EMORY HEALTHCARE

PROTOCOL TITLE: Kidney and Pancreas Post-Transplant: Immunosuppression							
APPLICABLE FACILITIES:							
☐EHC	☐EDH	☐EHH	☐EHI	☐EHN	☐EJCH	☐ELTAC	☒ESJH
☒EUH	☐EUHM	☐EUHS	☐EUOSH	☐EWWH	☐RJV-ERH	☐RJV-ESOP	☒TEC/ESA
EFFECTIVE DATE: 03/30/2022					**ORIGINATION DATE:** 3/4/2015		

CATEGORY:
Diagnostic/Therapeutic/Preventive, Medication Guidelines

LEVEL:
Independent

CONTENT:
The renal transplant program's primary immunosuppression protocol for renal transplant recipients will include basiliximab induction and maintenance therapy with belatacept plus tacrolimus overlap, mycophenolate mofetil and corticosteroids. Patients who do not meet criteria to receive belatacept maintenance long-term will receive either basiliximab or thymoglobulin induction along with tacrolimus, mycophenolate mofetil andcorticosteroids.

Primary – Belatacept 2.7 (with tacrolimus overlap)
1. Belatacept criteria for use:

   a. EBV positive serology (positive viral capsid antigen IgG)

   b. DDRT, LDT, or DDRT/LDT after liver transplant
   c. Includes ECD

   d. Includes re-transplant

   e. Includes high PRA

   f. Includes 6 antigen LDT

   g. Includes Hepatitis B & C

2. Exclusion criteria:

   a. EBV negative (negative viral capsid antigen IgG)

   b. PAK, SKPT or other combination transplant

   c. HIV+

d. ANY History of PTLD, lymphoma or hematologic malignancy
Note: EBV seropositive patients are defined as having evidence of acquired immunity shown by the presence of IgG antibodies to viral capsid antigen (VCA). IgM antibodies to viral capsid antigen or IgG antibodies to EBV nuclear antigen (EBNA) may be positive or negative.

e. CMV high risk (donor CMV positive and recipient CMV negative).
- May consider belatacept initiation in select patients:
  - If no h/o viremia by 18 months post-transplant
  - If h/o viremia, must be CMV viremia free for 1 year and have adequate CMV specific CD4 and CD8 T-cell immunity

3. Other patient considerations:

a. Transportation/Location

b. Difficult intravenous access

4. Patients admitted for DDRT will receive tacrolimus po 4mg q12h and mycophenolate mofetil 1000mg po q12h on admission, prior to and following transplant. Living donor recipients will take one time tacrolimus and mycophenolate dose the night before admission, and receive 4mg tacrolimus and mycophenolate 1000mg in pre-op holding. Belatacept, basiliximab, and corticosteroids will be given intra-op. Post-operatively, tacrolimus, mycophenolate mofetil and corticosteroids will continue as outlinedbelow.

	Intra-op	POD1	POD2	POD3	POD4
Belatacept	10mg/kg	x	x	x	x
Basiliximab	20mg IV	x	x	x	x
Tacrolimus	4 mg po q12h begun prior to transplant ----------				
MMF	1000mg po q12h begun prior to transplant ----------				
Corticosteroids	500mg IV	250mg IV	125mg IV	5mg PO qd----------	

5. Belatacept Schedule with Confirmation of Eligibility Status

a. 10mg/kg – Day 0 (intra-operatively)

b. 5mg/kg – beginning month 1 and monthly thereafter

c. Refer to ETC Belatacept Dosing for Solid Organ Transplant Recipients protocol for additional dosing and infusion information

6. Tacrolimus Dosing and Schedule

a. Tacrolimus 4mg q12h will be initiated on admission and continued post-operatively.

b. Tacrolimus goal trough levels:

- 5-8 ng/ml for months 0-1 post-transplant
- 3-5 ng/ml for months 1-9 post-transplant

Note: For patients receiving Thymoglobulin for rejection, goal trough level should be reduced to 3-5 ng/ml until month 9, and then tapered.

c. Begin taper off of tacrolimus at month 9 with eventual discontinuation by month 11. At month 9, decrease tacrolimus dose by 1/3. Decrease tacrolimus dose by another 1/3 at month 10. Discontinue tacrolimus at month 11.

