HIV Organ Policy Equity (HOPE) Act Research Criteria: follow-up discussion

Advisory Committee on Organ Transplantation
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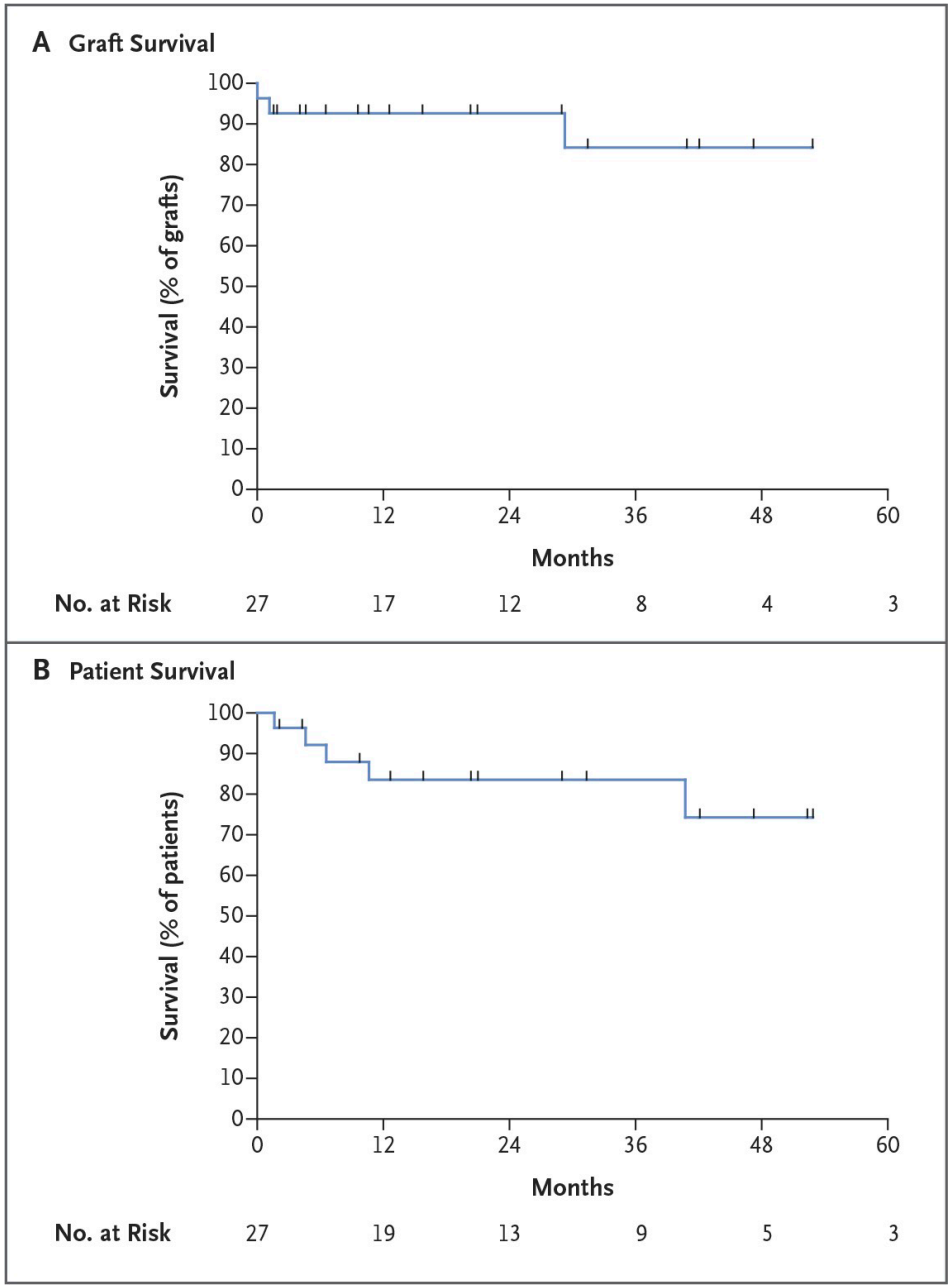

