Abdominal Transplant Immunosuppression Management - Adult - Inpatient/Ambulatory

Consensus Care Guideline

Population/Problem:

The information presented in this document is intended to guide the use of immunosuppressive medications in adult patients who have a history of an abdominal organ transplant (i.e. kidney, liver, and pancreas). Guidance is provided to use immunosuppressive medications safely and effectively in the inpatient and outpatient settings. Guidance is provided for the use of azathioprine, belatacept, cyclosporine, everolimus, mycophenolate, prednisone, sirolimus, and tacrolimus. Guidance is also provided for the use of alemtuzumab, basiliximab, dexamethasone, IVIG, rituximab, and thymoglobulin in the setting of renal transplant induction, desensitization, and rejection.

Information is provided for dosing, target blood levels, common drug interactions, monitoring, and common adverse effects.[1-5]

The guideline assists in the decision making of physicians, mid-level providers, pharmacists, and nursing staff.

Recommendations:

UW Health recommendations are based on long-standing experience with clinical care. The recommendations are supported by very low quality evidence.

Disclaimer
Consensus care models assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Content Expert(s):
David Hager, PharmD – Director, Pharmacy Clinical Services
Phone Number: (608) 890-8993
Email Address: dhager@uwhealth.org

Contact for Changes:
Philip Trapskin, PharmD – Director, Pharmacy Policy, Safety, Compliance and Informatics
Phone Number: (608) 263-1328
Email Address: ptrapskin@uwhealth.org

Guideline Author(s):
Melissa Durst, PharmD – Pharmacy Transplant Services

Workgroup Members:
Daniel Felix, PharmD
Jillian Fose, PharmD
David Hager, PharmD
Anthony Hennes, PharmD
Kimberly Holdener, PharmD
Mei Jorgenson, PharmD
Jamie Myers, RN
Nancy Radke, RN
Josh Wiegel, PharmD

Reviewer(s):
Dixon Kaufman, MD
Arjang Djamali, MD
Dave Foley, MD
Didier Mandelbrot, MD
Jon Odorico, MD
John Rice, MD

Committee Approval(s):

Pharmacy & Therapeutics Committee (06/17/21)

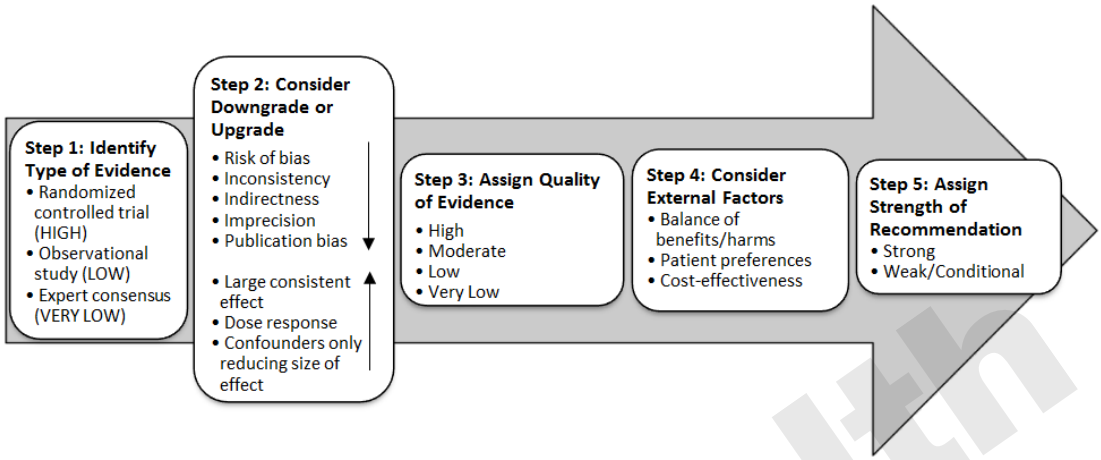

Table 1. GRADE Ranking of Evidence

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

Table 2. GRADE Ratings for Recommendations for or Against Practice

Strong (S)	Generally, should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.)
Conditional (C)	May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.)

Collateral Tools & Resources

The following collateral tools and resources support staff execution and performance of the evidence-based model recommendations in everyday clinical practice.

Metrics

Relevant metrics include graft survival, rejection rates and rates of opportunistic infections.

Order Sets & Smart Sets

- IP - Renal/Pancreas Transplant - Rejection - Adult - Medical Admission [766]
- IP - Liver Transplant - Adult - Intensive Care Unit - Postoperative [2885]
- IP - Renal/Pancreas Transplant - Adult - Postoperative [2927]
- IP - Transplant - Immunosuppression - Antithymocyte Globulin (Rabbit) - Adult - Supplemental [771]

References-

1. Kidney Disease: Improving Global Outcomes Transplant Work G. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant.* 2009;9 Suppl 3:S1-155.
2. Ekberg H, Tedesco-Silva H, Demirbas A, et al. Reduced exposure to calcineurin inhibitors in renal transplantation. *N Engl J Med.* 2007;357(25):2562-2575.
3. Hanaway MJ, Woodle ES, Mulgaonkar S, et al. Alemtuzumab induction in renal transplantation. *N Engl J Med.* 2011;364(20):1909-1919.
4. Lucey MR, Terrault N, Ojo L, et al. Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Liver Transpl.* 2013;19(1):3-26.
5. Scott LJ, McKeage K, Keam SJ, Plosker GL. Tacrolimus: a further update of its use in the management of organ transplantation. *Drugs.* 2003;63(12):1247-1297.