Month 9 tacrolimus dose	Initial dose reduction	Month 10 dose reduction	Month 11
0.5 mg q12h (Prograf level < 5 ng/ml)	0.5 mg daily	Discontinue	--
0.5mg q12h (Prograf level > 5 ng/ml)	0.5 mg daily	0.5mg every other day	Discontinue
1mg daily (Prograf level < 5 ng/ml)	0.5 mg daily	Discontinue	--
1mg daily (Prograf level > 5 ng/ml)	0.5 mg daily	0.5mg every other day	Discontinue
1mg q12h (Prograf level < 5 ng/ml)	1 mg daily	Discontinue	--
1mg q12h (Prograf level > 5 ng/ml)	0.5 mg q12h	0.5 mg daily	Discontinue
2mg q12h (Prograf level < 5 ng/ml)	1 mg q12	1 mg daily	Discontinue
2mg q12h (Prograf level > 5 ng/ml)	1.5 mg q12h	1 mg q12h	Discontinue
3 mg q12h	2 mg q12h	1 mg q12h	Discontinue
4 mg q12h	3 mg q12h	2 mg q12h	Discontinue
5 mg q12h	3 mg q12h	2 mg q12h	Discontinue
6 mg q12h	4 mg q12h	2 mg q12h	Discontinue
7 mg q12h	5 mg q12h	3 mg q12h	Discontinue
8 mg q12h	6 mg q12h	3 mg q12h	Discontinue
9 mg q12h	6 mg q12h	3 mg q12h	Discontinue
10 mg q12h	7 mg q12h	4 mg q12h	Discontinue

d. Additional every 2 week lab checks from month 9 thru month 13 (for 3 months after discontinuation of tacrolimus).

7. Mycophenolate mofetil will be dosed based on weight at time of transplant per “Weight based dosing of MMF” Protocol.

Secondary – Tacrolimus 1.5

Patients who do not meet criteria for belatacept will receive basiliximab induction withtacrolimus, mycophenolate mofetil and corticosteroids maintenance therapy. This includes combination transplants (such as kidney-liver or kidney-heart), HIV positive, or are ineligible to receive belatacept.

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1. Patients will receive doses of tacrolimus and mycophenolate mofetil orally pre-op and continue post- op as outlined below.

    a. **Exception:** HIV patients on protease inhibitors such as ritonivir, atazanavir,darunavir, saquinavir, on cobicistat, or on a combination agent containing one of these medications, warrant a modification of their tacrolimus dosing due to a major drug interaction with their antiretroviral agents. Only a single pre-op dose of tacrolimus should be ordered. Subsequent
    doses will be based on tacrolimus levels.

    b. Second dose of basiliximab will be given on POD3 instead of POD4 to facilitate discharging patient in an efficient manner.

	Intra-op	POD1	POD2	POD3	POD4
Basiliximab	20mg IV	x	x	20mg IV	x
Tacrolimus	4 mg po q12h begun prior to transplant ----------				
MMF	1000mg po q12h begun prior to transplant ----------				
Corticosteroids	500mg IV	250mg IV	125mg IV	5mg PO qd----------	

2. Tacrolimus Dosing and Schedule

    a. Tacrolimus 4mg q12h will be initiated on admission and continuedpost-operatively.

    b. Tacrolimus goal trough levels:
        i. 8-12 ng/ml for months 0-6 post-transplant
        ii. At month 6, reduce tacrolimus goal trough level to 5-8 ng/ml

3. Mycophenolate mofetil will be dosed based on weight at time of transplant per "Weight based dosing of MMF" Protocol.

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Tertiary – For + DSA or + B-cell crossmatch - Thymo1.2

1. Patients who have a positive DSA but negative crossmatch will receive thymoglobulin induction, and then continue on the belatacept/tacrolimus/mycophenolate/prednisone for maintenance immunosuppression (if eligible based on above criteria).

