initially, Muller et al (2010) reported 100 percent patient and graft survival in a four-patient pilot study. Subsequently, the same group reported an additional 10 HIV-positive to HIV-positive renal transplants (Muller, 2012). All patients were restarted on ART early postoperatively in the immunosuppressive setting of T-cell-depleting induction therapy, tacrolimus, mycophenolatemofetil, and prednisone. One to 4 years after transplantation, outcomes remained excellent and all patients had undetectable viral loads (Muller, 2012). The cumulative University of Cape Town experience of 27 HIV-positive to HIV-positive transplant procedures was recently summarized in the New England Journal of Medicine (Muller, 2015). The 1- and 5-year death-censored graft survival was 93 and 84 percent, respectively, and 1- and 5-year patient survival was 83 and 74 percent, respectively. Of note, the South African HIV-positive deceased donors were ART-naive, without history of opportunistic infection or proteinuria, and had normal pre-transplant renal biopsies. While renal function has remained normal in the recipients, three have had routine post-transplant renal biopsies demonstrating new changes typical

of early HIV-associated nephropathy that were not present in baseline biopsy specimens. The long- term significance of these findings remains unknown and awaits longer follow-up. All patients had undetectable plasma HIV viral loads after transplantation. Graft rejection rates were 8 percent at 1 year and 22 percentat 3 years.

The HOPE Act permits HIV-positive to HIV-positive organ transplantation under IRB-approved research protocols conforming to the Final Human Immunodeficiency Virus (HIV) Organ Policy Equity (HOPE) Act Safeguards and Research Criteria for Transplantation of Organs Infected with HIV, which were developed as directed in the HOPE Act. Patients receiving HIV-positive kidneys from deceased HIV-positive donors in South Africa (Muller, 2015) had survival rates of 84 percent and 74 percent at 1 and 5 years, respectively; however, there is presently no evidence for the safety, efficacy, and effectiveness of HIV-positive to HIV- positive transplantation in North America. The Final Safeguards and Research Criteria are meant to support the acquisition of new clinical knowledge and mechanistic insights about HIV-positive to HIV-positive organ transplantation in the United States. The results of this research will be evaluated by the Secretary of HHS and the OPTN to determine whether and how the OPTN standards for organ transplantation shall be revised to address HIV-positive organ donors.

The research protocol described below was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH thatestablishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States. The criteria address the minimum safety and data requirements of clinical research in HIV-positive to HIV-positive transplantation. As mandated by the HOPE Act, the Secretary, together with the OPTN, is charged with reviewing the results of scientific research conducted under these criteria to determine whether the OPTN's standards of quality should be further modified and whether some HIV- positive to HIV-positive transplants should proceed outside the auspices of research conducted under such criteria (see attached the original document).

Montefiore Medical Center and the Montefiore-Einstein Center for Transplantation meet the institutional standards and requirements to carry on a research protocol on HIV-positive to HIV-positive kidney transplantation with a collective experience of 14 kidney transplants on HIV positive recipients since 2008. The Montefiore AIDS center provides care to over 2500 HIV positive individuals in the Bronx. Potential transplant candidates as per protocol are evaluated by transplant ID clinicians with expertise also in HIV. The AIDS center providers and the Montefiore infectious disease faculty practice follow these patients closely for the first year after transplantation, and over two thirds of these patients have elected to remain at Montefiore for their HIV care. Multidisciplinary transplant protocols include management of HIV recipients and the outcomes of these cases have met the national standards without affecting our program-specific reports (SRTR reports).

4. Objectives and outcome measures

Montefiore's research in HIV-positive to HIV-positive transplantation will addressquestions related to HIV superinfection; incidence and severity of opportunistic infections (including transmission of occult

OIs from donor to recipient); immunologic mechanisms contributing to the increased rate of kidney rejection observed in HIV-positive recipients and quality of life for recipients of HIV- positive to HIV-positive transplantation.To ensure that all nationwide studies of HIV-positive to HIV- positive transplantation can contribute to evaluation of the safety of the procedure, the following key donor and recipient characteristics and outcome measures must be incorporated into the design of all clinical trials of HIV- positive to HIV-positive transplantation.

Wait List Candidates

- HIV status
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Removal from wait list (death or other reason)
- Time on wait list

Donors (all)

- Type (living or deceased)
- HIV status (HIV-positive new diagnosis, HIV-positive known diagnosis)
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Pre-transplant donor allograft biopsy

Note regarding Living Donors: Montefiore Einstein Center for Transplantation has decided to exclude living donors from the participation in this research protocol.

Transplant Recipients

- Rejection rate (annual up to 5 years)
- Progression to AIDS
- New Opportunistic Infections
- Failure to suppress viral replication (persistent viremia)
- HIV-associated organ failure
- Malignancy
- Graft failure
- Mismatched ART resistance versus donor
- Death

5. Methods:

-Donor Eligibility

Montefiore Einstein Center for Transplantation has decided to exclude living donors from this research protocol. HIV- positive deceased donors of organs for transplantation into an HIV-positive recipient must fulfill applicable clinical criteria in place for HIV-uninfected organ donors.

There is substantial concern about the consequences of transplanting an organ from an HIV-positive donor to a recipient infected with a strain of HIV that differs from the donor's in terms of its responsiveness to antiretroviral therapy (ART). The likelihood and impact of HIV superinfection in this context are unknown. Adverse consequences could range from transient loss of viral suppression, necessitating a change in antiretroviral regimen to a worst-case scenario in which the new infecting strain of HIV is unresponsive to available antiretroviral treatment and the recipient progresses to AIDS (Redd, 2013). Information relevant to understanding the known or potential extent of antiretroviral resistance in the strain of HIV infecting the organ donor may be incomplete for many reasons:

- There may be inadequate virus in donor specimens for antiretroviral resistance testing;
- If the specimen is adequate, there may not be enough time within the decision-making evaluation window to fully assess antiretroviral resistance before the clinical deterioration of the donor, organ procurement, and implantation;
- The donor's history of antiretroviral treatment may be unknown or incomplete;
- Results from prior antiretroviral resistance testing may be unavailable.

These issues might be especially challenging when considering organ donation from deceased donors whose HIV infection is first identified during donor evaluation. As of 2011, an estimated 1 in 6 U.S. adults living with HIV infection were undiagnosed (Prevention, 2013) and an estimated 16 percent of newly diagnosed, untreated individuals were infected with virus resistant to at least one class of antiretroviral drug (Kim, 2013; Megens, 2013).

It is anticipated that the risk of transmission of resistant HIV strains may be lower from deceased donors with a well-documented history of antiretroviral treatment, undetectable virus at demise, and robust and persistent undetectable viral load for at least 1 year prior to death. However, to impose this as an eligibility criterion would limit the pool of suitable donors and severely limit the ability to study transplantation of HIV-positive organs under the HOPE Act. In addition, it will not be possible in all cases to obtain viral loads and/or antiretroviral resistance profiles in the time available for donor evaluation. Transplant teams evaluating a donor must review all available donor and recipient information and be able to propose an antiretroviral regimen that will be equally or more safe, tolerable, and effective for the recipient after transplantation as the regimen in place in the recipient before transplantation. For instance, a donor who only achieves viral suppression with a regimen known to be intolerable to the

recipient must not be accepted. If there is doubt about the ability to suppress viral replication after transplantation, the transplant must not move forward.

Donors co-infected with hepatitis are not excluded from HIV-positive to HIV- positive transplant; however, careful consideration must be given when evaluating a donor co-infected with HBV and/or HCV (Terrault, 2012; Miro, 2012; Moreno, 2012; Sherman, 2014; Chen, 2014). Although HCV therapeutic strategies are rapidly evolving (Liang, 2013), it is possible that mixed genotype HCV infections may influence post- transplant treatment of HCV in the recipient. Prior antiretroviral treatment of the donor and/or recipient with agents active against HBV (i.e., lamivudine, emtricitabine, adefovir, and tenofovir) has the potential for inducing or uncovering archived HBV drug resistance in the recipient (Dieterich, 2007; Soriano, 2009; Pais, 2010).

HIV-positive transplant candidates who are listed for a transplant in the context of a research study of HIV- positive to HIV-positive transplantation must have the same opportunity as other transplant candidates to receive an organ from an HIV-negative donor, should one become available for them.

1.1 HIV-Positive Donor Eligibility Criteria

The HIV-specific donor eligibility criteria for deceased donors is listed (Table 1). Co-infection with HBV and/or HCV is not an exclusion criterion.

1.1.1 HIV-Positive Deceased Donors

When evaluating HIV-positive deceased donors, it is understood that limited medical history may be available and/or known at the time of the donor evaluation. The OPO must make reasonable efforts to obtain prior medical history so that a transplant center team may best determine the suitability of the potential donor based on the information available. A complete history of antiretroviral regimens and a history of viral load tests and resistance testing are especially valuable for evaluating the likelihood of donor HIV resistance to antiretroviral regimens. A history of OIs or cancers is also of high importance, due to the increased risk for both attributable to HIV, and the additional difficulty of treating some infections and neoplasms in a post-transplant setting. It is possible that deceased donors with lower CD4+ T-cell counts may pose an increased risk of harboring transmissible diseases (e.g., opportunistic infections or neoplasms) that may be difficult to detect during organ harvest and transplantation; teams conducting transplants under the HOPE Act are urged to assess donors with low CD4+ T-cell counts (e.g., <200/mL) with special caution and to promptly inform IRBs and the PI of known or suspected disease transmission events.

Minimum eligibility criteria for all HIV-positive deceased donors:

i. Documented HIV infection using an FDA-licensed, approved, or cleared test device(s).

ii. No evidence of invasive opportunistic complications of HIV infection.

iii. Pre-implant donor organ biopsy to be stored, at a minimum, for the duration of the study (or at least 5 years); additional specimens may be obtained to support specific research goals.

Additional eligibility criteria for HIV- positive deceased donors with a known history of HIV and prior treatment with ART:

i. The study team must describe the anticipated post-transplant antiretroviral regimen(s) to be prescribed for the recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Recipient Eligibility

A key consideration when evaluating potential HIV-positive transplant candidates is the ability to suppress HIV viral load post-transplant. This includes a thorough assessment by the transplant team of the candidate recipient's prescribed antiretroviral medications, HIV RNA levels while on medications, adherence to HIV treatment, and any available HIV resistance testing; a similar evaluation of the donor must also be carried out. A transplant should only take place if, after evaluating both recipient and donor, the team is confident they can define a post- transplant antiretroviral regimen that will be safe, tolerable, and effective. If there is any doubt on the part of the transplant team about the ability to suppress viral replication post- transplant, the transplant should not move forward. Concerns about transmitted drug resistance must be included in the recipient informed consent process for the research study. At the time of an organ offer, the recipient informed consent must address the transplant team's assessment of risk specific to the organ they are being offered.

2.1 HIV-Positive Recipient Eligibility Criteria

The following HIV-specific criteria must be met when screening for an HIV- positive to HIV-positive organ transplant (also refer to Table 1):

i. CD4+ T-cell count >200/mL (kidney) within 16 weeks prior to transplant; any patient with history of OI must have a CD4 positive T-cell count >200/uL.

ii. HIV RNA less than 50 copies/mL and on a stable antiretroviral regimen.*+

iii. No evidence of active opportunistic complications of HIV infection.

iv. No history of primary CNS lymphoma orPML.

v. Concurrence by the study team that, based on medical history and ART, viral suppression can be achieved in the recipient post-transplant.

*Patients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen for the patient once organ function is restored after transplantation.

+Those patients on a protease based regimen and fully suppressed with no available resistance studies, should be tested with an assay that looks at archived resistance (e.g. Genosure Archive®).

TABLE 1—SUMMARY OF DONOR AND RECIPIENT ELIGIBILITY CRITERIA FOR HIV-POSITIVE SERO-CONCORDANT ORGAN TRANSPLANT PAIRS UNDER THE HOPE ACT

HIV-Relatedvariables	Deceaseddonor	Livingdonor	HIV-Positiverecipient
Current CD4+ T-cell count (T lymphocytes/μL).....	No requirement	≥500 for 6 months prior to organ donation.	If no history ofOI •≥200 If history ofOI • ≥200(kidney) •≥100(liver) CD4+ T-cell count measured within 16 weeks oftransplantation
Plasma HIV RNA viral load(copies/mL).	No requirement**.....	<50	<50*
Opportunistic infection.....	No invasive OI.....	No invasive OI.....	Currently, • No active OI Historically,no • CNS lymphoma • PML

* Organ recipients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen to be used by the recipient once organ function is restored after transplantation.

** In deceased donors with a known history of HIV infection and prior treatment with ART, the study team must describe the anticipated post- transplant antiretroviral regimen(s) to be used by the organ recipient and justify their conclusion that the proposed regimen will be safe, tolerable, andeffective.

- Transplant processand post-transplant considerations

Organ recovery, transplant procedure, handling and storage of donor organs/tissues, as well as management of kidney transplant recipients at Montefiore-Einstein Center for Transplantation are well described in our policies and procedures section (intranet), including the multidisciplinary management and immunosuppression protocols of HIV-positivekidney recipients

Waitlist acceptance criteria:Once an IRB- approved research protocol in HIV- positive to HIV-positive transplantation is finalized, the transplant center will inform the OPTN of additional organ-specific acceptance criteria for organs from HIV-positive donors. Those HIV-positive kidney candidates on the wait list willing to accept an HIV- positive organ must specify any additional acceptance criteria to the OPO.

Consent process and Independent HIV-Positive Recipient Advocate: One of Montefiore's senior transplant coordinator is actively collaborating with an NIH initiative to train and credential independent advocates for protecting and promoting the rights and interests of the HIV-positive recipient (or prospective recipient). The independent advocate for the HIV- positive recipient will:

i. Promote and protect the interests of the HIV-positive recipient (including with respect to having access to a suitable HIV-negative organ if it becomes available) and take steps to ensure that the HIV-positive recipient's decision is informed and free from coercion.

ii. Review whether the potential HIV-positive recipient has received information regarding the results of SOT in general and transplantation in HIV- positive recipients in particular and the unknown risks associated with HIV- positive to HIV-positive transplant.

iii. Demonstrate knowledge of HIV infection and transplantation.

Attached: -Informed consent for research

Post-transplant care

After discharge, patients are seen by the multidisciplinary transplant team according to the below schedule. During weekly morbidity and mortality meeting the post-transplant team meets and reviews the transplant recipients seen during the week to discuss patients, complications (infections, rejection, bleeding, readmission, re-surgery, malignancy, patient death, and graft loss), and allograft function. These events are stored in the transplant computerized database and communicated to the OPTN in accordance with regulations. Recipients are also assessed and contacted in respect to QAPI initiatives to further improve patient care initiatives.

Adult Transplant Patients are generally evaluated according to the following schedule after kidney transplantation:

First month: twice a week labs, once a week clinic visit

2-3 months: once a week labs and every other week clinic visit

4-5 months: every other week labs and one month clinic visit

6-12 months: once a month labs and every other month clinic visit

Second year: every 2 months labs and 4 months clinic visit

3-5 years every 3 month labs and 6 months clinic visit

> 5 years every 3 months labs and once a year clinic visit

During each clinical visit, bloods and vital signs are obtained, a physical exam is performed and medications are reviewed with each patient. Medical and surgical problems will be addressed on an ongoing basis and appropriate referrals are made to specialists. Pharmacist, nutritional and social service support is available at each clinic. The Transplant Patient will receive specific instructions from the Transplant Multi-Disciplinary Team as to their follow-up care.

Additional transplant allograft biopsy will be performed at 3 months and one year from transplant.

All patients will be assigned to one respective transplant nephrologist for routine follow-up. Patients will be seen at least once within a month after transplantation by a transplant surgeon.

In order to promptly detect viral breakthrough or possibility of viral superinfection, HIV viral loads should be performed every week for the first four weeks after transplantation, every three months for

the first year post transplantation, and every 6 months in patients who have achieved sustained viral suppression. If viral breakthrough is detected on two consecutive assays, genotypic resistance studies will be sent. In addition tropism assays and resistance testing looking for mutations in the integrase gene will be performed. CD4 monitoring can be done less frequently. Monthly CD4 monitoring for the first three months, every three months for the first year, and every 6 months in stable patient. The Montefiore transplant infectious disease provider will see the patient monthly the first three months after transplantation and every three months for the first year post transplant. After the first year, stable transplant patients may return to their outside provider, however the transplant ID attending will maintain close contact with the primary care provider, and also see the recipient twice a year for the duration of the study. To assist patients with urgent infectious disease issues the Montefiore AIDS center provides walk in services Monday through Friday, and 24 hour service coverage for established patients.

Transplant physicians will give 24 hour coverage service for posttransplant patients with any questions and complaints.

6– Potential risks

Risk considerations and pertinent safeguards to potential recipients have been described in detail above under donor and recipient eligibility sections.

Prevention of Inadvertent Transmission of HIV

Although the use of HIV-positive organs may help alleviate transplant shortages and reduce patient waiting list times, there also are patient safety concerns to consider. Prevention or management of inadvertent transmission of HIV or exposure of an HIV-negative recipient to organs or tissues from an HIV-positive donor due to identification error is paramount (Ison, 2009, 2011a, 2011b). Thetransplant community, with regulatory oversight at multiple levels, has been able to achieve a high level of safety through routine procedures and clinical practice. The precautions taken with ABO compatible donor-recipient pairs and HCV-infected donor organs in HCV- infected recipients (Morales, 2010; Kucirka, 2010; Mandal, 2000; Tector, 2006) are existing models. However, vulnerabilities still exist, and mishaps still occur. For instance, the risks of error during manual transcription of information are well documented.

Montefiore medical center and the transplant centeralready count with an institutional biohazard plan for handling of HCV-positive organsand tissue disposal for HCV-positive recipients and ABO compatibility verification policies. HIV-positive status of donor organ, donor tissues and intended recipient will be added to the organ-to-recipient verification form

7- Confidentiality and safeguards to minimize risks.

The research protocol was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States (attached document and informed consent).

8- Study benefits

The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV. It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients

9-References

Bertani, A., Grossi, P., Vitulo, P., et al. (2009).Successful lung transplantation in an HIV- and HBV-positive patient with cystic fibrosis. American Journal of Transplantation, 9, 2190–2196.

Bisleri, G., Morgan, J. A., Deng, M. C., et al. (2003). Should HIV-positive recipients undergo heart transplantation? Journal of Thoracic and Cardiovascular Surgery, 126, 1639–1640.

Blumberg, E. A., & Stock, P. (2009).Solid organ transplantation in the HIV-infected patient.American Journal of Transplantation, 9 Suppl 4, S131–135.

Blumberg, E. A., & Rogers, C. C.(2013a).Human immunodeficiency virus in solid organ transplantation. American Journal of Transplantation, 13 Suppl 4, 169–178.

Blumberg, E. A., Ison, M. G., Pruett, T. L., &Segev, D. L. (2013b). Optimal testing of the live organ donor for blood-borne viral pathogens: the report of a consensus conference. American Journal of Transplantation, 13(6), 1405–1415.

Boyarsky, B. J., Hall, E. C., Singer, A. L., Montgomery, R. A., Gebo, K. A., &Segev,D. L. (2011). Estimating the potential pool of HIV-infected deceased organdonors in the United States. American Journal of Transplantation, 11(6), 1209–1217.

Boyarsky, B. J., Durand C. M., Palella F. J., Segev D.L., (2015). Challenges and clinical decision-making in HIV-to-HIV transplantation: insights from the HIV literature. American Journal of Transplantation, 15:2023–2030.

Brucato, A., Colombo, T., Bonacina, E., et al. (2004). Fulminant myocarditis during HIV seroconversion: recovery with temporary left ventricular mechanical assistance. Italian Heart Journal, 5, 228–231.

Calabrese, L. H., Albrecht, M., Young, J., et al. (2003). Successful cardiac transplantation in an HIV–1-infected patient with advanced disease. New England Journal of Medicine, 348, 2323–2328.

Castel, M. A., Pe´rez-Villa, F., Roig, E., &Miro´ ,J. M. (2011a). Heart transplantation in an HIV–1-infected patient with ischemic cardiomyopathy and severe pulmonary hypertension.Revista Espan˜ ola de Cardiologı´a, 64, 1066–1067.

Castel, M. A., Pe´rez-Villa, F., & Miro´ , J. M. (2011b). Heart transplantation in HIV- infected patients: more cases in Europe. The Journal of Heart and Lung Transplantation, 30, 1418.

Chen, J. Y., Feeney, E. R., & Chung, R. T. (2014). HCV and HIV co-infection: mechanisms and management. Nature Reviews: Gastroenterology &Hepatology, 11(6), 362–371.

Cooper, C., Kanters, S., Klein, M., Chaudhury, P., Marotta, P., Wong, P., et al. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with synthetic cohort. AIDS, 25(6), 777–786.

Dieterich, D.T. (2007). Special considerations and treatment of patients with HBV–HIV coinfection.Antiviral Therapy, 12, H43– H51.

Duclos-Vallee, J. C., Falissard, B., & Samuel,D. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with a synthetic cohort. AIDS, 25(13), 1675– 1676.

Durante-Mangoni, E., Maiello, C., &Sbreglia,C. (2011). A European first: successful heart transplant in a human immunodeficiency virus-positive recipient. The Journal of Heart and Lung Transplantation, 30, 845.

Durante-Mangoni, E., Maiello, C., Limongelli, G., et al. (2014). Management of immunosuppression and antiretroviral treatment before and after heart transplant for HIV-associated dilated cardiomyopathy. International Journal of Immunopathology and Pharmacology, 27(1), 113–120.

Fieno, D. S., Czer, L. S., Schwarz, E. R., et al. (2009). Left ventricular assist device placement in a patient with end-stage heart failure and human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 919–920.

Fox, A. N., Vagefi, P. A., & Stock, P. G. (2012). Liver transplantation in HIVpatients. Seminars in Liver Disease, 32(2), 177–185.

Frassetto, L. A., Browne, M., Cheng, A., et al. (2007). Immunosuppressant pharmacokinetics and dosing modifications in HIV–1 Infected liver and kidney transplant recipients.

American Journal of Transplantation, 7(12), 2816–2820.Frassetto, L. A., Tan-Tam, C., & Stock, P. G. (2009).Renal transplantation in patients with HIV. Nature Review: Nephrology, 5(10), 582–589.

Frassetto, L. A., Tan-Tam, C. C., Barin, B.,Browne, M., Wolfe, A. R., Stock, P. G., et al. (2014). Best Single Time Point Correlations with AUC for Cyclosporine and Tacrolimus in HIV-Infected Kidney and Liver Transplant Recipients.Transplantation, 97(6), 701–707.

Freedman, B.I. (2013).APOL1 and nephropathy progression in populations of African ancestry. Seminars in Nephrology, 33(5):425–432.

Freedman, B.I., Julian, B. A., Pastan, S. O. et al. (2015). Apolipoprotein L1 gene variants in deceased organ donors are associated with renal allograft failure. American Journal of Transplantation, 15:1615–1622.

Genovese, G., Friedman, D. J., Ross, M. D., Lecordier, L., Uzureau, P., Freedman, B. I., et al. (2010). Association of trypanolytic APOL1 variants with kidney disease in African Americans.Science, 329(5993), 841–845.

Gomez, V., Fernandez, A., Galeano, C., Oliva, J., Diez, V., Bueno, C., et al. (2013). Renal transplantation in HIV-infected patients: experience at a tertiary hospital in Spain and review of the literature. Transplant Proceedings, 45(3), 1255–1259.

Grossi, P. A. (2012). Update in HIV infection in organ transplantation. Current Opinion Organ Transplantation, 17(6), 586–593.

Harbell, J., Terrault, N. A., & Stock, P. (2013). Solid organ transplants in HIV-infected patients. Current HIV/AIDS Reports, 10(3), 217–225.

Humbert, M., Sitbon, O., Chaouat A., et al. (2006). Pulmonary arterial hypertension in France: results from a national registry. American Journal of Respiratory and Critical Care Medicine, 173, 1023.

Huprikar, S. (2009). Solid organ transplantation in HIV-infected individuals: an update. Reviews in Medical Virology, 19(6), 317–323.

Ison, M. G., Hager, J., Blumberg, E., Burdick, J., Carney, K., Cutler, J., et al. (2009).Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS Disease Transmission Advisory Committee. American Journal of Transplantation, 9(8), 1929–1935.

Ison, M. G., Llata, E., Conover, C. S., Friedewald, J. J., Gerber, S. I., Grigoryan, A., et al. (2011a). Transmission of human immunodeficiency virus and hepatitis C virus from an organ donor to four transplant recipients. American Journal of Transplantation, 11(6), 1218–1225.

Ison, M. G., &Nalesnik, M. A. (2011b). An update on donor-derived diseasetransmission in organ transplantation. American Journal of Transplantation, 11(6), 1123–1130.

Kaplan, J. E., Masur, H., Holmes, K.K., et al. (1995a). USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: introduction. USPHS/IDSA Prevention of Opportunistic Infections Working Group. Clinical Infectious Diseases, 21 Suppl 1:S1–11. Available at http:// www.ncbi.nlm.nih.gov/pubmed/ 8547495.

Kaplan, J. E., Masur, H., Jaffe, H.W., Holmes,K.K. (1995b). Reducing the impact of opportunistic infections in patients with HIV infection.New guidelines. Journal of the American Medical Association, 274(4):347–348. Available at http:// www.ncbi.nlm.nih.gov/pubmed/7609267.

Kern, R. M., Seethamraju, H., Blanc, P. D., et al. (2014a). The feasibility of lung transplantation in HIV seropositive patients.Annals of the American Thoracic Society (in press, online).

Kern, R., Seethamraju, H., Blanc, P., Sinha,N., Loebe, M., Golden, J., et al. (2014b).Lung Transplantation in HIV Seropositive Patients.Chest, 145(3 Suppl), 642A.

Kim, D., Ziebell, R., Sadulvala, N., Kline, R., Ocfemia, C., Prejean, J., et al. (2013).Trends in Transmitted Drug Resistance Associated Mutations: 10 HIV Surveillance Areas, US, 2001–2010.

Paper presented at the 20th Conference on Retroviruses and Opportunistic Infections.Kim, W. R., Smith, J. M., Skeans, M. A., et al. (2014). OPTN/SRTR 2012 AnnualData Report: Liver. American Journal of Transplantation, 1, 69–96.

Kucirka, L. M., Singer, A. L., Ross, R. L., et al. (2010). Underutilization of hepatitis C-positive kidneys for hepatitis C- positive recipients. American Journal of Transplantation, 10(5), 1238–1246.

Kucirka, L.M., Bowring, M. G., Massie, A. B., et al, (2015) Landscape of deceased donors labeled increased risk for disease transmission under new guidelines.American Journal of Transplantation, (in press).

Liang, T. J., &Ghany, M. G. (2013).Current and future therapies for hepatitis C virus infection. New England Journal of Medicine, 368(20), 1907–1917.

Locke, J. E., James, N. T., Mannon, R. B.,Mehta, S. G., Pappas, P. G., Baddley, J. W., et al. (2014). Immunosuppression Regimen and the Risk of Acute Rejection in HIV-Infected Kidney Transplant Recipients. Transplantation, 97(4), 446–450.

Locke, J. E., Reed R. D., Mehta S. G., et al. (2015a). Center-level experience and kidney transplant outcomes in HIV- infected recipients. American Journal of Transplantation, 15:2096–2104.

Locke, J. E., Mehta, S., Reed, R. D., et al. (2015b).A national study of outcomes among HIV-infected kidney transplant recipients. Journal of the American Society of Nephrology, 26:1–8.

Mandal, A. K., Kraus, E.S., Samaniego, M., et al. (2000). Shorter waiting times for hepatitis C virus seropositive recipients of cadaveric renal allografts from hepatitis C virus seropositive donors.Clinical Transplantation, 14, 391–396.

Mascolini, M. (2014). Four to Five HIV+ Dying in Care Yearly in Philadelphia Are Potential Organ Donors. 54th Interscience Conference on Antimicrobial Agents and Chemotherapy: Abstract H–1199a.Presented September 7, 2014.

Matas, A. J., Smith, J. M., Skeans, M. A., etal. (2014) OPTN/SRTR 2012 Annual Data Report: Kidney. American Journal of Transplantation, 1, 11–44.

Megens, S., &Laethem, K. V. (2013). HIV–1 genetic variation and drug resistance development. Expert Review of Anti- Infective Therapy, 11(11), 1159–1178.

Mehmood, S., Blais, D., Martin S., &Sai- Sudhakar, C. (2009).Heartmate XVE destination therapy for end-stage heart failure in a patient with human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 909–910.

Mehta, N. J., Khan, I. A., Mehta, R. N., et al. (2000). HIV-related pulmonary hypertension: analytic review of 131 cases. Chest, 118, 1133.

Mgbako, O., Glazier, A., Blumberg, E., & Reese, P. P. (2013). Allowing HIV- positive organ donation: ethical, legal and operational considerations.American Journal of Transplantation,13(7), 1636–1642.

Miro, J. M., Montejo, M., Castells, L., Rafecas, A., Moreno, S., Aguero, F., et al. (2012). Outcome of HCV/HIV-coinfected liver transplant recipients: a prospective and multicenter cohort study. American Journal of Transplantation, 12(7), 1866–1876.

Miro, J. M., Stock, P., Teicher, E., et al, (2015).Outcome and management of HCV/HIV coinfection pre- and post-liver transplantation.A 205 update. Journal of Hepatology, 62:701–711.

Morales, J. M., Campistol, J. M., Dominguez- Gil, B., Andres, A., Esforzado, N., Oppenheimer, F., et al. (2010). Long-term experience with kidney transplantation from hepatitis C-positive donors into hepatitis C-positive recipients. American Journal of Transplantation, 10(11), 2453–2462.

Moreno, A., Cervera, C., Fortun, J., et al. (2012). Epidemiology and outcome of infections in human immunodeficiency virus/hepatitis C virus-coinfected liver transplant recipients: a FIPSE/GESIDA prospective cohort study. Liver Transplantation, 18, 70–81.

Muller, E., Kahn, D., &Mendelson, M. (2010).Renal transplantation between HIV- positive donors and recipients. New England Journal of Medicine, 362(24), 2336–2337.

Muller, E., Barday, Z., Mendelson, M., & Kahn, D. (2012). Renal transplantation between HIV-positive donors and recipients justified. South African Medical Journal, 102(6), 497–498.

Muller, E., Barday, Z., Mendelson, M., Kahn,D., et al. (2015). HIV-positive-to-HIV- positive kidney transplantation—results at 3 to 5 years. New England Journal of Medicine, 372:613–20.

Neuhaus, J., Angus, B., Kowalska, J. D., et al. (2010). Risk of all-cause mortality associated with nonfatal AIDS and serious non-AIDS events among adults infected with HIV. AIDS, 24(5), 697–706.

OPTN Policies and Bylaws.From http:// optn.transplant.hrsa.gov/ policiesandbylaws/policies.asp.

Pais, R. &Benhamou, Y. (2010). Long-term therapy for chronic hepatitis B in HIV co-infected patients. Gastroente´ rologieClinique et Biologique, 34, 136–41.

Parsa, A., Kao, W. H. L., Xie, D., et al, (2013).APOL1 risk variants, race, and progression of chronic kidney disease. New England Journal of Medicine, 369:2183–96.

Panel on Opportunistic Infections in HIV- Infected Adults and Adolescents.Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents; recommendations

from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/ contentfiles/lvguidelines/adult oi.pdf.(Accessed September 2015).

Pelletier S. J., Norman S. P., Christensen L. L., et al. (2004). Review of transplantation in HIV patients during the HAART era. Clinical Transplantation, 63–82.

Petrosillo, N., Chinello, P., &Cicalini, S. (2006). Pulmonary hypertension in individuals with HIV infection.AIDS, 20, 2128.

Prevention, C. f. D. C. a. (2013). HIV Surveillance Supplemental Report.Ragni, M. V., Dodson, S. F., Hunt, S. C., et al. (1999). Liver transplantation in a hemophilia patient with acquiredimmunodeficiency syndrome. Blood, 93, 1113–1114.

Redd A. D., Quinn T. C., Tobian A. A. (2013).Frequency and implications of HIV superinfection. The Lancet Infectious Diseases, 13(7), 622–628.

Reeves-Daniel, A. M., DePalma, J. A., Bleyer,A. J., Rocco, M. V., Murea, M., Adams,P. L., et al. (2011). The APOL1 Gene and Allograft Survival after Transplantation. American Journal of Transplantation, 11(5), 1025–1030.

Richterman, A., Blumberg, E., (2015). The challenges and promise of HIV-infected donors for solid organ transplantation.Current Infectious Disease Reports, 17:1– 8.

Richterman, A., Sawinski, D., Reese, P.P., et al, (2015).An assessment of HIV-infected patients dying in care for deceased organ donation in a United States urban center. American Journal of Transplantation, 15:2105–2116.

Riella, L.V., Sheridan, A.M., (2015). Testing for high-risk APOL1 alleles in potential living kidney donors. American Journal of Kidney Disease, (in press).

Roland, M., Carlson, L., & Stock, P. (2002).Solid organ transplantation in HIV- infected individuals. AIDS Clinical Care, 14(7), 59–63.

Roland, M. E., Adey, D., Carlson, L. L., &Terrault, N. A. (2003a). Kidney and liver transplantation in HIV-infected patients: case presentations and review. AIDS Patient Care STDS, 17(10), 501–507.

Roland, M. E., Lo, B., Braff, J., & Stock, P. G. (2003b).Key clinical, ethical, and policy issues in the evaluation of the safety and effectiveness of solid organ transplantation in HIV-infected patients. Archives of Internal Medicine, 163(15), 1773–1778.

Roland, M. E., & Stock, P. G. (2003c). Review of solid-organ transplantation in HIV- infected patients. Transplantation, 75(4), 425–429.

Sawinski, D., Goldberg, D. S., Blumberg, E., et al. (2015) Beyond the NIH multicenter HIV transplant trial experience: Outcomes of HIV+ liver transplant recipients compared to HCV+ or HIV+/ HCV+ coinfected recipients in the United States. Clinical InfectiousDisease, (in Press).

Sherman, K. E., Thomas, D., & Chung, R. T. (2014).Human immunodeficiency virus and liver disease forum 2012.Hepatology, 59(1), 307–317.

Sims, D. B., Uriel, N., Gonza´lez-Costello, J., et al. (2011). Human immunodeficiency virus infection and left ventricular assist devices: a case series. Journal of Heart and Lung Transplantation, 30, 1060–1064.

