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| **PROTOCOL TITLE:** HIV positive Kidney and Simultaneous Kidney Pancreas Transplant Candidate and Recipient Management |
| **APPLICABLE FACILITIES:**☐EHC ☐EDH ☐EHH☒EUH ☐EUHM ☐EUHS | ☐EHI☐EUOSH | ☐EHN☐EWWH | ☐EJCH☐RJV-ERH | ☐ELTAC ☐ESJH☐RJV-ESOP ☐TEC/ESA |
| **EFFECTIVE DATE:** 10/21/2020 | **ORIGINATION DATE:** 02/15/2017 |

# CONTENT:

**Referral:**

* Referrals will be received through the ETC Renal Transplant intake process using the standard program referral forms and requirements.
* Patient will be scheduled to attend day 1 evaluation.

# Evaluation:

* **Day 1 evaluation**: per standard procedure (see Kidney and Pancreas Recipient Evaluation).

# ID visit

* Following day one evaluation, patients will be scheduled for Transplant ID consultation.
* Historical ID records should be available and scanned into EeMR prior to the consult appointment. If records have not been received, the patient may still have the ID and surgical consult appointments. However, a determination about candidacy for continuing evaluation may be deferred until additional records are available.
* If the patient is a “No Show” for this consult visit, please refer to “Patient Appointment No Show Policy.”
* The Transplant ID provider will make a determination regarding the patient’s candidacy relative to his/her HIV medical status, with the following eligibility criteria guidelines:

# Medical criteria:

To be eligible to proceed with listing, Kidney transplant alone patients should have:

* CD4 count of > 200/µL or =15% on 2 consecutive occasions at least 3 months apart.
	+ For Simultaneous Kidney Pancreas candidates, CD4 count of > 350/µL on 2 consecutive occasions at least 3 months apart
* HIV viral load of < 1000 copies OR the reasonable expectation of the Transplant ID provider that viral suppression can be achieved with medical management
	+ For Simultaneous Kidney Pancreas candidates, HIV viral load of < 100 IU/mL (<2.0 Log) OR the reasonable expectation of the Transplant ID provider that viral suppression can be achieved with medical management
* Must be on effective antiretroviral therapy regimen for > 6 months (exception: patient who has never been on ART and has undetectable VL and eligible CD4 count without medications, ART will be started at the time of transplantation). Patients not already on effective antiretroviral therapy prior to transplant must be willing to start therapy in the early post-transplant period.

The following are EXCLUSIONS to transplantation::

* history of Progressive multifocal leukoencephalopathy (PML)
* history of Chronic intestinal cryptosporidiosis of > 1 month duration
* history of Primary CNS lymphoma
* history of pulmonary coccidiodomycosis treated per recommended treatment guidelines and generally should require a 5-year disease-free off of antifungals
* history of any neoplasm except for the following: cutaneous Kaposi’s sarcoma, *in situ* anogenital carcinoma, adequately treated basal or squamous cell carcinoma of the skin, and solid tumors (except primary CNS lymphoma) treated with curative therapy and disease free for more than 5 years.
* History of renal cell carcinoma requires disease-free state for 2 years.
* History of leukemia will be evaluated on an individual basis in consultation with Hematology/Oncology service
* current BMI < 17

Simultaneous Kidney Pancreas candidates, in addition to the above medical conditions, who have or had any of the following are NOT medically eligible to proceed with transplant evaluation:

* any Kaposi’s sarcoma
* history of Cryptococcal infections
* history of histoplasmosis, coccidiomycoses or other invasive fungal infections with the exception of Candidiasis
* history of Toxoplasmosis of the brain
* Disseminated *Mycobacterium avium* infection

If the patient is found to not a candidate for transplant at the consultation visit, NAC letters will be drafted and mailed to the patient and referring provider (reference: Correspondence Procedure).

# HCV co-infected patients:

Patients who are HCV antibody positive will have HCV viral load by PCR measured.

* HCV ab positive with an undetectable HCV viral load (PCR) patients will be eligible for transplant without additional work-up.
* HCV ab positive patients with a detectable HCV viral load (PCR) will be referred to Hepatology for evaluation.
	+ Treatment of HCV should be deferred until after transplant so as to increase the possible donor pool, unless treatment is deemed urgent by hepatology or Infectious Diseases.
	+ Patients should be willing and able to take therapy post-transplant.
	+ Development of a post-transplant HCV treatment plan will be developed by Transplant ID and Hepatology readdressed at the time of transplant and instituted within 3 months post-transplant.\
* Patients in whom the liver biopsy indicates cirrhosis and likely need for liver transplant will not be eligible to proceed with evaluation for kidney transplant.