	Intra-op	POD1	POD2	POD3	POD4
Thymoglobulin	1.5mg/kg	1.5mg/kg	1.5mg/kg	1.5mg/kg	x
Intravenous Immunoglobulin (only for + cross-match)	30g x 1 dose	2g/kg (less 30g, max 140g)			
Belatacept	10 mg/kg	x	x	x	x
Tacrolimus	4 mg po q12h begun prior to transplant----------				
MMF	1000mg po q12h begun prior to transplant----------				
Corticosteroids	500mg IV	250mg IV	125mg IV	5mg PO qd----------	

2. Patients with a "true" positive B-cell crossmatch will receive the same regimen but with the addition of intravenous immunoglobulin. Dose of 30g should be started pre-operatively. Remainder of 2g/kg dose (less the 30g already given, max 140g total dose) should be given post-operatively.

3. Belatacept
   a. Confirm belatacept eligibility status per Belatacept 2.7 protocol.
   b. Dosing per Belatacept 2.7 protocol (10mg/kg – Day 0 (intra-operatively), 5mg/kg – Beginning month 1 and monthly thereafter).
   c. Administration per Belatacept 2.7 protocol.

4. Tacrolimus Dosing and Schedule
   a. Tacrolimus 4mg q12h will be initiated on admission and continued post-operatively.
   b. Tacrolimus goal trough levels:
      i. 5-8 ng/ml for months 0-1 post-transplant
      ii. 3-5 ng/ml for months 2-9 post-transplant
      iii. **Note:** For patients receiving Thymoglobulin for rejection, goal trough level should be reduced to 3-5 ng/ml until month 9, and then tapered.
   c. Begin taper off of tacrolimus at month 9 with eventual discontinuation by month 11. Taper per Belatacept 2.7 protocol.

Quaternary – For Living Donor HLA identical transplants – HLA identical Bela 1.0 and HLA identical Tac 1.0

1. HLA Identical Bela 1.0. For patients eligible for belatacept (based on primary protocol criteria).
   a. Patients will receive mycophenolate mofetil 1000mg po night prior to admission and in pre- op holding. No CNIs. Belatacept, basiliximab, corticosteroids will be given intra-op.

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	Intra-op	POD1	POD2	POD3	POD4
Belatacept	10 mg/kg	x	x	x	x
Basiliximab	20mg IV	x	x	x	x
MMF	1000mg po pre-op, then 1000mg po q12h post-op ----------				
Corticosteroids	500mg IV	250mg IV	125mg IV	5mg PO qd----------	

b. Belatacept

i. Confirm belatacept eligibility status per Belatacept 2.7 protocol.

ii. Dosing per Belatacept 2.7 protocol (10mg/kg on day 0 (intra-operatively) 5mg/kg beginning month 1 and monthly thereafter).

iii. Administration per Belatacept 2.7 protocol.

c. Mycophenolate

i. 1000mg x 1 dose the night before admission, 1000mg x 1 dose pre-operatively, then 1000mg q12h post-operatively.

ii. At month 9, reduce dose to 500mg q12h. Continue this dose indefinitely.

d. Prednisone

i. After completing IV methylprednisone, begin prednisone 5mg daily. At month 6, begin taper as follows:

1. Reduce dose to 2.5mg daily for 1 month.

2. Reduce dose to 2.5mg qod for 1 month.

3. Discontinue prednisone.

2. HLA Identical Tac 1.0. For patients ineligible for belatacept.

a. Patients will receive tacrolimus po 5mg and mycophenolate mofetil 1000mg po x1 the night before admission, and receive tacrolimus 4mg and mycophenolate 1000mg x 1 in pre-op holding. Basiliximab and corticosteroids will be given intra-op. Post-operatively, patient will receive tacrolimus, mycophenolate mofetil and corticosteroids as outlined below.

	Intra-op	POD1	POD2	POD3	POD4
Basiliximab	20mg IV	x	x	20mg IV	x
Tacrolimus	4 mg po pre-op, then 4 mg po q12h post-op ----------				
MMF	1000mg po pre-op, then 1000mg po q12h post-op ----------				
Corticosteroids	500mg IV	250mg IV	125mg IV	5mg PO qd----------	

b. Tacrolimus

i. Tacrolimus 5mg x 1 dose the night before admission, 4mg x 1 dose pre-operatively, then 4mg q12h post-operatively.

ii. Tacrolimus goal trough levels:

1. 5-8 ng/ml for months 0-12 post-transplant

2. At month 12, reduce tacrolimus goal trough level to 3-5 ng/ml

c. Mycophenolate

i. 1000mg x 1 dose the night before admission, 1000mg x 1 dose pre-operatively, then 1000mg q12h post-operatively.

ii. At month 9, reduce dose to 500mg q12h. Continue this dose indefinitely.

d. Prednisone

i. Begin prednisone taper from 5mg daily dose at month 6 as follows:

1. Reduce dose to 2.5mg daily for 1 month

2. Reduce dose to 2.5mg qod for 1 month

3. Discontinue prednisone

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Pancreas Transplant – Bela/Thymo 2.0

1. Patients who are eligible for belatacept (see criteria above) receiving a SKPT, PAK or PTA will receive thymoglobulin induction. Maintenance therapy will consist of belatacept, tacrolimus, and mycophenolate mofetil.

	Intra-op	POD1	POD2	POD3	POD4
Thymoglobulin	1.5mg/kg	1.5mg/kg	1.5mg/kg	1.5mg/kg	x
Belatacept	10mg/kg	x	x	x	x
Tacrolimus*	4 mg po q12h pre-op, then 2 mg po q12h post-op ----------				
MMF	1000mg po q12h begun prior to transplant----------				
Corticosteroids	500mg IV	250mg IV	125mg IV	60mg IV	20mg po

*Reduction in post-operative tacrolimus dosing secondary to fluconazole interaction.

2. Belatacept Schedule with Confirmation of Eligibility Status

   a. 10mg/kg – Day 0 (intra-operatively)

   b. 5mg/kg – beginning month 1 and monthly thereafter

   c. Refer to ETC Belatacept Dosing for Solid Organ Transplant Recipients protocol for additional dosing and infusion information

3. Tacrolimus Dosing and Schedule

   a. Tacrolimus 4mg q12h will be given pre-operatively and then 2mg q12h will be initiated post- operatively.

   b. Tacrolimus goal trough levels:
      i. 5-8 ng/ml for months 0-6 post-transplant
      ii. 3-5 ng/ml > 6 months post-transplant

4. Mycophenolate mofetil will be dosed based on weight at time of transplant per "Weight based dosing of MMF" Protocol.

5. Corticosteroids
   a. 5 days of corticosteroids will be completed inpatient and patient will be discharged off steroids

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Pancreas Transplant – Tac/Thymo 1.0

1. Patients who are not eligible for belatacept receiving a SKPT, PAK or PTA will receive Tac/Thymo 1.0 protocol. Maintenance therapy will consist of tacrolimus, mycophenolate mofetil and corticosteroids.

	Intra-op	POD1	POD2	POD3	POD4
Thymoglobulin	1.5mg/kg	1.5mg/kg	1.5mg/kg	1.5mg/kg	x
Tacrolimus*	4 mg po q12h pre-op, then 2 mg po q12h post-op ----------				
MMF	1000mg po q12h begun prior to transplant----------				
Corticosteroids	500mg IV	250mg IV	125mg IV	5mg po qd ----------	

*Reduction in post-operative tacrolimus dosing secondary to fluconazole interaction.

2. Tacrolimus Dosing and Schedule

    a. Tacrolimus 4mg q12h will be given pre-operatively and then 2mg q12h will be initiated post- operatively.

    b. Tacrolimus goal trough levels:
        i. 8-12 ng/ml for months 0-6 post-transplant
        ii. Reduce tacrolimus goal trough level to 5-8 ng/ml as clinically indicated

3. Mycophenolate mofetil will be dosed based on weight at time of transplant per "Weight based dosing of MMF" Protocol.

RELATED DOCUMENTS/LINKS:

ETC Belatacept Dosing for Solid Organ Transplant Recipients
Kidney and Pancreas post-transplant weight based dosing of mycophenolate mofetil

DEFINITIONS:

DDRT: deceased donor renal
EBV: Epstein Barr Virus
ECD: expanded criteria donor
HLA: human leukocyte antigen
PAK: pancreas after kidney Tac-tacrolimus
PRA: panel reactive antibody
PTA: pancreas transplant alone
PTLD: post-transplant lymphoproliferative disorder DSA-donor specific antibody
SKPT: simultaneous kidney pancreas transplant

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