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Table 1. Characteristics of HIV-Positive Kidney-Transplant Recipients at Baseline.*

Characteristic	Patients (N = 27)
Age — yr	
Median	41
Interquartile range	39–43
Male sex — no. (%)	15 (56)
Race — no (%)†	
Black	26 (96)
Mixed race	1 (4)
Cause of chronic kidney disease — no. (%)	
Hypertension	1 (4)
Membranous glomerulonephritis	1 (4)
Biopsy-confirmed HIV-associated nephropathy	5 (19)
Presumed HIV-associated nephropathy	20 (74)
CD4 T-cell count — cells/mm^3	
Median	288
Interquartile range	236–511
Positive for hepatitis B surface antigen — no. (%)	3 (11)
ART regimen — no. (%)	
Protease inhibitor–based therapy	11 (41)
NNRTI-based therapy	16 (59)
Antibody induction therapy‡	
ATG	
No. of patients (%)	10 (37)
Cumulative dose — mg	
Median	475
Interquartile range	400–750
Thymoglobuline	
No. of patients (%)	17 (63)
Cumulative dose — mg	
Median	600
Interquartile range	450–1000

* ART denotes antiretroviral therapy, HIV human immunodeficiency virus, and NNRTI nonnucleoside reverse-transcriptase inhibitor.
† Race was self-reported.
‡ Antibody induction therapy was performed with the use of rabbit antithymocyte globulin (ATG [Fresenius] or Thymoglobuline [Sanofi]).

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Table 2. Rejection Episodes after Transplantation.

Time from Transplantation to Rejection Episode	Treatment		Outcome
	Medication or Other Treatment	Total Dose	
Patient 5			
2 yr	Methylprednisolone	2000 mg	Functioning graft
3 yr 3 mo	ATG	700 mg	Functioning graft
Patient 7			
1 yr 7 mo	Methylprednisolone	2000 mg	Functioning graft
2 yr 3 mo	Methylprednisolone	2000 mg	Graft failure
Patient 9			
4 mo	Methylprednisolone	2000 mg	Functioning graft
2 yr 9 mo	Methylprednisolone	2000 mg	Functioning graft
Patient 17			
1 wk	Thymoglobuline and plasmapheresis	800 mg	Graft failure
Patient 27			
1 wk	Thymoglobuline and plasmapheresis	500 mg	Functioning graft

Research Criteria - Overview

1) Protect safety of research subjects and the general public

2) Transplant centers must have experience with HIV- to HIV+ transplantation before embarking on medically more complex and less well-defined HIV+ to HIV+ transplantation

3) Currently, that experience in the US exists only for kidney and liver transplantation

Research Criteria – Overview (2)

4) Address minimum safety and data requirements of clinical research

4) Does not describe all the details and necessary components of an IRB-approved research protocol for HIV+ to HIV+ organ transplantation

5) Criteria do not supplant current policies and regulations governing organ transplantation, human subjects research, consent process, confidentiality & privacy; rather these criteria serve to supplement existing policies and regulations

Categories

1) Donor eligibility

2) Recipient eligibility

3) Transplant program qualifications

4) OPO responsibilities

5) Prevention of inadvertent transmission of HIV

6) Outcome measures (minimum)
   - Wait list
   - Donor organs (deceased and living)
   - Living donors (post donation)
   - Transplant recipients

Donor eligibility

Deceased donor with known history of HIV infection	CD4+ T cell count ≥ 200/uL or ≥14%
	HIV-1 RNA < 50 copies/mL; No history of viral load > 1000 copies/ml in the prior 12 months
	No active opportunistic infection
Deceased donor with newly diagnosed HIV infection	CD4+ T cell count ≥ 200/uL or ≥14%
	Viral load: no requirement
	No active opportunistic infection
Living HIV+ donor	Well controlled HIV infection
	CD4+ T cell count (lifetime nadir) ≥ 200/uL
	CD4+ T cell count ≥ 500/uL for the 6-month period before donation
	HIV-1 RNA < 50 copies/mL
	No opportunistic infections
	Pre-transplant donor allograft biopsy