Soriano, V., Tuma, P., Labarga, P., et al. (2009). Hepatitis B in HIV patients: what is the current treatment and what are the challenges? Journal of HIV Therapy, 14(1), 13–18.

Stock, P. G., Barin, B., Murphy, B., Hanto, D.,Diego, J. M., Light, J., et al. (2010). Outcomes of kidney transplantation in HIV-infected recipients. New England Journal of Medicine, 363(21), 2004–2014.

Taege, A. (2013). Organ transplantation and HIV progress or success?A review of current status.Curr Infectious Disease Reports, 15, 67–76.

Tector, A. J., Mangu, R. S., Chestovich, P., et al. (2006). Use of extended criteria livers decreases wait time for liver transplantation without adversity impacting posttransplant survival.

Annals of Surgery, 244, 439–450.Terrault, N. A., Roland, M. E., Schiano, T., Dove, L., Wong, M. T., Poordad, F., et al. (2012). Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection.

Liver Transplantation, 18(6), 716–726.Touzot, M., Pillebout, E., Matignon, M., Tricot, L., Viard, J. P., Rondeau, E., et al. (2010). Renal transplantation in HIV- infected patients: the Paris experience. American Journal of Transplantation, 10(10), 2263–2269.

Uriel, N., Jorde, U. P., Cotarlan, V., et al. (2009). Heart transplantation in human immunodeficiency virus-positive patients. Journal of Heart and Lung Transplant, 28, 667–669.

Uriel, N., Nahumi, N., Colombo, P. C., et al. (2014). Advance heart failure in patientsinfected with human immunodeficiency virus: is there equal access to care?

Journal of Heart and Lung Transplantation (in press, online).Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2013). Cause- specific life expectancies after 35 years of age for human immunodeficiency syndrome-infected and human immunodeficiency syndrome-negative individuals followed simultaneously in long-term cohort studies, 1984–2008.American Journal of Epidemiology,177(2), 116–125.

Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2014). Cause- specific mortality among HIV-infected individuals, by CD4 (+) cell count at HAART initiation, compared with HIV-uninfected individuals. AIDS, 28(2), 257–265.

Yoon, S. C., Hurst, F. P., Jindal, R. M.,George, S. A., Neff, R. T., Agodoa, L. Y., et al. (2011). Trends in renal transplantation in patients with human immunodeficiency virus infection: an analysis of the United States renal data system. Transplantation, 91(8), 864–868.

Protocol Version 1.2

Amendment #1 May **29, 2018**

1. Title:

Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.

2. Investigators:

PI: Juan P Rocca[1], MD.

AIs: Victoria Muggia[3], MD; Grace Minamoto[3], MD; Yoram Puius[3] Enver Akalin[2], MD;; Maria Ajaimy[2], MD;; Stuart Greenstein[1], MD, Jay Graham[1], MD; Milan Kinkhabwala [1], MD.

[1] Montefiore-Einstein Center for Transplantation, Transplant Surgery, Department of Surgery.

[2] Montefiore-Einstein Center for Transplantation, Transplant nephrology, Department of Medicine.

[3] Montefiore-Einstein Center for Transplantation, Transplant Infectious Diseases, Department of Medicine.

3. Background and purposes:

The advent of effective antiretroviral therapy (ART) in the mid-1990s for treatment of individuals infected with HIV transformed a rapidly fatal disease into a well-controlled chronic illness. Currently, the life expectancy of individuals infected with HIV and receiving ART early in the course of their disease approaches that of individuals without HIV infection (Wada, 2013, 2014). In this era of greater longevity, liver failure, end-stage renal disease, and cardiovascular disease have emerged as important causes of morbidity and mortality in patients with HIV infection (Neuhaus, 2010).

Organ transplantation prolongs survival and improves quality of life for individuals with end-stage organ disease (Matas, 2014; Kim, 2014). Until recently, however, organ transplantation was unavailable to those infected with HIV due to concerns that pharmacologic immunosuppression to prevent organ rejection would hasten the progression from HIV infection to AIDS, concerns about disease transmission, and reluctance to allocate organs to a population whose outcome was unpredictable (Blumberg, 2009, 2013a, 2013b; Mgbako, 2013; Taege, 2013).

Nevertheless, a few transplant programs accepted HIV-positive patients on their transplant waiting lists and accumulated data showing kidney or liver transplantation could be done safely in these patients (Roland, 2002, 2003a, 2003b, 2003c; Blumberg, 2009; Stock, 2010; Yoon, 2011; Terrault, 2012). Subsequently, a prospective, multicenter clinical trial of kidney and liver transplantation in 275 patients demonstrated that, among HIV-positive kidney and liver transplant recipients, patient and graft survival

rates were acceptable and within the range of outcomes currently achieved among non-infected transplant recipients.

However, the rate of kidney rejection was unexpectedly high, demonstrating that the immune dysregulation resulting from HIV infection, HCV co-infection, and antirejection drugs is complex and incompletely understood. Some of the challenges encountered in that study remain relevant for clinical sites offering organ transplantation to HIV-positive individuals today (e.g., management of drug interactions and toxicities when combining complex medical regimens, management of combined morbidities of two or more active diseases, and the need for ongoing collaboration among medical professionals from different specialties) (Frassetto, 2007, 2014; Locke, 2014). Despite the complexities, this study and others (Ragni, 1999; Frassetto, 2009; Huprikar, 2009; Stock, 2010; Touzot, 2010; Cooper, 2011; Duclos-Vallee, 2011; Reeves-Daniel, 2011; Fox, 2012; Terrault, 2012; Grossi, 2012; Gomez, 2013; Harbell, 2013) demonstrate that kidney and liver transplantation are appropriate in HIV- positive individuals with liver or kidney failure, although gaps in knowledge and many research questions remain. There is much less experience with heart (Calabrese, 2003; Bisleri, 2003; Pelletier, 2004; Uriel, 2009, 2014; Castel, 2011a, 2011b; Durante-Mangoni, 2011 and 2014) and lung (Mehta, 2000; Humbert,2006; Petrosillo, 2006; Bertani, 2009; Kern, 2014a, 2014b) transplantation in HIV-positive recipients, or mechanical circulatory assistance (Brucato, 2004; Fieno, 2009; Mehmood, 2009; Sims, 2011) as a bridge to transplantation, although case reports and small case series suggest acceptable short-term outcomes are possible.

Prior to the passage of the HOPE Act, U.S. law required that all U.S. transplants for HIV-positive recipients utilize organs from HIV-uninfected donors. (See 42 U.S.C. 273(b)(3)(C), 274(b) and 18 U.S.C. 1122, all prior to amendment by the HOPE Act). The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV (hereinafter referred to as ‘‘HIV-positive to HIV-positive transplantation’’) is recognized (Boyarsky, 2011, 2015; Mgbako, 2013; Mascolini, 2014; Kucirka, 2015; Richterman, 2015). It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients (Boyarsky, 2011). The published experience with HIV-positive to HIV- positive SOT at this time comes from Muller et al from the University of Cape Town in South Africa. Initially, Muller et al (2010) reported 100 percent patient and graft survival in a four-patient pilot study. Subsequently, the same group reported an additional 10 HIV-positive to HIV-positive renal transplants (Muller, 2012). All patients were restarted on ART early postoperatively in the immunosuppressive setting of T- cell-depleting induction therapy, tacrolimus, mycophenolate mofetil, and prednisone. One to 4 years after transplantation, outcomes remained excellent and all patients had undetectable viral loads (Muller, 2012). The cumulative University of Cape Town experience of 27 HIV-positive to HIV-positive transplant procedures was recently summarized in the New England Journal of Medicine (Muller, 2015). The 1- and 5-year death-censored graft survival was 93 and 84 percent, respectively, and 1- and 5-year patient survival was 83 and 74 percent, respectively. Of note, the South African HIV-positive deceased donors were ART-naive, without history of opportunistic infection or proteinuria, and had normal pre-transplant renal biopsies. While renal function has remained normal in the recipients, three have had routine post-transplant renal biopsies

demonstrating new changes typical of early HIV-associated nephropathy that were not present in baseline biopsy specimens. The long- term significance of these findings remains unknown and awaits longer follow-up. All patients had undetectable plasma HIV viral loads after transplantation. Graft rejection rates were 8 percent at 1 year and 22 percent at 3 years.

The HOPE Act permits HIV-positive to HIV-positive organ transplantation under IRB-approved research protocols conforming to the Final Human Immunodeficiency Virus (HIV) Organ Policy Equity (HOPE) Act Safeguards and Research Criteria for Transplantation of Organs Infected with HIV, which were developed as directed in the HOPE Act. Patients receiving HIV-positive kidneys from deceased HIV-positive donors in South Africa (Muller, 2015) had survival rates of 84 percent and 74 percent at 1 and 5 years, respectively; however, there is presently no evidence for the safety, efficacy, and effectiveness of HIV-positive to HIV- positive transplantation in North America. The Final Safeguards and Research Criteria are meant to support the acquisition of new clinical knowledge and mechanistic insights about HIV-positive to HIV-positive organ transplantation in the United States. The results of this research will be evaluated by the Secretary of HHS and the OPTN to determine whether and how the OPTN standards for organ transplantation shall be revised to address HIV-positive organ donors.

The research protocol described below was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States. The criteria address the minimum safety and data requirements of clinical research in HIV-positive to HIV-positive transplantation. As mandated by the HOPE Act, the Secretary, together with the OPTN, is charged with reviewing the results of scientific research conducted under these criteria to determine whether the OPTN's standards of quality should be further modified and whether some HIV- positive to HIV-positive transplants should proceed outside the auspices of research conducted under such criteria (see attached the original document).

Montefiore Medical Center and the Montefiore-Einstein Center for Transplantation meet the institutional standards and requirements to carry on a research protocol on HIV-positive to HIV-positive kidney transplantation with a collective experience of 14 kidney transplants on HIV positive recipients since 2008. The Montefiore AIDS center provides care to over 2500 HIV positive individuals in the Bronx. Potential transplant candidates as per protocol are evaluated by transplant ID clinicians with expertise also in HIV. The AIDS center providers and the Montefiore infectious disease faculty practice follow these patients closely for the first year after transplantation, and over two thirds of these patients have elected to remain at Montefiore for their HIV care. Multidisciplinary transplant protocols include management of HIV recipients and the outcomes of these cases have met the national standards without affecting our program-specific reports (SRTR reports).

4. Objectives and outcome measures

Montefiore's research in HIV-positive to HIV-positive transplantation will address questions related to HIV superinfection; incidence and severity of opportunistic infections (including transmission of occult

OIs from donor to recipient); immunologic mechanisms contributing to the increased rate of kidney rejection observed in HIV-positive recipients and quality of life for recipients of HIV- positive to HIV-positive transplantation. To ensure that all nationwide studies of HIV-positive to HIV- positive transplantation can contribute to evaluation of the safety of the procedure, the following key donor and recipient characteristics and outcome measures must be incorporated into the design of all clinical trials of HIV- positive to HIV-positive transplantation.

Wait List Candidates

- HIV status
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Removal from wait list (death or other reason)
- Time on wait list

Donors (all)

- Type (living or deceased)
- HIV status (HIV-positive new diagnosis, HIV-positive known diagnosis)
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Pre-transplant donor allograft biopsy

Note regarding Living Donors: Montefiore Einstein Center for Transplantation has decided to exclude living donors from the participation in this research protocol.

Transplant Recipients

- Rejection rate (annual up to 5 years)
- Progression to AIDS
- New Opportunistic Infections
- Failure to suppress viral replication (persistent viremia)
- HIV-associated organ failure
- Malignancy
- Graft failure
- Mismatched ART resistance versus donor
- Death

5. Methods:

- Donor Eligibility

Montefiore Einstein Center for Transplantation has decided to exclude living donors from this research protocol. HIV- positive deceased donors of organs for transplantation into an HIV-positive recipient must fulfill applicable clinical criteria in place for HIV-uninfected organ donors.

There is substantial concern about the consequences of transplanting an organ from an HIV-positive donor to a recipient infected with a strain of HIV that differs from the donor's in terms of its responsiveness to antiretroviral therapy (ART). The likelihood and impact of HIV superinfection in this context are unknown. Adverse consequences could range from transient loss of viral suppression, necessitating a change in antiretroviral regimen to a worst-case scenario in which the new infecting strain of HIV is unresponsive to available antiretroviral treatment and the recipient progresses to AIDS (Redd, 2013). Information relevant to understanding the known or potential extent of antiretroviral resistance in the strain of HIV infecting the organ donor may be incomplete for many reasons:

- There may be inadequate virus in donor specimens for antiretroviral resistance testing;
- If the specimen is adequate, there may not be enough time within the decision-making evaluation window to fully assess antiretroviral resistance before the clinical deterioration of the donor, organ procurement, and implantation;
- The donor's history of antiretroviral treatment may be unknown or incomplete;
- Results from prior antiretroviral resistance testing may be unavailable.

These issues might be especially challenging when considering organ donation from deceased donors whose HIV infection is first identified during donor evaluation. As of 2011, an estimated 1 in 6 U.S. adults living with HIV infection were undiagnosed (Prevention, 2013) and an estimated 16 percent of newly diagnosed, untreated individuals were infected with virus resistant to at least one class of antiretroviral drug (Kim, 2013; Megens, 2013).

It is anticipated that the risk of transmission of resistant HIV strains may be lower from deceased donors with a well-documented history of antiretroviral treatment, undetectable virus at demise, and robust and persistent undetectable viral load for at least 1 year prior to death. However, to impose this as an eligibility criterion would limit the pool of suitable donors and severely limit the ability to study transplantation of HIV-positive organs under the HOPE Act. In addition, it will not be possible in all cases to obtain viral loads and/or antiretroviral resistance profiles in the time available for donor evaluation. Transplant teams evaluating a donor must review all available donor and recipient information and be able to propose an antiretroviral regimen that will be equally or more safe, tolerable, and effective for the recipient after transplantation as the regimen in place in the recipient before transplantation. For instance, a donor who only achieves viral suppression with a regimen known to be intolerable to the

recipient must not be accepted. If there is doubt about the ability to suppress viral replication after transplantation, the transplant must not move forward.

Donors co-infected with hepatitis are not excluded from HIV-positive to HIV- positive transplant; however, careful consideration must be given when evaluating a donor co-infected with HBV and/or HCV (Terrault, 2012; Miro, 2012; Moreno, 2012; Sherman, 2014; Chen, 2014). Although HCV therapeutic strategies are rapidly evolving (Liang, 2013), it is possible that mixed genotype HCV infections may influence post- transplant treatment of HCV in the recipient. Prior antiretroviral treatment of the donor and/or recipient with agents active against HBV (i.e., lamivudine, emtricitabine, adefovir, and tenofovir) has the potential for inducing or uncovering archived HBV drug resistance in the recipient (Dieterich, 2007; Soriano, 2009; Pais, 2010).

HIV-positive transplant candidates who are listed for a transplant in the context of a research study of HIV- positive to HIV-positive transplantation must have the same opportunity as other transplant candidates to receive an organ from an HIV-negative donor, should one become available for them.

1.1 HIV-Positive Donor Eligibility Criteria

The HIV-specific donor eligibility criterion for deceased donors is listed (Table 1). Co-infection with HBV and/or HCV is not an exclusion criterion.

1.1.1 HIV-Positive Deceased Donors

When evaluating HIV-positive deceased donors, it is understood that limited medical history may be available and/or known at the time of the donor evaluation. The OPO must make reasonable efforts to obtain prior medical history so that a transplant center team may best determine the suitability of the potential donor based on the information available. A complete history of antiretroviral regimens and a history of viral load tests and resistance testing are especially valuable for evaluating the likelihood of donor HIV resistance to antiretroviral regimens. A history of OIs or cancers is also of high importance, due to the increased risk for both attributable to HIV, and the additional difficulty of treating some infections and neoplasms in a post-transplant setting. It is possible that deceased donors with lower CD4+ T-cell counts may pose an increased risk of harboring transmissible diseases (e.g., opportunistic infections or neoplasms) that may be difficult to detect during organ harvest and transplantation; teams conducting transplants under the HOPE Act are urged to assess donors with low CD4+ T-cell counts (e.g., <200/mL) with special caution and to promptly inform IRBs and the PI of known or suspected disease transmission events.

Minimum eligibility criteria for all HIV-positive deceased donors:

i. Documented HIV infection using an FDA-licensed, approved, or cleared test device(s).

ii. No evidence of invasive opportunistic complications of HIV infection.

iii. Pre-implant donor organ biopsy to be stored, at a minimum, for the duration of the study (or at least 5 years); additional specimens may be obtained to support specific research goals.

Additional eligibility criteria for HIV- positive deceased donors with a known history of HIV and prior treatment with ART:

i. The study team must describe the anticipated post-transplant antiretroviral regimen(s) to be prescribed for the recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Recipient Eligibility

A key consideration when evaluating potential HIV-positive transplant candidates is the ability to suppress HIV viral load post-transplant. This includes a thorough assessment by the transplant team of the candidate recipient's prescribed antiretroviral medications, HIV RNA levels while on medications, adherence to HIV treatment, and any available HIV resistance testing; a similar evaluation of the donor must also be carried out. A transplant should only take place if, after evaluating both recipient and donor, the team is confident they can define a post- transplant antiretroviral regimen that will be safe, tolerable, and effective. If there is any doubt on the part of the transplant team about the ability to suppress viral replication post- transplant, the transplant should not move forward. Concerns about transmitted drug resistance must be included in the recipient informed consent process for the research study. At the time of an organ offer, the recipient informed consent must address the transplant team's assessment of risk specific to the organ they are being offered.

2.1 HIV-Positive Recipient Eligibility Criteria

The following HIV-specific criteria must be met when screening for an HIV- positive to HIV-positive organ transplant (also refer to Table 1):

i. Last CD4+ T-cell count >200/mL (kidney) Prior to enrollment; any patient with history of OI must have a CD4 positive T-cell count >200/uL.

ii. HIV RNA less than 50 copies/mL and on a stable antiretroviral regimen.*+

iii. No evidence of active opportunistic complications of HIV infection.

iv. No history of primary CNS lymphoma or PML.

v. Concurrence by the study team that based on medical history and ART, viral suppression can be achieved in the recipient post-transplant.

*Patients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen for the patient once organ function is restored after transplantation.

+Those patients on a protease based regimen and fully suppressed with no available resistance studies, should be tested with an assay that looks at archived resistance (e.g. Genosure Archive®).

TABLE 1—SUMMARY OF DONOR AND RECIPIENT ELIGIBILITY CRITERIA FOR HIV-POSITIVE SERO-CONCORDANT ORGAN TRANSPLANT PAIRS UNDER THE HOPE ACT

HIV-Related variables	Deceased donor	Living donor	HIV-Positive recipient
Current CD4+ T-cell count (T lymphocytes/μL)	No requirement	≥500 for 6 months prior to organ donation.	If no history of OI • ≥200 If history of OI • ≥200 (kidney) • ≥100 (liver) Last CD4+ T-cell count Prior to enrollment
Plasma HIV RNA viral load (copies/mL).	No requirement**	<50	<50*
Opportunistic infection	No invasive OI	No invasive OI	Currently, • No active OI Historically, no • CNS lymphoma • PML

* Organ recipients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen to be used by the recipient once organ function is restored after transplantation.

** In deceased donors with a known history of HIV infection and prior treatment with ART, the study team must describe the anticipated post- transplant antiretroviral regimen(s) to be used by the organ recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Transplant process and post-transplant considerations

Organ recovery, transplant procedure, handling and storage of donor organs/tissues, as well as management of kidney transplant recipients at Montefiore-Einstein Center for Transplantation are well described in our policies and procedures section (intranet), including the multidisciplinary management and immunosuppression protocols of HIV-positive kidney recipients

Waitlist acceptance criteria: Once an IRB- approved research protocol in HIV- positive to HIV-positive transplantation is finalized, the transplant center will inform the OPTN of additional organ-specific acceptance criteria for organs from HIV-positive donors. Those HIV-positive kidney candidates on the wait list willing to accept an HIV- positive organ must specify any additional acceptance criteria to the OPO.

Consent process and Independent HIV-Positive Recipient Advocate: One of Montefiore's senior transplant coordinator is actively collaborating with an NIH initiative to train and credential independent advocates for protecting and promoting the rights and interests of the HIV-positive recipient (or prospective recipient). The independent advocate for the HIV- positive recipient will:

i. Promote and protect the interests of the HIV-positive recipient (including with respect to having access to a suitable HIV-negative organ if it becomes available) and take steps to ensure that the HIV-positive recipient's decision is informed and free from coercion.

ii. Review whether the potential HIV-positive recipient has received information regarding the results of SOT in general and transplantation in HIV- positive recipients in particular and the unknown risks associated with HIV- positive to HIV-positive transplant.

iii. Demonstrate knowledge of HIV infection and transplantation.

Attached: -Informed consent for research

Post-transplant care

After discharge, patients are seen by the multidisciplinary transplant team according to the below schedule. During weekly morbidity and mortality meeting the post-transplant team meets and reviews the transplant recipients seen during the week to discuss patients, complications (infections, rejection, bleeding, readmission, re-surgery, malignancy, patient death, and graft loss), and allograft function. These events are stored in the transplant computerized database and communicated to the OPTN in accordance with regulations. Recipients are also assessed and contacted in respect to QAPI initiatives to further improve patient care initiatives.

Adult Transplant Patients are generally evaluated according to the following schedule after kidney transplantation:

First month: twice a week labs, once a week clinic visit

2-3 months: once a week labs and every other week clinic visit

4-5 months: every other week labs and one month clinic visit

6-12 months: once a month labs and every other month clinic visit

Second year: every 2 months labs and 4 months clinic visit

3-5 years every 3 month labs and 6 months clinic visit

> 5 years every 3 months labs and once a year clinic visit

During each clinical visit, bloods and vital signs are obtained, a physical exam is performed and medications are reviewed with each patient. Medical and surgical problems will be addressed on an ongoing basis and appropriate referrals are made to specialists. Pharmacist, nutritional and social service support is available at each clinic. The Transplant Patient will receive specific instructions from the Transplant Multi-Disciplinary Team as to their follow-up care.

Additional transplant allograft biopsy will be performed at 3 months and one year from transplant.

All patients will be assigned to one respective transplant nephrologist for routine follow-up. Patients will be seen at least once within a month after transplantation by a transplant surgeon.

In order to promptly detect viral breakthrough or possibility of viral superinfection, HIV viral loads should be performed every week for the first four weeks after transplantation, every three months for

the first year post transplantation, and every 6 months in patients who have achieved sustained viral suppression. If viral breakthrough is detected on two consecutive assays, genotypic resistance studies will be sent. In addition tropism assays and resistance testing looking for mutations in the integrase gene will be performed. CD4 monitoring can be done less frequently. Monthly CD4 monitoring for the first three months, every three months for the first year, and every 6 months in stable patient. The Montefiore transplant infectious disease provider will see the patient monthly the first three months after transplantation and every three months for the first year post transplant. After the first year, stable transplant patients may return to their outside provider, however the transplant ID attending will maintain close contact with the primary care provider, and also see the recipient twice a year for the duration of the study. To assist patients with urgent infectious disease issues the Montefiore AIDS center provides walk in services Monday through Friday, and 24 hour service coverage for established patients.

Transplant physicians will give 24 hour coverage service for post-transplant patients with any questions and complaints.

6 – Potential risks

Risk considerations and pertinent safeguards to potential recipients have been described in detail above under donor and recipient eligibility sections.

Prevention of Inadvertent Transmission of HIV

Although the use of HIV-positive organs may help alleviate transplant shortages and reduce patient waiting list times, there also are patient safety concerns to consider. Prevention or management of inadvertent transmission of HIV or exposure of an HIV-negative recipient to organs or tissues from an HIV-positive donor due to identification error is paramount (Ison, 2009, 2011a, 2011b). The transplant community, with regulatory oversight at multiple levels, has been able to achieve a high level of safety through routine procedures and clinical practice. The precautions taken with ABO compatible donor-recipient pairs and HCV-infected donor organs in HCV- infected recipients (Morales, 2010; Kucirka, 2010; Mandal, 2000; Tector, 2006) are existing models. However, vulnerabilities still exist, and mishaps still occur. For instance, the risks of error during manual transcription of information are well documented.

Montefiore medical center and the transplant center already count with an institutional biohazard plan for handling of HCV-positive organs and tissue disposal for HCV-positive recipients and ABO compatibility verification policies. HIV-positive status of donor organ, donor tissues and intended recipient will be added to the organ-to-recipient verification form

7- Confidentiality and safeguards to minimize risks.

The research protocol was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States (attached document and informed consent).

8- Study benefits

The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV. It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients

9- Data Safety Monitoring Board

A DSMB comprised of a three physicians (not involved in the study) will be assembled every 12 months to review safety data.

9-References

Bertani, A., Grossi, P., Vitulo, P., et al. (2009). Successful lung transplantation in an HIV- and HBV-positive patient with cystic fibrosis. American Journal of Transplantation, 9, 2190–2196.

Bisleri, G., Morgan, J. A., Deng, M. C., et al. (2003). Should HIV-positive recipients undergo heart transplantation? Journal of Thoracic and Cardiovascular Surgery, 126, 1639–1640.

Blumberg, E. A., & Stock, P. (2009). Solid organ transplantation in the HIV-infected patient. American Journal of Transplantation, 9 Suppl 4, S131–135.

Blumberg, E. A., & Rogers, C. C. (2013a). Human immunodeficiency virus in solid organ transplantation. American Journal of Transplantation, 13 Suppl 4, 169–178.

Blumberg, E. A., Ison, M. G., Pruett, T. L., & Segev, D. L. (2013b). Optimal testing of the live organ donor for blood-borne viral pathogens: the report of a consensus conference. American Journal of Transplantation, 13(6), 1405–1415.

Boyarsky, B. J., Hall, E. C., Singer, A. L., Montgomery, R. A., Gebo, K. A., & Segev,D. L. (2011). Estimating the potential pool of HIV-infected deceased organ donors in the United States. American Journal of Transplantation, 11(6), 1209–1217.

Boyarsky, B. J., Durand C. M., Palella F. J., Segev D.L., (2015). Challenges and clinical decision-making in HIV-to-HIV transplantation: insights from the HIV literature. American Journal of Transplantation, 15:2023–2030.

Brucato, A., Colombo, T., Bonacina, E., et al. (2004). Fulminant myocarditis during HIV seroconversion: recovery with temporary left ventricular mechanical assistance. Italian Heart Journal, 5, 228–231.

Calabrese, L. H., Albrecht, M., Young, J., et al. (2003). Successful cardiac transplantation in an HIV–1-infected patient with advanced disease. New England Journal of Medicine, 348, 2323–2328.

Castel, M. A., Pe´rez-Villa, F., Roig, E., & Miro´ , J. M. (2011a). Heart transplantation in an HIV–1-infected patient with ischemic cardiomyopathy and severe pulmonary hypertension. Revista Espan˜ ola de Cardiologı´a, 64, 1066–1067.

Castel, M. A., Pe´rez-Villa, F., & Miro´ , J. M. (2011b). Heart transplantation in HIV- infected patients: more cases in Europe. The Journal of Heart and Lung Transplantation, 30, 1418.

Chen, J. Y., Feeney, E. R., & Chung, R. T. (2014). HCV and HIV co-infection: mechanisms and management. Nature Reviews: Gastroenterology & Hepatology, 11(6), 362–371.

Cooper, C., Kanters, S., Klein, M., Chaudhury, P., Marotta, P., Wong, P., et al. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with synthetic cohort. AIDS, 25(6), 777–786.

Dieterich, D.T. (2007). Special considerations and treatment of patients with HBV–HIV coinfection. Antiviral Therapy, 12, H43– H51.

Duclos-Vallee, J. C., Falissard, B., & Samuel, D. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with a synthetic cohort. AIDS, 25(13), 1675– 1676.

Durante-Mangoni, E., Maiello, C., & Sbreglia, C. (2011). A European first: successful heart transplant in a human immunodeficiency virus-positive recipient. The Journal of Heart and Lung Transplantation, 30, 845.

Durante-Mangoni, E., Maiello, C., Limongelli, G., et al. (2014). Management of immunosuppression and antiretroviral treatment before and after heart transplant for HIV-associated dilated cardiomyopathy. International Journal of Immunopathology and Pharmacology, 27(1), 113–120.

Fieno, D. S., Czer, L. S., Schwarz, E. R., et al. (2009). Left ventricular assist device placement in a patient with end-stage heart failure and human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 919–920.

Fox, A. N., Vagefi, P. A., & Stock, P. G. (2012). Liver transplantation in HIV patients. Seminars in Liver Disease, 32(2), 177–185.

Frassetto, L. A., Browne, M., Cheng, A., et al. (2007). Immunosuppressant pharmacokinetics and dosing modifications in HIV–1 Infected liver and kidney transplant recipients.

American Journal of Transplantation, 7(12), 2816–2820. Frassetto, L. A., Tan-Tam, C., & Stock, P. G. (2009). Renal transplantation in patients with HIV. Nature Review: Nephrology, 5(10), 582–589.

Frassetto, L. A., Tan-Tam, C. C., Barin, B., Browne, M., Wolfe, A. R., Stock, P. G., et al. (2014). Best Single Time Point Correlations with AUC for Cyclosporine and Tacrolimus in HIV-Infected Kidney and Liver Transplant Recipients.Transplantation, 97(6), 701–707.

Freedman, B.I. (2013). APOL1 and nephropathy progression in populations of African ancestry. Seminars in Nephrology, 33(5):425–432.

Freedman, B.I., Julian, B. A., Pastan, S. O. et al. (2015). Apolipoprotein L1 gene variants in deceased organ donors are associated with renal allograft failure. American Journal of Transplantation, 15:1615–1622.

Genovese, G., Friedman, D. J., Ross, M. D., Lecordier, L., Uzureau, P., Freedman, B. I., et al. (2010). Association of trypanolytic APOL1 variants with kidney disease in African Americans. Science, 329(5993), 841–845.

Gomez, V., Fernandez, A., Galeano, C., Oliva, J., Diez, V., Bueno, C., et al. (2013). Renal transplantation in HIV-infected patients: experience at a tertiary hospital in Spain and review of the literature. Transplant Proceedings, 45(3), 1255–1259.

Grossi, P. A. (2012). Update in HIV infection in organ transplantation. Current Opinion Organ Transplantation, 17(6), 586–593.

Harbell, J., Terrault, N. A., & Stock, P. (2013). Solid organ transplants in HIV-infected patients. Current HIV/AIDS Reports, 10(3), 217–225.

Humbert, M., Sitbon, O., Chaouat A., et al. (2006). Pulmonary arterial hypertension in France: results from a national registry. American Journal of Respiratory and Critical Care Medicine, 173, 1023.

Huprikar, S. (2009). Solid organ transplantation in HIV-infected individuals: an update. Reviews in Medical Virology, 19(6), 317–323.

Ison, M. G., Hager, J., Blumberg, E., Burdick, J., Carney, K., Cutler, J., et al. (2009).Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS Disease Transmission Advisory Committee. American Journal of Transplantation, 9(8), 1929–1935.

Ison, M. G., Llata, E., Conover, C. S., Friedewald, J. J., Gerber, S. I., Grigoryan, A., et al. (2011a). Transmission of human immunodeficiency virus and hepatitis C virus from an organ donor to four transplant recipients. American Journal of Transplantation, 11(6), 1218–1225.

Ison, M. G., & Nalesnik, M. A. (2011b). An update on donor-derived disease transmission in organ transplantation. American Journal of Transplantation, 11(6), 1123–1130.

Kaplan, J. E., Masur, H., Holmes, K.K., et al. (1995a). USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: introduction. USPHS/IDSA Prevention of Opportunistic Infections Working Group. Clinical Infectious Diseases, 21 Suppl 1:S1–11. Available at http:// www.ncbi.nlm.nih.gov/pubmed/ 8547495.

Kaplan, J. E., Masur, H., Jaffe, H.W., Holmes, K.K. (1995b). Reducing the impact of opportunistic infections in patients with HIV infection. New guidelines. Journal of the American Medical Association, 274(4):347–348. Available at http:// www.ncbi.nlm.nih.gov/pubmed/7609267.

Kern, R. M., Seethamraju, H., Blanc, P. D., et al. (2014a). The feasibility of lung transplantation in HIV seropositive patients. Annals of the American Thoracic Society (in press, online).

Kern, R., Seethamraju, H., Blanc, P., Sinha, N., Loebe, M., Golden, J., et al. (2014b). Lung Transplantation in HIV Seropositive Patients. Chest, 145(3 Suppl), 642A.

Kim, D., Ziebell, R., Sadulvala, N., Kline, R., Ocfemia, C., Prejean, J., et al. (2013).Trends in Transmitted Drug Resistance Associated Mutations: 10 HIV Surveillance Areas, US, 2001–2010.

Paper presented at the 20th Conference on Retroviruses and Opportunistic Infections. Kim, W. R., Smith, J. M., Skeans, M. A., et al. (2014). OPTN/SRTR 2012 Annual Data Report: Liver. American Journal of Transplantation, 1, 69–96.

Kucirka, L. M., Singer, A. L., Ross, R. L., et al. (2010). Underutilization of hepatitis C-positive kidneys for hepatitis C- positive recipients. American Journal of Transplantation, 10(5), 1238–1246.

Kucirka, L.M., Bowring, M. G., Massie, A. B., et al, (2015) Landscape of deceased donors labeled increased risk for disease transmission under new guidelines.American Journal of Transplantation, (in press).

Liang, T. J., & Ghany, M. G. (2013). Current and future therapies for hepatitis C virus infection. New England Journal of Medicine, 368(20), 1907–1917.

Locke, J. E., James, N. T., Mannon, R. B.,Mehta, S. G., Pappas, P. G., Baddley, J. W., et al. (2014). Immunosuppression Regimen and the Risk of Acute Rejection in HIV-Infected Kidney Transplant Recipients. Transplantation, 97(4), 446–450.

Locke, J. E., Reed R. D., Mehta S. G., et al. (2015a). Center-level experience and kidney transplant outcomes in HIV- infected recipients. American Journal of Transplantation, 15:2096–2104.

Locke, J. E., Mehta, S., Reed, R. D., et al. (2015b). A national study of outcomes among HIV-infected kidney transplant recipients. Journal of the American Society of Nephrology, 26:1–8.

Mandal, A. K., Kraus, E.S., Samaniego, M., et al. (2000). Shorter waiting times for hepatitis C virus seropositive recipients of cadaveric renal allografts from hepatitis C virus seropositive donors.Clinical Transplantation, 14, 391–396.