Tacrolimus – liver transplant

<table>
<tr><th></th><th>Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td>Post-operative day 1</td><td rowspan="3">• Initiation of tacrolimus should on post-operative day 1 after transplant (UW Health, Very Low, Conditional)
• Capsules and suspension may be taken with or without food. Since the presence of food affects the bioavailability of tacrolimus, if taken with food, it should be taken consistently the same way each time. (UW Health, Very Low, Conditional)
• Tacrolimus may be given sublingually in patients unable to adequately absorb enteral formulations or in those unable to take oral. If a patient is being transitioned to tacrolimus sublingual from tacrolimus IR, each dose should be divided by 2 and given sublingually. (UW Health, Very Low, Conditional)
• Use of IV should be considered rare and risky and only considered in the inpatient setting. Only after discussion with an experienced transplant pharmacist and the faculty of record can it be considered. Conversion from IV to oral tacrolimus is recommended as soon as enteral therapy can be tolerated to minimize risk of anaphylactic reactions that occur with injectables containing castor oil derivatives. (UW Health, Very Low, Conditional)
• LCP-Tacrolimus (Envarsus®) may be utilized in patients with documented intolerable adverse effects with tacrolimus IR or who are unable to obtain a therapeutic drug concentration with the IR formulation. If a patient is being transitioned to LCP-tacrolimus from tacrolimus IR, the total daily dose should be multiplied by 0.8, then rounded to the nearest tablet size. Astagraf, Envarsus, and Prograf are not interchangeable (UW Health, Very Low, Conditional)</td></tr>
<tr><td>Dosing (initial)</td><td>Standard dosing: Fixed dose 2 mg by mouth twice daily
Increased sensitivity (on CYP3A4 inhibitor - see list below): Fixed dose 1 mg by mouth twice daily</td></tr>
<tr><td>Drug-drug Interactions (not an all-inclusive list)</td><td>Increases tacrolimus concentration
Check Lexicomp for dose adjustments
<u>Adjust tacrolimus dose empirically for the following CYP4 inhibitors:</u>
• Fluconazole
• Posaconazole
• Voriconazole
• Ritonavir
• Letermovir
<u>Monitor tacrolimus levels and adjust as needed:</u>
• Clarithromycin
• Erythromycin</td><td>Decreases tacrolimus concentration
Check Lexicomp for dose adjustments
<u>Monitor tacrolimus levels and adjust as needed:</u>
• Rifampin
• Phenytoin
• Carbamazepine
• Phenobarbital</td></tr>
<tr><td>Target levels

Dose Adjustments

Labs</td><td>
<table>
<tr><th></th><th>Autoimmune disease and not on MPA</th><th>NOT autoimmune OR on MPA</th></tr>
<tr><td>0-3 months:</td><td>8-10 ng/mL</td><td>5-7 ng/mL</td></tr>
<tr><td>3-6 months:</td><td>8-10 ng/mL</td><td>5-7ng/mL</td></tr>
<tr><td>6-12 months:</td><td>6-8 ng/mL</td><td>3-5 ng/mL</td></tr>
<tr><td>>12 months:</td><td>4-6 ng/mL</td><td>2-5 ng/mL</td></tr>
</table>
Above trough goals are general guidance, and immunosuppression should be tailored to patient's immunologic risk and tolerance of medications

<table>
<tr><th>Below/Above Target</th><th></th></tr>
<tr><td><u>≥</u>50%</td><td>Adjust dose by 25-50%*</td></tr>
<tr><td><50%</td><td>Adjust dose by 25%</td></tr>
</table>
*Holding doses may be necessary</td><td><u>Laboratory Monitoring:</u>
Tacrolimus (trough), potassium, and creatinine
Inpatient: Daily
Outpatient:
<table>
<tr><th>Day after discharge</th><th>Frequency</th></tr>
<tr><td>0-30</td><td>Twice weekly</td></tr>
<tr><td>31-90</td><td>Not less than weekly</td></tr>
<tr><td>91-180</td><td>Not less than twice monthly</td></tr>
<tr><td>181-365</td><td>Not less than once monthly</td></tr>
</table>
Modify as Needed on a Patient-by-Patient basis:
• Change in medication formulation, patient status, or creatinine increase <u>≥</u>0.3 mg/dL above baseline
• 3 to 7 days (ideally 4 days) following dose adjustment</td></tr>
</table>

Adverse effects	Acute kidney injury	• Assess tacrolimus trough level for correlation with elevated creatinine • If trough level is above goal and creatinine has increased ≥ 0.3 mg/dL above baseline: o Decrease tacrolimus dose if trough is <4 ng/mL above goal o Hold tacrolimus if trough ≥5 ng/mL above goal and consider increasing current prednisone dose • Consult transplant physician regarding further work up elevated creatinine
	Neurological symptoms (tremor, headache)	• Assess tacrolimus trough level for correlation with tremors or headache • If trough level is above goal, adjust tacrolimus dose and follow up with patient • If trough level within target range, no dose adjustment is recommended, follow-up with patient in 1 week to assess continued symptoms and trend severity • If adverse effects are persistent, not improving, or interfering with daily activities and there is no other known cause: • Consult the transplant physician to consider splitting IR tacrolimus to three times daily or converting the patient to LCP-tacrolimus or cyclosporine • Addition of a low dose propranolol may also be considered if heart rate >60 BPM, systolic blood pressure >120 mmHg, and patient is not already on a beta blocker
	New onset diabetes after transplantation (NODAT) *Diagnosis (2 of the following)* • Sx of DM + casual PG concentrations ≥200 mg/dL • FPG ≥126 mg/dL • 2-hr PG ≥200 mg/dL during an oral glucose tolerance test • Hba1c > 7.0% for more than 2 months	• No tacrolimus dose adjustment is recommended • Consult diabetes management & nutrition services • Diagnosis of new onset diabetes after transplant (NODAT) is defined by the World Health Organization (WHO) and American Diabetes Association (ADA) that develops for the first time after transplantation • Continue planned discontinuation of glucocorticoids by 2 months • If there is no improvement in glucose control 6 months after transplant (NODAT requiring insulin OR A1c >7% with glucose lowering agent): o Consult transplant physician and consider reassessment of steroid dosing or conversion to LCP-tacrolimus

Cyclosporine – liver transplant

<table>
<tr><th></th><th colspan="2">Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">Post-operative day 1</td><td>• The initiation of cyclosporine should start post-operative day 1 after transplant (UW Health, Very Low, Conditional)</td></tr>
<tr><td>Dosing (initial)</td><td>Standard dosing
Increased sensitivity (on CYP3A4 inhibitor - see list below)</td><td>Fixed dose 150 mg by mouth twice daily
Fixed dose 100 mg by mouth twice daily</td><td rowspan="3">• Neoral/Gengraf (cyclosporine modified) and Sandimmune (cyclosporine non-modified) are not bioequivalent and cannot be used interchangeably (UW Health, Very Low, Conditional)
• Cyclosporine modified is preferred over cyclosporine non-modified (UW Health, Very Low, Conditional)
• Capsules and suspension may be taken with or without food. However, since the presence of food affects the bioavailability of cyclosporine, if taken with food, it should be taken consistently the same way each time. (UW Health, Very Low, Conditional)</td></tr>
<tr><td>Drug-Drug Interactions (not an all-inclusive list)</td><td>Increases cyclosporine concentration
Check Lexicomp for dose adjustments
<u>Adjust cyclosporine dose empirically for the following CYP4 inhibitors:</u>
• Fluconazole
• Posaconazole
• Voriconazole
• Ritonavir
• Letermovir
<u>Monitor cyclosporine levels and adjust as needed:</u>
• Clarithromycin
• Erythromycin</td><td>Decreases cyclosporine concentration
Check Lexicomp for dose adjustments
<u>Monitor cyclosporine levels and adjust as needed:</u>
• Rifampin
• Phenytoin
• Carbamazepine
• Phenobarbital</td></tr>
<tr><td>Target levels