# Medical Testing and Day 2 evaluation.

* If the patient is found to be a suitable candidate by Transplant ID and Transplant Surgery, additional testing orders will be signed and processed for scheduling. Medical Testing and Day 2 consults will be scheduled.
* Day 2 evaluation will be completed per standard procedure (see Kidney and Pancreas Recipient Evaluation).

# UNOS Listing:

Once the evaluation process is complete and the patient is found to be a suitable candidate for transplant, a listing packet will be sent to patient per the Kidney and Pancreas Waitlist Management protocol. The patient will be informed (with the HIV patient criteria information sheet) of their obligation to provide updated records of follow-up with their ID provider every 6 months and the need for updated CD4 count and an HIV viral load laboratory test results every 6 months. These results should be forwarded to the transplant center every 6 months in order for them to remain active for transplant. The patient’s primary HIV Provider (carbon copy the referring nephrologist as well) will be informed of these requirements in the HIV Provider Listing Letter.

# Wait List Management:

Status of Wait-listed patients will be reviewed every 6 months as per the Procedure for HIV Lab Monitoring by the Organ Placement Program.

# Transplant:

To be eligible for transplantation, at the time of the organ offer, patients must have**:**

* HIV viral load of **<1000** copies (<100 copies for Kidney/Pancreas) within the 6 months (plus one month grace period) prior to the organ offer
* CD4 count **>200/µL or = 15%** (>350/uL for Kidney/Pancreas) within the 6 months (plus one month grace period) prior to the organ offer
* For HIV-related research studies (HOPE in Action and HIV-TR CCR5) the lab interval is 4 months (see OPP Procedure for Review of Hope In Action Potential Kidney Recipients)
* no active infections
* be on antiretroviral therapy (exception: patient who has never been on ART and still meets viral load and CD4 count criteria)

# Post-Transplant Management:

Infectious Disease service will be consulted upon admission for transplant on all HIV positive transplant patients.

# IMMUNOSUPPRESSION: RECOMMENDED REGIMENS

*Induction:*

* For most patients: Basiliximab per Tacrolimus 1.5 protocol
* For SKPT or PTA: Thymoglobulin per Thymoglobulin 1.0 protocol

*Maintenance calcineurin Inhibitor*

* Tacrolimus dosing should be initiated as follows:
	+ If patient is taking a ritonavir (Norvir, Kaletra), or cobicistat (Stribild, Genvoya, Tybost, Evotaz, Prezcobix) containing regimen, then a single load dose should be

given in the OR, then daily levels should be obtained. Subsequent dosing should be done under the direction of the clinical pharmacist and inpatient ID team.

* + If patient is not taking ritonavir or cobicistat, then Tacrolimus 1.5 standard of care protocol should be used.
		- Please note that patients on unboosted protease inhibitors (eg Atazanavir, Fosamprenavir) should have tacrolimus levels watched very closely due to possible interactions\*\*

*Mycophenolate mofetil (Cellcept)*

* Per the Tacrolimus 1.5 standard of care protocol

*Prednisone*

* Per the Tacrolimus 1.5 standard of care protocol

# OPPORTUNISTIC INFECTION PROPHYLAXIS: RECOMMENDED REGIMENS

*Pneumocystis jirovecii* Pneumonia (PCP)

* Regimen: Bactrim 1 single strength tablet (80 mg trimethoprim/400 mg sulfamethoxazole) PO daily for **6 months, or until CD4 > 200 or > 14, whichever is longer.**

# \*\*For patients that receive ATG induction, they should be on PCP prophylaxis for at least a year, or until CD4 > 200 or > 14, whichever is longer.\*\*

* Alternatives: dapsone 100 mg PO QD (dapsone contraindicated if G6PD deficient).
* If Bactrim and dapsone allergic (or G6PD deficient), consider atovaquone 1500 mg PO daily or aerosolized pentamidine 300 mg via Respirgard II nebulizer monthly.

*Toxoplasmosis*

* Indication: Primary prophylaxis is indicated for Toxoplasma IgG positive pts with CD4 count

< 200. Secondary prophylaxis should be reinstituted immediately post-transplant for one month for any patient with prior history of Toxoplasmosis and whenever CD4 count drops below 200 cells. May be discontinued when CD4 count is >200 for 6 months.

* Preferred Regimen: Bactrim SS 1 tab PO q day
* Alternatives: dapsone 100 mg PO daily + pyrimethamine 50 mg PO QD + leucovorin 25 mg PO QD; atovaquone 1500 mg PO QD with dinner; Alternative: for patients who cannot tolerate sulfa drugs pyrimethamine 25 mg PO QD plus clindamycin 300 mg PO QID. (Note that only the combination of pyrimethamine plus sulfadiazine appears to provide protection against PCP, thus PCP prophylaxis must be continued with this regimen.)