Mascolini, M. (2014). Four to Five HIV+ Dying in Care Yearly in Philadelphia Are Potential Organ Donors. 54th Interscience Conference on Antimicrobial Agents and Chemotherapy: Abstract H–1199a.Presented September 7, 2014.

Matas, A. J., Smith, J. M., Skeans, M. A., etal. (2014) OPTN/SRTR 2012 Annual Data Report: Kidney. American Journal of Transplantation, 1, 11–44.

Megens, S., & Laethem, K. V. (2013). HIV–1 genetic variation and drug resistance development. Expert Review of Anti- Infective Therapy, 11(11), 1159–1178.

Mehmood, S., Blais, D., Martin S., & Sai- Sudhakar, C. (2009). Heartmate XVE destination therapy for end-stage heart failure in a patient with human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 909–910.

Mehta, N. J., Khan, I. A., Mehta, R. N., et al. (2000). HIV-related pulmonary hypertension: analytic review of 131 cases. Chest, 118, 1133.

Mgbako, O., Glazier, A., Blumberg, E., & Reese, P. P. (2013). Allowing HIV- positive organ donation: ethical, legal and operational considerations. American Journal of Transplantation, 13(7), 1636–1642.

Miro, J. M., Montejo, M., Castells, L., Rafecas, A., Moreno, S., Aguero, F., et al. (2012). Outcome of HCV/HIV-coinfected liver transplant recipients: a prospective and multicenter cohort study. American Journal of Transplantation, 12(7), 1866–1876.

Miro, J. M., Stock, P., Teicher, E., et al, (2015). Outcome and management of HCV/HIV coinfection pre- and post-liver transplantation. A 205 update. Journal of Hepatology, 62:701–711.

Morales, J. M., Campistol, J. M., Dominguez- Gil, B., Andres, A., Esforzado, N., Oppenheimer, F., et al. (2010). Long-term experience with kidney transplantation from hepatitis C-positive donors into hepatitis C-positive recipients. American Journal of Transplantation, 10(11), 2453–2462.

Moreno, A., Cervera, C., Fortun, J., et al. (2012). Epidemiology and outcome of infections in human immunodeficiency virus/hepatitis C virus-coinfected liver transplant recipients: a FIPSE/GESIDA prospective cohort study. Liver Transplantation, 18, 70–81.

Muller, E., Kahn, D., & Mendelson, M. (2010). Renal transplantation between HIV- positive donors and recipients. New England Journal of Medicine, 362(24), 2336–2337.

Muller, E., Barday, Z., Mendelson, M., & Kahn, D. (2012). Renal transplantation between HIV-positive donors and recipients justified. South African Medical Journal, 102(6), 497–498.

Muller, E., Barday, Z., Mendelson, M., Kahn, D., et al. (2015). HIV-positive-to-HIV- positive kidney transplantation—results at 3 to 5 years. New England Journal of Medicine, 372:613–20.

Neuhaus, J., Angus, B., Kowalska, J. D., et al. (2010). Risk of all-cause mortality associated with nonfatal AIDS and serious non-AIDS events among adults infected with HIV. AIDS, 24(5), 697–706.

OPTN Policies and Bylaws. From http:// optn.transplant.hrsa.gov/ policiesandbylaws/policies.asp.

Pais, R. & Benhamou, Y. (2010). Long-term therapy for chronic hepatitis B in HIV co-infected patients. Gastroente´ rologie Clinique et Biologique, 34, 136–41.

Parsa, A., Kao, W. H. L., Xie, D., et al, (2013). APOL1 risk variants, race, and progression of chronic kidney disease. New England Journal of Medicine, 369:2183–96.

Panel on Opportunistic Infections in HIV- Infected Adults and Adolescents.Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents; recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/ contentfiles/lvguidelines/adult oi.pdf. (Accessed September 2015).

Pelletier S. J., Norman S. P., Christensen L. L., et al. (2004). Review of transplantation in HIV patients during the HAART era. Clinical Transplantation, 63–82.

Petrosillo, N., Chinello, P., & Cicalini, S. (2006). Pulmonary hypertension in individuals with HIV infection. AIDS, 20, 2128.

Prevention, C. f. D. C. a. (2013). HIV Surveillance Supplemental Report. Ragni, M. V., Dodson, S. F., Hunt, S. C., et al. (1999). Liver transplantation in a hemophilia patient with acquired immunodeficiency syndrome. Blood, 93, 1113–1114.

Redd A. D., Quinn T. C., Tobian A. A. (2013). Frequency and implications of HIV superinfection. The Lancet Infectious Diseases, 13(7), 622–628.

Reeves-Daniel, A. M., DePalma, J. A., Bleyer, A. J., Rocco, M. V., Murea, M., Adams, P. L., et al. (2011). The APOL1 Gene and Allograft Survival after Transplantation. American Journal of Transplantation, 11(5), 1025–1030.

Richterman, A., Blumberg, E., (2015). The challenges and promise of HIV-infected donors for solid organ transplantation. Current Infectious Disease Reports, 17:1– 8.

Richterman, A., Sawinski, D., Reese, P.P., et al, (2015). An assessment of HIV-infected patients dying in care for deceased organ donation in a United States urban center. American Journal of Transplantation, 15:2105–2116.

Riella, L.V., Sheridan, A.M., (2015). Testing for high-risk APOL1 alleles in potential living kidney donors. American Journal of Kidney Disease, (in press).

Roland, M., Carlson, L., & Stock, P. (2002). Solid organ transplantation in HIV- infected individuals. AIDS Clinical Care, 14(7), 59–63.

Roland, M. E., Adey, D., Carlson, L. L., & Terrault, N. A. (2003a). Kidney and liver transplantation in HIV-infected patients: case presentations and review. AIDS Patient Care STDS, 17(10), 501–507.

Roland, M. E., Lo, B., Braff, J., & Stock, P. G. (2003b). Key clinical, ethical, and policy issues in the evaluation of the safety and effectiveness of solid organ transplantation in HIV-infected patients. Archives of Internal Medicine, 163(15), 1773–1778.

Roland, M. E., & Stock, P. G. (2003c). Review of solid-organ transplantation in HIV- infected patients. Transplantation, 75(4), 425–429.

Sawinski, D., Goldberg, D. S., Blumberg, E., et al. (2015) Beyond the NIH multicenter HIV transplant trial experience: Outcomes of HIV+ liver transplant recipients compared to HCV+ or HIV+/ HCV+ coinfected recipients in the United States. Clinical Infectious Disease, (in Press).

Sherman, K. E., Thomas, D., & Chung, R. T. (2014). Human immunodeficiency virus and liver disease forum 2012. Hepatology, 59(1), 307–317.

Sims, D. B., Uriel, N., Gonza´lez-Costello, J., et al. (2011). Human immunodeficiency virus infection and left ventricular assist devices: a case series. Journal of Heart and Lung Transplantation, 30, 1060–1064.

Soriano, V., Tuma, P., Labarga, P., et al. (2009). Hepatitis B in HIV patients: what is the current treatment and what are the challenges? Journal of HIV Therapy, 14(1), 13–18.

Stock, P. G., Barin, B., Murphy, B., Hanto, D., Diego, J. M., Light, J., et al. (2010). Outcomes of kidney transplantation in HIV-infected recipients. New England Journal of Medicine, 363(21), 2004–2014.

Taege, A. (2013). Organ transplantation and HIV progress or success? A review of current status. Curr Infectious Disease Reports, 15, 67–76.

Tector, A. J., Mangu, R. S., Chestovich, P., et al. (2006). Use of extended criteria livers decreases wait time for liver transplantation without adversity impacting posttransplant survival.

Annals of Surgery, 244, 439–450. Terrault, N. A., Roland, M. E., Schiano, T., Dove, L., Wong, M. T., Poordad, F., et al. (2012). Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection.

Liver Transplantation, 18(6), 716–726. Touzot, M., Pillebout, E., Matignon, M., Tricot, L., Viard, J. P., Rondeau, E., et al. (2010). Renal transplantation in HIV- infected patients: the Paris experience. American Journal of Transplantation, 10(10), 2263–2269.

Uriel, N., Jorde, U. P., Cotarlan, V., et al. (2009). Heart transplantation in human immunodeficiency virus-positive patients. Journal of Heart and Lung Transplant, 28, 667–669.

Uriel, N., Nahumi, N., Colombo, P. C., et al. (2014). Advance heart failure in patients infected with human immunodeficiency virus: is there equal access to care?

Journal of Heart and Lung Transplantation (in press, online). Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2013). Cause- specific life expectancies after 35 years of age for human immunodeficiency syndrome-infected and human immunodeficiency syndrome-negative individuals followed simultaneously in long-term cohort studies, 1984–2008.American Journal of Epidemiology, 177(2), 116–125.

Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2014). Cause- specific mortality among HIV-infected individuals, by CD4 (+) cell count at HAART initiation, compared with HIV-uninfected individuals. AIDS, 28(2), 257–265.

Yoon, S. C., Hurst, F. P., Jindal, R. M., George, S. A., Neff, R. T., Agodoa, L. Y., et al. (2011). Trends in renal transplantation in patients with human immunodeficiency virus infection: an analysis of the United States renal data system. Transplantation, 91(8), 864–868.

Protocol Version 1.2

Amendment #1 May **29, 2018**

1. Title:

Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.

2. Investigators:

PI: Yorg al Azzi[2], MD.
AIs: Vagish Hemmige, MD[3], Victoria Muggia, MD[3], Grace Minamoto, MD[3], Yoram Puius, MD[3] Margaret McCort MD[3], Enver Akalin MD[2], Maria Ajaimy MD[2], Stuart Greenstein MD[1], Jay Graham MD[1], Milan Kinkhabwala MD[1]

[1] Montefiore-Einstein Center for Transplantation, Transplant Surgery, Department of Surgery.
[2] Montefiore-Einstein Center for Transplantation, Transplant Nephrology, Department of Medicine.
[3] Montefiore-Einstein Center for Transplantation, Transplant Infectious Diseases, Department of Medicine.

3. Background and purposes:

The advent of effective antiretroviral therapy (ART) in the mid-1990s for treatment of individuals infected with HIV transformed a rapidly fatal disease into a well-controlled chronic illness. Currently, the life expectancy of individuals infected with HIV and receiving ART early in the course of their disease approaches that of individuals without HIV infection (Wada, 2013, 2014). In this era of greater longevity, liver failure, end-stage renal disease, and cardiovascular disease have emerged as important causes of morbidity and mortality in patients with HIV infection (Neuhaus, 2010).

Organ transplantation prolongs survival and improves quality of life for individuals with end-stage organ disease (Matas, 2014; Kim, 2014). Until recently, however, organ transplantation was unavailable to those infected with HIV due to concerns that pharmacologic immunosuppression to prevent organ rejection would hasten the progression from HIV infection to AIDS, concerns about disease transmission, and reluctance to allocate organs to a population whose outcome was unpredictable (Blumberg, 2009, 2013a, 2013b; Mgbako, 2013; Taege, 2013).

Nevertheless, a few transplant programs accepted HIV-positive patients on their transplant waiting lists and accumulated data showing kidney or liver transplantation could be done safely in these patients (Roland, 2002, 2003a, 2003b, 2003c; Blumberg, 2009; Stock, 2010; Yoon, 2011; Terrault, 2012). Subsequently, a prospective, multicenter clinical trial of kidney and liver transplantation in 275 patients demonstrated that, among HIV-positive kidney and liver transplant recipients, patient and graft survival rates were acceptable and within the range of outcomes currently achieved among non-infected transplant recipients.

However, the rate of kidney rejection was unexpectedly high, demonstrating that the immune dysregulation resulting from HIV infection, HCV co-infection, and antirejection drugs is complex and incompletely understood. Some of the challenges encountered in that study remain relevant for clinical sites offering organ transplantation to HIV-positive individuals today (e.g., management of drug interactions and toxicities when combining complex medical regimens, management of combined morbidities of two or more active diseases, and the need for ongoing collaboration among medical professionals from different specialties) (Frassetto, 2007, 2014; Locke, 2014). Despite the complexities, this study and others (Ragni, 1999; Frassetto, 2009; Huprikar, 2009; Stock, 2010; Touzot, 2010; Cooper, 2011; Duclos-Vallee, 2011; Reeves-Daniel, 2011; Fox, 2012; Terrault, 2012; Grossi, 2012; Gomez, 2013; Harbell, 2013) demonstrate that kidney and liver transplantation are appropriate in HIV- positive individuals with liver or kidney failure, although gaps in knowledge and many research questions remain. There is much less experience with heart (Calabrese, 2003; Bisleri, 2003; Pelletier, 2004; Uriel, 2009, 2014; Castel, 2011a, 2011b; Durante-Mangoni, 2011 and 2014) and lung (Mehta, 2000; Humbert,2006; Petrosillo, 2006; Bertani, 2009; Kern, 2014a, 2014b) transplantation in HIV-positive recipients, or mechanical circulatory assistance (Brucato, 2004; Fieno, 2009; Mehmood, 2009; Sims, 2011) as a bridge to transplantation, although case reports and small case series suggest acceptable short-term outcomes are possible.

Prior to the passage of the HOPE Act, U.S. law required that all U.S. transplants for HIV-positive recipients utilize organs from HIV-uninfected donors. (See 42 U.S.C. 273(b)(3)(C), 274(b) and 18 U.S.C. 1122, all prior to amendment by the HOPE Act). The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV (hereinafter referred to as ‘‘HIV-positive to HIV-positive transplantation’’) is recognized (Boyarsky, 2011, 2015; Mgbako, 2013; Mascolini, 2014; Kucirka, 2015; Richterman, 2015). It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients (Boyarsky, 2011). The published experience with HIV-positive to HIV- positive SOT at this time comes from Muller et al from the University of Cape Town in South Africa. Initially, Muller et al (2010) reported 100 percent patient and graft survival in a four-patient pilot study. Subsequently, the same group reported an additional 10 HIV-positive to HIV-positive renal transplants (Muller, 2012). All patients were restarted on ART early postoperatively in the immunosuppressive setting of T- cell-depleting induction therapy, tacrolimus, mycophenolate mofetil, and prednisone. One to 4 years after transplantation, outcomes remained excellent and all patients had undetectable viral loads (Muller, 2012). The cumulative University of Cape Town experience of 27 HIV-positive to HIV-positive transplant procedures was recently summarized in the New England Journal of Medicine (Muller, 2015). The 1- and 5-year death-censored graft survival was 93 and 84 percent, respectively, and 1- and 5-year patient survival was 83 and 74 percent, respectively. Of note, the South African HIV-positive deceased donors were ART-naive, without history of opportunistic infection or proteinuria, and had normal pre-transplant renal biopsies. While renal function has remained normal in the recipients, three have had routine post-transplant renal biopsies demonstrating new changes typical of early HIV-associated nephropathy that were not present in baseline biopsy specimens. The long- term significance of these findings remains unknown and awaits

longer follow-up. All patients had undetectable plasma HIV viral loads after transplantation. Graft rejection rates were 8 percent at 1 year and 22 percent at 3 years.

The HOPE Act permits HIV-positive to HIV-positive organ transplantation under IRB-approved research protocols conforming to the Final Human Immunodeficiency Virus (HIV) Organ Policy Equity (HOPE) Act Safeguards and Research Criteria for Transplantation of Organs Infected with HIV, which were developed as directed in the HOPE Act. Patients receiving HIV-positive kidneys from deceased HIV-positive donors in South Africa (Muller, 2015) had survival rates of 84 percent and 74 percent at 1 and 5 years, respectively; however, there is presently no evidence for the safety, efficacy, and effectiveness of HIV-positive to HIV- positive transplantation in North America. The Final Safeguards and Research Criteria are meant to support the acquisition of new clinical knowledge and mechanistic insights about HIV-positive to HIV-positive organ transplantation in the United States. The results of this research will be evaluated by the Secretary of HHS and the OPTN to determine whether and how the OPTN standards for organ transplantation shall be revised to address HIV-positive organ donors.

The research protocol described below was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States. The criteria address the minimum safety and data requirements of clinical research in HIV-positive to HIV-positive transplantation. As mandated by the HOPE Act, the Secretary, together with the OPTN, is charged with reviewing the results of scientific research conducted under these criteria to determine whether the OPTN's standards of quality should be further modified and whether some HIV- positive to HIV-positive transplants should proceed outside the auspices of research conducted under such criteria (see attached the original document).

Montefiore Medical Center and the Montefiore-Einstein Center for Transplantation meet the institutional standards and requirements to carry on a research protocol on HIV-positive to HIV-positive kidney transplantation with a collective experience of 14 kidney transplants on HIV positive recipients since 2008. The Montefiore AIDS center provides care to over 2500 HIV positive individuals in the Bronx. Potential transplant candidates as per protocol are evaluated by transplant ID clinicians with expertise also in HIV. The AIDS center providers and the Montefiore infectious disease faculty practice follow these patients closely for the first year after transplantation, and over two thirds of these patients have elected to remain at Montefiore for their HIV care. Multidisciplinary transplant protocols include management of HIV recipients and the outcomes of these cases have met the national standards without affecting our program-specific reports (SRTR reports).

4. Objectives and outcome measures

Montefiore's research in HIV-positive to HIV-positive transplantation will address questions related to HIV superinfection; incidence and severity of opportunistic infections (including transmission of occult OIs from donor to recipient); immunologic mechanisms contributing to the increased rate of kidney rejection observed in HIV-positive recipients and quality of life for recipients of HIV- positive to HIV-

positive transplantation. To ensure that all nationwide studies of HIV-positive to HIV- positive transplantation can contribute to evaluation of the safety of the procedure, the following key donor and recipient characteristics and outcome measures must be incorporated into the design of all clinical trials of HIV- positive to HIV-positive transplantation.

Wait List Candidates

- HIV status
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Removal from wait list (death or other reason)
- Time on wait list

Donors (all)

- Type (living or deceased)
- HIV status (HIV-positive new diagnosis, HIV-positive known diagnosis)
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Pre-transplant donor allograft biopsy

Note regarding Living Donors: Montefiore Einstein Center for Transplantation has decided to exclude living donors from the participation in this research protocol.

Transplant Recipients

- Rejection rate (annual up to 5 years)
- Progression to AIDS
- New Opportunistic Infections
- Failure to suppress viral replication (persistent viremia)
- HIV-associated organ failure
- Malignancy
- Graft failure
- Mismatched ART resistance versus donor
- Death

5. Methods:

- Donor Eligibility

Montefiore Einstein Center for Transplantation has decided to exclude living donors from this research protocol. HIV- positive deceased donors of organs for transplantation into an HIV-positive recipient must fulfill applicable clinical criteria in place for HIV-uninfected organ donors.

There is substantial concern about the consequences of transplanting an organ from an HIV-positive donor to a recipient infected with a strain of HIV that differs from the donor's in terms of its responsiveness to antiretroviral therapy (ART). The likelihood and impact of HIV superinfection in this context are unknown. Adverse consequences could range from transient loss of viral suppression, necessitating a change in antiretroviral regimen to a worst-case scenario in which the new infecting strain of HIV is unresponsive to available antiretroviral treatment and the recipient progresses to AIDS (Redd, 2013). Information relevant to understanding the known or potential extent of antiretroviral resistance in the strain of HIV infecting the organ donor may be incomplete for many reasons:

- There may be inadequate virus in donor specimens for antiretroviral resistance testing;
- If the specimen is adequate, there may not be enough time within the decision-making evaluation window to fully assess antiretroviral resistance before the clinical deterioration of the donor, organ procurement, and implantation;
- The donor's history of antiretroviral treatment may be unknown or incomplete;
- Results from prior antiretroviral resistance testing may be unavailable.

These issues might be especially challenging when considering organ donation from deceased donors whose HIV infection is first identified during donor evaluation. As of 2011, an estimated 1 in 6 U.S. adults living with HIV infection were undiagnosed (Prevention, 2013) and an estimated 16 percent of newly diagnosed, untreated individuals were infected with virus resistant to at least one class of antiretroviral drug (Kim, 2013; Megens, 2013).

It is anticipated that the risk of transmission of resistant HIV strains may be lower from deceased donors with a well-documented history of antiretroviral treatment, undetectable virus at demise, and robust and persistent undetectable viral load for at least 1 year prior to death. However, to impose this as an eligibility criterion would limit the pool of suitable donors and severely limit the ability to study transplantation of HIV-positive organs under the HOPE Act. In addition, it will not be possible in all cases to obtain viral loads and/or antiretroviral resistance profiles in the time available for donor evaluation. Transplant teams evaluating a donor must review all available donor and recipient information and be able to propose an antiretroviral regimen that will be equally or more safe, tolerable, and effective for the recipient after transplantation as the regimen in place in the recipient before transplantation. For instance, a donor who only achieves viral suppression with a regimen known to be intolerable to the recipient must not be accepted. If there is doubt about the ability to suppress viral replication after transplantation, the transplant must not move forward.

Donors co-infected with hepatitis are not excluded from HIV-positive to HIV- positive transplant; however, careful consideration must be given when evaluating a donor co-infected with HBV and/or HCV (Terrault, 2012; Miro, 2012; Moreno, 2012; Sherman, 2014; Chen, 2014). Although HCV therapeutic strategies are rapidly evolving (Liang, 2013), it is possible that mixed genotype HCV infections may influence post- transplant treatment of HCV in the recipient. Prior antiretroviral treatment of the donor and/or recipient with agents active against HBV (i.e., lamivudine, emtricitabine, adefovir, and tenofovir) has the potential for inducing or uncovering archived HBV drug resistance in the recipient (Dieterich, 2007; Soriano, 2009; Pais, 2010).

HIV-positive transplant candidates who are listed for a transplant in the context of a research study of HIV- positive to HIV-positive transplantation must have the same opportunity as other transplant candidates to receive an organ from an HIV-negative donor, should one become available for them.

1.1 HIV-Positive Donor Eligibility Criteria

The HIV-specific donor eligibility criterion for deceased donors is listed (Table 1). Co-infection with HBV and/or HCV is not an exclusion criterion.

1.1.1 HIV-Positive Deceased Donors

When evaluating HIV-positive deceased donors, it is understood that limited medical history may be available and/or known at the time of the donor evaluation. The OPO must make reasonable efforts to obtain prior medical history so that a transplant center team may best determine the suitability of the potential donor based on the information available. A complete history of antiretroviral regimens and a history of viral load tests and resistance testing are especially valuable for evaluating the likelihood of donor HIV resistance to antiretroviral regimens. A history of OIs or cancers is also of high importance, due to the increased risk for both attributable to HIV, and the additional difficulty of treating some infections and neoplasms in a post-transplant setting. It is possible that deceased donors with lower CD4+ T-cell counts may pose an increased risk of harboring transmissible diseases (e.g., opportunistic infections or neoplasms) that may be difficult to detect during organ harvest and transplantation; teams conducting transplants under the HOPE Act are urged to assess donors with low CD4+ T-cell counts (e.g., <200/mL) with special caution and to promptly inform IRBs and the PI of known or suspected disease transmission events.

Minimum eligibility criteria for all HIV-positive deceased donors:

i. Documented HIV infection using an FDA-licensed, approved, or cleared test device(s).

ii. No evidence of invasive opportunistic complications of HIV infection.

iii. Pre-implant donor organ biopsy to be stored, at a minimum, for the duration of the study (or at least 5 years); additional specimens may be obtained to support specific research goals.

Additional eligibility criteria for HIV- positive deceased donors with a known history of HIV and prior treatment with ART:

i. The study team must describe the anticipated post-transplant antiretroviral regimen(s) to be prescribed for the recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Recipient Eligibility

A key consideration when evaluating potential HIV-positive transplant candidates is the ability to suppress HIV viral load post-transplant. This includes a thorough assessment by the transplant team of the candidate recipient's prescribed antiretroviral medications, HIV RNA levels while on medications, adherence to HIV treatment, and any available HIV resistance testing; a similar evaluation of the donor must also be carried out. A transplant should only take place if, after evaluating both recipient and donor, the team is confident they can define a post- transplant antiretroviral regimen that will be safe, tolerable, and effective. If there is any doubt on the part of the transplant team about the ability to suppress viral replication post- transplant, the transplant should not move forward. Concerns about transmitted drug resistance must be included in the recipient informed consent process for the research study. At the time of an organ offer, the recipient informed consent must address the transplant team's assessment of risk specific to the organ they are being offered.

2.1 HIV-Positive Recipient Eligibility Criteria

The following HIV-specific criteria must be met when screening for an HIV- positive to HIV-positive organ transplant (also refer to Table 1):

i. Last CD4+ T-cell count >200/mL (kidney) Prior to enrollment; any patient with history of OI must have a CD4 positive T-cell count >200/uL.

ii. HIV RNA less than 50 copies/mL and on a stable antiretroviral regimen.*+

iii. No evidence of active opportunistic complications of HIV infection.

iv. No history of primary CNS lymphoma or PML.

v. Concurrence by the study team that based on medical history and ART, viral suppression can be achieved in the recipient post-transplant.

*Patients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen for the patient once organ function is restored after transplantation.

+Those patients on a protease based regimen and fully suppressed with no available resistance studies, should be tested with an assay that looks at archived resistance (e.g. Genosure Archive®).

+ We enroll 100 HIV positive patients who are eligible for kidney transplant.

TABLE 1—SUMMARY OF DONOR AND RECIPIENT ELIGIBILITY CRITERIA FOR HIV-POSITIVE SERO-CONCORDANT ORGAN TRANSPLANT PAIRS UNDER THE HOPE ACT

HIV-Related variables	Deceased donor	Living donor	HIV-Positive recipient
Current CD4+ T-cell count (T lymphocytes/μL)	No requirement	≥500 for 6 months prior to organ donation.	If no history of OI • ≥200 If history of OI • ≥200 (kidney) • ≥100 (liver) Last CD4+ T-cell count Prior to enrollment
Plasma HIV RNA viral load (copies/mL).	No requirement**	<50	<50*
Opportunistic infection	No invasive OI	No invasive OI	Currently, • No active OI Historically, no • CNS lymphoma • PML

* Organ recipients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen to be used by the recipient once organ function is restored after transplantation.

** In deceased donors with a known history of HIV infection and prior treatment with ART, the study team must describe the anticipated post- transplant antiretroviral regimen(s) to be used by the organ recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Transplant process and post-transplant considerations

Organ recovery, transplant procedure, handling and storage of donor organs/tissues, as well as management of kidney transplant recipients at Montefiore-Einstein Center for Transplantation are well described in our policies and procedures section (intranet), including the multidisciplinary management and immunosuppression protocols of HIV-positive kidney recipients

Waitlist acceptance criteria: Once an IRB- approved research protocol in HIV- positive to HIV-positive transplantation is finalized, the transplant center will inform the OPTN of additional organ-specific acceptance criteria for organs from HIV-positive donors. Those HIV-positive kidney candidates on the wait list willing to accept an HIV- positive organ must specify any additional acceptance criteria to the OPO.

Consent process and Independent HIV-Positive Recipient Advocate: One of Montefiore's senior transplant coordinator is actively collaborating with an NIH initiative to train and credential independent advocates for protecting and promoting the rights and interests of the HIV-positive recipient (or prospective recipient). The independent advocate for the HIV- positive recipient will:

i. Promote and protect the interests of the HIV-positive recipient (including with respect to having access to a suitable HIV-negative organ if it becomes available) and take steps to ensure that the HIV-positive recipient's decision is informed and free from coercion.

ii. Review whether the potential HIV-positive recipient has received information regarding the results of SOT in general and transplantation in HIV- positive recipients in particular and the unknown risks associated with HIV- positive to HIV-positive transplant.

iii. Demonstrate knowledge of HIV infection and transplantation.

Attached: -Informed consent for research

Post-transplant care

After discharge, patients are seen by the multidisciplinary transplant team according to the below schedule. During weekly morbidity and mortality meeting the post-transplant team meets and reviews the transplant recipients seen during the week to discuss patients, complications (infections, rejection, bleeding, readmission, re-surgery, malignancy, patient death, and graft loss), and allograft function. These events are stored in the transplant computerized database and communicated to the OPTN in accordance with regulations. Recipients are also assessed and contacted in respect to QAPI initiatives to further improve patient care initiatives.

Adult Transplant Patients are generally evaluated according to the following schedule after kidney transplantation:

First month: twice a week labs, once a week clinic visit

2-3 months: once a week labs and every other week clinic visit

4-5 months: every other week labs and one month clinic visit

6-12 months: once a month labs and every other month clinic visit

Second year: every 2 months labs and 4 months clinic visit

3-5 years every 3 month labs and 6 months clinic visit

> 5 years every 3 months labs and once a year clinic visit

During each clinical visit, bloods and vital signs are obtained, a physical exam is performed and medications are reviewed with each patient. Medical and surgical problems will be addressed on an ongoing basis and appropriate referrals are made to specialists. Pharmacist, nutritional and social service support is available at each clinic. The Transplant Patient will receive specific instructions from the Transplant Multi-Disciplinary Team as to their follow-up care.

Additional transplant allograft biopsy will be performed at 3 months and one year from transplant.

All patients will be assigned to one respective transplant nephrologist for routine follow-up. Patients will be seen at least once within a month after transplantation by a transplant surgeon.

In order to promptly detect viral breakthrough or possibility of viral superinfection, HIV viral loads should be performed every week for the first four weeks after transplantation, every three months for

the first year post transplantation, and every 6 months in patients who have achieved sustained viral suppression. If viral breakthrough is detected on two consecutive assays, genotypic resistance studies will be sent. In addition tropism assays and resistance testing looking for mutations in the integrase gene will be performed. CD4 monitoring can be done less frequently. Monthly CD4 monitoring for the first three months, every three months for the first year, and every 6 months in stable patient. The Montefiore transplant infectious disease provider will see the patient monthly the first three months after transplantation and every three months for the first year post transplant. After the first year, stable transplant patients may return to their outside provider, however the transplant ID attending will maintain close contact with the primary care provider, and also see the recipient twice a year for the duration of the study. To assist patients with urgent infectious disease issues the Montefiore AIDS center provides walk in services Monday through Friday, and 24 hour service coverage for established patients.

Transplant physicians will give 24 hour coverage service for post-transplant patients with any questions and complaints.

6 – Potential risks

Risk considerations and pertinent safeguards to potential recipients have been described in detail above under donor and recipient eligibility sections.

Prevention of Inadvertent Transmission of HIV

Although the use of HIV-positive organs may help alleviate transplant shortages and reduce patient waiting list times, there also are patient safety concerns to consider. Prevention or management of inadvertent transmission of HIV or exposure of an HIV-negative recipient to organs or tissues from an HIV-positive donor due to identification error is paramount (Ison, 2009, 2011a, 2011b). The transplant community, with regulatory oversight at multiple levels, has been able to achieve a high level of safety through routine procedures and clinical practice. The precautions taken with ABO compatible donor-recipient pairs and HCV-infected donor organs in HCV- infected recipients (Morales, 2010; Kucirka, 2010; Mandal, 2000; Tector, 2006) are existing models. However, vulnerabilities still exist, and mishaps still occur. For instance, the risks of error during manual transcription of information are well documented.

Montefiore medical center and the transplant center already count with an institutional biohazard plan for handling of HCV-positive organs and tissue disposal for HCV-positive recipients and ABO compatibility verification policies. HIV-positive status of donor organ, donor tissues and intended recipient will be added to the organ-to-recipient verification form

7- Confidentiality and safeguards to minimize risks.

The research protocol was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States (attached document and informed consent).

8- Study benefits

The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV. It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients

9- Data Safety Monitoring Board

A DSMB comprised of a three physicians (not involved in the study) will be assembled every 12 months to review safety data.

9-References

Bertani, A., Grossi, P., Vitulo, P., et al. (2009). Successful lung transplantation in an HIV- and HBV-positive patient with cystic fibrosis. American Journal of Transplantation, 9, 2190–2196.

Bisleri, G., Morgan, J. A., Deng, M. C., et al. (2003). Should HIV-positive recipients undergo heart transplantation? Journal of Thoracic and Cardiovascular Surgery, 126, 1639–1640.

Blumberg, E. A., & Stock, P. (2009). Solid organ transplantation in the HIV-infected patient. American Journal of Transplantation, 9 Suppl 4, S131–135.

Blumberg, E. A., & Rogers, C. C. (2013a). Human immunodeficiency virus in solid organ transplantation. American Journal of Transplantation, 13 Suppl 4, 169–178.

Blumberg, E. A., Ison, M. G., Pruett, T. L., & Segev, D. L. (2013b). Optimal testing of the live organ donor for blood-borne viral pathogens: the report of a consensus conference. American Journal of Transplantation, 13(6), 1405–1415.

Boyarsky, B. J., Hall, E. C., Singer, A. L., Montgomery, R. A., Gebo, K. A., & Segev,D. L. (2011). Estimating the potential pool of HIV-infected deceased organ donors in the United States. American Journal of Transplantation, 11(6), 1209–1217.

Boyarsky, B. J., Durand C. M., Palella F. J., Segev D.L., (2015). Challenges and clinical decision-making in HIV-to-HIV transplantation: insights from the HIV literature. American Journal of Transplantation, 15:2023–2030.

Brucato, A., Colombo, T., Bonacina, E., et al. (2004). Fulminant myocarditis during HIV seroconversion: recovery with temporary left ventricular mechanical assistance. Italian Heart Journal, 5, 228–231.

Calabrese, L. H., Albrecht, M., Young, J., et al. (2003). Successful cardiac transplantation in an HIV–1-infected patient with advanced disease. New England Journal of Medicine, 348, 2323–2328.

Castel, M. A., Pe´rez-Villa, F., Roig, E., & Miro´ , J. M. (2011a). Heart transplantation in an HIV–1-infected patient with ischemic cardiomyopathy and severe pulmonary hypertension. Revista Espan˜ ola de Cardiologı´a, 64, 1066–1067.

Castel, M. A., Pe´rez-Villa, F., & Miro´ , J. M. (2011b). Heart transplantation in HIV- infected patients: more cases in Europe. The Journal of Heart and Lung Transplantation, 30, 1418.

Chen, J. Y., Feeney, E. R., & Chung, R. T. (2014). HCV and HIV co-infection: mechanisms and management. Nature Reviews: Gastroenterology & Hepatology, 11(6), 362–371.

Cooper, C., Kanters, S., Klein, M., Chaudhury, P., Marotta, P., Wong, P., et al. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with synthetic cohort. AIDS, 25(6), 777–786.

Dieterich, D.T. (2007). Special considerations and treatment of patients with HBV–HIV coinfection. Antiviral Therapy, 12, H43– H51.