Dose Adjustments

Labs</td><td colspan="2">
<table>
<tr><th></th><th>Autoimmune disease and not on MPA</th><th>NOT autoimmune OR on MPA</th></tr>
<tr><td>0-3 mo:</td><td>150-200 ng/mL</td><td>125-175 ng/mL</td></tr>
<tr><td>3-6 mo:</td><td>125-150 ng/mL</td><td>125-150 ng/mL</td></tr>
<tr><td>6-12 mo:</td><td>100-125 ng/mL</td><td>75-100 ng/mL</td></tr>
<tr><td>>12 mo:</td><td>100 ng/mL</td><td>50-75 ng/mL</td></tr>
</table>
Above trough goals are general guidance, and immunosuppression should be tailored to patient's immunologic risk and tolerance of medications

<table>
<tr><th>Below/Above Target</th><th></th></tr>
<tr><td><u>≥</u>50%</td><td>Adjust dose 25% to 50%</td></tr>
<tr><td><u>≤</u>50%</td><td>Adjust dose by 25%</td></tr>
</table>
*Holding doses may be necessary</td><td><u>Laboratory Monitoring:</u>
Cyclosporine (trough), potassium, and creatinine
Inpatient: Daily
Post-Discharge:
<table>
<tr><th>Day</th><th>Frequency</th></tr>
<tr><td>0-30</td><td>Twice weekly</td></tr>
<tr><td>31-90</td><td>Not less than weekly</td></tr>
<tr><td>91-180</td><td>Not less than twice monthly</td></tr>
<tr><td>181-365</td><td>Not less than once monthly</td></tr>
</table>
Modify as Needed on a Patient-by-Patient basis:
• Change in medication formulation, patient status, or creatinine increase <u>≥</u>0.3 mg/dL above baseline
• 3 to 7 days (ideally 4 days) following dose adjustment</td></tr>
</table>

Adverse effects	Acute kidney injury	• Assess cyclosporine trough level for correlation with elevated creatinine • If trough level is above goal and creatinine has increased ≥ 0.3 mg/dL above baseline: o Decrease cyclosporine dose if trough is <50 ng/mL above goal o Hold cyclosporine if trough ≥50 ng/mL above goal and consider increasing current prednisone dose • Consult transplant physician regarding further work up elevated creatinine
	Neurological symptoms (tremor, headache)	• Assess cyclosporine trough level for correlation with tremors or headache • If trough level is above goal, adjust cyclosporine dose and follow up with patient • If trough level within target range, no dose adjustment is recommended, follow-up with patient in 1 week to assess continued symptoms and trend severity • If adverse effects are intolerable or interacting with daily activities and there is no other known cause of symptom: o Consult the transplant physician to consider converting the patient to LCP-tacrolimus o Addition of a low dose propranolol may also be considered if heart rate >60 BPM, systolic blood pressure >120 mmHg, and patient is not already on a beta blocker
	New onset diabetes after transplantation (NODAT) *Diagnosis (2 of the following)* • Sx of DM + casual PG concentrations ≥200 mg/dL • FPG ≥126 mg/dL • 2-hr PG ≥200 mg/dL during an oral glucose tolerance test • Hba1c > 7.0% for more than 2 months	• No cyclosporine dose adjustment is recommended • Consult diabetes management & nutrition services • Diagnosis of new onset diabetes after transplant (NODAT) is defined by the World Health Organization (WHO) and American Diabetes Association (ADA) that develops for the first time after transplantation • Continue planned discontinuation of glucocorticoids by 60 days • If there is no improvement in glucose control 6 months after transplant (NODAT requiring insulin OR A1c >7% with glucose lowering agent): • Consult transplant physician and consider reassessment of steroid dosing or conversion to other immunosuppressant

Mycophenolate – liver transplant

<table>
<tr><th></th><th>Recommendation</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td>Post-operative day 0</td><td rowspan="3">• Full dose mycophenolic acid is the preferred anti-proliferative medication used for liver transplant patients (UW Health, Very Low, Conditional)
• IV mycophenolate mofetil is indicated if the patient has an acute condition that affects gastrointestinal absorption (i.e., GI bleed or obstruction, malabsorption syndromes, severe diarrhea or severe vomiting) (UW Health, Very Low, Conditional)
• Mycophenolate mofetil suspension is utilized for patients receiving medications via nasogastric or orogastric tube</td></tr>
<tr><td>Dosing (initial)</td><td><table>
<tr><td rowspan="2">Mycophenolate mofetil</td><td>1000 mg IV x 1 dose</td><td>POD0</td></tr>
<tr><td>1000 mg IV twice daily x 4 doses</td><td>POD1-2</td></tr>
<tr><td>Mycophenolate sodium</td><td>720 mg PO twice daily and after</td><td>POD3</td></tr>
</table></td></tr>
<tr><td>Drug-drug interactions (not an all-inclusive list)</td><td>Medications that decrease mycophenolate concentration
• Cyclosporine
• Bile acid sequestrants
Mycophenolate decreases concentration of estrogen derivatives. Women of childbearing potential who are receiving mycophenolate mofetil should consider using an alternative and/or additional form of contraception.
Check Lexicomp for dose adjustments</td></tr>
<tr><td>Target levels