*Mycobacterium avium* Complex (MAC)

* *Primary Prophylaxis (Patients with No Prior History of MAC)*
* Indication: If CD4 count drops < 75 cells/µL. May be discontinued when CD4 count is above 100 cells/µL
* Preferred Regimen: azithromycin 1200 mg PO weekly
* Alternative: Because of the risk of rejection due to drug interaction with calcineurin inhibitors, rifabutin and rifampin should be avoided for prophylaxis unless all other alternatives have been exhausted. If unable to tolerate a macrolide, consider rifabutin 300 mg PO QD. Rifabutin must be administered at one-half the usual daily dose (i.e., reduce

from 300 mg to 150 mg PO QD) with protease inhibitors. Should discuss with pharmacy or Transplant ID changes to CNI dosing.

* *Secondary Prophylaxis (Patients with a Prior History of MAC)*
* Indication: Reinstitute immediately post-transplant for one month and whenever the CD4 count drops below 75 cells/µL. May be discontinued when CD4 count is above 100 for 6 months. Should also be reinstituted during treatment for AR and for one month following completion of AR therapy (unless CD4 count drops below 75)
* Preferred Regimen: azithromycin 600 mg PO QD in combination with ethambutol 15 mg/kg/day. Regimen may be modified based on previous MAC treatment.
* Alternative: clarithromycin 500 mg PO BID plus ethambutol 15 mg/kg/day (Clarithromycin inhibits clearance of tacrolimus and the tacrolimus dose should be decreased by half unless the patient is already taking ritonavir.). Because of the risk of rejection due to drug interaction with calcineurin inhibitors, **rifabutin and rifampin should be avoided for prophylaxis** unless all other alternatives have been exhausted.

*Cytomegalovirus (CMV)*

* *Primary Prophylaxis (Patients with No Prior History of CMV)*
* Per to CMV protocol
* *Secondary Prophylaxis (Patients with a Prior History of CMV)*
* Preferred Regimen: valganciclovir 900 mg PO QD

*Epstein Barr Virus (EBV)*

Patients who are EBV negative and receive a transplant from EBV positive donor will be monitored for EBV infection per standard of care.

# OPPORTUNISTIC INFECTION MONITORING GUIDELINES

Retinitis is the major manifestation of HIV-associated CMV end-organ disease. This is a sight threatening disorder. Floaters and peripheral visual defects are common but may not be present, thus screening is standard of care in HIV-infected patients with CD4 counts < 50. Thus, any newly CMV viremic subject should have an ophthalmologic dilated fundoscopic examination within 3 - 7 days, or immediately if any visual symptoms including floaters or peripheral visual defects are present.

# Post-transplant monitoring

* Patients will be followed per the ETC Renal Transplant clinical pathway, with the following additions:
* Due to the known drug interactions, this patient population will require careful follow-up and monitoring of drug levels, therefore, patients will be educated that more frequent lab and clinic appointments may be necessary in the immediate post-transplant period.
* Additional laboratory monitoring:
* HIV RNA and CD4 counts will be drawn at month 1, 3, 6, 9, and 12 and annually thereafter.
* HCV ab positive patients (for patients not under active treatment for HCV) HCV viral load will be drawn at 1, 3, and 12 months and annually.
* Patients will be seen by transplant ID at month 1 post-transplant. Additional consultation will be made on a PRN basis. Transplant ID physician will contact the pts primary ID provider at time of transplant and 1 month visit to communicate any ART changes and coordinate pts care recommendations going forward.

# Treatment of acute rejection

* AR events will be treated per standard of care for renal transplant. If Thymoglobulin therapy is indicated, patient should undergo close monitoring of CD4 count.
* All patients on Thymoglobulin will have CMV prophylaxis and PCP prophylaxis resumed.
* Re-institution of other secondary opportunistic infection prophylaxis will be required if CD4 count drops below 200/µL. (reference Section 5.2)

# RELATED POLICIES / PROCEDURES:

Kidney and Pancreas Recipient Evaluation protocol

Organ Placement Program Management: Procedure for HIV Lab Monitoring Audit for Renal/Pancreas HIV Provider Listing Letter

HIV Patient criteria information sheet

# DEFINITIONS:

N/A

# REFERENCES AND SOURCES OF EVIDENCE:

Grossi et al. AJT 2012

Akhtar et al. Transplant Proc 2011 Genzini et al. Transplant Proc 2010 Miro et al. Transplant Proc 2012 Mittal et al. Int J AIDS 2016

Toso et al AJT 2003

Stock PG, et al. NEJM 2010 Roland ME, et al. AIDS 2016

# KEY WORDS:

HIV, kidney transplant, pancreas transplant