Duclos-Vallee, J. C., Falissard, B., & Samuel, D. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with a synthetic cohort. AIDS, 25(13), 1675– 1676.

Durante-Mangoni, E., Maiello, C., & Sbreglia, C. (2011). A European first: successful heart transplant in a human immunodeficiency virus-positive recipient. The Journal of Heart and Lung Transplantation, 30, 845.

Durante-Mangoni, E., Maiello, C., Limongelli, G., et al. (2014). Management of immunosuppression and antiretroviral treatment before and after heart transplant for HIV-associated dilated cardiomyopathy. International Journal of Immunopathology and Pharmacology, 27(1), 113–120.

Fieno, D. S., Czer, L. S., Schwarz, E. R., et al. (2009). Left ventricular assist device placement in a patient with end-stage heart failure and human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 919–920.

Fox, A. N., Vagefi, P. A., & Stock, P. G. (2012). Liver transplantation in HIV patients. Seminars in Liver Disease, 32(2), 177–185.

Frassetto, L. A., Browne, M., Cheng, A., et al. (2007). Immunosuppressant pharmacokinetics and dosing modifications in HIV–1 Infected liver and kidney transplant recipients.

American Journal of Transplantation, 7(12), 2816–2820. Frassetto, L. A., Tan-Tam, C., & Stock, P. G. (2009). Renal transplantation in patients with HIV. Nature Review: Nephrology, 5(10), 582–589.

Frassetto, L. A., Tan-Tam, C. C., Barin, B., Browne, M., Wolfe, A. R., Stock, P. G., et al. (2014). Best Single Time Point Correlations with AUC for Cyclosporine and Tacrolimus in HIV-Infected Kidney and Liver Transplant Recipients.Transplantation, 97(6), 701–707.

Freedman, B.I. (2013). APOL1 and nephropathy progression in populations of African ancestry. Seminars in Nephrology, 33(5):425–432.

Freedman, B.I., Julian, B. A., Pastan, S. O. et al. (2015). Apolipoprotein L1 gene variants in deceased organ donors are associated with renal allograft failure. American Journal of Transplantation, 15:1615–1622.

Genovese, G., Friedman, D. J., Ross, M. D., Lecordier, L., Uzureau, P., Freedman, B. I., et al. (2010). Association of trypanolytic APOL1 variants with kidney disease in African Americans. Science, 329(5993), 841–845.

Gomez, V., Fernandez, A., Galeano, C., Oliva, J., Diez, V., Bueno, C., et al. (2013). Renal transplantation in HIV-infected patients: experience at a tertiary hospital in Spain and review of the literature. Transplant Proceedings, 45(3), 1255–1259.

Grossi, P. A. (2012). Update in HIV infection in organ transplantation. Current Opinion Organ Transplantation, 17(6), 586–593.

Harbell, J., Terrault, N. A., & Stock, P. (2013). Solid organ transplants in HIV-infected patients. Current HIV/AIDS Reports, 10(3), 217–225.

Humbert, M., Sitbon, O., Chaouat A., et al. (2006). Pulmonary arterial hypertension in France: results from a national registry. American Journal of Respiratory and Critical Care Medicine, 173, 1023.

Huprikar, S. (2009). Solid organ transplantation in HIV-infected individuals: an update. Reviews in Medical Virology, 19(6), 317–323.

Ison, M. G., Hager, J., Blumberg, E., Burdick, J., Carney, K., Cutler, J., et al. (2009).Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS Disease Transmission Advisory Committee. American Journal of Transplantation, 9(8), 1929–1935.

Ison, M. G., Llata, E., Conover, C. S., Friedewald, J. J., Gerber, S. I., Grigoryan, A., et al. (2011a). Transmission of human immunodeficiency virus and hepatitis C virus from an organ donor to four transplant recipients. American Journal of Transplantation, 11(6), 1218–1225.

Ison, M. G., & Nalesnik, M. A. (2011b). An update on donor-derived disease transmission in organ transplantation. American Journal of Transplantation, 11(6), 1123–1130.

Kaplan, J. E., Masur, H., Holmes, K.K., et al. (1995a). USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: introduction. USPHS/IDSA Prevention of Opportunistic Infections Working Group. Clinical Infectious Diseases, 21 Suppl 1:S1–11. Available at http:// www.ncbi.nlm.nih.gov/pubmed/ 8547495.

Kaplan, J. E., Masur, H., Jaffe, H.W., Holmes, K.K. (1995b). Reducing the impact of opportunistic infections in patients with HIV infection. New guidelines. Journal of the American Medical Association, 274(4):347–348. Available at http:// www.ncbi.nlm.nih.gov/pubmed/7609267.

Kern, R. M., Seethamraju, H., Blanc, P. D., et al. (2014a). The feasibility of lung transplantation in HIV seropositive patients. Annals of the American Thoracic Society (in press, online).

Kern, R., Seethamraju, H., Blanc, P., Sinha, N., Loebe, M., Golden, J., et al. (2014b). Lung Transplantation in HIV Seropositive Patients. Chest, 145(3 Suppl), 642A.

Kim, D., Ziebell, R., Sadulvala, N., Kline, R., Ocfemia, C., Prejean, J., et al. (2013).Trends in Transmitted Drug Resistance Associated Mutations: 10 HIV Surveillance Areas, US, 2001–2010.

Paper presented at the 20th Conference on Retroviruses and Opportunistic Infections. Kim, W. R., Smith, J. M., Skeans, M. A., et al. (2014). OPTN/SRTR 2012 Annual Data Report: Liver. American Journal of Transplantation, 1, 69–96.

Kucirka, L. M., Singer, A. L., Ross, R. L., et al. (2010). Underutilization of hepatitis C-positive kidneys for hepatitis C- positive recipients. American Journal of Transplantation, 10(5), 1238–1246.

Kucirka, L.M., Bowring, M. G., Massie, A. B., et al, (2015) Landscape of deceased donors labeled increased risk for disease transmission under new guidelines.American Journal of Transplantation, (in press).

Liang, T. J., & Ghany, M. G. (2013). Current and future therapies for hepatitis C virus infection. New England Journal of Medicine, 368(20), 1907–1917.

Locke, J. E., James, N. T., Mannon, R. B.,Mehta, S. G., Pappas, P. G., Baddley, J. W., et al. (2014). Immunosuppression Regimen and the Risk of Acute Rejection in HIV-Infected Kidney Transplant Recipients. Transplantation, 97(4), 446–450.

Locke, J. E., Reed R. D., Mehta S. G., et al. (2015a). Center-level experience and kidney transplant outcomes in HIV- infected recipients. American Journal of Transplantation, 15:2096–2104.

Locke, J. E., Mehta, S., Reed, R. D., et al. (2015b). A national study of outcomes among HIV-infected kidney transplant recipients. Journal of the American Society of Nephrology, 26:1–8.

Mandal, A. K., Kraus, E.S., Samaniego, M., et al. (2000). Shorter waiting times for hepatitis C virus seropositive recipients of cadaveric renal allografts from hepatitis C virus seropositive donors.Clinical Transplantation, 14, 391–396.

Mascolini, M. (2014). Four to Five HIV+ Dying in Care Yearly in Philadelphia Are Potential Organ Donors. 54th Interscience Conference on Antimicrobial Agents and Chemotherapy: Abstract H–1199a.Presented September 7, 2014.

Matas, A. J., Smith, J. M., Skeans, M. A., etal. (2014) OPTN/SRTR 2012 Annual Data Report: Kidney. American Journal of Transplantation, 1, 11–44.

Megens, S., & Laethem, K. V. (2013). HIV–1 genetic variation and drug resistance development. Expert Review of Anti- Infective Therapy, 11(11), 1159–1178.

Mehmood, S., Blais, D., Martin S., & Sai- Sudhakar, C. (2009). Heartmate XVE destination therapy for end-stage heart failure in a patient with human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 909–910.

Mehta, N. J., Khan, I. A., Mehta, R. N., et al. (2000). HIV-related pulmonary hypertension: analytic review of 131 cases. Chest, 118, 1133.

Mgbako, O., Glazier, A., Blumberg, E., & Reese, P. P. (2013). Allowing HIV- positive organ donation: ethical, legal and operational considerations. American Journal of Transplantation, 13(7), 1636–1642.

Miro, J. M., Montejo, M., Castells, L., Rafecas, A., Moreno, S., Aguero, F., et al. (2012). Outcome of HCV/HIV-coinfected liver transplant recipients: a prospective and multicenter cohort study. American Journal of Transplantation, 12(7), 1866–1876.

Miro, J. M., Stock, P., Teicher, E., et al, (2015). Outcome and management of HCV/HIV coinfection pre- and post-liver transplantation. A 205 update. Journal of Hepatology, 62:701–711.

Morales, J. M., Campistol, J. M., Dominguez- Gil, B., Andres, A., Esforzado, N., Oppenheimer, F., et al. (2010). Long-term experience with kidney transplantation from hepatitis C-positive donors into hepatitis C-positive recipients. American Journal of Transplantation, 10(11), 2453–2462.

Moreno, A., Cervera, C., Fortun, J., et al. (2012). Epidemiology and outcome of infections in human immunodeficiency virus/hepatitis C virus-coinfected liver transplant recipients: a FIPSE/GESIDA prospective cohort study. Liver Transplantation, 18, 70–81.

Muller, E., Kahn, D., & Mendelson, M. (2010). Renal transplantation between HIV- positive donors and recipients. New England Journal of Medicine, 362(24), 2336–2337.

Muller, E., Barday, Z., Mendelson, M., & Kahn, D. (2012). Renal transplantation between HIV-positive donors and recipients justified. South African Medical Journal, 102(6), 497–498.

Muller, E., Barday, Z., Mendelson, M., Kahn, D., et al. (2015). HIV-positive-to-HIV- positive kidney transplantation—results at 3 to 5 years. New England Journal of Medicine, 372:613–20.

Neuhaus, J., Angus, B., Kowalska, J. D., et al. (2010). Risk of all-cause mortality associated with nonfatal AIDS and serious non-AIDS events among adults infected with HIV. AIDS, 24(5), 697–706.

OPTN Policies and Bylaws. From http:// optn.transplant.hrsa.gov/ policiesandbylaws/policies.asp.

Pais, R. & Benhamou, Y. (2010). Long-term therapy for chronic hepatitis B in HIV co-infected patients. Gastroente´ rologie Clinique et Biologique, 34, 136–41.

Parsa, A., Kao, W. H. L., Xie, D., et al, (2013). APOL1 risk variants, race, and progression of chronic kidney disease. New England Journal of Medicine, 369:2183–96.

Panel on Opportunistic Infections in HIV- Infected Adults and Adolescents.Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents; recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/ contentfiles/lvguidelines/adult oi.pdf. (Accessed September 2015).

Pelletier S. J., Norman S. P., Christensen L. L., et al. (2004). Review of transplantation in HIV patients during the HAART era. Clinical Transplantation, 63–82.

Petrosillo, N., Chinello, P., & Cicalini, S. (2006). Pulmonary hypertension in individuals with HIV infection. AIDS, 20, 2128.

Prevention, C. f. D. C. a. (2013). HIV Surveillance Supplemental Report. Ragni, M. V., Dodson, S. F., Hunt, S. C., et al. (1999). Liver transplantation in a hemophilia patient with acquired immunodeficiency syndrome. Blood, 93, 1113–1114.

Redd A. D., Quinn T. C., Tobian A. A. (2013). Frequency and implications of HIV superinfection. The Lancet Infectious Diseases, 13(7), 622–628.

Reeves-Daniel, A. M., DePalma, J. A., Bleyer, A. J., Rocco, M. V., Murea, M., Adams, P. L., et al. (2011). The APOL1 Gene and Allograft Survival after Transplantation. American Journal of Transplantation, 11(5), 1025–1030.

Richterman, A., Blumberg, E., (2015). The challenges and promise of HIV-infected donors for solid organ transplantation. Current Infectious Disease Reports, 17:1– 8.

Richterman, A., Sawinski, D., Reese, P.P., et al, (2015). An assessment of HIV-infected patients dying in care for deceased organ donation in a United States urban center. American Journal of Transplantation, 15:2105–2116.

Riella, L.V., Sheridan, A.M., (2015). Testing for high-risk APOL1 alleles in potential living kidney donors. American Journal of Kidney Disease, (in press).

Roland, M., Carlson, L., & Stock, P. (2002). Solid organ transplantation in HIV- infected individuals. AIDS Clinical Care, 14(7), 59–63.

Roland, M. E., Adey, D., Carlson, L. L., & Terrault, N. A. (2003a). Kidney and liver transplantation in HIV-infected patients: case presentations and review. AIDS Patient Care STDS, 17(10), 501–507.

Roland, M. E., Lo, B., Braff, J., & Stock, P. G. (2003b). Key clinical, ethical, and policy issues in the evaluation of the safety and effectiveness of solid organ transplantation in HIV-infected patients. Archives of Internal Medicine, 163(15), 1773–1778.

Roland, M. E., & Stock, P. G. (2003c). Review of solid-organ transplantation in HIV- infected patients. Transplantation, 75(4), 425–429.

Sawinski, D., Goldberg, D. S., Blumberg, E., et al. (2015) Beyond the NIH multicenter HIV transplant trial experience: Outcomes of HIV+ liver transplant recipients compared to HCV+ or HIV+/ HCV+ coinfected recipients in the United States. Clinical Infectious Disease, (in Press).

Sherman, K. E., Thomas, D., & Chung, R. T. (2014). Human immunodeficiency virus and liver disease forum 2012. Hepatology, 59(1), 307–317.

Sims, D. B., Uriel, N., Gonza´lez-Costello, J., et al. (2011). Human immunodeficiency virus infection and left ventricular assist devices: a case series. Journal of Heart and Lung Transplantation, 30, 1060–1064.

Soriano, V., Tuma, P., Labarga, P., et al. (2009). Hepatitis B in HIV patients: what is the current treatment and what are the challenges? Journal of HIV Therapy, 14(1), 13–18.

Stock, P. G., Barin, B., Murphy, B., Hanto, D., Diego, J. M., Light, J., et al. (2010). Outcomes of kidney transplantation in HIV-infected recipients. New England Journal of Medicine, 363(21), 2004–2014.

Taege, A. (2013). Organ transplantation and HIV progress or success? A review of current status. Curr Infectious Disease Reports, 15, 67–76.

Tector, A. J., Mangu, R. S., Chestovich, P., et al. (2006). Use of extended criteria livers decreases wait time for liver transplantation without adversity impacting posttransplant survival.

Annals of Surgery, 244, 439–450. Terrault, N. A., Roland, M. E., Schiano, T., Dove, L., Wong, M. T., Poordad, F., et al. (2012). Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection.

Liver Transplantation, 18(6), 716–726. Touzot, M., Pillebout, E., Matignon, M., Tricot, L., Viard, J. P., Rondeau, E., et al. (2010). Renal transplantation in HIV- infected patients: the Paris experience. American Journal of Transplantation, 10(10), 2263–2269.

Uriel, N., Jorde, U. P., Cotarlan, V., et al. (2009). Heart transplantation in human immunodeficiency virus-positive patients. Journal of Heart and Lung Transplant, 28, 667–669.

Uriel, N., Nahumi, N., Colombo, P. C., et al. (2014). Advance heart failure in patients infected with human immunodeficiency virus: is there equal access to care?

Journal of Heart and Lung Transplantation (in press, online). Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2013). Cause- specific life expectancies after 35 years of age for human immunodeficiency syndrome-infected and human immunodeficiency syndrome-negative individuals followed simultaneously in long-term cohort studies, 1984–2008.American Journal of Epidemiology, 177(2), 116–125.

Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2014). Cause- specific mortality among HIV-infected individuals, by CD4 (+) cell count at HAART initiation, compared with HIV-uninfected individuals. AIDS, 28(2), 257–265.

Yoon, S. C., Hurst, F. P., Jindal, R. M., George, S. A., Neff, R. T., Agodoa, L. Y., et al. (2011). Trends in renal transplantation in patients with human immunodeficiency virus infection: an analysis of the United States renal data system. Transplantation, 91(8), 864–868.

Protocol Version 1.3

Amendment #2 Dec **27, 2021**

1. Title:

Research protocol for organ transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.

2. Investigators:

PI: Yorg al-Azzi, MD.

AIs: Vagish Hemmige, MD[3], Victoria Muggia, MD[3], Grace Minamoto, MD[3], Yoram Puius, MD[3] Margaret McCort MD[3,] Sam Sigal MD[4], Enver Akalin MD[2], Maria Ajaimy MD[2], Stuart Greenstein MD[1], Jay Graham MD[1], Milan Kinkhabwala MD[1], Daniel Goldstein[5], Snehal Patel[6]

[1] Montefiore-Einstein Center for Transplantation, Transplant Surgery, Department of Surgery.

[2] Montefiore-Einstein Center for Transplantation, Transplant Nephrology, Department of Medicine.

[3] Montefiore-Einstein Center for Transplantation, Transplant Infectious Diseases, Department of Medicine.

[4] Montefiore-Einstein Center for Transplantation, Transplant Hepatology, Department of Medicine

[5] Center for Advanced Cardiac Therapies, Department of Cardiothoracic Surgery

[6] Center for Advanced Cardiac Therapies, Transplant Cardiology, Department of Medicine

3. Background and purpose:

The advent of effective antiretroviral therapy (ART) in the mid-1990s for treatment of individuals infected with HIV transformed a rapidly fatal disease into a well-controlled chronic illness. Currently, the life expectancy of individuals infected with HIV and receiving ART early in the course of their disease approaches that of individuals without HIV infection (Wada, 2013, 2014). In this era of greater longevity, liver failure, end-stage renal disease, and cardiovascular disease have emerged as important causes of morbidity and mortality in patients with HIV infection (Neuhaus, 2010).

Organ transplantation prolongs survival and improves quality of life for individuals with end-stage organ disease (Matas, 2014; Kim, 2014). Until recently, however, organ transplantation was unavailable to those infected with HIV due to concerns that pharmacologic immunosuppression to prevent organ rejection would hasten the progression from HIV infection to AIDS, leading to increase rates of opportunistic infections, concerns about disease transmission, and reluctance to allocate organs to a

population whose outcome was unpredictable (Blumberg, 2009, 2013a, 2013b; Mgbako, 2013; Taege, 2013).

Nevertheless, a few transplant programs accepted HIV-positive patients on their transplant waiting lists and accumulated data showing kidney or liver transplantation could be done safely in these patients (Roland, 2002, 2003a, 2003b, 2003c; Blumberg, 2009; Stock, 2010; Yoon, 2011; Terrault, 2012). Subsequently, a prospective, multicenter clinical trial of kidney and liver transplantation in 275 patients demonstrated that, among HIV-positive kidney and liver transplant recipients, patient and graft survival rates were acceptable and within the range of outcomes currently achieved among non-infected transplant recipients.

However, the rate of kidney rejection was unexpectedly high, demonstrating that the immune dysregulation resulting from HIV infection, HCV co-infection, and antirejection drugs is complex and incompletely understood. Some of the challenges encountered in that study remain relevant for clinical sites offering organ transplantation to HIV-positive individuals today (e.g., management of drug interactions and toxicities when combining complex medical regimens, management of combined morbidities of two or more active diseases, and the need for ongoing collaboration among medical professionals from different specialties) (Frassetto, 2007, 2014; Locke, 2014). Despite the complexities, this study and others (Ragni, 1999; Frassetto, 2009; Huprikar, 2009; Stock, 2010; Touzot, 2010; Cooper, 2011; Duclos-Vallee, 2011; Reeves-Daniel, 2011; Fox, 2012; Terrault, 2012; Grossi, 2012; Gomez, 2013; Harbell, 2013) demonstrate that kidney and liver transplantation are appropriate in HIV- positive individuals with liver or kidney failure, although gaps in knowledge and many research questions remain. There is much less experience with heart (Calabrese, 2003; Bisleri, 2003; Pelletier, 2004; Uriel, 2009, 2014; Castel, 2011a, 2011b; Durante-Mangoni, 2011 and 2014; Madan 2019) and lung (Mehta, 2000; Humbert,2006; Petrosillo, 2006; Bertani, 2009; Kern, 2014a, 2014b) transplantation in HIV-positive recipients, or mechanical circulatory assistance (Brucato, 2004; Fieno, 2009; Mehmood, 2009; Sims, 2011) as a bridge to transplantation. However, case reports, small case series, and our own institutional experience with four heart transplant recipients with HIV suggest acceptable outcomes are possible with selected patients at experienced centers with the appropriate expertise.

Prior to the passage of the HOPE Act, U.S. law required that all U.S. transplants for HIV-positive recipients utilize organs from HIV-uninfected donors. (See 42 U.S.C. 273(b)(3)(C), 274(b) and 18 U.S.C. 1122, all prior to amendment by the HOPE Act). The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV (hereinafter referred to as ‘‘HIV-positive to HIV-positive transplantation’’) is recognized (Boyarsky, 2011, 2015; Mgbako, 2013; Mascolini, 2014; Kucirka, 2015; Richterman, 2015). It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients (Boyarsky, 2011). The first published experience with HIV-positive to HIV- positive SOT at this time came from Muller et al from the University of Cape Town in South Africa. Initially, Muller et al (2010) reported 100 percent patient and graft survival in a four-patient pilot study. Subsequently, the same group reported an additional 10 HIV-positive to HIV-positive renal transplants (Muller, 2012). All patients were restarted on ART early postoperatively in the immunosuppressive setting of T- cell-depleting induction therapy,

tacrolimus, mycophenolate mofetil, and prednisone. One to 4 years after transplantation, outcomes remained excellent and all patients had undetectable viral loads (Muller, 2012). The cumulative University of Cape Town experience of 27 HIV-positive to HIV-positive transplant procedures was recently summarized in the New England Journal of Medicine (Muller, 2015). The 1- and 5-year death-censored graft survival was 93 and 84 percent, respectively, and 1- and 5-year patient survival was 83 and 74 percent, respectively. Of note, the South African HIV-positive deceased donors were ART-naive, without history of opportunistic infection or proteinuria, and had normal pre-transplant renal biopsies. While renal function has remained normal in the recipients, three have had routine post-transplant renal biopsies demonstrating new changes typical of early HIV-associated nephropathy that were not present in baseline biopsy specimens. The long- term significance of these findings remains unknown and awaits longer follow-up. All patients had undetectable plasma HIV viral loads after transplantation. Graft rejection rates were 8 percent at 1 year and 22 percent at 3 years.

The HOPE Act permits HIV-positive to HIV-positive organ transplantation under IRB-approved research protocols conforming to the Final Human Immunodeficiency Virus (HIV) Organ Policy Equity (HOPE) Act Safeguards and Research Criteria for Transplantation of Organs Infected with HIV, which were developed as directed in the HOPE Act. Patients receiving HIV-positive kidneys from deceased HIV-positive donors in South Africa (Muller, 2015) had survival rates of 84 percent and 74 percent at 1 and 5 years, respectively; however, there is presently no evidence for the safety, efficacy, and effectiveness of HIV-positive to HIV- positive transplantation in North America. The Final Safeguards and Research Criteria are meant to support the acquisition of new clinical knowledge and mechanistic insights about HIV-positive to HIV-positive organ transplantation in the United States. The results of this research will be evaluated by the Secretary of HHS and the OPTN to determine whether and how the OPTN standards for organ transplantation shall be revised to address HIV-positive organ donors.

The research protocol described below was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States. The criteria address the minimum safety and data requirements of clinical research in HIV-positive to HIV-positive transplantation. As mandated by the HOPE Act, the Secretary, together with the OPTN, is charged with reviewing the results of scientific research conducted under these criteria to determine whether the OPTN's standards of quality should be further modified and whether some HIV- positive to HIV-positive transplants should proceed outside the auspices of research conducted under such criteria (see attached the original document).

Montefiore Medical Center and the Montefiore-Einstein Center for Transplantation meet the institutional standards and requirements to carry on a research protocol on HIV-positive to HIV-positive kidney transplantation with a collective experience of over 15 kidney transplants on HIV positive recipients since 2008. In terms of liver transplantation, the physicians of the Montefiore Transplant Center have been involved in the care of 5 liver transplants in HIV positive recipients in the previous 4 years, as of February 2022. Similarly, the physicians of the Montefiore heart transplant program have been involved in the care of 5 cardiac transplants in HIV positive recipients in the previous 4 years, as of February 2022. The Montefiore AIDS Center for Positive Living provides care to over 2500 HIV positive

individuals in the Bronx. Potential transplant candidates, as per protocol, are evaluated by transplant ID clinicians with expertise also in HIV. The Center for Positive Living providers and the Montefiore infectious disease faculty practice follow these patients closely for the first year after transplantation. The majority of these patients have elected to remain at Montefiore for their HIV care. Multidisciplinary transplant protocols include management of HIV recipients and the outcomes of these cases have met the national standards without affecting our program-specific reports (SRTR reports).**As of February 2022, Montefiore Medical Center has performed three kidney transplants under the HOPE protocol, and the abdominal transplant and infectious diseases faculty meet regularly to discuss organ offers made under the study.**

4. Objectives and outcome measures

Montefiore's research in HIV-positive to HIV-positive transplantation will address questions related to HIV superinfection; incidence and severity of opportunistic infections (including transmission of occult OIs from donor to recipient); immunologic mechanisms contributing to the increased rate of kidney rejection observed in HIV-positive recipients and quality of life for recipients of HIV- positive to HIV-positive transplantation. To ensure that all nationwide studies of HIV-positive to HIV- positive transplantation can contribute to evaluation of the safety of the procedure, the following key donor and recipient characteristics and outcome measures must be incorporated into the design of all clinical trials of HIV- positive to HIV-positive transplantation.

Wait List Candidates

- HIV status
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Removal from wait list (death or other reason)
- Time on wait list

Donors (all)

- Type (deceased)*
- HIV status (HIV-positive new diagnosis, HIV-positive known diagnosis)
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load

- ART resistance
- Pre-transplant donor allograft biopsy

*Living Donors will be excluded from this protocol

Transplant Recipients

- Rejection rate (annual up to 5 years)
- New Opportunistic Infections
- Failure to suppress viral replication (persistent viremia)
- HIV-associated organ failure
- Malignancy
- Graft failure
- Acquisition of resistant viral strain
- Death

5. Methods:

- Donor Eligibility

Montefiore Einstein Center for Transplantation has decided to exclude living donors from this research protocol. HIV- positive deceased donors of organs for transplantation into an HIV-positive recipient must fulfill applicable clinical criteria in place for HIV-uninfected organ donors.

One concern about the consequences of transplanting an organ from an HIV-positive donor to a HIV-positive recipient is the acquisition of a resistant strain with subsequent poor viral control and decreased responsiveness to antiretroviral therapy (ART). Adverse consequences could range from transient loss of viral suppression, necessitating a change in antiretroviral regimen to a worst-case scenario in which the new infecting strain of HIV is unresponsive to available antiretroviral treatment and subsequently the recipient develops progression of their HIV infection and the development of opportunistic infections or HIV related malignancies (Redd, 2013).

Information relevant to understanding the known or potential extent of antiretroviral resistance in the strain of HIV infecting the organ donor may be incomplete for many reasons:

- There may be inadequate virus in donor specimens for antiretroviral resistance testing;
- If the specimen is adequate, there may not be enough time within the decision-making evaluation window to fully assess antiretroviral resistance before the clinical deterioration of the donor, organ procurement, and implantation;
- The donor's history of antiretroviral treatment may be unknown or incomplete;
- Results from prior antiretroviral resistance testing may be unavailable.

These issues might be especially challenging when considering organ donation from deceased donors whose HIV infection is first identified during donor evaluation. As of 2011, an estimated 1 in 6 U.S. adults living with HIV infection were undiagnosed (Prevention, 2013) and an estimated 16 percent of newly diagnosed, untreated individuals were infected with virus resistant to at least one class of antiretroviral drug (Kim, 2013; Megens, 2013).

It is anticipated that the risk of transmission of resistant HIV strains may be lower from deceased donors with a well-documented history of adherence to antiretroviral treatment, undetectable viral load at demise. However, to impose this as an eligibility criterion would limit the pool of suitable donors. In addition, it will not be possible in all cases to obtain viral loads and/or antiretroviral resistance profiles in the time available for donor evaluation. Transplant teams evaluating a donor must review all available donor and recipient information available and if necessary, be able to propose an antiretroviral regimen that will be safe, tolerable, and effective for the recipient after transplantation as the regimen in place in the recipient before transplantation. If there is doubt about the ability to suppress viral replication after transplantation, the transplant must not move forward. Fortunately, with the development of newer antivirals, including integrase strand transfer inhibitors (INSTI), acquisition of resistance is much less likely. In the HOPE pilot study involving the care of 75 renal transplants, there were no cases of donor derived drug resistance. (Durand, et al Am J transplantation 2021a;21:1754-1764)

Donors co-infected with hepatitis are not excluded from HIV-positive to HIV- positive transplant; however, careful consideration must be given when evaluating a donor co-infected with HBV and/or HCV (Terrault, 2012; Miro, 2012; Moreno, 2012; Sherman, 2014; Chen, 2014). Although HCV therapeutic strategies are rapidly evolving (Liang, 2013), it is possible that mixed genotype HCV infections may influence post- transplant treatment of HCV in the recipient. Prior antiretroviral treatment of the donor and/or recipient with agents active against HBV (i.e., lamivudine, emtricitabine, adefovir, and tenofovir) has the potential for inducing or uncovering archived HBV drug resistance in the recipient (Dieterich, 2007; Soriano, 2009; Pais, 2010).

HIV-positive transplant candidates who are listed for a transplant in the context of a research study of HIV- positive to HIV-positive transplantation must have the same opportunity as other transplant candidates to receive an organ from an HIV-negative donor, should one become available for them.

1.1 HIV-Positive Donor Eligibility Criteria

The HIV-specific donor eligibility criterion for deceased donors is listed (Table 1). Co-infection with HBV and/or HCV is not an exclusion criterion.

1.1.1 HIV-Positive Deceased Donors

When evaluating HIV-positive deceased donors, it is understood that limited medical history may be available and/or known at the time of the donor evaluation. The OPO must make reasonable efforts to obtain prior medical history so that a transplant center team may best determine the suitability of the potential donor based on the information available. A complete history of antiretroviral regimens and a history of viral load tests and resistance testing are especially valuable for evaluating the likelihood of donor HIV resistance to antiretroviral regimens. A history of OIs or cancers is also of high importance,

due to the increased risk for both attributable to HIV, and the additional difficulty of treating some infections and neoplasms in a post-transplant setting. It is possible that deceased donors with lower CD4+ T-cell counts may pose an increased risk of harboring transmissible diseases (e.g., opportunistic infections or neoplasms) that may be difficult to detect during organ harvest and transplantation; teams conducting transplants under the HOPE Act are urged to assess donors with low CD4+ T-cell counts (e.g., <200/mL) with special caution and to promptly inform IRBs and the PI of known or suspected disease transmission events.

Minimum eligibility criteria for all HIV-positive deceased donors:

i. Documented HIV infection using an FDA-licensed, approved, or cleared test device(s).

ii. No evidence of invasive opportunistic complications of HIV infection.

iii. Pre-implant donor organ biopsy to be stored, at a minimum, for the duration of the study (or at least 5 years); additional specimens may be obtained to support specific research goals.

Additional eligibility criteria for HIV- positive deceased donors with a known history of HIV and prior treatment with ART:

i. The study team must describe the anticipated post-transplant antiretroviral regimen(s) to be prescribed for the recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Recipient Eligibility

A key consideration when evaluating potential HIV-positive transplant candidates is the ability to suppress HIV viral load post-transplant. This includes a thorough assessment by the transplant team of the candidate recipient's prescribed antiretroviral medications, HIV RNA levels while on medications, adherence to HIV treatment, and any available HIV resistance testing; a similar evaluation of the donor must also be carried out. A transplant should only take place if, after evaluating both recipient and donor, the team is confident they can define a post- transplant antiretroviral regimen that will be safe, tolerable, and effective. If there is any doubt on the part of the transplant team about the ability to suppress viral replication post- transplant, the transplant should not move forward. Concerns about transmitted drug resistance must be included in the recipient informed consent process for the research study. At the time of an organ offer, the recipient informed consent must address the transplant team's assessment of risk specific to the organ they are being offered.

2.1 HIV-Positive Recipient Eligibility Criteria

The following HIV-specific criteria must be met when screening for an HIV- positive to HIV-positive organ transplant (also refer to Table 1):

i. Last CD4+ T-cell count >200/mL (kidney, heart, lung). Patients with end stage liver disease may be lymphopenic due to cirrhosis and splenic sequestration, so a cutoff of 100 will be applied to them if

there is no history of opportunistic infection or malignancy. Potential liver transplant patients with a history of opportunistic infection or malignancy must have a CD4 positive T-cell count >200/uL unless the transplant team feels that an effective prophylactic strategy would make transplant safe in the CD4 100-200 range.

ii. HIV RNA less than 50 copies/mL and on a stable antiretroviral regimen.*+

iii. No evidence of active opportunistic complications of HIV infection.

iv. No history of primary CNS lymphoma or PML.

v. Concurrence by the study team that based on medical history and ART, viral suppression can be achieved in the recipient post-transplant.

*Patients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen for the patient once organ function is restored after transplantation.

+Those patients on a protease based regimen will be evaluated prior to transplant by our HIV/Transplant infectious disease service to attempt transition to INSTI regimen

+ We enroll 100 HIV positive patients who are eligible for solid organ transplant.

TABLE 1—SUMMARY OF DONOR AND RECIPIENT ELIGIBILITY CRITERIA FOR HIV-POSITIVE SERO-CONCORDANT ORGAN TRANSPLANT PAIRS UNDER THE HOPE ACT

HIV-Related variables	Deceased donor	Living donor	HIV-Positive recipient
Current CD4+ T-cell count (T lymphocytes/μL)	No requirement	≥500 for 6 months prior to organ donation.	If no history of OI • ≥200 (kidney, heart) • ≥100 (liver) If history of OI • ≥200 Last CD4+ T-cell count Prior to enrollment
Plasma HIV RNA viral load (copies/mL).	No requirement**	<50	<50*
Opportunistic infection	No invasive OI	No invasive OI	Currently, • No active OI Historically, no • CNS lymphoma • PML

* Organ recipients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen to be used by the recipient once organ function is restored after transplantation.