Labs</td><td><table>
<tr><th></th><th>Goal MPA Trough</th></tr>
<tr><td>CsA or TAC based regimens</td><td>1.0-3.5 mg/L</td></tr>
</table>
<u>Laboratory Monitoring:</u>
• Lab monitoring of MPA levels is not recommended to assess for toxicity or efficacy
• If levels are requested, they are only appropriate for mycophenolate mofetil and should be drawn as a trough</td><td>• MPA AUC is a better predictor of clinical events than MPA trough. Trough levels are poorly correlated with AUC and are not recommended (UW Health, Very Low, Conditional)
• Levels may be utilized for assessing safety; not recommended to assess efficacy</td></tr>
<tr><td rowspan="2">Adverse effects</td><td>Diarrhea
If a patient has ≥50% increase in their frequency of daily bowel movements for ≥ 5-7 days
• 0-3 months post-transplant:
o C. difficile, C. difficile toxin B PCR
o CMV PCR
• ≥3 months post-transplant:
o CMV PCR
o Complete blood count
o Clostridium difficile toxin B PCR
o Cryptosporidium
o Giardia PCR
o Norovirus PCR
o Rotavirus AG
o Stool culture, with E. Coli (Shiga) toxin
o Stool O&P (parasitology, isospora, cyclospora, pinworm)
o Consider colonoscopy if diarrhea persists and all stool studies are negative
*In any patient post-liver transplant with diarrhea in the first 6 months, consider graft-versus-host disease</td><td colspan="2">• If diarrhea work-up is negative for an infectious cause of diarrhea and it is affecting activities of daily living or the patient is having limited and/or decreased oral intake:
o Decrease mycophenolate by 25% and increase dosing frequency (ex. 720 mg BID → 360 mg TID)
▪ If fails, decrease mycophenolate by 50%
o Follow up with patient in 1 week to assess continued symptoms and trend severity
o If dose is decreased to 180 mg twice daily (MYF) or 250 mg twice daily (MMF) consult provider to determine if other immunosuppression needs to be adjusted
o Consider adding the following:
▪ Add loperamide (Imodium®) 2 mg as needed after each loose stool (max dose: 16 mg daily)
▪ Diphenoxylate/atropine (Lomotil®) 5 mg four times daily as needed (max dose: 20 mg/day)
▪ Psyllium fiber (Metamucil®) 3.4 g daily as needed
• If patient is continuing to have symptoms despite lowering immunosuppression, discuss with transplant provider</td></tr>
<tr><td>Leukopenia</td><td colspan="2">• Consult transplant physician regarding further work up leukopenia
• Adjust dose based on following recommendations:
o WBC 2-4 x 10^9/L: Could consider decrease in total daily dose by 50%
o WBC <2 x 10^9/L: Hold doses until leukopenia resolves</td></tr>
</table>

		• Consider dose modifications or discontinuations of other medications that may cause leukopenia • If leukopenia persists despite medication changes, consider graft-versus-host disease
	Heartburn/nausea	• Counsel patient on taking MYF or MMF with food if not already doing so • Convert from MMF to MYF if only upper GI complaints (heartburn, nausea) • Add calcium carbonate as needed, or the addition of an H2RA or PPI if not already on • If symptoms continue following 1 week of daily therapy increase H2RA or PPI dose to twice daily, reassess in 1 week • If symptoms persist for ≥1 week, consider EGD to rule out infection vs. ulceration

Azathioprine – liver transplant

	Recommendation	Notes/Evidence
Initiation	Failure to tolerate mycophenolate	• Azathioprine is recommended for use in patients unable to tolerate adverse effects of mycophenolate (UW Health, Very Low, Conditional)
Dosing (initial)	1-3 mg/kg by mouth daily rounded to nearest 25 mg dose	• Azathioprine is considered to be less effective than MPA in preventing rejection. Prior to initiating azathioprine, consider the total immunosuppression for the patient and timing out from transplant • Azathioprine 50 mg tablets should be prescribed as azathioprine 75 and 100 mg tablets are not available as generic and are more expensive
Drug-drug interactions (not an all-inclusive list)	**Increases** azathioprine concentration: ***Check Lexicomp for dose adjustments**** <u>Avoid concurrent use:</u> • Febuxostat <u>Adjust azathioprine dose empirically:</u> • Allopurinol	
Labs	<u>Laboratory Monitoring:</u> • Monitor CBC with differential and platelets weekly during first month, twice monthly for months 2 and 3, then monthly thereafter; monitor more frequently with dose modifications • Monitor LFTs every 3 months while on treatment • There is no recommended azathioprine level for monitoring purposes. However, if toxicity is suspected, check thiopurine methyltransferase (TPMT)	

Adverse effects	Leukopenia	• Consult transplant provider if WBC <3 and consider checking thiopurine methyltransferase (TPMT)
	Gastrointestinal If a patient has ≥50% increase in their frequency of daily bowel movements for ≥ 5-7 days • 0-3 months post-transplant: o C. difficile, C. difficile toxin B PCR o CMV PCR • ≥3 months post-transplant: o CMV PCR o Complete blood count o Clostridium difficile toxin B PCR o Cryptosporidium o Giardia PCR o Norovirus PCR o Rotavirus AG o Stool culture, with E. Coli (Shiga) toxin o Stool O&P (parasitology, isospora, cyclospora, pinworm) Consider colonoscopy if diarrhea persists and all stool studies are negative	• See diarrhea work-up algorithm
	Pancreatitis	• Consult transplant provider if suspected based on patient symptoms

Sirolimus/everolimus – liver transplant

<table>
<tr><th></th><th colspan="2">Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">For use in patients with:
CNI toxicity
Skin cancer
Recurrent hepatocellular carcinoma
Renal dysfunction
Quadruple therapy</td><td>Sirolimus/everolimus may impair or delay wound healing, and should be used with caution in the peri-surgical period (UW Health, Very Low, Conditional)
Sirolimus should not be used within 30 days of liver transplant due to risk of hepatic artery thrombosis (UW Health, Very Low, Conditional)
May be indicated for use in patients with recurrent skin cancers as a replacement for azathioprine, MPA, or CNIs (UW Health, Very Low, Conditional)</td></tr>
<tr><td rowspan="2">Dosing (initial)</td><td>Sirolimus</td><td>2 mg by mouth once daily</td><td rowspan="3"></td></tr>
<tr><td>Everolimus</td><td>0.75 mg by mouth twice daily</td></tr>
<tr><td>Drug-drug interactions (not an all-inclusive list)</td><td>Increase mTOR concentration (not an all-inclusive list):
Check Lexicomp for dose adjustments
<u>Avoid concurrent use:</u>
Posaconazole
Voriconazole
Ritonavir
<u>Monitor mTOR levels and adjust as needed:</u>
Fluconazole
Ritonavir
Letermovir
Clarithromycin
Erythromycin</td><td>Decrease mTOR concentration (not an all-inclusive list)
Check Lexicomp for dose adjustments
<u>Monitor mTOR levels and adjust as needed:</u>
Rifampin
Phenytoin
Carbamazepine
Phenobarbital</td></tr>
<tr><td>Target levels