Recipient eligibility

Recipient (HIV+) Eligibility	
	CD4+ T cell count ≥ 200/uL (kidney) CD4+ T cell count ≥ 100uL (liver) within 16 weeks prior to transplant; or ≥ 200uL with history of opportunistic infection
	HIV-1 RNA < 50 copies/mL and on a stable antiretroviral regimen
	No active opportunistic infection or neoplasm
	No history of chronic cryptosporidiosis, primary CNS lymphoma, or progressive multifocal leukoencephalopathy

Transplant programs

Transplant Program Criteria	
	Medical center with established program for care of HIV+ subjects HIV program expertise on the transplant team
	Experience with HIV- to HIV+ organ transplantation
	Standard operating procedures (SOPs) and training for the organ procurement, implanting/operative, and postoperative care teams for handling HIV infected subjects, organs, and tissues.
	IRB-approved research protocol in HIV+ to HIV+ transplantation Institutional biohazard plan outlining measures to prevent and manage inadvertent exposure and/or transmission of HIV
	Provide each living HIV+ donor and HIV+ recipient with an "Independent Advocate"
	Policies and SOPs governing the necessary knowledge, experience, skills, and training for independent advocates Experience with at least 5 HIV uninfected to HIV+ transplants with designated organ(s) over last 4 years (minimum). IRB will evaluate key personnel in the context of total expertise and experience

OPOs

OPO Responsibilities	
	SOPs and staff training procedures for working with deceased HIV+ donors and their family and kin in pertinent history taking, medical chart abstraction, the consent process and handling blood, tissues, organs and biospecimens Biohazard plan to prevent and manage HIV exposure and/or transmission

HIV Transmission

Prevention of Inadvertent HIV Transmission	**Each participating Transplant Program and OPO shall develop an institutional biohazard plan for handling of HIV+ organs designed to prevent and/or manage inadvertent transmission or exposure to HIV** **Procedures must be in place to ensure that human cells, tissues, and cellular and tissue-based products (HCT/Ps) are not recovered from HIV+ donors for implantation, transplantation, infusion, or transfer into a human recipient; however, HCT/Ps from a donor determined to be ineligible may be made available for nonclinical purposes.**

Outcome measures (bare bones)

Required Outcome Measures	
Wait List (all)	HIV status
	CD4+ T cell counts
	Co-infection (HCV, HBV)
	HIV viral load
	ART resistance
	Removal from wait list (death or other reason)
Donors (all)	Living or deceased
	HIV status (new diagnosis or known diagnosis)
	CD4+ T cell count
	Co-infection (HCV, HBV)
	HIV viral load
	ART resistance

Outcome measures (2)

Required Outcome Measures	
Living Donors	Progression to renal insufficiency in kidney donors (serum creatinine > 2 mg/dl, serum creatinine level twice the pre-donation creatinine level, or proteinuria)
	Progression to hepatic insufficiency in living donors (INR > 1.5 and/or total bilirubin > 2.0)
	Change in ART regimen as a result of organ dysfunction
	Progression to AIDS
	Failure to suppress viral replication (persistent HIV viremia)
	Death

Outcome measures (3)

Transplant Recipients	Rejection rate (Years 1 & 2)
	Progression to AIDS
	New opportunistic infections
	Failure to suppress viral replication (persistent HIV viremia)
	HIV-associated organ failure
	Malignancy
	Graft failure
	Mismatched ART resistance versus donor
	Death

ACOT

1) Need for prior transplant experience in HIV- to HIV+ solid organ transplantation

2) Pre-implant biopsies (? Required)

3) Living HIV+ donors (? Excluded)

4) Mechanism by which the Secretary will gather and assemble outcome data from research protocols (under HOPE Act) in order to re-evaluate and tweak the on-going program

5) Other issues