** In deceased donors with a known history of HIV infection and prior treatment with ART, the study team must describe the anticipated post- transplant antiretroviral regimen(s) to be used by the organ recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Transplant process and post-transplant considerations

Organ recovery, transplant procedure, handling and storage of donor organs/tissues, as well as management of solid organ transplant recipients are well described in our policies and procedures section (intranet), including the multidisciplinary management and immunosuppression protocols of HIV-positive recipients.

Waitlist acceptance criteria: Once an IRB- approved research protocol in HIV- positive to HIV-positive transplantation is finalized, the transplant center will inform the OPTN of additional organ-specific acceptance criteria for organs from HIV-positive donors. Those HIV-positive solid organ transplant candidates on the wait list willing to accept an HIV- positive organ must specify any additional acceptance criteria to the OPO.

Consent process and Independent HIV-Positive Recipient Advocate: One of Montefiore's senior transplant coordinators is actively collaborating with an NIH initiative to train and credential independent advocates for protecting and promoting the rights and interests of the HIV-positive recipient (or prospective recipient). The independent advocate for the HIV- positive recipient will:

i. Promote and protect the interests of the HIV-positive recipient (including with respect to having access to a suitable HIV-negative organ if it becomes available) and take steps to ensure that the HIV-positive recipient's decision is informed and free from coercion.

ii. Review whether the potential HIV-positive recipient has received information regarding the results of SOT in general and transplantation in HIV- positive recipients in particular and the unknown risks associated with HIV- positive to HIV-positive transplant.

iii. Demonstrate knowledge of HIV infection and transplantation.

Attached: -Informed consent for research

Post-transplant care

After discharge, patients are seen by the multidisciplinary transplant team according to the below schedule. During weekly morbidity and mortality meeting the post-transplant team meets and reviews the transplant recipients seen during the week to discuss patients, complications (infections, rejection, bleeding, readmission, re-surgery, malignancy, patient death, and graft loss), and allograft function. These events are stored in the transplant computerized database and communicated to the OPTN in accordance with regulations. Recipients are also assessed and contacted in respect to QAPI initiatives to further improve patient care initiatives.

Adult Transplant Patients are generally evaluated according to the following schedule after abdominal transplantation:

First month: twice a week labs (kidney) or once a week labs (liver), once a week clinic visit

2-3 months: once a week labs and every other week clinic visit

4-5 months: every other week labs and one month clinic visit

6-12 months: once a month labs and every other month clinic visit

Second year: every 2 months labs and 4 months clinic visit

3-5 years every 3 month labs and 6 months clinic visit

> 5 years every 3 months labs and once a year clinic visit

During each clinical visit, bloods and vital signs are obtained, a physical exam is performed and medications are reviewed with each patient. Medical and surgical problems will be addressed on an ongoing basis and appropriate referrals are made to specialists. Pharmacist, nutritional and social service support is available at each clinic. The Transplant Patient will receive specific instructions from the Transplant Multi-Disciplinary Team as to their follow-up care.

Additional transplant allograft biopsy will be performed either as clinically indicated (kidney, liver) or as per the standard post-transplant protocol (heart).

All patients will be assigned to one respective transplant clinician for outpatient follow-up. Patients will be seen at least once within a month after transplantation by a transplant surgeon.

In order to promptly detect viral breakthrough or possibility of viral superinfection, HIV viral loads should be performed at baseline and four weeks after transplantation, every three months for the first year post transplantation, and every 4-6 months in patients who have achieved sustained viral suppression. If viral breakthrough is detected on two consecutive assays, genotypic resistance studies will be sent. T cell subsets will be monitored every three months for the first year, and every 4-6 months in stable patient. A Montefiore transplant infectious disease provider will see the patient at the time of transplant, one month after transplantation and every three months for the first year post transplant. After the first year, should they wish, stable transplant patients may return to their outside provider. The Montefiore transplant ID attending will maintain close contact with the primary care provider, and also see the recipient twice a year for the duration of the study. To assist patients with urgent infectious disease issues the Montefiore AIDS center provides walk in services Monday through Friday, and 24 hour service coverage for established patients.

Transplant physicians will give 24 hour coverage service for post-transplant patients with any questions and complaints.

6 – Potential risks

Risk considerations and pertinent safeguards to potential recipients have been described in detail above under donor and recipient eligibility sections.

Prevention of Inadvertent Transmission of HIV

Although the use of HIV-positive organs may help alleviate transplant shortages and reduce patient waiting list times, there also are patient safety concerns to consider. Prevention or management of inadvertent transmission of HIV or exposure of an HIV-negative recipient to organs or tissues from an HIV-positive donor due to identification error is paramount (Ison, 2009, 2011a, 2011b). The transplant community, with regulatory oversight at multiple levels, has been able to achieve a high level of safety through routine procedures and clinical practice. The precautions taken with ABO compatible donor-recipient pairs and HCV-infected donor organs in HCV- infected recipients (Morales, 2010; Kucirka, 2010; Mandal, 2000; Tector, 2006) are existing models. However, vulnerabilities still exist, and mishaps still occur. For instance, the risks of error during manual transcription of information are well documented.

Montefiore Medical Center and the transplant center already count with an institutional biohazard plan for handling of HCV-positive organs and tissue disposal for HCV-positive recipients and ABO compatibility verification policies. HIV-positive status of donor organ, donor tissues and intended recipient will be added to the organ-to-recipient verification form.

7- Confidentiality and safeguards to minimize risks.

The research protocol was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States (attached document and informed consent).

8- Study benefits

The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV. It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients. Preliminary data nationally suggest earlier access to transplantation in patients with HIV who accept organs from donors with HIV (Durand 2021a; Durand 2021b).

9- Data Safety Monitoring Board

A DSMB comprised of three physicians (not involved in the study) will continue to be assembled every 12 months to review safety data.

9-References

Bertani, A., Grossi, P., Vitulo, P., et al. (2009). Successful lung transplantation in an HIV- and HBV-positive patient with cystic fibrosis. American Journal of Transplantation, 9, 2190–2196.

Bisleri, G., Morgan, J. A., Deng, M. C., et al. (2003). Should HIV-positive recipients undergo heart transplantation? Journal of Thoracic and Cardiovascular Surgery, 126, 1639–1640.

Blumberg, E. A., & Stock, P. (2009). Solid organ transplantation in the HIV-infected patient. American Journal of Transplantation, 9 Suppl 4, S131–135.

Blumberg, E. A., & Rogers, C. C. (2013a). Human immunodeficiency virus in solid organ transplantation. American Journal of Transplantation, 13 Suppl 4, 169–178.

Blumberg, E. A., Ison, M. G., Pruett, T. L., & Segev, D. L. (2013b). Optimal testing of the live organ donor for blood-borne viral pathogens: the report of a consensus conference. American Journal of Transplantation, 13(6), 1405–1415.

Boyarsky, B. J., Hall, E. C., Singer, A. L., Montgomery, R. A., Gebo, K. A., & Segev,D. L. (2011). Estimating the potential pool of HIV-infected deceased organ donors in the United States. American Journal of Transplantation, 11(6), 1209–1217.

Boyarsky, B. J., Durand C. M., Palella F. J., Segev D.L., (2015). Challenges and clinical decision-making in HIV-to-HIV transplantation: insights from the HIV literature. American Journal of Transplantation, 15:2023–2030.

Brucato, A., Colombo, T., Bonacina, E., et al. (2004). Fulminant myocarditis during HIV seroconversion: recovery with temporary left ventricular mechanical assistance. Italian Heart Journal, 5, 228–231.

Calabrese, L. H., Albrecht, M., Young, J., et al. (2003). Successful cardiac transplantation in an HIV–1-infected patient with advanced disease. New England Journal of Medicine, 348, 2323–2328.

Castel, M. A., Pe´rez-Villa, F., Roig, E., & Miro´ , J. M. (2011a). Heart transplantation in an HIV–1-infected patient with ischemic cardiomyopathy and severe pulmonary hypertension. Revista Espan˜ ola de Cardiologı´a, 64, 1066–1067.

Castel, M. A., Pe´rez-Villa, F., & Miro´ , J. M. (2011b). Heart transplantation in HIV- infected patients: more cases in Europe. The Journal of Heart and Lung Transplantation, 30, 1418.

Chen, J. Y., Feeney, E. R., & Chung, R. T. (2014). HCV and HIV co-infection: mechanisms and management. Nature Reviews: Gastroenterology & Hepatology, 11(6), 362–371.

Cooper, C., Kanters, S., Klein, M., Chaudhury, P., Marotta, P., Wong, P., et al. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with synthetic cohort. AIDS, 25(6), 777–786.

Dieterich, D.T. (2007). Special considerations and treatment of patients with HBV–HIV coinfection. Antiviral Therapy, 12, H43– H51.

Duclos-Vallee, J. C., Falissard, B., & Samuel, D. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with a synthetic cohort. AIDS, 25(13), 1675– 1676.

Durand, C et al. A prospective multicenter pilot study of HIV-positive deceased donor to HIV-positive recipient kidney transplantation: HOPE in action. American Journal of Transplantation. 2021a;21:p1754-1764.

Durand, C *et al*. HOPE in action: A prospective multicenter pilot study of liver transplantation from donors with HIV to recipients with HIV. *Am J Transplant*. 2021b Nov 6. doi: 10.1111/ajt.16886. Online ahead of print.

Durante-Mangoni, E., Maiello, C., & Sbreglia, C. (2011). A European first: successful heart transplant in a human immunodeficiency virus-positive recipient. The Journal of Heart and Lung Transplantation, 30, 845.

Durante-Mangoni, E., Maiello, C., Limongelli, G., et al. (2014). Management of immunosuppression and antiretroviral treatment before and after heart transplant for HIV-associated dilated cardiomyopathy. International Journal of Immunopathology and Pharmacology, 27(1), 113–120.

Fieno, D. S., Czer, L. S., Schwarz, E. R., et al. (2009). Left ventricular assist device placement in a patient with end-stage heart failure and human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 919–920.

Fox, A. N., Vagefi, P. A., & Stock, P. G. (2012). Liver transplantation in HIV patients. Seminars in Liver Disease, 32(2), 177–185.

Frassetto, L. A., Browne, M., Cheng, A., et al. (2007). Immunosuppressant pharmacokinetics and dosing modifications in HIV–1 Infected liver and kidney transplant recipients. American Journal of Transplantation, 7(12), 2816–2820.

Frassetto, L. A., Tan-Tam, C., & Stock, P. G. (2009). Renal transplantation in patients with HIV. Nature Review: Nephrology, 5(10), 582–589.

Frassetto, L. A., Tan-Tam, C. C., Barin, B., Browne, M., Wolfe, A. R., Stock, P. G., et al. (2014). Best Single Time Point Correlations with AUC for Cyclosporine and Tacrolimus in HIV-Infected Kidney and Liver Transplant Recipients.Transplantation, 97(6), 701–707.

Freedman, B.I. (2013). APOL1 and nephropathy progression in populations of African ancestry. Seminars in Nephrology, 33(5):425–432.

Freedman, B.I., Julian, B. A., Pastan, S. O. et al. (2015). Apolipoprotein L1 gene variants in deceased organ donors are associated with renal allograft failure. American Journal of Transplantation, 15:1615–1622.

Genovese, G., Friedman, D. J., Ross, M. D., Lecordier, L., Uzureau, P., Freedman, B. I., et al. (2010). Association of trypanolytic APOL1 variants with kidney disease in African Americans. Science, 329(5993), 841–845.

Gomez, V., Fernandez, A., Galeano, C., Oliva, J., Diez, V., Bueno, C., et al. (2013). Renal transplantation in HIV-infected patients: experience at a tertiary hospital in Spain and review of the literature. Transplant Proceedings, 45(3), 1255–1259.

Grossi, P. A. (2012). Update in HIV infection in organ transplantation. Current Opinion Organ Transplantation, 17(6), 586–593.

Harbell, J., Terrault, N. A., & Stock, P. (2013). Solid organ transplants in HIV-infected patients. Current HIV/AIDS Reports, 10(3), 217–225.

Humbert, M., Sitbon, O., Chaouat A., et al. (2006). Pulmonary arterial hypertension in France: results from a national registry. American Journal of Respiratory and Critical Care Medicine, 173, 1023.

Huprikar, S. (2009). Solid organ transplantation in HIV-infected individuals: an update. Reviews in Medical Virology, 19(6), 317–323.

Ison, M. G., Hager, J., Blumberg, E., Burdick, J., Carney, K., Cutler, J., et al. (2009).Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS Disease Transmission Advisory Committee. American Journal of Transplantation, 9(8), 1929–1935.

Ison, M. G., Llata, E., Conover, C. S., Friedewald, J. J., Gerber, S. I., Grigoryan, A., et al. (2011a). Transmission of human immunodeficiency virus and hepatitis C virus from an organ donor to four transplant recipients. American Journal of Transplantation, 11(6), 1218–1225.

Ison, M. G., & Nalesnik, M. A. (2011b). An update on donor-derived disease transmission in organ transplantation. American Journal of Transplantation, 11(6), 1123–1130.

Kaplan, J. E., Masur, H., Holmes, K.K., et al. (1995a). USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: introduction. USPHS/IDSA Prevention of Opportunistic Infections Working Group. Clinical Infectious Diseases, 21 Suppl 1:S1–11. Available at http:// www.ncbi.nlm.nih.gov/pubmed/ 8547495.

Kaplan, J. E., Masur, H., Jaffe, H.W., Holmes, K.K. (1995b). Reducing the impact of opportunistic infections in patients with HIV infection. New guidelines. Journal of the American Medical Association, 274(4):347–348. Available at http:// www.ncbi.nlm.nih.gov/pubmed/7609267.

Kern, R. M., Seethamraju, H., Blanc, P. D., et al. (2014a). The feasibility of lung transplantation in HIV seropositive patients. Annals of the American Thoracic Society. 2014 Jul;11(6):882-9.

Kern, R., Seethamraju, H., Blanc, P., Sinha, N., Loebe, M., Golden, J., et al. (2014b). Lung Transplantation in HIV Seropositive Patients. Chest, 145(3 Suppl), 642A.

Kim, D., Ziebell, R., Sadulvala, N., Kline, R., Ocfemia, C., Prejean, J., et al. (2013).Trends in Transmitted Drug Resistance Associated Mutations: 10 HIV Surveillance Areas, US, 2001–2010.

Paper presented at the 20th Conference on Retroviruses and Opportunistic Infections. Kim, W. R., Smith, J. M., Skeans, M. A., et al. (2014). OPTN/SRTR 2012 Annual Data Report: Liver. American Journal of Transplantation, 1, 69–96.

Kucirka, L. M., Singer, A. L., Ross, R. L., et al. (2010). Underutilization of hepatitis C-positive kidneys for hepatitis C- positive recipients. American Journal of Transplantation, 10(5), 1238–1246.

Kucirka, L.M., Bowring, M. G., Massie, A. B., et al, (2015) Landscape of deceased donors labeled increased risk for disease transmission under new guidelines. American Journal of Transplantation. Dec;15(12):3215-23.

Liang, T. J., & Ghany, M. G. (2013). Current and future therapies for hepatitis C virus infection. New England Journal of Medicine, 368(20), 1907–1917.

Locke, J. E., James, N. T., Mannon, R. B.,Mehta, S. G., Pappas, P. G., Baddley, J. W., et al. (2014). Immunosuppression Regimen and the Risk of Acute Rejection in HIV-Infected Kidney Transplant Recipients. Transplantation, 97(4), 446–450.

Locke, J. E., Reed R. D., Mehta S. G., et al. (2015a). Center-level experience and kidney transplant outcomes in HIV- infected recipients. American Journal of Transplantation, 15:2096–2104.

Locke, J. E., Mehta, S., Reed, R. D., et al. (2015b). A national study of outcomes among HIV-infected kidney transplant recipients. Journal of the American Society of Nephrology, 26:1–8.

Madan, S., Patel, S. P., Saeed,O., et al. (2019). Outcomes of heart transplantation in patients with human immunodeficiency virus. Am J Transplant. 2019 May;19(5):1529-1535.

Mandal, A. K., Kraus, E.S., Samaniego, M., et al. (2000). Shorter waiting times for hepatitis C virus seropositive recipients of cadaveric renal allografts from hepatitis C virus seropositive donors.Clinical Transplantation, 14, 391–396.

Mascolini, M. (2014). Four to Five HIV+ Dying in Care Yearly in Philadelphia Are Potential Organ Donors. 54th Interscience Conference on Antimicrobial Agents and Chemotherapy: Abstract H–1199a.Presented September 7, 2014.

Matas, A. J., Smith, J. M., Skeans, M. A., etal. (2014) OPTN/SRTR 2012 Annual Data Report: Kidney. American Journal of Transplantation, 1, 11–44.

Megens, S., & Laethem, K. V. (2013). HIV–1 genetic variation and drug resistance development. Expert Review of Anti- Infective Therapy, 11(11), 1159–1178.

Mehmood, S., Blais, D., Martin S., & Sai- Sudhakar, C. (2009). Heartmate XVE destination therapy for end-stage heart failure in a patient with human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 909–910.

Mehta, N. J., Khan, I. A., Mehta, R. N., et al. (2000). HIV-related pulmonary hypertension: analytic review of 131 cases. Chest, 118, 1133.

Mgbako, O., Glazier, A., Blumberg, E., & Reese, P. P. (2013). Allowing HIV- positive organ donation: ethical, legal and operational considerations. American Journal of Transplantation, 13(7), 1636–1642.

Miro, J. M., Montejo, M., Castells, L., Rafecas, A., Moreno, S., Aguero, F., et al. (2012). Outcome of HCV/HIV-coinfected liver transplant recipients: a prospective and multicenter cohort study. American Journal of Transplantation, 12(7), 1866–1876.

Miro, J. M., Stock, P., Teicher, E., et al, (2015). Outcome and management of HCV/HIV coinfection pre- and post-liver transplantation. A 205 update. Journal of Hepatology, 62:701–711.

Morales, J. M., Campistol, J. M., Dominguez- Gil, B., Andres, A., Esforzado, N., Oppenheimer, F., et al. (2010). Long-term experience with kidney transplantation from hepatitis C-positive donors into hepatitis C-positive recipients. American Journal of Transplantation, 10(11), 2453–2462.

Moreno, A., Cervera, C., Fortun, J., et al. (2012). Epidemiology and outcome of infections in human immunodeficiency virus/hepatitis C virus-coinfected liver transplant recipients: a FIPSE/GESIDA prospective cohort study. Liver Transplantation, 18, 70–81.

Muller, E., Kahn, D., & Mendelson, M. (2010). Renal transplantation between HIV- positive donors and recipients. New England Journal of Medicine, 362(24), 2336–2337.

Muller, E., Barday, Z., Mendelson, M., & Kahn, D. (2012). Renal transplantation between HIV-positive donors and recipients justified. South African Medical Journal, 102(6), 497–498.

Muller, E., Barday, Z., Mendelson, M., Kahn, D., et al. (2015). HIV-positive-to-HIV- positive kidney transplantation—results at 3 to 5 years. New England Journal of Medicine, 372:613–20.

Neuhaus, J., Angus, B., Kowalska, J. D., et al. (2010). Risk of all-cause mortality associated with nonfatal AIDS and serious non-AIDS events among adults infected with HIV. AIDS, 24(5), 697–706.

OPTN Policies and Bylaws. From http:// optn.transplant.hrsa.gov/ policiesandbylaws/policies.asp.

Pais, R. & Benhamou, Y. (2010). Long-term therapy for chronic hepatitis B in HIV co-infected patients. Gastroente´ rologie Clinique et Biologique, 34, 136–41.

Parsa, A., Kao, W. H. L., Xie, D., et al, (2013). APOL1 risk variants, race, and progression of chronic kidney disease. New England Journal of Medicine, 369:2183–96.

Panel on Opportunistic Infections in HIV- Infected Adults and Adolescents.Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents; recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/ contentfiles/lvguidelines/adult□oi.pdf. (Accessed September 2015).

Pelletier S. J., Norman S. P., Christensen L. L., et al. (2004). Review of transplantation in HIV patients during the HAART era. Clinical Transplantation, 63–82.

Petrosillo, N., Chinello, P., & Cicalini, S. (2006). Pulmonary hypertension in individuals with HIV infection. AIDS, 20, 2128.

Prevention, C. f. D. C. a. (2013). HIV Surveillance Supplemental Report. Ragni, M. V., Dodson, S. F., Hunt, S. C., et al. (1999). Liver transplantation in a hemophilia patient with acquired immunodeficiency syndrome. Blood, 93, 1113–1114.

Redd A. D., Quinn T. C., Tobian A. A. (2013). Frequency and implications of HIV superinfection. The Lancet Infectious Diseases, 13(7), 622–628.

Reeves-Daniel, A. M., DePalma, J. A., Bleyer, A. J., Rocco, M. V., Murea, M., Adams, P. L., et al. (2011). The APOL1 Gene and Allograft Survival after Transplantation. American Journal of Transplantation, 11(5), 1025–1030.

Richterman, A., Blumberg, E., (2015). The challenges and promise of HIV-infected donors for solid organ transplantation. Current Infectious Disease Reports, 17:1– 8.

Richterman, A., Sawinski, D., Reese, P.P., et al, (2015). An assessment of HIV-infected patients dying in care for deceased organ donation in a United States urban center. American Journal of Transplantation, 15:2105–2116.

Riella, L.V., Sheridan, A.M., (2015). Testing for high-risk APOL1 alleles in potential living kidney donors. American Journal of Kidney Disease. Sep;66(3):396-401.

Roland, M., Carlson, L., & Stock, P. (2002). Solid organ transplantation in HIV- infected individuals. AIDS Clinical Care, 14(7), 59–63.

Roland, M. E., Adey, D., Carlson, L. L., & Terrault, N. A. (2003a). Kidney and liver transplantation in HIV-infected patients: case presentations and review. AIDS Patient Care STDS, 17(10), 501–507.

Roland, M. E., Lo, B., Braff, J., & Stock, P. G. (2003b). Key clinical, ethical, and policy issues in the evaluation of the safety and effectiveness of solid organ transplantation in HIV-infected patients. Archives of Internal Medicine, 163(15), 1773–1778.

Roland, M. E., & Stock, P. G. (2003c). Review of solid-organ transplantation in HIV- infected patients. Transplantation, 75(4), 425–429.

Sawinski, D., Goldberg, D. S., Blumberg, E., et al. (2015) Beyond the NIH multicenter HIV transplant trial experience: Outcomes of HIV+ liver transplant recipients compared to HCV+ or HIV+/ HCV+ coinfected recipients in the United States. Clinical Infectious Disease. Oct 1;61(7):1054-62.

Sherman, K. E., Thomas, D., & Chung, R. T. (2014). Human immunodeficiency virus and liver disease forum 2012. Hepatology, 59(1), 307–317.

Sims, D. B., Uriel, N., Gonza´lez-Costello, J., et al. (2011). Human immunodeficiency virus infection and left ventricular assist devices: a case series. Journal of Heart and Lung Transplantation, 30, 1060–1064.

Soriano, V., Tuma, P., Labarga, P., et al. (2009). Hepatitis B in HIV patients: what is the current treatment and what are the challenges? Journal of HIV Therapy, 14(1), 13–18.

Stock, P. G., Barin, B., Murphy, B., Hanto, D., Diego, J. M., Light, J., et al. (2010). Outcomes of kidney transplantation in HIV-infected recipients. New England Journal of Medicine, 363(21), 2004–2014.

Taege, A. (2013). Organ transplantation and HIV progress or success? A review of current status. Curr Infectious Disease Reports, 15, 67–76.

Tector, A. J., Mangu, R. S., Chestovich, P., et al. (2006). Use of extended criteria livers decreases wait time for liver transplantation without adversity impacting posttransplant survival.

Annals of Surgery, 244, 439–450. Terrault, N. A., Roland, M. E., Schiano, T., Dove, L., Wong, M. T., Poordad, F., et al. (2012). Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection.Liver Transplantation, 18(6), 716–726.

Touzot, M., Pillebout, E., Matignon, M., Tricot, L., Viard, J. P., Rondeau, E., et al. (2010). Renal transplantation in HIV- infected patients: the Paris experience. American Journal of Transplantation, 10(10), 2263–2269.

Uriel, N., Jorde, U. P., Cotarlan, V., et al. (2009). Heart transplantation in human immunodeficiency virus-positive patients. Journal of Heart and Lung Transplant, 28, 667–669.

Uriel, N., Nahumi, N., Colombo, P. C., et al. (2014). Advance heart failure in patients infected with human immunodeficiency virus: is there equal access to care?Journal of Heart and Lung Transplantation. 2014 Sep;33(9):924-30.

Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2013). Cause- specific life expectancies after 35 years of age for human immunodeficiency syndrome-infected and human immunodeficiency syndrome-negative individuals followed simultaneously in long-term cohort studies, 1984–2008.American Journal of Epidemiology, 177(2), 116–125.

Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2014). Cause- specific mortality among HIV-infected individuals, by CD4 (+) cell count at HAART initiation, compared with HIV-uninfected individuals. AIDS, 28(2), 257–265.

Yoon, S. C., Hurst, F. P., Jindal, R. M., George, S. A., Neff, R. T., Agodoa, L. Y., et al. (2011). Trends in renal transplantation in patients with human immunodeficiency virus infection: an analysis of the United States renal data system. Transplantation, 91(8), 864–868.

Protocol Version 1.3

Amendment #2 Dec **27, 2021**

1. Title:

Research protocol for organ transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.

2. Investigators:

PI: Yorg al-Azzi, MD.

AIs: Vagish Hemmige, MD[3], Victoria Muggia, MD[3], Grace Minamoto, MD[3], Yoram Puius, MD[3] Margaret McCort MD[3,] Sam Sigal MD[4], Enver Akalin MD[2], Maria Ajaimy MD[2], Stuart Greenstein MD[1], Jay Graham MD[1], Milan Kinkhabwala MD[1], Daniel Goldstein[5], Snehal Patel[6]

[1] Montefiore-Einstein Center for Transplantation, Transplant Surgery, Department of Surgery.

[2] Montefiore-Einstein Center for Transplantation, Transplant Nephrology, Department of Medicine.

[3] Montefiore-Einstein Center for Transplantation, Transplant Infectious Diseases, Department of Medicine.

[4] Montefiore-Einstein Center for Transplantation, Transplant Hepatology, Department of Medicine

[5] Center for Advanced Cardiac Therapies, Department of Cardiothoracic Surgery

[6] Center for Advanced Cardiac Therapies, Transplant Cardiology, Department of Medicine

3. Background and purpose:

The advent of effective antiretroviral therapy (ART) in the mid-1990s for treatment of individuals infected with HIV transformed a rapidly fatal disease into a well-controlled chronic illness. Currently, the life expectancy of individuals infected with HIV and receiving ART early in the course of their disease approaches that of individuals without HIV infection (Wada, 2013, 2014). In this era of greater longevity, liver failure, end-stage renal disease, and cardiovascular disease have emerged as important causes of morbidity and mortality in patients with HIV infection (Neuhaus, 2010).

Organ transplantation prolongs survival and improves quality of life for individuals with end-stage organ disease (Matas, 2014; Kim, 2014). Until recently, however, organ transplantation was unavailable to those infected with HIV due to concerns that pharmacologic immunosuppression to prevent organ rejection would hasten the progression from HIV infection to AIDS, leading to increase rates of opportunistic infections, concerns about disease transmission, and reluctance to allocate organs to a

population whose outcome was unpredictable (Blumberg, 2009, 2013a, 2013b; Mgbako, 2013; Taege, 2013).

Nevertheless, a few transplant programs accepted HIV-positive patients on their transplant waiting lists and accumulated data showing kidney or liver transplantation could be done safely in these patients (Roland, 2002, 2003a, 2003b, 2003c; Blumberg, 2009; Stock, 2010; Yoon, 2011; Terrault, 2012). Subsequently, a prospective, multicenter clinical trial of kidney and liver transplantation in 275 patients demonstrated that, among HIV-positive kidney and liver transplant recipients, patient and graft survival rates were acceptable and within the range of outcomes currently achieved among non-infected transplant recipients.

However, the rate of kidney rejection was unexpectedly high, demonstrating that the immune dysregulation resulting from HIV infection, HCV co-infection, and antirejection drugs is complex and incompletely understood. Some of the challenges encountered in that study remain relevant for clinical sites offering organ transplantation to HIV-positive individuals today (e.g., management of drug interactions and toxicities when combining complex medical regimens, management of combined morbidities of two or more active diseases, and the need for ongoing collaboration among medical professionals from different specialties) (Frassetto, 2007, 2014; Locke, 2014). Despite the complexities, this study and others (Ragni, 1999; Frassetto, 2009; Huprikar, 2009; Stock, 2010; Touzot, 2010; Cooper, 2011; Duclos-Vallee, 2011; Reeves-Daniel, 2011; Fox, 2012; Terrault, 2012; Grossi, 2012; Gomez, 2013; Harbell, 2013) demonstrate that kidney and liver transplantation are appropriate in HIV- positive individuals with liver or kidney failure, although gaps in knowledge and many research questions remain. There is much less experience with heart (Calabrese, 2003; Bisleri, 2003; Pelletier, 2004; Uriel, 2009, 2014; Castel, 2011a, 2011b; Durante-Mangoni, 2011 and 2014; Madan 2019) and lung (Mehta, 2000; Humbert,2006; Petrosillo, 2006; Bertani, 2009; Kern, 2014a, 2014b) transplantation in HIV-positive recipients, or mechanical circulatory assistance (Brucato, 2004; Fieno, 2009; Mehmood, 2009; Sims, 2011) as a bridge to transplantation. However, case reports, small case series, and our own institutional experience with four heart transplant recipients with HIV suggest acceptable outcomes are possible with selected patients at experienced centers with the appropriate expertise.

Prior to the passage of the HOPE Act, U.S. law required that all U.S. transplants for HIV-positive recipients utilize organs from HIV-uninfected donors. (See 42 U.S.C. 273(b)(3)(C), 274(b) and 18 U.S.C. 1122, all prior to amendment by the HOPE Act). The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV (hereinafter referred to as ‘‘HIV-positive to HIV-positive transplantation’’) is recognized (Boyarsky, 2011, 2015; Mgbako, 2013; Mascolini, 2014; Kucirka, 2015; Richterman, 2015). It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients (Boyarsky, 2011). The first published experience with HIV-positive to HIV- positive SOT at this time came from Muller et al from the University of Cape Town in South Africa. Initially, Muller et al (2010) reported 100 percent patient and graft survival in a four-patient pilot study. Subsequently, the same group reported an additional 10 HIV-positive to HIV-positive renal transplants (Muller, 2012). All patients were restarted on ART early postoperatively in the immunosuppressive setting of T- cell-depleting induction therapy,

tacrolimus, mycophenolate mofetil, and prednisone. One to 4 years after transplantation, outcomes remained excellent and all patients had undetectable viral loads (Muller, 2012). The cumulative University of Cape Town experience of 27 HIV-positive to HIV-positive transplant procedures was recently summarized in the New England Journal of Medicine (Muller, 2015). The 1- and 5-year death-censored graft survival was 93 and 84 percent, respectively, and 1- and 5-year patient survival was 83 and 74 percent, respectively. Of note, the South African HIV-positive deceased donors were ART-naive, without history of opportunistic infection or proteinuria, and had normal pre-transplant renal biopsies. While renal function has remained normal in the recipients, three have had routine post-transplant renal biopsies demonstrating new changes typical of early HIV-associated nephropathy that were not present in baseline biopsy specimens. The long- term significance of these findings remains unknown and awaits longer follow-up. All patients had undetectable plasma HIV viral loads after transplantation. Graft rejection rates were 8 percent at 1 year and 22 percent at 3 years.

The HOPE Act permits HIV-positive to HIV-positive organ transplantation under IRB-approved research protocols conforming to the Final Human Immunodeficiency Virus (HIV) Organ Policy Equity (HOPE) Act Safeguards and Research Criteria for Transplantation of Organs Infected with HIV, which were developed as directed in the HOPE Act. Patients receiving HIV-positive kidneys from deceased HIV-positive donors in South Africa (Muller, 2015) had survival rates of 84 percent and 74 percent at 1 and 5 years, respectively; however, there is presently no evidence for the safety, efficacy, and effectiveness of HIV-positive to HIV- positive transplantation in North America. The Final Safeguards and Research Criteria are meant to support the acquisition of new clinical knowledge and mechanistic insights about HIV-positive to HIV-positive organ transplantation in the United States. The results of this research will be evaluated by the Secretary of HHS and the OPTN to determine whether and how the OPTN standards for organ transplantation shall be revised to address HIV-positive organ donors.

The research protocol described below was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States. The criteria address the minimum safety and data requirements of clinical research in HIV-positive to HIV-positive transplantation. As mandated by the HOPE Act, the Secretary, together with the OPTN, is charged with reviewing the results of scientific research conducted under these criteria to determine whether the OPTN's standards of quality should be further modified and whether some HIV- positive to HIV-positive transplants should proceed outside the auspices of research conducted under such criteria (see attached the original document).

Montefiore Medical Center and the Montefiore-Einstein Center for Transplantation meet the institutional standards and requirements to carry on a research protocol on HIV-positive to HIV-positive kidney transplantation with a collective experience of over 15 kidney transplants on HIV positive recipients since 2008. In terms of liver transplantation, the physicians of the Montefiore Transplant Center have been involved in the care of 5 liver transplants in HIV positive recipients in the previous 4 years, as of February 2022. Similarly, the physicians of the Montefiore heart transplant program have been involved in the care of 5 cardiac transplants in HIV positive recipients in the previous 4 years, as of February 2022. The Montefiore AIDS Center for Positive Living provides care to over 2500 HIV positive

individuals in the Bronx. Potential transplant candidates, as per protocol, are evaluated by transplant ID clinicians with expertise also in HIV. The Center for Positive Living providers and the Montefiore infectious disease faculty practice follow these patients closely for the first year after transplantation. The majority of these patients have elected to remain at Montefiore for their HIV care. Multidisciplinary transplant protocols include management of HIV recipients and the outcomes of these cases have met the national standards without affecting our program-specific reports (SRTR reports).**As of February 2022, Montefiore Medical Center has performed three kidney transplants under the HOPE protocol, and the abdominal transplant and infectious diseases faculty meet regularly to discuss organ offers made under the study.**

4. Objectives and outcome measures

Montefiore's research in HIV-positive to HIV-positive transplantation will address questions related to HIV superinfection; incidence and severity of opportunistic infections (including transmission of occult OIs from donor to recipient); immunologic mechanisms contributing to the increased rate of kidney rejection observed in HIV-positive recipients and quality of life for recipients of HIV- positive to HIV-positive transplantation. To ensure that all nationwide studies of HIV-positive to HIV- positive transplantation can contribute to evaluation of the safety of the procedure, the following key donor and recipient characteristics and outcome measures must be incorporated into the design of all clinical trials of HIV- positive to HIV-positive transplantation.