Dose Adjustments

Labs</td><td colspan="2"><table><tr><th></th><th>Goal Trough Levels (Siro/Evr+FK)</th><th>Goal Trough Levels (Siro/Evr+MPA)</th></tr><tr><td>0-3 mo:</td><td>Siro/Evr: 4-7 ng/mL; FK: 5-7 ng/mL</td><td>Siro/Evr: 8-10 ng/mL</td></tr><tr><td>3-6 mo:</td><td>Siro/Evr: 4-7 ng/mL; FK: 5-7 ng/mL</td><td>Siro/Evr: 8-10 ng/mL</td></tr><tr><td>6-12 mo:</td><td>Siro/Evr: 3-5 ng/mL; FK: 3-5 ng/mL</td><td>Siro/Evr: 5-8 ng/mL</td></tr><tr><td>>12 mo:</td><td>Siro/Evr: 3-5 ng/mL; FK: 3-5 ng/mL</td><td>Siro/Evr: 5-8 ng/mL</td></tr></table>*Above trough goals are general guidance, and immunosuppression should be tailored to patient's immunologic risk and tolerance of medications*

<u>Laboratory Monitoring:</u>
Recommended monitoring trough level once weekly upon initiation and with any dose changes
When target trough level has been attained, recommend monitoring levels once monthly
Monitor fasting lipids profile annually, proteinuria at 6 months and then annually post-transplant, and LFTs and CBC while on therapy.</td><td></td></tr>
</table>

Adverse Effects	Proteinuria	• Consider administration of angiotensin-converting enzyme (ACE)-inhibitors and angiotensin II receptor antagonists and reducing mTOR levels
	Mouth ulcers	• Development of mouth ulcers seems to be dose-related because they usually appear after the loading dose and often improve after a dose reduction • Addition of a high-potency topical steroid may be considered
	Hyperlipidemia	• Follow current guidelines for management (diet, exercise, lipid lowering agents) • Immunosuppressive strategies minimizing doses of mTORs, CNIs, or corticosteroids may help in controlling hyperlipidemia
	Leukopenia	• Consider dose reduction or temporary drug suspension if appropriate
	Thrombocytopenia	• Consider dose reduction or temporary drug suspension if appropriate
	Anemia	• Consider dose reduction or temporary drug suspension if appropriate

Prednisone – liver transplant

<table>
<tr><th></th><th colspan="4">Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="4">Post-operative day 5 following dexamethasone taper</td><td>• Prednisone 10 mg twice daily will be started on POD 5 following dexamethasone taper and may be continued on discharge</td></tr>
<tr><td>Dosing (initial)</td><td>Standard steroid taper
• Prednisone taper should occur following POD5
• Assessment for prednisone taper should occur at 3-4 weeks post-operatively for patients without autoimmune disease
• Factors that may influence the duration of prednisone taper:
o Current and historical CNI levels
o Current and historical MPA dosing
o Current liver function
o Episodes of rejection
o Perceived rejection and infection risk</td><td colspan="2"><table>
<tr><td>Dexamethasone</td><td>100 mg</td><td>POD0</td></tr>
<tr><td></td><td>50 mg</td><td>POD1</td></tr>
<tr><td></td><td>25 mg</td><td>POD2</td></tr>
<tr><td></td><td>12 mg</td><td>POD3</td></tr>
<tr><td></td><td>6 mg</td><td>POD4</td></tr>
<tr><td>Prednisone</td><td>10 mg BID</td><td>POD5</td></tr>
<tr><td>Without autoimmune disease</td><td colspan="2">Decrease by 5 mg every 2 weeks until gone</td></tr>
<tr><td>With autoimmune disease</td><td colspan="2">Decrease by 5 mg every 2 weeks to a dose of 5 mg daily</td></tr>
</table></td><td>• Prednisone doses should be split to twice daily dosing for patients requiring insulin for glucose control (UW Health, Very Low, Conditional)
• Patient should be off prednisone by 2 months post-transplant and maintained on tacrolimus and mycophenolate but is based on provider discretion
• For patients on doses higher than 20 mg daily for anticipated duration of greater than 2 weeks, PJP prophylaxis should be initiated</td></tr>
<tr><td>Labs</td><td colspan="4"><u>Laboratory Monitoring:</u>
Glucose, bone mineral density</td></tr>
<tr><td rowspan="3">Adverse effects</td><td>Hyperglycemia</td><td colspan="3">• Prednisone doses should be split to twice daily dosing for patients requiring insulin for glucose control</td></tr>
<tr><td>Heartburn/reflux</td><td colspan="3">• Start a proton pump inhibitor (PPI) at time of transplant
• If a patient complains of heartburn on daily dosing of the PPI, frequency may be increased to twice daily (pending renal function)
• Discontinue PPI in patients with no history of heartburn/gastroesophageal reflux disease (GERD) prior to transplant if prednisone is discontinued</td></tr>
<tr><td>Osteoporosis</td><td colspan="3">• Recommend calcium 1200 mg daily (based on elemental calcium dosing)
• Recommend vitamin D 2000 units daily</td></tr>
</table>