Wait List Candidates

- HIV status
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Removal from wait list (death or other reason)
- Time on wait list

Donors (all)

- Type (deceased)*
- HIV status (HIV-positive new diagnosis, HIV-positive known diagnosis)
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load

- ART resistance
- Pre-transplant donor allograft biopsy

*Living Donors will be excluded from this protocol

Transplant Recipients

- Rejection rate (annual up to 5 years)
- New Opportunistic Infections
- Failure to suppress viral replication (persistent viremia)
- HIV-associated organ failure
- Malignancy
- Graft failure
- Acquisition of resistant viral strain
- Death

5. Methods:

- Donor Eligibility

Montefiore Einstein Center for Transplantation has decided to exclude living donors from this research protocol. HIV- positive deceased donors of organs for transplantation into an HIV-positive recipient must fulfill applicable clinical criteria in place for HIV-uninfected organ donors.

One concern about the consequences of transplanting an organ from an HIV-positive donor to a HIV-positive recipient is the acquisition of a resistant strain with subsequent poor viral control and decreased responsiveness to antiretroviral therapy (ART). Adverse consequences could range from transient loss of viral suppression, necessitating a change in antiretroviral regimen to a worst-case scenario in which the new infecting strain of HIV is unresponsive to available antiretroviral treatment and subsequently the recipient develops progression of their HIV infection and the development of opportunistic infections or HIV related malignancies (Redd, 2013).

Information relevant to understanding the known or potential extent of antiretroviral resistance in the strain of HIV infecting the organ donor may be incomplete for many reasons:

- There may be inadequate virus in donor specimens for antiretroviral resistance testing;
- If the specimen is adequate, there may not be enough time within the decision-making evaluation window to fully assess antiretroviral resistance before the clinical deterioration of the donor, organ procurement, and implantation;
- The donor's history of antiretroviral treatment may be unknown or incomplete;
- Results from prior antiretroviral resistance testing may be unavailable.

These issues might be especially challenging when considering organ donation from deceased donors whose HIV infection is first identified during donor evaluation. As of 2011, an estimated 1 in 6 U.S. adults living with HIV infection were undiagnosed (Prevention, 2013) and an estimated 16 percent of newly diagnosed, untreated individuals were infected with virus resistant to at least one class of antiretroviral drug (Kim, 2013; Megens, 2013).

It is anticipated that the risk of transmission of resistant HIV strains may be lower from deceased donors with a well-documented history of adherence to antiretroviral treatment, undetectable viral load at demise. However, to impose this as an eligibility criterion would limit the pool of suitable donors. In addition, it will not be possible in all cases to obtain viral loads and/or antiretroviral resistance profiles in the time available for donor evaluation. Transplant teams evaluating a donor must review all available donor and recipient information available and if necessary, be able to propose an antiretroviral regimen that will be safe, tolerable, and effective for the recipient after transplantation as the regimen in place in the recipient before transplantation. If there is doubt about the ability to suppress viral replication after transplantation, the transplant must not move forward. Fortunately, with the development of newer antivirals, including integrase strand transfer inhibitors (INSTI), acquisition of resistance is much less likely. In the HOPE pilot study involving the care of 75 renal transplants, there were no cases of donor derived drug resistance. (Durand, et al Am J transplantation 2021a;21:1754-1764)

Donors co-infected with hepatitis are not excluded from HIV-positive to HIV- positive transplant; however, careful consideration must be given when evaluating a donor co-infected with HBV and/or HCV (Terrault, 2012; Miro, 2012; Moreno, 2012; Sherman, 2014; Chen, 2014). Although HCV therapeutic strategies are rapidly evolving (Liang, 2013), it is possible that mixed genotype HCV infections may influence post- transplant treatment of HCV in the recipient. Prior antiretroviral treatment of the donor and/or recipient with agents active against HBV (i.e., lamivudine, emtricitabine, adefovir, and tenofovir) has the potential for inducing or uncovering archived HBV drug resistance in the recipient (Dieterich, 2007; Soriano, 2009; Pais, 2010).

HIV-positive transplant candidates who are listed for a transplant in the context of a research study of HIV- positive to HIV-positive transplantation must have the same opportunity as other transplant candidates to receive an organ from an HIV-negative donor, should one become available for them.

1.1 HIV-Positive Donor Eligibility Criteria

The HIV-specific donor eligibility criterion for deceased donors is listed (Table 1). Co-infection with HBV and/or HCV is not an exclusion criterion.

1.1.1 HIV-Positive Deceased Donors

When evaluating HIV-positive deceased donors, it is understood that limited medical history may be available and/or known at the time of the donor evaluation. The OPO must make reasonable efforts to obtain prior medical history so that a transplant center team may best determine the suitability of the potential donor based on the information available. A complete history of antiretroviral regimens and a history of viral load tests and resistance testing are especially valuable for evaluating the likelihood of donor HIV resistance to antiretroviral regimens. A history of OIs or cancers is also of high importance,

due to the increased risk for both attributable to HIV, and the additional difficulty of treating some infections and neoplasms in a post-transplant setting. It is possible that deceased donors with lower CD4+ T-cell counts may pose an increased risk of harboring transmissible diseases (e.g., opportunistic infections or neoplasms) that may be difficult to detect during organ harvest and transplantation; teams conducting transplants under the HOPE Act are urged to assess donors with low CD4+ T-cell counts (e.g., <200/mL) with special caution and to promptly inform IRBs and the PI of known or suspected disease transmission events.

Minimum eligibility criteria for all HIV-positive deceased donors:

i. Documented HIV infection using an FDA-licensed, approved, or cleared test device(s).

ii. No evidence of invasive opportunistic complications of HIV infection.

iii. Pre-implant donor organ biopsy to be stored, at a minimum, for the duration of the study (or at least 5 years); additional specimens may be obtained to support specific research goals.

Additional eligibility criteria for HIV- positive deceased donors with a known history of HIV and prior treatment with ART:

i. The study team must describe the anticipated post-transplant antiretroviral regimen(s) to be prescribed for the recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Recipient Eligibility

A key consideration when evaluating potential HIV-positive transplant candidates is the ability to suppress HIV viral load post-transplant. This includes a thorough assessment by the transplant team of the candidate recipient's prescribed antiretroviral medications, HIV RNA levels while on medications, adherence to HIV treatment, and any available HIV resistance testing; a similar evaluation of the donor must also be carried out. A transplant should only take place if, after evaluating both recipient and donor, the team is confident they can define a post- transplant antiretroviral regimen that will be safe, tolerable, and effective. If there is any doubt on the part of the transplant team about the ability to suppress viral replication post- transplant, the transplant should not move forward. Concerns about transmitted drug resistance must be included in the recipient informed consent process for the research study. At the time of an organ offer, the recipient informed consent must address the transplant team's assessment of risk specific to the organ they are being offered.

2.1 HIV-Positive Recipient Eligibility Criteria

The following HIV-specific criteria must be met when screening for an HIV- positive to HIV-positive organ transplant (also refer to Table 1):

i. Last CD4+ T-cell count >200/mL (kidney, heart, lung). Patients with end stage liver disease may be lymphopenic due to cirrhosis and splenic sequestration, so a cutoff of 100 will be applied to them if

there is no history of opportunistic infection or malignancy. Potential liver transplant patients with a history of opportunistic infection or malignancy must have a CD4 positive T-cell count >200/uL unless the transplant team feels that an effective prophylactic strategy would make transplant safe in the CD4 100-200 range.

ii. HIV RNA less than 50 copies/mL and on a stable antiretroviral regimen.*+

iii. No evidence of active opportunistic complications of HIV infection.

iv. No history of primary CNS lymphoma or PML.

v. Concurrence by the study team that based on medical history and ART, viral suppression can be achieved in the recipient post-transplant.

*Patients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen for the patient once organ function is restored after transplantation.

+Those patients on a protease based regimen will be evaluated prior to transplant by our HIV/Transplant infectious disease service to attempt transition to INSTI regimen

+ We enroll 100 HIV positive patients who are eligible for solid organ transplant.

TABLE 1—SUMMARY OF DONOR AND RECIPIENT ELIGIBILITY CRITERIA FOR HIV-POSITIVE SERO-CONCORDANT ORGAN TRANSPLANT PAIRS UNDER THE HOPE ACT

HIV-Related variables	Deceased donor	Living donor	HIV-Positive recipient
Current CD4+ T-cell count (T lymphocytes/μL)	No requirement	≥500 for 6 months prior to organ donation.	If no history of OI • ≥200 (kidney, heart) • ≥100 (liver) If history of OI • ≥200 Last CD4+ T-cell count Prior to enrollment
Plasma HIV RNA viral load (copies/mL).	No requirement**	<50	<50*
Opportunistic infection	No invasive OI	No invasive OI	Currently, • No active OI Historically, no • CNS lymphoma • PML

* Organ recipients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen to be used by the recipient once organ function is restored after transplantation.

** In deceased donors with a known history of HIV infection and prior treatment with ART, the study team must describe the anticipated post- transplant antiretroviral regimen(s) to be used by the organ recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Transplant process and post-transplant considerations

Organ recovery, transplant procedure, handling and storage of donor organs/tissues, as well as management of solid organ transplant recipients are well described in our policies and procedures section (intranet), including the multidisciplinary management and immunosuppression protocols of HIV-positive recipients.

Waitlist acceptance criteria: Once an IRB- approved research protocol in HIV- positive to HIV-positive transplantation is finalized, the transplant center will inform the OPTN of additional organ-specific acceptance criteria for organs from HIV-positive donors. Those HIV-positive solid organ transplant candidates on the wait list willing to accept an HIV- positive organ must specify any additional acceptance criteria to the OPO.

Consent process and Independent HIV-Positive Recipient Advocate: One of Montefiore's senior transplant coordinators is actively collaborating with an NIH initiative to train and credential independent advocates for protecting and promoting the rights and interests of the HIV-positive recipient (or prospective recipient). The independent advocate for the HIV- positive recipient will:

i. Promote and protect the interests of the HIV-positive recipient (including with respect to having access to a suitable HIV-negative organ if it becomes available) and take steps to ensure that the HIV-positive recipient's decision is informed and free from coercion.

ii. Review whether the potential HIV-positive recipient has received information regarding the results of SOT in general and transplantation in HIV- positive recipients in particular and the unknown risks associated with HIV- positive to HIV-positive transplant.

iii. Demonstrate knowledge of HIV infection and transplantation.

Attached: -Informed consent for research

Post-transplant care

After discharge, patients are seen by the multidisciplinary transplant team according to the below schedule. During weekly morbidity and mortality meeting the post-transplant team meets and reviews the transplant recipients seen during the week to discuss patients, complications (infections, rejection, bleeding, readmission, re-surgery, malignancy, patient death, and graft loss), and allograft function. These events are stored in the transplant computerized database and communicated to the OPTN in accordance with regulations. Recipients are also assessed and contacted in respect to QAPI initiatives to further improve patient care initiatives.

Adult Transplant Patients are generally evaluated according to the following schedule after abdominal transplantation:

First month: twice a week labs (kidney) or once a week labs (liver), once a week clinic visit

2-3 months: once a week labs and every other week clinic visit

4-5 months: every other week labs and one month clinic visit

6-12 months: once a month labs and every other month clinic visit

Second year: every 2 months labs and 4 months clinic visit

3-5 years every 3 month labs and 6 months clinic visit

> 5 years every 3 months labs and once a year clinic visit

During each clinical visit, bloods and vital signs are obtained, a physical exam is performed and medications are reviewed with each patient. Medical and surgical problems will be addressed on an ongoing basis and appropriate referrals are made to specialists. Pharmacist, nutritional and social service support is available at each clinic. The Transplant Patient will receive specific instructions from the Transplant Multi-Disciplinary Team as to their follow-up care.

Additional transplant allograft biopsy will be performed either as clinically indicated (kidney, liver) or as per the standard post-transplant protocol (heart).

All patients will be assigned to one respective transplant clinician for outpatient follow-up. Patients will be seen at least once within a month after transplantation by a transplant surgeon.

In order to promptly detect viral breakthrough or possibility of viral superinfection, HIV viral loads should be performed at baseline and four weeks after transplantation, every three months for the first year post transplantation, and every 4-6 months in patients who have achieved sustained viral suppression. If viral breakthrough is detected on two consecutive assays, genotypic resistance studies will be sent. T cell subsets will be monitored every three months for the first year, and every 4-6 months in stable patient. A Montefiore transplant infectious disease provider will see the patient at the time of transplant, one month after transplantation and every three months for the first year post transplant. After the first year, should they wish, stable transplant patients may return to their outside provider. The Montefiore transplant ID attending will maintain close contact with the primary care provider, and also see the recipient twice a year for the duration of the study. To assist patients with urgent infectious disease issues the Montefiore AIDS center provides walk in services Monday through Friday, and 24 hour service coverage for established patients.

Transplant physicians will give 24 hour coverage service for post-transplant patients with any questions and complaints.

6 – Potential risks

Risk considerations and pertinent safeguards to potential recipients have been described in detail above under donor and recipient eligibility sections.

Prevention of Inadvertent Transmission of HIV

Although the use of HIV-positive organs may help alleviate transplant shortages and reduce patient waiting list times, there also are patient safety concerns to consider. Prevention or management of inadvertent transmission of HIV or exposure of an HIV-negative recipient to organs or tissues from an HIV-positive donor due to identification error is paramount (Ison, 2009, 2011a, 2011b). The transplant community, with regulatory oversight at multiple levels, has been able to achieve a high level of safety through routine procedures and clinical practice. The precautions taken with ABO compatible donor-recipient pairs and HCV-infected donor organs in HCV- infected recipients (Morales, 2010; Kucirka, 2010; Mandal, 2000; Tector, 2006) are existing models. However, vulnerabilities still exist, and mishaps still occur. For instance, the risks of error during manual transcription of information are well documented.

Montefiore Medical Center and the transplant center already count with an institutional biohazard plan for handling of HCV-positive organs and tissue disposal for HCV-positive recipients and ABO compatibility verification policies. HIV-positive status of donor organ, donor tissues and intended recipient will be added to the organ-to-recipient verification form.

7- Confidentiality and safeguards to minimize risks.

The research protocol was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States (attached document and informed consent).

8- Study benefits

The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV. It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients. Preliminary data nationally suggest earlier access to transplantation in patients with HIV who accept organs from donors with HIV (Durand 2021a; Durand 2021b).

9- Data Safety Monitoring Board

A DSMB comprised of three physicians (not involved in the study) will continue to be assembled every 12 months to review safety data.

9-References

Bertani, A., Grossi, P., Vitulo, P., et al. (2009). Successful lung transplantation in an HIV- and HBV-positive patient with cystic fibrosis. American Journal of Transplantation, 9, 2190–2196.

Bisleri, G., Morgan, J. A., Deng, M. C., et al. (2003). Should HIV-positive recipients undergo heart transplantation? Journal of Thoracic and Cardiovascular Surgery, 126, 1639–1640.

Blumberg, E. A., & Stock, P. (2009). Solid organ transplantation in the HIV-infected patient. American Journal of Transplantation, 9 Suppl 4, S131–135.

Blumberg, E. A., & Rogers, C. C. (2013a). Human immunodeficiency virus in solid organ transplantation. American Journal of Transplantation, 13 Suppl 4, 169–178.

Blumberg, E. A., Ison, M. G., Pruett, T. L., & Segev, D. L. (2013b). Optimal testing of the live organ donor for blood-borne viral pathogens: the report of a consensus conference. American Journal of Transplantation, 13(6), 1405–1415.

Boyarsky, B. J., Hall, E. C., Singer, A. L., Montgomery, R. A., Gebo, K. A., & Segev,D. L. (2011). Estimating the potential pool of HIV-infected deceased organ donors in the United States. American Journal of Transplantation, 11(6), 1209–1217.

Boyarsky, B. J., Durand C. M., Palella F. J., Segev D.L., (2015). Challenges and clinical decision-making in HIV-to-HIV transplantation: insights from the HIV literature. American Journal of Transplantation, 15:2023–2030.

Brucato, A., Colombo, T., Bonacina, E., et al. (2004). Fulminant myocarditis during HIV seroconversion: recovery with temporary left ventricular mechanical assistance. Italian Heart Journal, 5, 228–231.

Calabrese, L. H., Albrecht, M., Young, J., et al. (2003). Successful cardiac transplantation in an HIV–1-infected patient with advanced disease. New England Journal of Medicine, 348, 2323–2328.

Castel, M. A., Pe´rez-Villa, F., Roig, E., & Miro´ , J. M. (2011a). Heart transplantation in an HIV–1-infected patient with ischemic cardiomyopathy and severe pulmonary hypertension. Revista Espan˜ ola de Cardiologı´a, 64, 1066–1067.

Castel, M. A., Pe´rez-Villa, F., & Miro´ , J. M. (2011b). Heart transplantation in HIV- infected patients: more cases in Europe. The Journal of Heart and Lung Transplantation, 30, 1418.

Chen, J. Y., Feeney, E. R., & Chung, R. T. (2014). HCV and HIV co-infection: mechanisms and management. Nature Reviews: Gastroenterology & Hepatology, 11(6), 362–371.

Cooper, C., Kanters, S., Klein, M., Chaudhury, P., Marotta, P., Wong, P., et al. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with synthetic cohort. AIDS, 25(6), 777–786.

Dieterich, D.T. (2007). Special considerations and treatment of patients with HBV–HIV coinfection. Antiviral Therapy, 12, H43– H51.

Duclos-Vallee, J. C., Falissard, B., & Samuel, D. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with a synthetic cohort. AIDS, 25(13), 1675– 1676.

Durand, C et al. A prospective multicenter pilot study of HIV-positive deceased donor to HIV-positive recipient kidney transplantation: HOPE in action. American Journal of Transplantation. 2021a;21:p1754-1764.

Durand, C *et al*. HOPE in action: A prospective multicenter pilot study of liver transplantation from donors with HIV to recipients with HIV. *Am J Transplant*. 2021b Nov 6. doi: 10.1111/ajt.16886. Online ahead of print.

Durante-Mangoni, E., Maiello, C., & Sbreglia, C. (2011). A European first: successful heart transplant in a human immunodeficiency virus-positive recipient. The Journal of Heart and Lung Transplantation, 30, 845.

Durante-Mangoni, E., Maiello, C., Limongelli, G., et al. (2014). Management of immunosuppression and antiretroviral treatment before and after heart transplant for HIV-associated dilated cardiomyopathy. International Journal of Immunopathology and Pharmacology, 27(1), 113–120.

Fieno, D. S., Czer, L. S., Schwarz, E. R., et al. (2009). Left ventricular assist device placement in a patient with end-stage heart failure and human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 919–920.

Fox, A. N., Vagefi, P. A., & Stock, P. G. (2012). Liver transplantation in HIV patients. Seminars in Liver Disease, 32(2), 177–185.

Frassetto, L. A., Browne, M., Cheng, A., et al. (2007). Immunosuppressant pharmacokinetics and dosing modifications in HIV–1 Infected liver and kidney transplant recipients. American Journal of Transplantation, 7(12), 2816–2820.

Frassetto, L. A., Tan-Tam, C., & Stock, P. G. (2009). Renal transplantation in patients with HIV. Nature Review: Nephrology, 5(10), 582–589.

Frassetto, L. A., Tan-Tam, C. C., Barin, B., Browne, M., Wolfe, A. R., Stock, P. G., et al. (2014). Best Single Time Point Correlations with AUC for Cyclosporine and Tacrolimus in HIV-Infected Kidney and Liver Transplant Recipients.Transplantation, 97(6), 701–707.

Freedman, B.I. (2013). APOL1 and nephropathy progression in populations of African ancestry. Seminars in Nephrology, 33(5):425–432.

Freedman, B.I., Julian, B. A., Pastan, S. O. et al. (2015). Apolipoprotein L1 gene variants in deceased organ donors are associated with renal allograft failure. American Journal of Transplantation, 15:1615–1622.

Genovese, G., Friedman, D. J., Ross, M. D., Lecordier, L., Uzureau, P., Freedman, B. I., et al. (2010). Association of trypanolytic APOL1 variants with kidney disease in African Americans. Science, 329(5993), 841–845.

Gomez, V., Fernandez, A., Galeano, C., Oliva, J., Diez, V., Bueno, C., et al. (2013). Renal transplantation in HIV-infected patients: experience at a tertiary hospital in Spain and review of the literature. Transplant Proceedings, 45(3), 1255–1259.

Grossi, P. A. (2012). Update in HIV infection in organ transplantation. Current Opinion Organ Transplantation, 17(6), 586–593.

Harbell, J., Terrault, N. A., & Stock, P. (2013). Solid organ transplants in HIV-infected patients. Current HIV/AIDS Reports, 10(3), 217–225.

Humbert, M., Sitbon, O., Chaouat A., et al. (2006). Pulmonary arterial hypertension in France: results from a national registry. American Journal of Respiratory and Critical Care Medicine, 173, 1023.

Huprikar, S. (2009). Solid organ transplantation in HIV-infected individuals: an update. Reviews in Medical Virology, 19(6), 317–323.

Ison, M. G., Hager, J., Blumberg, E., Burdick, J., Carney, K., Cutler, J., et al. (2009).Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS Disease Transmission Advisory Committee. American Journal of Transplantation, 9(8), 1929–1935.

Ison, M. G., Llata, E., Conover, C. S., Friedewald, J. J., Gerber, S. I., Grigoryan, A., et al. (2011a). Transmission of human immunodeficiency virus and hepatitis C virus from an organ donor to four transplant recipients. American Journal of Transplantation, 11(6), 1218–1225.

Ison, M. G., & Nalesnik, M. A. (2011b). An update on donor-derived disease transmission in organ transplantation. American Journal of Transplantation, 11(6), 1123–1130.

Kaplan, J. E., Masur, H., Holmes, K.K., et al. (1995a). USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: introduction. USPHS/IDSA Prevention of Opportunistic Infections Working Group. Clinical Infectious Diseases, 21 Suppl 1:S1–11. Available at http:// www.ncbi.nlm.nih.gov/pubmed/ 8547495.

Kaplan, J. E., Masur, H., Jaffe, H.W., Holmes, K.K. (1995b). Reducing the impact of opportunistic infections in patients with HIV infection. New guidelines. Journal of the American Medical Association, 274(4):347–348. Available at http:// www.ncbi.nlm.nih.gov/pubmed/7609267.

Kern, R. M., Seethamraju, H., Blanc, P. D., et al. (2014a). The feasibility of lung transplantation in HIV seropositive patients. Annals of the American Thoracic Society. 2014 Jul;11(6):882-9.

Kern, R., Seethamraju, H., Blanc, P., Sinha, N., Loebe, M., Golden, J., et al. (2014b). Lung Transplantation in HIV Seropositive Patients. Chest, 145(3 Suppl), 642A.

Kim, D., Ziebell, R., Sadulvala, N., Kline, R., Ocfemia, C., Prejean, J., et al. (2013).Trends in Transmitted Drug Resistance Associated Mutations: 10 HIV Surveillance Areas, US, 2001–2010.

Paper presented at the 20th Conference on Retroviruses and Opportunistic Infections. Kim, W. R., Smith, J. M., Skeans, M. A., et al. (2014). OPTN/SRTR 2012 Annual Data Report: Liver. American Journal of Transplantation, 1, 69–96.

Kucirka, L. M., Singer, A. L., Ross, R. L., et al. (2010). Underutilization of hepatitis C-positive kidneys for hepatitis C- positive recipients. American Journal of Transplantation, 10(5), 1238–1246.

Kucirka, L.M., Bowring, M. G., Massie, A. B., et al, (2015) Landscape of deceased donors labeled increased risk for disease transmission under new guidelines. American Journal of Transplantation. Dec;15(12):3215-23.

Liang, T. J., & Ghany, M. G. (2013). Current and future therapies for hepatitis C virus infection. New England Journal of Medicine, 368(20), 1907–1917.

Locke, J. E., James, N. T., Mannon, R. B.,Mehta, S. G., Pappas, P. G., Baddley, J. W., et al. (2014). Immunosuppression Regimen and the Risk of Acute Rejection in HIV-Infected Kidney Transplant Recipients. Transplantation, 97(4), 446–450.

Locke, J. E., Reed R. D., Mehta S. G., et al. (2015a). Center-level experience and kidney transplant outcomes in HIV- infected recipients. American Journal of Transplantation, 15:2096–2104.

Locke, J. E., Mehta, S., Reed, R. D., et al. (2015b). A national study of outcomes among HIV-infected kidney transplant recipients. Journal of the American Society of Nephrology, 26:1–8.

Madan, S., Patel, S. P., Saeed,O., et al. (2019). Outcomes of heart transplantation in patients with human immunodeficiency virus. Am J Transplant. 2019 May;19(5):1529-1535.

Mandal, A. K., Kraus, E.S., Samaniego, M., et al. (2000). Shorter waiting times for hepatitis C virus seropositive recipients of cadaveric renal allografts from hepatitis C virus seropositive donors.Clinical Transplantation, 14, 391–396.

Mascolini, M. (2014). Four to Five HIV+ Dying in Care Yearly in Philadelphia Are Potential Organ Donors. 54th Interscience Conference on Antimicrobial Agents and Chemotherapy: Abstract H–1199a.Presented September 7, 2014.

Matas, A. J., Smith, J. M., Skeans, M. A., etal. (2014) OPTN/SRTR 2012 Annual Data Report: Kidney. American Journal of Transplantation, 1, 11–44.

Megens, S., & Laethem, K. V. (2013). HIV–1 genetic variation and drug resistance development. Expert Review of Anti- Infective Therapy, 11(11), 1159–1178.

Mehmood, S., Blais, D., Martin S., & Sai- Sudhakar, C. (2009). Heartmate XVE destination therapy for end-stage heart failure in a patient with human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 909–910.

Mehta, N. J., Khan, I. A., Mehta, R. N., et al. (2000). HIV-related pulmonary hypertension: analytic review of 131 cases. Chest, 118, 1133.

Mgbako, O., Glazier, A., Blumberg, E., & Reese, P. P. (2013). Allowing HIV- positive organ donation: ethical, legal and operational considerations. American Journal of Transplantation, 13(7), 1636–1642.

Miro, J. M., Montejo, M., Castells, L., Rafecas, A., Moreno, S., Aguero, F., et al. (2012). Outcome of HCV/HIV-coinfected liver transplant recipients: a prospective and multicenter cohort study. American Journal of Transplantation, 12(7), 1866–1876.

Miro, J. M., Stock, P., Teicher, E., et al, (2015). Outcome and management of HCV/HIV coinfection pre- and post-liver transplantation. A 205 update. Journal of Hepatology, 62:701–711.

Morales, J. M., Campistol, J. M., Dominguez- Gil, B., Andres, A., Esforzado, N., Oppenheimer, F., et al. (2010). Long-term experience with kidney transplantation from hepatitis C-positive donors into hepatitis C-positive recipients. American Journal of Transplantation, 10(11), 2453–2462.

Moreno, A., Cervera, C., Fortun, J., et al. (2012). Epidemiology and outcome of infections in human immunodeficiency virus/hepatitis C virus-coinfected liver transplant recipients: a FIPSE/GESIDA prospective cohort study. Liver Transplantation, 18, 70–81.

Muller, E., Kahn, D., & Mendelson, M. (2010). Renal transplantation between HIV- positive donors and recipients. New England Journal of Medicine, 362(24), 2336–2337.

Muller, E., Barday, Z., Mendelson, M., & Kahn, D. (2012). Renal transplantation between HIV-positive donors and recipients justified. South African Medical Journal, 102(6), 497–498.

Muller, E., Barday, Z., Mendelson, M., Kahn, D., et al. (2015). HIV-positive-to-HIV- positive kidney transplantation—results at 3 to 5 years. New England Journal of Medicine, 372:613–20.

Neuhaus, J., Angus, B., Kowalska, J. D., et al. (2010). Risk of all-cause mortality associated with nonfatal AIDS and serious non-AIDS events among adults infected with HIV. AIDS, 24(5), 697–706.

OPTN Policies and Bylaws. From http:// optn.transplant.hrsa.gov/ policiesandbylaws/policies.asp.

Pais, R. & Benhamou, Y. (2010). Long-term therapy for chronic hepatitis B in HIV co-infected patients. Gastroente´ rologie Clinique et Biologique, 34, 136–41.

Parsa, A., Kao, W. H. L., Xie, D., et al, (2013). APOL1 risk variants, race, and progression of chronic kidney disease. New England Journal of Medicine, 369:2183–96.

Panel on Opportunistic Infections in HIV- Infected Adults and Adolescents.Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents; recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/ contentfiles/lvguidelines/adult□oi.pdf. (Accessed September 2015).

Pelletier S. J., Norman S. P., Christensen L. L., et al. (2004). Review of transplantation in HIV patients during the HAART era. Clinical Transplantation, 63–82.

Petrosillo, N., Chinello, P., & Cicalini, S. (2006). Pulmonary hypertension in individuals with HIV infection. AIDS, 20, 2128.

Prevention, C. f. D. C. a. (2013). HIV Surveillance Supplemental Report. Ragni, M. V., Dodson, S. F., Hunt, S. C., et al. (1999). Liver transplantation in a hemophilia patient with acquired immunodeficiency syndrome. Blood, 93, 1113–1114.

Redd A. D., Quinn T. C., Tobian A. A. (2013). Frequency and implications of HIV superinfection. The Lancet Infectious Diseases, 13(7), 622–628.

Reeves-Daniel, A. M., DePalma, J. A., Bleyer, A. J., Rocco, M. V., Murea, M., Adams, P. L., et al. (2011). The APOL1 Gene and Allograft Survival after Transplantation. American Journal of Transplantation, 11(5), 1025–1030.

Richterman, A., Blumberg, E., (2015). The challenges and promise of HIV-infected donors for solid organ transplantation. Current Infectious Disease Reports, 17:1– 8.

Richterman, A., Sawinski, D., Reese, P.P., et al, (2015). An assessment of HIV-infected patients dying in care for deceased organ donation in a United States urban center. American Journal of Transplantation, 15:2105–2116.

Riella, L.V., Sheridan, A.M., (2015). Testing for high-risk APOL1 alleles in potential living kidney donors. American Journal of Kidney Disease. Sep;66(3):396-401.

Roland, M., Carlson, L., & Stock, P. (2002). Solid organ transplantation in HIV- infected individuals. AIDS Clinical Care, 14(7), 59–63.

Roland, M. E., Adey, D., Carlson, L. L., & Terrault, N. A. (2003a). Kidney and liver transplantation in HIV-infected patients: case presentations and review. AIDS Patient Care STDS, 17(10), 501–507.

Roland, M. E., Lo, B., Braff, J., & Stock, P. G. (2003b). Key clinical, ethical, and policy issues in the evaluation of the safety and effectiveness of solid organ transplantation in HIV-infected patients. Archives of Internal Medicine, 163(15), 1773–1778.

Roland, M. E., & Stock, P. G. (2003c). Review of solid-organ transplantation in HIV- infected patients. Transplantation, 75(4), 425–429.

Sawinski, D., Goldberg, D. S., Blumberg, E., et al. (2015) Beyond the NIH multicenter HIV transplant trial experience: Outcomes of HIV+ liver transplant recipients compared to HCV+ or HIV+/ HCV+ coinfected recipients in the United States. Clinical Infectious Disease. Oct 1;61(7):1054-62.

Sherman, K. E., Thomas, D., & Chung, R. T. (2014). Human immunodeficiency virus and liver disease forum 2012. Hepatology, 59(1), 307–317.

Sims, D. B., Uriel, N., Gonza´lez-Costello, J., et al. (2011). Human immunodeficiency virus infection and left ventricular assist devices: a case series. Journal of Heart and Lung Transplantation, 30, 1060–1064.

Soriano, V., Tuma, P., Labarga, P., et al. (2009). Hepatitis B in HIV patients: what is the current treatment and what are the challenges? Journal of HIV Therapy, 14(1), 13–18.

Stock, P. G., Barin, B., Murphy, B., Hanto, D., Diego, J. M., Light, J., et al. (2010). Outcomes of kidney transplantation in HIV-infected recipients. New England Journal of Medicine, 363(21), 2004–2014.

Taege, A. (2013). Organ transplantation and HIV progress or success? A review of current status. Curr Infectious Disease Reports, 15, 67–76.

Tector, A. J., Mangu, R. S., Chestovich, P., et al. (2006). Use of extended criteria livers decreases wait time for liver transplantation without adversity impacting posttransplant survival.

Annals of Surgery, 244, 439–450. Terrault, N. A., Roland, M. E., Schiano, T., Dove, L., Wong, M. T., Poordad, F., et al. (2012). Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection.Liver Transplantation, 18(6), 716–726.

Touzot, M., Pillebout, E., Matignon, M., Tricot, L., Viard, J. P., Rondeau, E., et al. (2010). Renal transplantation in HIV- infected patients: the Paris experience. American Journal of Transplantation, 10(10), 2263–2269.

Uriel, N., Jorde, U. P., Cotarlan, V., et al. (2009). Heart transplantation in human immunodeficiency virus-positive patients. Journal of Heart and Lung Transplant, 28, 667–669.

Uriel, N., Nahumi, N., Colombo, P. C., et al. (2014). Advance heart failure in patients infected with human immunodeficiency virus: is there equal access to care?Journal of Heart and Lung Transplantation. 2014 Sep;33(9):924-30.

Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2013). Cause- specific life expectancies after 35 years of age for human immunodeficiency syndrome-infected and human immunodeficiency syndrome-negative individuals followed simultaneously in long-term cohort studies, 1984–2008.American Journal of Epidemiology, 177(2), 116–125.

Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2014). Cause- specific mortality among HIV-infected individuals, by CD4 (+) cell count at HAART initiation, compared with HIV-uninfected individuals. AIDS, 28(2), 257–265.

Yoon, S. C., Hurst, F. P., Jindal, R. M., George, S. A., Neff, R. T., Agodoa, L. Y., et al. (2011). Trends in renal transplantation in patients with human immunodeficiency virus infection: an analysis of the United States renal data system. Transplantation, 91(8), 864–868.

Protocol Version 1.2

Amendment #1 May **29, 2018**

1. Title:

Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.

2. Investigators:

PI: Juan P Rocca[1], MD.