Tacrolimus – pancreas transplant

<table>
<tr><th></th><th colspan="2">Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">Post-operative day 1</td><td>• Initiation of tacrolimus should start before or at the time of transplant, rather than delayed until the onset of graft function (UW Health, Very Low, Conditional)</td></tr>
<tr><td>Dosing (initial)</td><td>Non-African American</td><td>NPO - 1 mg twice daily
PO - 0.025 mg/kg (use ABW) by mouth twice daily, rounded to the nearest capsule size</td><td rowspan="4">• Capsules and suspension may be taken with or without food. Since the presence of food affects the bioavailability of tacrolimus, if taken with food, it should be taken consistently the same way each time. (UW Health, Very Low, Conditional)
• Tacrolimus may be given sublingually in patients unable to adequately absorb enteral formulations or in those unable to take oral. If a patient is being transitioned to tacrolimus sublingual from tacrolimus IR, each dose should be divided by 2 and given sublingually. (UW Health, Very Low, Conditional)
• Use of IV tacrolimus should be considered rare and risky. Only after discussion with an experienced transplant pharmacist and the faculty of record can it be considered for patients unable to adequately absorb enteral formulations[a,b]. Conversion from IV to oral tacrolimus is recommended as soon as enteral therapy can be tolerated to minimize risk of anaphylactic reactions that occur with injectables containing castor oil derivatives (UW Health, Very Low, Conditional). Transplant Pharmacist should be consulted to assist in dosing and monitoring therapeutic levels
• LCP-Tacrolimus (Envarsus®) may be utilized in patients with documented intolerable adverse effects with tacrolimus IR or who are unable to obtain a therapeutic drug concentration with the IR formulation. If a patient is being transitioned to LCP-tacrolimus from tacrolimus IR, the total daily dose should be multiplied by 0.8, then rounded to the nearest capsule size. Astagraf, Envarsus, and Prograf are not interchangeable (UW Health, Very Low, Conditional)</td></tr>
<tr><td></td><td>African American</td><td>NPO - 2 mg twice daily
PO - 0.05 mg/kg (use ABW) by mouth twice daily, rounded to the nearest capsule size</td></tr>
<tr><td>Drug-drug Interactions (not an all-inclusive list)</td><td colspan="2">Increases tacrolimus concentration
Check Lexicomp for dose adjustments
<u>Adjust tacrolimus dose empirically:</u>
• Fluconazole
• Posaconazole
• Voriconazole
• Ritonavir
• Letermovir
<u>Monitor tacrolimus levels and adjust as needed:</u>
• Clarithromycin
• Erythromycin</td><td>Decreases tacrolimus concentration
Check Lexicomp for dose adjustments
<u>Monitor tacrolimus levels and adjust as needed:</u>
• Rifampin
• Phenytoin
• Carbamazepine
• Phenobarbital
• Octreotide</td></tr>
<tr><td>Target levels

Dose Adjustments

Labs</td><td colspan="2">Concurrent use of mycophenolate +/- prednisone

Tacrolimus goals may differ if patient is not on mycophenolate +/- prednisone regimen. Goal level should be discussed with provider.

<table>
<tr><th></th><th colspan="2">Target TAC Level</th></tr>
<tr><th></th><th>SPK*</th><th>PTA/PAK</th></tr>
<tr><td>0-3 months:</td><td>8-10 ng/mL</td><td>9-11 ng/mL</td></tr>
<tr><td>3-12 months:</td><td>8-10 ng/mL</td><td>9-11 ng/mL</td></tr>
<tr><td>1-3 years:</td><td>6-8 ng/mL</td><td>7-9 ng/mL</td></tr>
<tr><td>>3 years:</td><td colspan="2">Per provider discretion</td></tr>
</table>
*Follow PTA/PAK goals if secondary SPK or MFI ≥ 100
<table>
<tr><th>Below/Above Target</th><th></th></tr>
<tr><td>≥50%*</td><td>Adjust dose by 25-50%</td></tr>
<tr><td><50%</td><td>Adjust dose by 25%</td></tr>
</table>
*Holding doses may be necessary</td><td><u>Laboratory Monitoring:</u>
Tacrolimus (trough), potassium, and creatinine
Inpatient: Daily
Post-Discharge:
<table>
<tr><th>Day</th><th>Frequency</th></tr>
<tr><td>0-60</td><td>Not less than twice weekly</td></tr>
<tr><td>60-90</td><td>Not less than once weekly</td></tr>
<tr><td>91-120</td><td>Not less than twice monthly</td></tr>
<tr><td>120-360</td><td>Not less than once monthly</td></tr>
</table>
As Needed:
• Change in medication formulation, patient status, or creatinine increase ≥0.3 mg/dL above baseline
• 3 to 7 days (ideally 4 days) following dose adjustment</td></tr>
</table>

[a]Scott LJ, McKeage K, Keam SJ, Plosker GL. Tacrolimus a further update of its use in management of organ transplantation. *Drugs*. 2003;63(12):1247-1297.
[b]Prograf (tacrolimus) capsules/injection. Package insert. Astellas Pharma US, Inc; 2012.

Adverse effects	Acute kidney injury	• Assess tacrolimus trough level for correlation with elevated creatinine • If all other causes are ruled out and an elevated level is found, discuss with physician the appropriateness of dose reduction • Consult transplant physician regarding further work up elevated creatinine
	Neurological symptoms (tremor, headache)	• Assess tacrolimus trough level for correlation with tremors or headache • If trough level is above goal, adjust tacrolimus dose and follow up with patient • If trough level within target range, no dose adjustment is recommended, follow-up with patient in 1 week to assess continued symptoms and trend severity • If adverse effects are persistent, not improving, or interfering with daily activities and there is no other known cause: o Consult the transplant physician to consider splitting IR tacrolimus to three times daily, converting the patient to LCP-tacrolimus, belatacept, or cyclosporine, or refer to primary care provider for supportive therapy, such as addition of low dose beta blocker (propranolol)
	Post-transplant diabetes mellitus (PTDM) *Diagnosis (2 of the following)* • Sx of DM + casual PG concentrations ≥200 mg/dL • FPG ≥126 mg/dL • 2-hr PG ≥200 mg/dL during an oral glucose tolerance test • Hba1c > 7.0% for more than 2 months	• Diagnosis of Post-transplant diabetes mellitus (PTDM) is defined by the World Health Organization (WHO) and American Diabetes Association (ADA) that develops for the first time after transplantation • Consult transplant physician regarding further work up of hyperglycemia • Consult transplant physician and consider converting the patient to cyclosporine, reassessment of steroid dosing, conversion to LCP-tacrolimus or belatacept with lowered tacrolimus goals

Cyclosporine – pancreas transplant

<table>
<tr><th></th><th colspan="2">Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">Post-operative day 1</td><td>• The initiation of cyclosporine should start before or at the time of transplantation, rather than delayed until the onset of graft function (UW Health, Very Low, Conditional)
• Tacrolimus is the preferred therapy in pancreas transplant (UW Health, Very Low, Conditional)
• If cyclosporine was necessary, cyclosporine modified should be used to prevent variability in absorption. Sandimmune and other non-modified products should not be used in the pancreas transplant population (UW Health, Very Low, Conditional)</td></tr>
<tr><td rowspan="2">Dosing (initial)</td><td>Decreased sensitivity (African-American, >80kg)</td><td>Fixed dose 150 mg by mouth twice daily</td><td rowspan="3">• Neoral/Gengraf (cyclosporine modified) and Sandimmune (cyclosporine non-modified) are not bioequivalent and cannot be used interchangeably (UW Health, Very Low, Conditional)
• Cyclosporine modified is preferred over cyclosporine non-modified (UW Health, Very Low, Conditional)
• Capsules and suspension may be taken with or without food. However, since the presence of food affects the bioavailability of cyclosporine, if taken with food, it should be taken consistently the same way each time. (UW Health, Very Low, Conditional)</td></tr>
<tr><td>Increased sensitivity (NPO, <80kg)</td><td>Fixed dose 100 mg by mouth twice daily</td></tr>
<tr><td>Drug-Drug Interactions (not an all-inclusive list)</td><td>Increases cyclosporine concentration
Check Lexicomp for dose adjustments
<u>Adjust cyclosporine dose empirically:</u>
• Fluconazole
• Posaconazole
• Voriconazole
• Ritonavir
• Letermovir
<u>Monitor cyclosporine levels and adjust as needed:</u>
• Clarithromycin
• Erythromycin</td><td>Decreases cyclosporine concentration
Check Lexicomp for dose adjustments
<u>Monitor cyclosporine levels and adjust as needed:</u>
• Rifampin
• Phenytoin
• Carbamazepine
• Phenobarbital</td></tr>
<tr><td>Target levels