AIs: Victoria Muggia[3], MD; Grace Minamoto[3], MD; Yoram Puius[3] Enver Akalin[2], MD;; Maria Ajaimy[2], MD;; Stuart Greenstein[1], MD, Jay Graham[1], MD; Milan Kinkhabwala [1], MD.

[1] Montefiore-Einstein Center for Transplantation, Transplant Surgery, Department of Surgery.

[2] Montefiore-Einstein Center for Transplantation, Transplant nephrology, Department of Medicine.

[3] Montefiore-Einstein Center for Transplantation, Transplant Infectious Diseases, Department of Medicine.

3. Background and purposes:

The advent of effective antiretroviral therapy (ART) in the mid-1990s for treatment of individuals infected with HIV transformed a rapidly fatal disease into a well-controlled chronic illness. Currently, the life expectancy of individuals infected with HIV and receiving ART early in the course of their disease approaches that of individuals without HIV infection (Wada, 2013, 2014). In this era of greater longevity, liver failure, end-stage renal disease, and cardiovascular disease have emerged as important causes of morbidity and mortality in patients with HIV infection (Neuhaus, 2010).

Organ transplantation prolongs survival and improves quality of life for individuals with end-stage organ disease (Matas, 2014; Kim, 2014). Until recently, however, organ transplantation was unavailable to those infected with HIV due to concerns that pharmacologic immunosuppression to prevent organ rejection would hasten the progression from HIV infection to AIDS, concerns about disease transmission, and reluctance to allocate organs to a population whose outcome was unpredictable (Blumberg, 2009, 2013a, 2013b; Mgbako, 2013; Taege, 2013).

Nevertheless, a few transplant programs accepted HIV-positive patients on their transplant waiting lists and accumulated data showing kidney or liver transplantation could be done safely in these patients (Roland, 2002, 2003a, 2003b, 2003c; Blumberg, 2009; Stock, 2010; Yoon, 2011; Terrault, 2012). Subsequently, a prospective, multicenter clinical trial of kidney and liver transplantation in 275 patients demonstrated that, among HIV-positive kidney and liver transplant recipients, patient and graft survival

rates were acceptable and within the range of outcomes currently achieved among non-infected transplant recipients.

However, the rate of kidney rejection was unexpectedly high, demonstrating that the immune dysregulation resulting from HIV infection, HCV co-infection, and antirejection drugs is complex and incompletely understood. Some of the challenges encountered in that study remain relevant for clinical sites offering organ transplantation to HIV-positive individuals today (e.g., management of drug interactions and toxicities when combining complex medical regimens, management of combined morbidities of two or more active diseases, and the need for ongoing collaboration among medical professionals from different specialties) (Frassetto, 2007, 2014; Locke, 2014). Despite the complexities, this study and others (Ragni, 1999; Frassetto, 2009; Huprikar, 2009; Stock, 2010; Touzot, 2010; Cooper, 2011; Duclos-Vallee, 2011; Reeves-Daniel, 2011; Fox, 2012; Terrault, 2012; Grossi, 2012; Gomez, 2013; Harbell, 2013) demonstrate that kidney and liver transplantation are appropriate in HIV- positive individuals with liver or kidney failure, although gaps in knowledge and many research questions remain. There is much less experience with heart (Calabrese, 2003; Bisleri, 2003; Pelletier, 2004; Uriel, 2009, 2014; Castel, 2011a, 2011b; Durante-Mangoni, 2011 and 2014) and lung (Mehta, 2000; Humbert,2006; Petrosillo, 2006; Bertani, 2009; Kern, 2014a, 2014b) transplantation in HIV-positive recipients, or mechanical circulatory assistance (Brucato, 2004; Fieno, 2009; Mehmood, 2009; Sims, 2011) as a bridge to transplantation, although case reports and small case series suggest acceptable short-term outcomes are possible.

Prior to the passage of the HOPE Act, U.S. law required that all U.S. transplants for HIV-positive recipients utilize organs from HIV-uninfected donors. (See 42 U.S.C. 273(b)(3)(C), 274(b) and 18 U.S.C. 1122, all prior to amendment by the HOPE Act). The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV (hereinafter referred to as ‘‘HIV-positive to HIV-positive transplantation’’) is recognized (Boyarsky, 2011, 2015; Mgbako, 2013; Mascolini, 2014; Kucirka, 2015; Richterman, 2015). It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients (Boyarsky, 2011). The published experience with HIV-positive to HIV- positive SOT at this time comes from Muller et al from the University of Cape Town in South Africa. Initially, Muller et al (2010) reported 100 percent patient and graft survival in a four-patient pilot study. Subsequently, the same group reported an additional 10 HIV-positive to HIV-positive renal transplants (Muller, 2012). All patients were restarted on ART early postoperatively in the immunosuppressive setting of T- cell-depleting induction therapy, tacrolimus, mycophenolate mofetil, and prednisone. One to 4 years after transplantation, outcomes remained excellent and all patients had undetectable viral loads (Muller, 2012). The cumulative University of Cape Town experience of 27 HIV-positive to HIV-positive transplant procedures was recently summarized in the New England Journal of Medicine (Muller, 2015). The 1- and 5-year death-censored graft survival was 93 and 84 percent, respectively, and 1- and 5-year patient survival was 83 and 74 percent, respectively. Of note, the South African HIV-positive deceased donors were ART-naive, without history of opportunistic infection or proteinuria, and had normal pre-transplant renal biopsies. While renal function has remained normal in the recipients, three have had routine post-transplant renal biopsies

demonstrating new changes typical of early HIV-associated nephropathy that were not present in baseline biopsy specimens. The long- term significance of these findings remains unknown and awaits longer follow-up. All patients had undetectable plasma HIV viral loads after transplantation. Graft rejection rates were 8 percent at 1 year and 22 percent at 3 years.

The HOPE Act permits HIV-positive to HIV-positive organ transplantation under IRB-approved research protocols conforming to the Final Human Immunodeficiency Virus (HIV) Organ Policy Equity (HOPE) Act Safeguards and Research Criteria for Transplantation of Organs Infected with HIV, which were developed as directed in the HOPE Act. Patients receiving HIV-positive kidneys from deceased HIV-positive donors in South Africa (Muller, 2015) had survival rates of 84 percent and 74 percent at 1 and 5 years, respectively; however, there is presently no evidence for the safety, efficacy, and effectiveness of HIV-positive to HIV- positive transplantation in North America. The Final Safeguards and Research Criteria are meant to support the acquisition of new clinical knowledge and mechanistic insights about HIV-positive to HIV-positive organ transplantation in the United States. The results of this research will be evaluated by the Secretary of HHS and the OPTN to determine whether and how the OPTN standards for organ transplantation shall be revised to address HIV-positive organ donors.

The research protocol described below was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States. The criteria address the minimum safety and data requirements of clinical research in HIV-positive to HIV-positive transplantation. As mandated by the HOPE Act, the Secretary, together with the OPTN, is charged with reviewing the results of scientific research conducted under these criteria to determine whether the OPTN's standards of quality should be further modified and whether some HIV- positive to HIV-positive transplants should proceed outside the auspices of research conducted under such criteria (see attached the original document).

Montefiore Medical Center and the Montefiore-Einstein Center for Transplantation meet the institutional standards and requirements to carry on a research protocol on HIV-positive to HIV-positive kidney transplantation with a collective experience of 14 kidney transplants on HIV positive recipients since 2008. The Montefiore AIDS center provides care to over 2500 HIV positive individuals in the Bronx. Potential transplant candidates as per protocol are evaluated by transplant ID clinicians with expertise also in HIV. The AIDS center providers and the Montefiore infectious disease faculty practice follow these patients closely for the first year after transplantation, and over two thirds of these patients have elected to remain at Montefiore for their HIV care. Multidisciplinary transplant protocols include management of HIV recipients and the outcomes of these cases have met the national standards without affecting our program-specific reports (SRTR reports).

4. Objectives and outcome measures

Montefiore's research in HIV-positive to HIV-positive transplantation will address questions related to HIV superinfection; incidence and severity of opportunistic infections (including transmission of occult

OIs from donor to recipient); immunologic mechanisms contributing to the increased rate of kidney rejection observed in HIV-positive recipients and quality of life for recipients of HIV- positive to HIV-positive transplantation. To ensure that all nationwide studies of HIV-positive to HIV- positive transplantation can contribute to evaluation of the safety of the procedure, the following key donor and recipient characteristics and outcome measures must be incorporated into the design of all clinical trials of HIV- positive to HIV-positive transplantation.

Wait List Candidates

- HIV status
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Removal from wait list (death or other reason)
- Time on wait list

Donors (all)

- Type (living or deceased)
- HIV status (HIV-positive new diagnosis, HIV-positive known diagnosis)
- CD4+ T-cell count
- Co-infection (HCV, HBV)
- HIV viral load
- ART resistance
- Pre-transplant donor allograft biopsy

Note regarding Living Donors: Montefiore Einstein Center for Transplantation has decided to exclude living donors from the participation in this research protocol.

Transplant Recipients

- Rejection rate (annual up to 5 years)
- Progression to AIDS
- New Opportunistic Infections
- Failure to suppress viral replication (persistent viremia)
- HIV-associated organ failure
- Malignancy
- Graft failure
- Mismatched ART resistance versus donor
- Death

5. Methods:

- Donor Eligibility

Montefiore Einstein Center for Transplantation has decided to exclude living donors from this research protocol. HIV- positive deceased donors of organs for transplantation into an HIV-positive recipient must fulfill applicable clinical criteria in place for HIV-uninfected organ donors.

There is substantial concern about the consequences of transplanting an organ from an HIV-positive donor to a recipient infected with a strain of HIV that differs from the donor's in terms of its responsiveness to antiretroviral therapy (ART). The likelihood and impact of HIV superinfection in this context are unknown. Adverse consequences could range from transient loss of viral suppression, necessitating a change in antiretroviral regimen to a worst-case scenario in which the new infecting strain of HIV is unresponsive to available antiretroviral treatment and the recipient progresses to AIDS (Redd, 2013). Information relevant to understanding the known or potential extent of antiretroviral resistance in the strain of HIV infecting the organ donor may be incomplete for many reasons:

- There may be inadequate virus in donor specimens for antiretroviral resistance testing;
- If the specimen is adequate, there may not be enough time within the decision-making evaluation window to fully assess antiretroviral resistance before the clinical deterioration of the donor, organ procurement, and implantation;
- The donor's history of antiretroviral treatment may be unknown or incomplete;
- Results from prior antiretroviral resistance testing may be unavailable.

These issues might be especially challenging when considering organ donation from deceased donors whose HIV infection is first identified during donor evaluation. As of 2011, an estimated 1 in 6 U.S. adults living with HIV infection were undiagnosed (Prevention, 2013) and an estimated 16 percent of newly diagnosed, untreated individuals were infected with virus resistant to at least one class of antiretroviral drug (Kim, 2013; Megens, 2013).

It is anticipated that the risk of transmission of resistant HIV strains may be lower from deceased donors with a well-documented history of antiretroviral treatment, undetectable virus at demise, and robust and persistent undetectable viral load for at least 1 year prior to death. However, to impose this as an eligibility criterion would limit the pool of suitable donors and severely limit the ability to study transplantation of HIV-positive organs under the HOPE Act. In addition, it will not be possible in all cases to obtain viral loads and/or antiretroviral resistance profiles in the time available for donor evaluation. Transplant teams evaluating a donor must review all available donor and recipient information and be able to propose an antiretroviral regimen that will be equally or more safe, tolerable, and effective for the recipient after transplantation as the regimen in place in the recipient before transplantation. For instance, a donor who only achieves viral suppression with a regimen known to be intolerable to the

recipient must not be accepted. If there is doubt about the ability to suppress viral replication after transplantation, the transplant must not move forward.

Donors co-infected with hepatitis are not excluded from HIV-positive to HIV- positive transplant; however, careful consideration must be given when evaluating a donor co-infected with HBV and/or HCV (Terrault, 2012; Miro, 2012; Moreno, 2012; Sherman, 2014; Chen, 2014). Although HCV therapeutic strategies are rapidly evolving (Liang, 2013), it is possible that mixed genotype HCV infections may influence post- transplant treatment of HCV in the recipient. Prior antiretroviral treatment of the donor and/or recipient with agents active against HBV (i.e., lamivudine, emtricitabine, adefovir, and tenofovir) has the potential for inducing or uncovering archived HBV drug resistance in the recipient (Dieterich, 2007; Soriano, 2009; Pais, 2010).

HIV-positive transplant candidates who are listed for a transplant in the context of a research study of HIV- positive to HIV-positive transplantation must have the same opportunity as other transplant candidates to receive an organ from an HIV-negative donor, should one become available for them.

1.1 HIV-Positive Donor Eligibility Criteria

The HIV-specific donor eligibility criterion for deceased donors is listed (Table 1). Co-infection with HBV and/or HCV is not an exclusion criterion.

1.1.1 HIV-Positive Deceased Donors

When evaluating HIV-positive deceased donors, it is understood that limited medical history may be available and/or known at the time of the donor evaluation. The OPO must make reasonable efforts to obtain prior medical history so that a transplant center team may best determine the suitability of the potential donor based on the information available. A complete history of antiretroviral regimens and a history of viral load tests and resistance testing are especially valuable for evaluating the likelihood of donor HIV resistance to antiretroviral regimens. A history of OIs or cancers is also of high importance, due to the increased risk for both attributable to HIV, and the additional difficulty of treating some infections and neoplasms in a post-transplant setting. It is possible that deceased donors with lower CD4+ T-cell counts may pose an increased risk of harboring transmissible diseases (e.g., opportunistic infections or neoplasms) that may be difficult to detect during organ harvest and transplantation; teams conducting transplants under the HOPE Act are urged to assess donors with low CD4+ T-cell counts (e.g., <200/mL) with special caution and to promptly inform IRBs and the PI of known or suspected disease transmission events.

Minimum eligibility criteria for all HIV-positive deceased donors:

i. Documented HIV infection using an FDA-licensed, approved, or cleared test device(s).

ii. No evidence of invasive opportunistic complications of HIV infection.

iii. Pre-implant donor organ biopsy to be stored, at a minimum, for the duration of the study (or at least 5 years); additional specimens may be obtained to support specific research goals.

Additional eligibility criteria for HIV- positive deceased donors with a known history of HIV and prior treatment with ART:

i. The study team must describe the anticipated post-transplant antiretroviral regimen(s) to be prescribed for the recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Recipient Eligibility

A key consideration when evaluating potential HIV-positive transplant candidates is the ability to suppress HIV viral load post-transplant. This includes a thorough assessment by the transplant team of the candidate recipient's prescribed antiretroviral medications, HIV RNA levels while on medications, adherence to HIV treatment, and any available HIV resistance testing; a similar evaluation of the donor must also be carried out. A transplant should only take place if, after evaluating both recipient and donor, the team is confident they can define a post- transplant antiretroviral regimen that will be safe, tolerable, and effective. If there is any doubt on the part of the transplant team about the ability to suppress viral replication post- transplant, the transplant should not move forward. Concerns about transmitted drug resistance must be included in the recipient informed consent process for the research study. At the time of an organ offer, the recipient informed consent must address the transplant team's assessment of risk specific to the organ they are being offered.

2.1 HIV-Positive Recipient Eligibility Criteria

The following HIV-specific criteria must be met when screening for an HIV- positive to HIV-positive organ transplant (also refer to Table 1):

i. Last CD4+ T-cell count >200/mL (kidney) Prior to enrollment; any patient with history of OI must have a CD4 positive T-cell count >200/uL.

ii. HIV RNA less than 50 copies/mL and on a stable antiretroviral regimen.*+

iii. No evidence of active opportunistic complications of HIV infection.

iv. No history of primary CNS lymphoma or PML.

v. Concurrence by the study team that based on medical history and ART, viral suppression can be achieved in the recipient post-transplant.

*Patients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen for the patient once organ function is restored after transplantation.

+Those patients on a protease based regimen and fully suppressed with no available resistance studies, should be tested with an assay that looks at archived resistance (e.g. Genosure Archive®).

+ We enroll 100 HIV positive patients who are eligible for kidney transplant.

TABLE 1—SUMMARY OF DONOR AND RECIPIENT ELIGIBILITY CRITERIA FOR HIV-POSITIVE SERO-CONCORDANT ORGAN TRANSPLANT PAIRS UNDER THE HOPE ACT

HIV-Related variables	Deceased donor	Living donor	HIV-Positive recipient
Current CD4+ T-cell count (T lymphocytes/μL)	No requirement	≥500 for 6 months prior to organ donation.	If no history of OI • ≥200 If history of OI • ≥200 (kidney) • ≥100 (liver) Last CD4+ T-cell count Prior to enrollment
Plasma HIV RNA viral load (copies/mL).	No requirement**	<50	<50*
Opportunistic infection	No invasive OI	No invasive OI	Currently, • No active OI Historically, no • CNS lymphoma • PML

* Organ recipients who are unable to tolerate ART due to organ failure or who have only recently started ART may have detectable viral load and still be considered eligible if the study team is confident there will be a safe, tolerable, and effective antiretroviral regimen to be used by the recipient once organ function is restored after transplantation.

** In deceased donors with a known history of HIV infection and prior treatment with ART, the study team must describe the anticipated post- transplant antiretroviral regimen(s) to be used by the organ recipient and justify their conclusion that the proposed regimen will be safe, tolerable, and effective.

- Transplant process and post-transplant considerations

Organ recovery, transplant procedure, handling and storage of donor organs/tissues, as well as management of kidney transplant recipients at Montefiore-Einstein Center for Transplantation are well described in our policies and procedures section (intranet), including the multidisciplinary management and immunosuppression protocols of HIV-positive kidney recipients

Waitlist acceptance criteria: Once an IRB- approved research protocol in HIV- positive to HIV-positive transplantation is finalized, the transplant center will inform the OPTN of additional organ-specific acceptance criteria for organs from HIV-positive donors. Those HIV-positive kidney candidates on the wait list willing to accept an HIV- positive organ must specify any additional acceptance criteria to the OPO.

Consent process and Independent HIV-Positive Recipient Advocate: One of Montefiore's senior transplant coordinator is actively collaborating with an NIH initiative to train and credential independent advocates for protecting and promoting the rights and interests of the HIV-positive recipient (or prospective recipient). The independent advocate for the HIV- positive recipient will:

i. Promote and protect the interests of the HIV-positive recipient (including with respect to having access to a suitable HIV-negative organ if it becomes available) and take steps to ensure that the HIV-positive recipient's decision is informed and free from coercion.

ii. Review whether the potential HIV-positive recipient has received information regarding the results of SOT in general and transplantation in HIV- positive recipients in particular and the unknown risks associated with HIV- positive to HIV-positive transplant.

iii. Demonstrate knowledge of HIV infection and transplantation.

Attached: -Informed consent for research

Post-transplant care

After discharge, patients are seen by the multidisciplinary transplant team according to the below schedule. During weekly morbidity and mortality meeting the post-transplant team meets and reviews the transplant recipients seen during the week to discuss patients, complications (infections, rejection, bleeding, readmission, re-surgery, malignancy, patient death, and graft loss), and allograft function. These events are stored in the transplant computerized database and communicated to the OPTN in accordance with regulations. Recipients are also assessed and contacted in respect to QAPI initiatives to further improve patient care initiatives.

Adult Transplant Patients are generally evaluated according to the following schedule after kidney transplantation:

First month: twice a week labs, once a week clinic visit

2-3 months: once a week labs and every other week clinic visit

4-5 months: every other week labs and one month clinic visit

6-12 months: once a month labs and every other month clinic visit

Second year: every 2 months labs and 4 months clinic visit

3-5 years every 3 month labs and 6 months clinic visit

> 5 years every 3 months labs and once a year clinic visit

During each clinical visit, bloods and vital signs are obtained, a physical exam is performed and medications are reviewed with each patient. Medical and surgical problems will be addressed on an ongoing basis and appropriate referrals are made to specialists. Pharmacist, nutritional and social service support is available at each clinic. The Transplant Patient will receive specific instructions from the Transplant Multi-Disciplinary Team as to their follow-up care.

Additional transplant allograft biopsy will be performed at 3 months and one year from transplant.

All patients will be assigned to one respective transplant nephrologist for routine follow-up. Patients will be seen at least once within a month after transplantation by a transplant surgeon.

In order to promptly detect viral breakthrough or possibility of viral superinfection, HIV viral loads should be performed every week for the first four weeks after transplantation, every three months for the first year post transplantation, and every 6 months in patients who have achieved sustained viral suppression. If viral breakthrough is detected on two consecutive assays, genotypic resistance studies will be sent. In addition tropism assays and resistance testing looking for mutations in the integrase gene will be performed. CD4 monitoring can be done less frequently. Monthly CD4 monitoring for the first three months, every three months for the first year, and every 6 months in stable patient. The Montefiore transplant infectious disease provider will see the patient monthly the first three months after transplantation and every three months for the first year post transplant. After the first year, stable transplant patients may return to their outside provider, however the transplant ID attending will maintain close contact with the primary care provider, and also see the recipient twice a year for the duration of the study. To assist patients with urgent infectious disease issues the Montefiore AIDS center provides walk in services Monday through Friday, and 24 hour service coverage for established patients.

Transplant physicians will give 24 hour coverage service for post-transplant patients with any questions and complaints.

6 – Potential risks

Risk considerations and pertinent safeguards to potential recipients have been described in detail above under donor and recipient eligibility sections.

Prevention of Inadvertent Transmission of HIV

Although the use of HIV-positive organs may help alleviate transplant shortages and reduce patient waiting list times, there also are patient safety concerns to consider. Prevention or management of inadvertent transmission of HIV or exposure of an HIV-negative recipient to organs or tissues from an HIV-positive donor due to identification error is paramount (Ison, 2009, 2011a, 2011b). The transplant community, with regulatory oversight at multiple levels, has been able to achieve a high level of safety through routine procedures and clinical practice. The precautions taken with ABO compatible donor-recipient pairs and HCV-infected donor organs in HCV- infected recipients (Morales, 2010; Kucirka, 2010; Mandal, 2000; Tector, 2006) are existing models. However, vulnerabilities still exist, and mishaps still occur. For instance, the risks of error during manual transcription of information are well documented.

Montefiore medical center and the transplant center already count with an institutional biohazard plan for handling of HCV-positive organs and tissue disposal for HCV-positive recipients and ABO compatibility verification policies. HIV-positive status of donor organ, donor tissues and intended recipient will be added to the organ-to-recipient verification form

7- Confidentiality and safeguards to minimize risks.

The research protocol was drafted in accordance to the Final Safeguard and Research Criteria for Transplantation of HIV-positive donor organs in HIV-positive recipients as published by the HHS through the NIH that establishes the criteria for conducting research in HIV-positive to HIV-positive organ transplantation in the United States (attached document and informed consent).

8- Study benefits

The potential for increasing the pool of available organ donors for all recipients by allowing the use of organs from donors infected with HIV for transplantation into recipients infected with HIV. It is estimated that an additional 500 organ donors per year might be available if HIV-positive individuals were accepted as organ donors for HIV-positive recipients

9- Data Safety Monitoring Board

A DSMB comprised of a three physicians (not involved in the study) will be assembled every 12 months to review safety data.

9-References

Bertani, A., Grossi, P., Vitulo, P., et al. (2009). Successful lung transplantation in an HIV- and HBV-positive patient with cystic fibrosis. American Journal of Transplantation, 9, 2190–2196.

Bisleri, G., Morgan, J. A., Deng, M. C., et al. (2003). Should HIV-positive recipients undergo heart transplantation? Journal of Thoracic and Cardiovascular Surgery, 126, 1639–1640.

Blumberg, E. A., & Stock, P. (2009). Solid organ transplantation in the HIV-infected patient. American Journal of Transplantation, 9 Suppl 4, S131–135.

Blumberg, E. A., & Rogers, C. C. (2013a). Human immunodeficiency virus in solid organ transplantation. American Journal of Transplantation, 13 Suppl 4, 169–178.

Blumberg, E. A., Ison, M. G., Pruett, T. L., & Segev, D. L. (2013b). Optimal testing of the live organ donor for blood-borne viral pathogens: the report of a consensus conference. American Journal of Transplantation, 13(6), 1405–1415.

Boyarsky, B. J., Hall, E. C., Singer, A. L., Montgomery, R. A., Gebo, K. A., & Segev,D. L. (2011). Estimating the potential pool of HIV-infected deceased organ donors in the United States. American Journal of Transplantation, 11(6), 1209–1217.

Boyarsky, B. J., Durand C. M., Palella F. J., Segev D.L., (2015). Challenges and clinical decision-making in HIV-to-HIV transplantation: insights from the HIV literature. American Journal of Transplantation, 15:2023–2030.

Brucato, A., Colombo, T., Bonacina, E., et al. (2004). Fulminant myocarditis during HIV seroconversion: recovery with temporary left ventricular mechanical assistance. Italian Heart Journal, 5, 228–231.

Calabrese, L. H., Albrecht, M., Young, J., et al. (2003). Successful cardiac transplantation in an HIV–1-infected patient with advanced disease. New England Journal of Medicine, 348, 2323–2328.

Castel, M. A., Pe´rez-Villa, F., Roig, E., & Miro´ , J. M. (2011a). Heart transplantation in an HIV–1-infected patient with ischemic cardiomyopathy and severe pulmonary hypertension. Revista Espan˜ ola de Cardiologı´a, 64, 1066–1067.

Castel, M. A., Pe´rez-Villa, F., & Miro´ , J. M. (2011b). Heart transplantation in HIV- infected patients: more cases in Europe. The Journal of Heart and Lung Transplantation, 30, 1418.

Chen, J. Y., Feeney, E. R., & Chung, R. T. (2014). HCV and HIV co-infection: mechanisms and management. Nature Reviews: Gastroenterology & Hepatology, 11(6), 362–371.

Cooper, C., Kanters, S., Klein, M., Chaudhury, P., Marotta, P., Wong, P., et al. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with synthetic cohort. AIDS, 25(6), 777–786.

Dieterich, D.T. (2007). Special considerations and treatment of patients with HBV–HIV coinfection. Antiviral Therapy, 12, H43– H51.

Duclos-Vallee, J. C., Falissard, B., & Samuel, D. (2011). Liver transplant outcomes in HIV-infected patients: a systematic review and meta-analysis with a synthetic cohort. AIDS, 25(13), 1675– 1676.

Durante-Mangoni, E., Maiello, C., & Sbreglia, C. (2011). A European first: successful heart transplant in a human immunodeficiency virus-positive recipient. The Journal of Heart and Lung Transplantation, 30, 845.

Durante-Mangoni, E., Maiello, C., Limongelli, G., et al. (2014). Management of immunosuppression and antiretroviral treatment before and after heart transplant for HIV-associated dilated cardiomyopathy. International Journal of Immunopathology and Pharmacology, 27(1), 113–120.

Fieno, D. S., Czer, L. S., Schwarz, E. R., et al. (2009). Left ventricular assist device placement in a patient with end-stage heart failure and human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 919–920.

Fox, A. N., Vagefi, P. A., & Stock, P. G. (2012). Liver transplantation in HIV patients. Seminars in Liver Disease, 32(2), 177–185.

Frassetto, L. A., Browne, M., Cheng, A., et al. (2007). Immunosuppressant pharmacokinetics and dosing modifications in HIV–1 Infected liver and kidney transplant recipients.

American Journal of Transplantation, 7(12), 2816–2820. Frassetto, L. A., Tan-Tam, C., & Stock, P. G. (2009). Renal transplantation in patients with HIV. Nature Review: Nephrology, 5(10), 582–589.

Frassetto, L. A., Tan-Tam, C. C., Barin, B., Browne, M., Wolfe, A. R., Stock, P. G., et al. (2014). Best Single Time Point Correlations with AUC for Cyclosporine and Tacrolimus in HIV-Infected Kidney and Liver Transplant Recipients.Transplantation, 97(6), 701–707.

Freedman, B.I. (2013). APOL1 and nephropathy progression in populations of African ancestry. Seminars in Nephrology, 33(5):425–432.

Freedman, B.I., Julian, B. A., Pastan, S. O. et al. (2015). Apolipoprotein L1 gene variants in deceased organ donors are associated with renal allograft failure. American Journal of Transplantation, 15:1615–1622.

Genovese, G., Friedman, D. J., Ross, M. D., Lecordier, L., Uzureau, P., Freedman, B. I., et al. (2010). Association of trypanolytic APOL1 variants with kidney disease in African Americans. Science, 329(5993), 841–845.

Gomez, V., Fernandez, A., Galeano, C., Oliva, J., Diez, V., Bueno, C., et al. (2013). Renal transplantation in HIV-infected patients: experience at a tertiary hospital in Spain and review of the literature. Transplant Proceedings, 45(3), 1255–1259.

Grossi, P. A. (2012). Update in HIV infection in organ transplantation. Current Opinion Organ Transplantation, 17(6), 586–593.

Harbell, J., Terrault, N. A., & Stock, P. (2013). Solid organ transplants in HIV-infected patients. Current HIV/AIDS Reports, 10(3), 217–225.

Humbert, M., Sitbon, O., Chaouat A., et al. (2006). Pulmonary arterial hypertension in France: results from a national registry. American Journal of Respiratory and Critical Care Medicine, 173, 1023.

Huprikar, S. (2009). Solid organ transplantation in HIV-infected individuals: an update. Reviews in Medical Virology, 19(6), 317–323.

Ison, M. G., Hager, J., Blumberg, E., Burdick, J., Carney, K., Cutler, J., et al. (2009).Donor-derived disease transmission events in the United States: data reviewed by the OPTN/UNOS Disease Transmission Advisory Committee. American Journal of Transplantation, 9(8), 1929–1935.

Ison, M. G., Llata, E., Conover, C. S., Friedewald, J. J., Gerber, S. I., Grigoryan, A., et al. (2011a). Transmission of human immunodeficiency virus and hepatitis C virus from an organ donor to four transplant recipients. American Journal of Transplantation, 11(6), 1218–1225.

Ison, M. G., & Nalesnik, M. A. (2011b). An update on donor-derived disease transmission in organ transplantation. American Journal of Transplantation, 11(6), 1123–1130.

Kaplan, J. E., Masur, H., Holmes, K.K., et al. (1995a). USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: introduction. USPHS/IDSA Prevention of Opportunistic Infections Working Group. Clinical Infectious Diseases, 21 Suppl 1:S1–11. Available at http:// www.ncbi.nlm.nih.gov/pubmed/ 8547495.

Kaplan, J. E., Masur, H., Jaffe, H.W., Holmes, K.K. (1995b). Reducing the impact of opportunistic infections in patients with HIV infection. New guidelines. Journal of the American Medical Association, 274(4):347–348. Available at http:// www.ncbi.nlm.nih.gov/pubmed/7609267.

Kern, R. M., Seethamraju, H., Blanc, P. D., et al. (2014a). The feasibility of lung transplantation in HIV seropositive patients. Annals of the American Thoracic Society (in press, online).

Kern, R., Seethamraju, H., Blanc, P., Sinha, N., Loebe, M., Golden, J., et al. (2014b). Lung Transplantation in HIV Seropositive Patients. Chest, 145(3 Suppl), 642A.

Kim, D., Ziebell, R., Sadulvala, N., Kline, R., Ocfemia, C., Prejean, J., et al. (2013).Trends in Transmitted Drug Resistance Associated Mutations: 10 HIV Surveillance Areas, US, 2001–2010.

Paper presented at the 20th Conference on Retroviruses and Opportunistic Infections. Kim, W. R., Smith, J. M., Skeans, M. A., et al. (2014). OPTN/SRTR 2012 Annual Data Report: Liver. American Journal of Transplantation, 1, 69–96.

Kucirka, L. M., Singer, A. L., Ross, R. L., et al. (2010). Underutilization of hepatitis C-positive kidneys for hepatitis C- positive recipients. American Journal of Transplantation, 10(5), 1238–1246.

Kucirka, L.M., Bowring, M. G., Massie, A. B., et al, (2015) Landscape of deceased donors labeled increased risk for disease transmission under new guidelines.American Journal of Transplantation, (in press).

Liang, T. J., & Ghany, M. G. (2013). Current and future therapies for hepatitis C virus infection. New England Journal of Medicine, 368(20), 1907–1917.

Locke, J. E., James, N. T., Mannon, R. B.,Mehta, S. G., Pappas, P. G., Baddley, J. W., et al. (2014). Immunosuppression Regimen and the Risk of Acute Rejection in HIV-Infected Kidney Transplant Recipients. Transplantation, 97(4), 446–450.

Locke, J. E., Reed R. D., Mehta S. G., et al. (2015a). Center-level experience and kidney transplant outcomes in HIV- infected recipients. American Journal of Transplantation, 15:2096–2104.

Locke, J. E., Mehta, S., Reed, R. D., et al. (2015b). A national study of outcomes among HIV-infected kidney transplant recipients. Journal of the American Society of Nephrology, 26:1–8.

Mandal, A. K., Kraus, E.S., Samaniego, M., et al. (2000). Shorter waiting times for hepatitis C virus seropositive recipients of cadaveric renal allografts from hepatitis C virus seropositive donors.Clinical Transplantation, 14, 391–396.

Mascolini, M. (2014). Four to Five HIV+ Dying in Care Yearly in Philadelphia Are Potential Organ Donors. 54th Interscience Conference on Antimicrobial Agents and Chemotherapy: Abstract H–1199a.Presented September 7, 2014.

Matas, A. J., Smith, J. M., Skeans, M. A., etal. (2014) OPTN/SRTR 2012 Annual Data Report: Kidney. American Journal of Transplantation, 1, 11–44.

Megens, S., & Laethem, K. V. (2013). HIV–1 genetic variation and drug resistance development. Expert Review of Anti- Infective Therapy, 11(11), 1159–1178.

Mehmood, S., Blais, D., Martin S., & Sai- Sudhakar, C. (2009). Heartmate XVE destination therapy for end-stage heart failure in a patient with human immunodeficiency virus. Interactive Cardiovascular and Thoracic Surgery, 9, 909–910.

Mehta, N. J., Khan, I. A., Mehta, R. N., et al. (2000). HIV-related pulmonary hypertension: analytic review of 131 cases. Chest, 118, 1133.

Mgbako, O., Glazier, A., Blumberg, E., & Reese, P. P. (2013). Allowing HIV- positive organ donation: ethical, legal and operational considerations. American Journal of Transplantation, 13(7), 1636–1642.

Miro, J. M., Montejo, M., Castells, L., Rafecas, A., Moreno, S., Aguero, F., et al. (2012). Outcome of HCV/HIV-coinfected liver transplant recipients: a prospective and multicenter cohort study. American Journal of Transplantation, 12(7), 1866–1876.