Dose Adjustments

Labs</td><td>
<table>
<tr><th></th><th>Goal CSA Level</th></tr>
<tr><td>0-3 months:</td><td>200-300 ng/mL</td></tr>
<tr><td>3-6 months:</td><td>150-250 ng/mL</td></tr>
<tr><td>>6 months:</td><td>100-200 ng/mL</td></tr>
</table>
<table>
<tr><th>Below/Above Target</th><th></th></tr>
<tr><td><u>≥</u>50%</td><td>Adjust dose 25% to 50%</td></tr>
<tr><td><u>≤</u>50%</td><td>Adjust dose by 25%</td></tr>
</table>
*Holding doses may be necessary</td><td><u>Laboratory Monitoring:</u>
Cyclosporine (trough), potassium, and creatinine
Inpatient: Daily
Post-Discharge:
<table>
<tr><th>Day</th><th>Frequency</th></tr>
<tr><td>0-60</td><td>Not less than twice weekly</td></tr>
<tr><td>60-90</td><td>Not less than once weekly</td></tr>
<tr><td>91-180</td><td>Not less than twice monthly</td></tr>
<tr><td>181-240</td><td>Not less than once monthly</td></tr>
</table>
As Needed:
• Change in medication formulation, patient status, or creatinine increase <u>≥</u>0.3 mg/dL above baseline
• 3 to 7 days (ideally 4 days) following dose adjustment</td></tr>
</table>

Adverse effects	Acute kidney injury	• Assess cyclosporine trough level for correlation with elevated creatinine • If trough level is above goal and creatinine has increased ≥ 0.3 mg/dL above baseline: o Decrease cyclosporine dose if trough is <50 ng/mL above goal o Hold cyclosporine if trough ≥50 ng/mL above goal and consider increasing current prednisone dose • Consult transplant physician regarding further work up elevated creatinine
	Neurological symptoms (tremor, headache)	• Assess cyclosporine trough level for correlation with tremors or headache • If trough level is above goal, adjust cyclosporine dose and follow up with patient • If trough level within target range, no dose adjustment is recommended, follow-up with patient in 1 week to assess continued symptoms and trend severity • If adverse effects are intolerable or interacting with daily activities and there is no other known cause of symptom: o Consult the transplant physician to consider converting the patient to LCP-tacrolimus, belatacept, or refer to primary care provider for supportive therapy, such as addition of low dose beta blocker (propranolol)
	Post-transplant diabetes mellitus (PTDM) *Diagnosis (2 of the following)* • Sx of DM + casual PG concentrations ≥200 mg/dL • FPG ≥126 mg/dL • 2-hr PG ≥200 mg/dL during an oral glucose tolerance test • Hba1c > 7.0% for more than 2 months	• No cyclosporine dose adjustment is recommended • Consider consulting diabetes management & nutrition services • Diagnosis of Post-transplant diabetes mellitus (PTDM) is defined by the World Health Organization (WHO) and American Diabetes Association (ADA) that develops for the first time after transplantation • Consult transplant physician regarding further work up of hyperglycemia o Consult transplant physician and consider reassessment of steroid dosing, or conversion to belatacept with lowered tacrolimus goals

Mycophenolate – pancreas transplant

<table>
<tr><th></th><th>Recommendation</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td>Post-operative day 1</td><td rowspan="3">• Full dose mycophenolic acid is the preferred anti-proliferative medication used for PTA, PAK, and SPK transplant patients (UW Health, Very Low, Conditional)
• IV mycophenolate mofetil is administered for the first 4 doses after transplant and may also be indicated if the patient has an acute condition that affects gastrointestinal absorption (i.e., GI bleed or obstruction, malabsorption syndromes, severe diarrhea or severe vomiting) (UW Health, Very Low, Conditional)
• Mycophenolate mofetil suspension is utilized for patients receiving medications via nasogastric or orogastric tube</td></tr>
<tr><td>Dosing (initial)</td><td>
<table>
<tr><td rowspan="2">Mycophenolate mofetil</td><td>1000 mg IV x 1 dose</td><td>POD0</td></tr>
<tr><td>1000 mg IV twice daily x 4 doses</td><td>POD1-2</td></tr>
<tr><td>Mycophenolate sodium</td><td>720 mg PO twice daily</td><td>POD3</td></tr>
<tr><td colspan="3">*Note: if sum MFI 1000-4000 or patient is African American, consider 720 mg TID on POD3 and discharge</td></tr>
</table>
</td></tr>
<tr><td>Drug-drug interactions (not an all-inclusive list)</td><td>Decreases mycophenolate concentration
Check Lexicomp for dose adjustments
• Cyclosporine
• Bile acid sequestrants

Mycophenolate decreases concentration of estrogen derivatives. Women of childbearing potential who are receiving mycophenolate mofetil should consider using an alternative and/or additional form of contraception.</td></tr>
<tr><td>Target levels

Labs</td><td>
<table>
<tr><th></th><th>Goal MPA Trough[c]</th></tr>
<tr><td>CsA based regimens:</td><td>1.3-2.8 mg/L</td></tr>
<tr><td>TAC based regimens:</td><td>1.9-2.8 mg/L</td></tr>
</table>
</td><td><u>Laboratory Monitoring:</u>
• Lab monitoring of MPA levels is not recommended to assess for toxicity or efficacy
• If levels are requested, they are only appropriate for mycophenolate mofetil and should be drawn as a trough</td><td>• MPA AUC is a better predictor of clinical events than MPA trough. Trough levels are poorly correlated with AUC and are not recommended (UW Health, Very Low, Conditional)</td></tr>
<tr><td rowspan="2">Adverse effects</td><td>Diarrhea