Miro, J. M., Stock, P., Teicher, E., et al, (2015). Outcome and management of HCV/HIV coinfection pre- and post-liver transplantation. A 205 update. Journal of Hepatology, 62:701–711.

Morales, J. M., Campistol, J. M., Dominguez- Gil, B., Andres, A., Esforzado, N., Oppenheimer, F., et al. (2010). Long-term experience with kidney transplantation from hepatitis C-positive donors into hepatitis C-positive recipients. American Journal of Transplantation, 10(11), 2453–2462.

Moreno, A., Cervera, C., Fortun, J., et al. (2012). Epidemiology and outcome of infections in human immunodeficiency virus/hepatitis C virus-coinfected liver transplant recipients: a FIPSE/GESIDA prospective cohort study. Liver Transplantation, 18, 70–81.

Muller, E., Kahn, D., & Mendelson, M. (2010). Renal transplantation between HIV- positive donors and recipients. New England Journal of Medicine, 362(24), 2336–2337.

Muller, E., Barday, Z., Mendelson, M., & Kahn, D. (2012). Renal transplantation between HIV-positive donors and recipients justified. South African Medical Journal, 102(6), 497–498.

Muller, E., Barday, Z., Mendelson, M., Kahn, D., et al. (2015). HIV-positive-to-HIV- positive kidney transplantation—results at 3 to 5 years. New England Journal of Medicine, 372:613–20.

Neuhaus, J., Angus, B., Kowalska, J. D., et al. (2010). Risk of all-cause mortality associated with nonfatal AIDS and serious non-AIDS events among adults infected with HIV. AIDS, 24(5), 697–706.

OPTN Policies and Bylaws. From http:// optn.transplant.hrsa.gov/ policiesandbylaws/policies.asp.

Pais, R. & Benhamou, Y. (2010). Long-term therapy for chronic hepatitis B in HIV co-infected patients. Gastroente´ rologie Clinique et Biologique, 34, 136–41.

Parsa, A., Kao, W. H. L., Xie, D., et al, (2013). APOL1 risk variants, race, and progression of chronic kidney disease. New England Journal of Medicine, 369:2183–96.

Panel on Opportunistic Infections in HIV- Infected Adults and Adolescents.Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents; recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/ contentfiles/lvguidelines/adult oi.pdf. (Accessed September 2015).

Pelletier S. J., Norman S. P., Christensen L. L., et al. (2004). Review of transplantation in HIV patients during the HAART era. Clinical Transplantation, 63–82.

Petrosillo, N., Chinello, P., & Cicalini, S. (2006). Pulmonary hypertension in individuals with HIV infection. AIDS, 20, 2128.

Prevention, C. f. D. C. a. (2013). HIV Surveillance Supplemental Report. Ragni, M. V., Dodson, S. F., Hunt, S. C., et al. (1999). Liver transplantation in a hemophilia patient with acquired immunodeficiency syndrome. Blood, 93, 1113–1114.

Redd A. D., Quinn T. C., Tobian A. A. (2013). Frequency and implications of HIV superinfection. The Lancet Infectious Diseases, 13(7), 622–628.

Reeves-Daniel, A. M., DePalma, J. A., Bleyer, A. J., Rocco, M. V., Murea, M., Adams, P. L., et al. (2011). The APOL1 Gene and Allograft Survival after Transplantation. American Journal of Transplantation, 11(5), 1025–1030.

Richterman, A., Blumberg, E., (2015). The challenges and promise of HIV-infected donors for solid organ transplantation. Current Infectious Disease Reports, 17:1– 8.

Richterman, A., Sawinski, D., Reese, P.P., et al, (2015). An assessment of HIV-infected patients dying in care for deceased organ donation in a United States urban center. American Journal of Transplantation, 15:2105–2116.

Riella, L.V., Sheridan, A.M., (2015). Testing for high-risk APOL1 alleles in potential living kidney donors. American Journal of Kidney Disease, (in press).

Roland, M., Carlson, L., & Stock, P. (2002). Solid organ transplantation in HIV- infected individuals. AIDS Clinical Care, 14(7), 59–63.

Roland, M. E., Adey, D., Carlson, L. L., & Terrault, N. A. (2003a). Kidney and liver transplantation in HIV-infected patients: case presentations and review. AIDS Patient Care STDS, 17(10), 501–507.

Roland, M. E., Lo, B., Braff, J., & Stock, P. G. (2003b). Key clinical, ethical, and policy issues in the evaluation of the safety and effectiveness of solid organ transplantation in HIV-infected patients. Archives of Internal Medicine, 163(15), 1773–1778.

Roland, M. E., & Stock, P. G. (2003c). Review of solid-organ transplantation in HIV- infected patients. Transplantation, 75(4), 425–429.

Sawinski, D., Goldberg, D. S., Blumberg, E., et al. (2015) Beyond the NIH multicenter HIV transplant trial experience: Outcomes of HIV+ liver transplant recipients compared to HCV+ or HIV+/ HCV+ coinfected recipients in the United States. Clinical Infectious Disease, (in Press).

Sherman, K. E., Thomas, D., & Chung, R. T. (2014). Human immunodeficiency virus and liver disease forum 2012. Hepatology, 59(1), 307–317.

Sims, D. B., Uriel, N., Gonza´lez-Costello, J., et al. (2011). Human immunodeficiency virus infection and left ventricular assist devices: a case series. Journal of Heart and Lung Transplantation, 30, 1060–1064.

Soriano, V., Tuma, P., Labarga, P., et al. (2009). Hepatitis B in HIV patients: what is the current treatment and what are the challenges? Journal of HIV Therapy, 14(1), 13–18.

Stock, P. G., Barin, B., Murphy, B., Hanto, D., Diego, J. M., Light, J., et al. (2010). Outcomes of kidney transplantation in HIV-infected recipients. New England Journal of Medicine, 363(21), 2004–2014.

Taege, A. (2013). Organ transplantation and HIV progress or success? A review of current status. Curr Infectious Disease Reports, 15, 67–76.

Tector, A. J., Mangu, R. S., Chestovich, P., et al. (2006). Use of extended criteria livers decreases wait time for liver transplantation without adversity impacting posttransplant survival.

Annals of Surgery, 244, 439–450. Terrault, N. A., Roland, M. E., Schiano, T., Dove, L., Wong, M. T., Poordad, F., et al. (2012). Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection.

Liver Transplantation, 18(6), 716–726. Touzot, M., Pillebout, E., Matignon, M., Tricot, L., Viard, J. P., Rondeau, E., et al. (2010). Renal transplantation in HIV- infected patients: the Paris experience. American Journal of Transplantation, 10(10), 2263–2269.

Uriel, N., Jorde, U. P., Cotarlan, V., et al. (2009). Heart transplantation in human immunodeficiency virus-positive patients. Journal of Heart and Lung Transplant, 28, 667–669.

Uriel, N., Nahumi, N., Colombo, P. C., et al. (2014). Advance heart failure in patients infected with human immunodeficiency virus: is there equal access to care?

Journal of Heart and Lung Transplantation (in press, online). Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2013). Cause- specific life expectancies after 35 years of age for human immunodeficiency syndrome-infected and human immunodeficiency syndrome-negative individuals followed simultaneously in long-term cohort studies, 1984–2008.American Journal of Epidemiology, 177(2), 116–125.

Wada, N., Jacobson, L. P., Cohen, M., French, A., Phair, J., & Munoz, A. (2014). Cause- specific mortality among HIV-infected individuals, by CD4 (+) cell count at HAART initiation, compared with HIV-uninfected individuals. AIDS, 28(2), 257–265.

Yoon, S. C., Hurst, F. P., Jindal, R. M., George, S. A., Neff, R. T., Agodoa, L. Y., et al. (2011). Trends in renal transplantation in patients with human immunodeficiency virus infection: an analysis of the United States renal data system. Transplantation, 91(8), 864–868.

EINSTEIN
Albert Einstein College of Medicine
Office of Human Research Affairs
Montefiore
Science at the heart of medicine
Institutional Review Board
Albert Einstein College of Medicine
FWA #00023382
Montefiore Medical Center
FWA #00002558
North Bronx Healthcare Network
FWA #00009807
Yeshiva University
FWA #00000140
White Plains Hospital
FWA #00023382
East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817
West Campus IRB
Montefiore Medical Center
3306 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: June 26, 2024

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	115807
Amendment Approval Date:	06/26/2024	**Study Expiration Date:**	05/07/2025

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

This submission was approved with the following stipulations:

- Use only IRB stamped copies of the consent form(s). Do not use expired consent forms.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Data Use Agreements/ Material Transfer Agreements: If you are releasing data/specimens to an external site/entity/collaborator, you are required to obtain an executed DUA (Data Use Agreement)/ MTA (Material Transfer Agreement). This may be obtained through the Research Agreement Request Portal (https://einsteinmed.co1.qualtrics.com/jfe/form/SV_8fgVaus0Bpcpeux).

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: June 17, 2024

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	115356
Amendment Approval Date:	06/17/2024	**Study Expiration Date:**	05/07/2025

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual was added as Key Personnel: Olachi Wokonko

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Data Use Agreements/ Material Transfer Agreements: If you are releasing data/specimens to an external site/entity/collaborator, you are required to obtain an executed DUA (Data Use Agreement)/ MTA (Material Transfer Agreement). This may be obtained through the Research Agreement Request Portal (https://einsteinmed.co1.qualtrics.com/jfe/form/SV_8fgVaus0Bpcpeux).

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Re-approval

Date: May 09, 2024

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference # Study:**	113138
Approval Date:	05/08/2024	**Expiration Date:**	05/07/2025

This is to inform you that the Einstein IRB has reviewed and reapproved the above referenced human research project and informed consent document(s) for the period noted above at the IRB meeting held on 05/08/2024.

To access your reapproved/stamped consents: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

Expiration Notice: IRB approval for this full board study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report by 04/07/2025. To facilitate this, iRIS will send an email reminder 60 days prior to the due date. When this project is completed, submit a final Progress Report to close the file.

To prevent lapses in IRB approval the IRB recommends the following:

- Submission of Progress Report in iRIS 6 weeks prior to the expiration date
- Setting up a calendar reminder to submit the Progress Report (automatic iRIS notifications are often sent to SPAM).
- Maintaining a list of COI disclosures and CITI training for all Key Personnel, and proactively updating the disclosures and training on a regular basis. We recommend that COI disclosures be updated on a quarterly basis.
- Notifying the PI by phone or email to sign off on the Progress Report submission (automatic iRIS notifications are often sent to SPAM).
- Proactively tracking the Progress Report submission in IRIS to make sure the it is progressing in the system in a timely manner. You may track the status of your submission by going to Study Assistant > My Studies > Click on the notepad > Click on the colored icon under "Track Location" (right hand side of the page) and note the location of the submission by the first row in the list.

Reminders

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Data Use Agreements/ Material Transfer Agreements: If you are releasing data/specimens to an external site/entity/collaborator, you are required to obtain an executed DUA (Data Use Agreement)/ MTA (Material Transfer Agreement). This may be obtained through the Research Agreement Request Portal (https://einsteinmed.co1.qualtrics.com/jfe/form/SV_8fgVaus0Bpcpeux).

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Consent form posting requirement for federally sponsored clinical trials receiving initial approval from the IRB after January 20, 2019
The revised Common Rule requires that for each clinical trial conducted or supported by a Federal department or agency (such as the NIH), one IRB-approved informed consent form used to enroll subjects must be posted by the awardee on a publicly available Federal Web site.

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

At this time, there are two publicly available federal websites that will satisfy the consent form posting requirement: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

If additional information is needed, please contact the Administrative Office at 718-430-2237.

EINSTEIN
Albert Einstein College of Medicine
Office of Human Research Affairs
Montefiore

Science at the heart of medicine
Institutional Review Board
Albert Einstein College of Medicine
FWA #00023382
Montefiore Medical Center
FWA #00002558
North Bronx Healthcare Network
FWA #00009807
Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

https://www.einsteinmed.org/irb

Notification of Receipt of Reportable Event

Date: November 07, 2023

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	107253
Reportable Event Acknowledged Date:	11/02/2023	**Study Expiration Date:**	05/09/2024

The above noted reportable event was received by the Einstein IRB.

A follow-up report is not required.

Submissions Documents: To obtain a list of documents that were received with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: September 13, 2023

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	105994
Amendment Approval Date:	09/13/2023	**Study Expiration Date:**	05/09/2024

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual was added as Key Personnel: Paola Mejia.
The following individual was removed as Key Personnel: Samuel Sigal.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Data Use Agreements/ Material Transfer Agreements: If you are releasing data/specimens to an external site/entity/collaborator, you are required to obtain an executed DUA (Data Use Agreement)/ MTA (Material Transfer Agreement). This may be obtained through the Research Agreement Request Portal (https://einsteinmed.co1.qualtrics.com/jfe/form/SV_8fgVaus0Bpcpeux).

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: May 19, 2023

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	101505
Amendment Approval Date:	05/19/2023	**Study Expiration Date:**	05/09/2024

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual was added as Key Personnel: Milan Kinkhabwala

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Data Use Agreements/ Material Transfer Agreements: If you are releasing data/specimens to an external site/entity/collaborator, you are required to obtain an executed DUA (Data Use Agreement)/ MTA (Material Transfer Agreement). This may be obtained through the Research Agreement Request Portal (https://einsteinmed.co1.qualtrics.com/jfe/form/SV_8fgVaus0Bpcpeux).

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Re-approval

Date: May 11, 2023

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	099406
Approval Date:	05/10/2023	**Study Expiration Date:**	05/09/2024

This is to inform you that the Einstein IRB has reviewed and reapproved the above referenced human research project and informed consent document(s) for the period noted above at the IRB meeting held on 05/10/2023.

Prior to reapproval, IRB approval had lapsed from 4/26/23 to 5/9/23. To prevent future expirations, the following Corrective Action Plan has been implemented:

Submission of Progress Report in iRIS 6 weeks prior to the expiration date. Setting up a calendar reminder to submit the Progress Report. Maintaining a list of COI disclosures and CITI training for all Key Personnel, and proactively updating the disclosures and training on a regular basis. We recommend that COI disclosures be updated on a quarterly basis. Notifying the PI by phone or email to sign off on the Progress Report submission. Proactively tracking the Progress Report submission in IRIS to make sure it is progressing in the system in a timely manner.

Future lapses of approval may be considered serious or continuing noncompliance, and may be reportable to federal agencies.

To access your reapproved/stamped consents: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

Expiration Notice: IRB approval for this full board review study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report by 04/09/2024. To facilitate this, iRIS will send an email reminder 60 days prior to the due date. When this project is completed, submit a final Progress Report to close the file.

To prevent lapses in IRB approval the IRB recommends the following:

- Submission of Progress Report in iRIS 6 weeks prior to the expiration date

- Setting up a calendar reminder to submit the Progress Report (automatic iRIS notifications are often sent to SPAM).
- Maintaining a list of COI disclosures and CITI training for all Key Personnel, and proactively updating the disclosures and training on a regular basis. We recommend that COI disclosures be updated on a quarterly basis.
- Notifying the PI by phone or email to sign off on the Progress Report submission (automatic iRIS notifications are often sent to SPAM).
- Proactively tracking the Progress Report submission in IRIS to make sure the it is progressing in the system in a timely manner. You may track the status of your submission by going to Study Assistant > My Studies > Click on the notepad > Click on the colored icon under "Track Location" (right hand side of the page) and note the location of the submission by the first row in the list.

Reminders

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Data Use Agreements/ Material Transfer Agreements: If you are releasing data/specimens to an external site/entity/collaborator, you are required to obtain an executed DUA (Data Use Agreement)/ MTA (Material Transfer Agreement). This may be obtained through the Research Agreement Request Portal (https://einsteinmed.co1.qualtrics.com/jfe/form/SV_8fgVaus0Bpcpeux).

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Consent form posting requirement for federally sponsored clinical trials receiving initial approval from the IRB after January 20, 2019
The revised Common Rule requires that for each clinical trial conducted or supported by a Federal department or agency (such as the NIH), one IRB-approved informed consent form used to enroll subjects must be posted by the awardee on a publicly available Federal Web site.

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

At this time, there are two publicly available federal websites that will satisfy the consent form posting requirement: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

If additional information is needed, please contact the Administrative Office at 718-430-2237.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: April 24, 2023

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	099768
Amendment Approval Date:	04/24/2023	**Study Expiration Date:**	04/26/2023

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual was removed as Key Personnel: Milan Kinkhabwala

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Data Use Agreements/ Material Transfer Agreements: If you are releasing data/specimens to an external site/entity/collaborator, you are required to obtain an executed DUA (Data Use Agreement)/ MTA (Material Transfer Agreement). This may be obtained through the Research Agreement Request Portal (https://einsteinmed.co1.qualtrics.com/jfe/form/SV_8fgVaus0Bpcpeux).

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	099581
Amendment Approval Date:	04/17/2023	**Study Expiration Date:**	04/26/2023

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individuals were removed as Key Personnel: Stuart Greenstein,Pablo Loarte-Campos, Haider Al Anssari & Omar Al Ani

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Data Use Agreements/ Material Transfer Agreements: If you are releasing data/specimens to an external site/entity/collaborator, you are required to obtain an executed DUA (Data Use Agreement)/ MTA (Material Transfer Agreement). This may be obtained through the Research Agreement Request Portal (https://einsteinmed.co1.qualtrics.com/jfe/form/SV_8fgVaus0Bpcpeux).

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine | Office of Human Research Affairs | Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: September 14, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	092710
Amendment Approval Date:	09/14/2022	**Study Expiration Date:**	04/26/2023

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: June 27, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	090458
Amendment Approval Date:	06/27/2022	**Study Expiration Date:**	04/26/2023

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

This submission was approved with the following stipulation:

- Use only IRB stamped copies of the French (Creole) consent form. Do not use expired consent forms.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine
Office of Human Research Affairs
Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: June 09, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	089977
Amendment Approval Date:	06/09/2022	**Study Expiration Date:**	04/26/2023

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual(s) was added as Key Personnel: Fortune, Brett E. and Bellemare, Sarah

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: June 03, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	089796
Amendment Approval Date:	06/03/2022	**Study Expiration Date:**	04/26/2023

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

This submission was approved with the following stipulation:

- Use only IRB stamped copies of the French consent form. Do not use expired consent forms.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

https://www.einsteinmed.org/irb

Notification of Receipt of Reportable Event

Date: May 13, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	087727
Reportable Event Acknowledged Date:	05/11/2022	**Study Expiration Date:**	04/26/2023

The above noted reportable event was received by the Einstein IRB.

A follow-up report is not required.

Submissions Documents: To obtain a list of documents that were received with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: May 04, 2022

Principal Investigator: Yorg A Azzi

Study Title: Research protocol for kidney, Heart & Liver transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.

IRB #: 2016-6490

Reference #: 087815

Amendment Approval Date: 05/04/2022

Study Expiration Date: 04/26/2023

This amendment, (Title Change) was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Re-approval

Date: April 28, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	086733
Approval Date:	04/27/2022	**Study Expiration Date:**	04/26/2023

This is to inform you that the Einstein IRB has reviewed and reapproved the above referenced human research project and informed consent document(s) for the period noted above at the IRB meeting held on 04/27/2022.

To access your reapproved/stamped consents: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

Expiration Notice: IRB approval for this full board review study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report by 03/26/2023. To facilitate this, iRIS will send an email reminder 60 days prior to the due date. When this project is completed, submit a final Progress Report to close the file.

To prevent lapses in IRB approval the IRB recommends the following:

- Submission of Progress Report in iRIS 6 weeks prior to the expiration date
- Setting up a calendar reminder to submit the Progress Report (automatic iRIS notifications are often sent to SPAM).
- Maintaining a list of COI disclosures and CITI training for all Key Personnel, and proactively updating the disclosures and training on a regular basis. We recommend that COI disclosures be updated on a quarterly basis.
- Notifying the PI by phone or email to sign off on the Progress Report submission (automatic iRIS notifications are often sent to SPAM).
- Proactively tracking the Progress Report submission in IRIS to make sure the it is progressing in the system in a timely manner. You may track the status of your submission by going to Study Assistant > My Studies > Click on the notepad > Click on the colored icon under "Track Location" (right hand side of the page) and note the location of the submission by the first row in the list.

Reminders

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Consent form posting requirement for federally sponsored clinical trials receiving initial approval from the IRB after January 20, 2019
The revised Common Rule requires that for each clinical trial conducted or supported by a Federal department or agency (such as the NIH), one IRB-approved informed consent form used to enroll subjects must be posted by the awardee on a publicly available Federal Web site.

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

At this time, there are two publicly available federal websites that will satisfy the consent form posting requirement: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

If additional information is needed, please contact the Administrative Office at 718-430-2237.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: April 26, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	087093
Amendment Approval Date:	04/24/2022	**Study Expiration Date:**	04/27/2022

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual(s) was added as Key Personnel: Haider Al Anssari
The following individuals was removed as Key Personnel: Alani, Omar

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: April 21, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	087205
Amendment Approval Date:	04/21/2022	**Study Expiration Date:**	04/27/2022

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual(s) were added as Key Personnel: Cecilia Nucci, Christiana Gjelaj & Omar Saeed

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: April 15, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	087165
Amendment Approval Date:	04/15/2022	**Study Expiration Date:**	04/27/2022

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

This submission was approved with the following stipulations:

- Use only IRB stamped copies of the Spanish consent form. Do not use expired consent forms.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: April 13, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	087059
Amendment Approval Date:	04/12/2022	**Study Expiration Date:**	04/27/2022

This amendment, was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5687

Notification of Amendment Approval

Date: March 24, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	083614
Amendment Approval Date:	03/23/2022	**Study Expiration Date:**	04/27/2022

This amendment, was reviewed and approved at the IRB meeting held on 03/23/2022.

The following individual(s) were added as Key Personnel: **Samuel Sigal, Snehal R Patel,** and **Daniel Goldstein.**

This submission was approved with the following stipulations:

- Use only IRB stamped copies of the consent form(s). Do not use expired consent forms.
- A fully translated foreign language informed consent document must be approved by the Einstein IRB prior to enrolling non-English speaking participants.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-

approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine | Office of Human Research Affairs | Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: March 01, 2022

Principal Investigator: Yorg A Azzi

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	083973
Amendment Approval Date:	03/01/2022	**Study Expiration Date:**	04/27/2022

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual was added as Key Personnel: Yorg Azzi (Principal Investigator).
The following individuals were removed as Key Personnel: Juan Rocca (Principal Investigator) and Yorg Azzi (Co-Investigator)

This submission was approved with the following stipulations:

- Use only IRB stamped copies of the consent form(s). Do not use expired consent forms.
- Currently enrolled subjects must be informed of these changes at their next study visit and the research team must document this in the study records.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-

approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine | Office of Human Research Affairs | Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: October 15, 2021

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	081274
Amendment Approval Date:	10/15/2021	**Study Expiration Date:**	04/27/2022

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual was added as Key Personnel: Haider Al Anssari

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: September 13, 2021

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	080232
Amendment Approval Date:	09/12/2021	**Study Expiration Date:**	04/27/2022

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: August 31, 2021

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	079881
Amendment Approval Date:	08/31/2021	**Study Expiration Date:**	04/27/2022

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual(s) were added as Key Personnel: Vagish Hemmige

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5687

Notification of Amendment Approval

Date: August 26, 2021

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	077101
Amendment Approval Date:	08/25/2021	**Study Expiration Date:**	04/27/2022

This amendment was reviewed and approved at the IRB meeting held on 08/25/2021.

The following individual(s) were added as Key Personnel:
Harith Raees

This submission was approved with the following stipulations:

- Use only IRB stamped copies of the consent form(s). Do not use expired consent forms.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is

completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

White Plains Hospital
FWA #00023382

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

Notification of Amendment Approval

Date: June 18, 2021

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	077502
Amendment Approval Date:	06/18/2021	**Study Expiration Date:**	04/27/2022

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual(s) were added as Key Personnel: Harith Raees & Pablo M Loarte-Campos

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

Notification of Re-approval

Date: April 29, 2021

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	074324
Approval Date:	04/28/2021	**Study Expiration Date:**	04/27/2022

This is to inform you that the Einstein IRB has reviewed and reapproved the above referenced human research project and informed consent document(s) for the period noted above at the IRB meeting held on 04/28/2021.

To access your reapproved/stamped consents: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

Expiration Notice: IRB approval for this full board review study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report by 03/27/2022. To facilitate this, iRIS will send an email reminder 60 days prior to the due date. When this project is completed, submit a final Progress Report to close the file.

To prevent lapses in IRB approval the IRB recommends the following:

- Submission of Progress Report in iRIS 6 weeks prior to the expiration date
- Setting up a calendar reminder to submit the Progress Report (automatic iRIS notifications are often sent to SPAM).
- Maintaining a list of COI disclosures and CITI training for all Key Personnel, and proactively updating the disclosures and training on a regular basis. We recommend that COI disclosures be updated on a quarterly basis.
- Notifying the PI by phone or email to sign off on the Progress Report submission (automatic iRIS notifications are often sent to SPAM).
- Proactively tracking the Progress Report submission in IRIS to make sure the it is progressing in the system in a timely manner. You may track the status of your submission by going to Study Assistant > My Studies > Click on the notepad > Click on the colored icon under "Track Location" (right hand side of the page) and note the location of the submission by the first row in the list.

Reminders

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Consent form posting requirement for federally sponsored clinical trials receiving initial approval from the IRB after January 20, 2019
The revised Common Rule requires that for each clinical trial conducted or supported by a Federal department or agency (such as the NIH), one IRB-approved informed consent form used to enroll subjects must be posted by the awardee on a publicly available Federal Web site.

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

At this time, there are two publicly available federal websites that will satisfy the consent form posting requirement: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

If additional information is needed, please contact the Administrative Office at 718-430-2237.

EINSTEIN
Albert Einstein College of Medicine

Office of Human Research Affairs

Montefiore

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

https://www.einsteinmed.org/irb

Notification of Amendment Approval

Date: October 19, 2020

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	069629
Amendment Approval Date:	10/19/2020	**Study Expiration Date:**	05/05/2021

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual was added as Key Personnel: Harith Raees.
The following individual was removed as Key Personnel: Nawaf Hindosh

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Amendment Approval

Date: May 08, 2020

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	064544
Amendment Approval Date:	05/07/2020	**Study Expiration Date:**	05/05/2021

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Reapproval

Date: May 06, 2020

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	063779
Approval Date:	05/06/2020	**Study Expiration Date:**	05/05/2021

This is to inform you that the Einstein IRB has reviewed and reapproved the above referenced human research project and informed consent document(s) for the period noted above at the IRB meeting held on 05/06/2020.

To access your reapproved/stamped consents: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report by 04/05/2021. To facilitate this, iRIS will send an email reminder 60 days prior to the due date. When this project is completed, submit a final Progress Report to close the file.

Reminders

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Consent form posting requirement for federally sponsored clinical trials receiving initial approval from the IRB after January 20, 2019
The revised Common Rule requires that for each clinical trial conducted or supported by a Federal department or agency (such as the NIH), one IRB-approved informed consent form used to enroll subjects must be posted by the awardee on a publicly available Federal Web site.

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

At this time, there are two publicly available federal websites that will satisfy the consent form posting requirement: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

If additional information is needed, please contact the Administrative Office at 718-430-2237.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Amendment Approval

Date: April 06, 2020

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	063220
Amendment Approval Date:	04/06/2020	**Study Expiration Date:**	05/16/2020

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual was removed as Key Personnel: Oya Andacoglu

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Amendment Approval

Date: March 04, 2020

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	061111
Amendment Approval Date:	03/04/2020	**Study Expiration Date:**	05/16/2020

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual(s) were added as Key Personnel: Nawaf Hindosh & Vagish Hemmige.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Reapproval

Date: May 21, 2019

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	051464
Approval Date:	05/17/2019	**Study Expiration Date:**	05/16/2020

This is to inform you that the Einstein IRB has reviewed and reapproved the above referenced human research project and informed consent document(s) for the period noted above at the IRB meeting held on 05/17/2019.

To access your reapproved/stamped consents: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report by 04/01/2020. To facilitate this, iRIS will send an email reminder 60 days prior to the due date. When this project is completed, submit a final Progress Report to close the file.

Reminders

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Consent form posting requirement for federally sponsored clinical trials receiving initial approval from the IRB after January 20, 2019
The revised Common Rule requires that for each clinical trial conducted or supported by a Federal department or agency (such as the NIH), one IRB-approved informed consent form used to enroll subjects must be posted by the awardee on a publicly available Federal Web site.

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

At this time, there are two publicly available federal websites that will satisfy the consent form posting requirement: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

If additional information is needed, please contact the Administrative Office at 718-430-2237.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Amendment Approval

Date: April 03, 2019

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	051479
Amendment Approval Date:	04/03/2019	**Study Expiration Date:**	06/12/2019

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

This submission was approved with the following stipulation:

- Use only IRB stamped copies of the Spanish consent form. Do not use expired consent forms.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Amendment Approval

Date: March 28, 2019

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	050848
Amendment Approval Date:	03/28/2019	**Study Expiration Date:**	06/12/2019

This amendment, , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual was added as Key Personnel: Cindy Pynadath, Yorg Azzi & Oya Andacoglu.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Reapproval

Date: June 14, 2018

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	041957
		Study	
Approval Date:	06/13/2018	**Expiration Date:**	06/12/2019

This is to inform you that the Einstein IRB has reviewed and reapproved the above referenced human research project and informed consent document(s) for the period noted above at the IRB meeting held on 06/13/2018.

To access your reapproved/stamped consents: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report by 05/01/2019. To facilitate this, iRIS will send an email reminder 60 days prior to the due date. When this project is completed, submit a final Progress Report to close the file.

Reminders

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

If additional information is needed, please contact the Administrative Office at 718-430-2237.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Amendment Approval

Date: June 11, 2018

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	041953
Amendment Approval Date:	06/11/2018	**Study Expiration Date:**	07/11/2018

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

This submission was approved with the following stipulations:

- Use only IRB stamped copies of the consent form(s). Do not use expired consent forms.
- A fully translated foreign language informed consent document must be approved by the Einstein IRB prior to enrolling non-English speaking participants.
- Currently enrolled subjects must be informed of these changes at their next study visit and the research team must document this in the study records.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Amendment Approval

Date: April 10, 2018

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	040189
Amendment Approval Date:	04/10/2018	**Study Expiration Date:**	07/11/2018

This amendment, was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individuals were removed as Key Personnel: Mortadha Abd, Michelle Lubetzky & Layla Kamal.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Reapproval

Date: July 12, 2017

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	030110
		Study	
Approval Date:	07/12/2017	**Expiration Date:**	07/11/2018

This is to inform you that the Einstein IRB has reviewed and reapproved the above referenced human research project and informed consent document(s) for the period noted above at the IRB meeting held on 07/12/2017.

To access your reapproved/stamped consents: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report by 06/11/2018. To facilitate this, iRIS will send an email reminder 60 days prior to the due date. When this project is completed, submit a final Progress Report to close the file.

Reminders

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

If additional information is needed, please contact the Administrative Office at 718-430-2237.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Amendment Approval

Date: January 06, 2017

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	025620
Amendment Approval Date:	01/05/2017	**Study Expiration Date:**	07/12/2017

This amendment was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

This submission was approved with the following stipulations:

- Use only IRB stamped copies of the Spanish consent form. Do not use expired consent forms.
- The HIPAA Authorization was incorporated into the approved consent.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

EINSTEIN
Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Amendment Approval

Date: November 10, 2016

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	024053
Amendment Approval Date:	11/10/2016	**Study Expiration Date:**	07/12/2017

This amendment, Amendment 1 dated 24 October 2016 , was reviewed and approved by expedited review under 45 CFR 46.110 and 21 CFR 56.110.

The following individual(s) were added as Key Personnel obtaining informed consent: Omar Mohammed.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

Reminders

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report prior to the expiration of the study. When the research is completed, submit a final Progress Report. The iRIS system will generate an email notification 60 days prior to the expiration of this study's approval. However, it is your responsibility to ensure that a Progress Report has been submitted by the required time.

Albert Einstein College of Medicine

Science at the heart of medicine

Institutional Review Board

Albert Einstein College of Medicine
FWA #00023382

Montefiore Medical Center
FWA #00002558

North Bronx Healthcare Network
FWA #00009807

Yeshiva University
FWA #00000140

East Campus IRB
Jack and Pearl Resnick Campus
1300 Morris Park Ave., Belfer 1002
Bronx, NY 10461
718.430.2237 fax 718.430.8817

West Campus IRB
Montefiore Medical Center
3308 Rochambeau Avenue
Bronx, NY 10467
718.798.0406 fax 718.798.5657

http://www.einstein.yu.edu/irb

Notification of Approval

Date: August 02, 2016

Principal Investigator: Juan Rocca

Study Title:	Research protocol for kidney transplantation from HIV+ donors into HIV+ recipients under the Final HIV Organ Policy Equity (HOPE) Act.		
IRB #:	2016-6490	**Reference #:**	018876
Type of Submission:	Submission Response for Initial Review Submission form		
Approval Date:	08/01/2016	**Expiration Date:**	07/12/2017

The above referenced submission, made in response to stipulations put forth by the Einstein IRB at the Full Board meeting of 07/13/2016, was reviewed and approved by expedited procedures on 08/01/2016, in accordance with 45 CFR 46.110(b)(2) and 21 CFR 56.110(b)(2).

This submission was approved with the following stipulations:

- Use only IRB stamped copies of the consent form(s) in your research. Do not use expired consent forms.
- The HIPAA Authorization was incorporated into the approved consent.
- A fully translated foreign language informed consent document must be approved by the Einstein IRB prior to enrolling non-English speaking participants.
- The waiver of informed consent and HIPAA authorization for accessing medical/clinical records for recruitment purposes was approved.

All changes to a study must receive IRB approval before they are implemented. The only exception to the requirement for prior IRB review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(b)(4), 21 CFR 56.108(a)). In such cases, report the actions taken as a reportable event.

Reportable Events must be reported to the IRB in compliance with the Einstein IRB policy.

Expiration Notice: IRB approval for this study is limited to the period specified above. In order to gain re-approval, you must submit a Progress Report by 05/29/2017. To facilitate this, iRIS will send an email reminder 60 days prior to the due date. When this project is completed, submit a final Progress Report to close the file.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of

submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to Study Assistant – My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.