If a patient has ≥50% increase in their frequency of daily bowel movements for ≥ 5-7 days
• 0-3 months post-transplant:
o C. difficile, C. difficile toxin B PCR
o CMV PCR
• ≥3 months post-transplant:
o CMV PCR
o Complete blood count
o Clostridium difficile toxin B PCR
o Cryptosporidium
o Giardia PCR
o Norovirus PCR
o Rotavirus AG
o Stool culture, with E. Coli (Shiga) toxin
o Stool O&P (parasitology, isospora, cyclospora, pinworm)
o Consider colonoscopy if diarrhea persists and all stool studies are negative</td><td colspan="2">• If diarrhea work-up is negative for an infectious cause of diarrhea and it is affecting activities of daily living or the patient is having limited and/or decreased oral intake:
o Decrease mycophenolate by 25% and increase dosing frequency (ex. 720 mg BID → 360 mg TID)
▪ If fails, decrease mycophenolate by 50%
o Follow up with patient in 1 week to assess continued symptoms and trend severity
o If dose is decreased to 180 mg twice daily (MYF) or 250 mg twice daily (MMF) consult provider to determine if other immunosuppression needs to be adjusted
o Consider adding the following:
▪ Add loperamide (Imodium®) 2 mg as needed after each loose stool (max dose: 16 mg daily)
▪ Diphenoxylate/atropine (Lomotil®) 5 mg four times daily as needed (max dose: 20 mg/day)
▪ Psyllium fiber (Metamucil®) 3.4 g daily as needed</td></tr>
<tr><td>Leukopenia</td><td colspan="2">• Consult transplant physician regarding further work up of leukopenia and to determine if immunosuppression needs to be adjusted</td></tr>
</table>

	Heartburn/nausea	• Counsel patient on taking MYF or MMF with food if not already doing so • Convert from MMF to MYF if only upper GI complaints (heartburn, nausea) • Add calcium carbonate as needed, or the addition of an H2RA or PPI if not already on • If symptoms continue following one week of daily thearpy, increase H2RA or PPI dose to twice daily, reassess in 1 week • If symptoms persist for ≥1 week, consider EGD to rule out infection vs. ulceration

[c]Gaston RS, Kaplan B, Shah T, et al. Fixed- or controlled-dose mycophenolate mofetil with standard or reduced-dose calcineurin inhibitors: the opticept trial. *Am J Transplant*. 2009;9(7):1607-19.

Prednisone – pancreas transplant

<table>
<tr><th></th><th>Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td>Post-operative day 4 following dexamethasone taper</td><td>• Prednisone 30 mg once daily will be started on POD 4 following dexamethasone taper and may be continued on discharge</td></tr>
<tr><td>Dosing (initial)</td><td>Standard steroid taper
• Factors that may influence the duration of prednisone taper:
o Current and historical CNI levels
o Sensitization status
o Current MPA dose
o Episodes of rejection
<table>
<tr><td>Dexamethasone</td><td>100 mg</td><td>POD0</td></tr>
<tr><td></td><td>50 mg</td><td>POD1</td></tr>
<tr><td>Dexamethasone or Prednisone</td><td>18 mg (dex) or 90 mg (pred)</td><td>POD2</td></tr>
<tr><td></td><td>12 mg (dex) or 60 mg (pred)</td><td>POD3</td></tr>
<tr><td rowspan="2">Prednisone</td><td>30 mg</td><td>POD4</td></tr>
<tr><td colspan="2">Discharge on 30 mg and after 2 week follow up, decrease dose by 5 mg each week to a target dose of 10 mg daily</td></tr>
</table></td><td rowspan="3">• Steroid withdrawal can be considered for patients who receive alemtuzumab for induction (UW Health, Very Low, Conditional)
• Rapid steroid taper can be considered for patients who receive alemtuzumab or thymoglobulin for induction (UW Health, Very Low, Conditional)
• Prednisone doses should be split to twice daily dosing for patients requiring glucose control (UW Health, Very Low, Conditional)</td></tr>
<tr><td>Rapid steroid taper
<table>
<tr><td>Dexamethasone</td><td>100 mg</td><td>POD0</td></tr>
<tr><td></td><td>50 mg</td><td>POD1</td></tr>
<tr><td>Dexamethasone or Prednisone</td><td>18 mg (dex) or 90 mg (pred)</td><td>POD2</td></tr>
<tr><td></td><td>12 mg (dex) or 60 mg (pred)</td><td>POD3</td></tr>
<tr><td rowspan="4">Prednisone</td><td>30 mg</td><td>POD4</td></tr>
<tr><td>20 mg</td><td>POD5</td></tr>
<tr><td>10 mg</td><td>POD6</td></tr>
<tr><td colspan="2">Discharge on 10 mg daily and decrease to 5 mg daily after 2 weeks if tacrolimus is therapeutic</td></tr>
</table></td></tr>
<tr><td>Early steroid withdrawal
<table>
<tr><td>Dexamethasone</td><td>100 mg</td><td>POD0</td></tr>
<tr><td></td><td>50 mg</td><td>POD1</td></tr>
<tr><td>Dexamethasone or Prednisone</td><td>18 mg (dex) or 90 mg (pred)</td><td>POD2</td></tr>
<tr><td></td><td>12 mg (dex) or 60 mg (pred)</td><td>POD3</td></tr>
<tr><td rowspan="2">Prednisone</td><td>30 mg</td><td>POD4</td></tr>
<tr><td colspan="2">Steroid withdrawal on POD5</td></tr>
</table></td></tr>
<tr><td>Labs</td><td colspan="2"><u>Laboratory Monitoring:</u> Glucose, bone mineral density</td></tr>
<tr><td rowspan="3">Adverse effects</td><td>Hyperglycemia</td><td>• Prednisone doses should be split to twice daily dosing for patients with hyperglycemia</td></tr>
<tr><td>Heartburn/reflux</td><td>• Start proton pump inhibitor (PPI) at time of transplant. Should be continued for at least 3 months after transplant
• If a patient complains of heartburn on daily dosing of the PPI, frequency may be increased to twice daily (pending renal function)
• Discontinue PPI in patients with no history of heartburn/gastroesophageal reflux disease (GERD) prior to transplant if prednisone is discontinued</td></tr>
<tr><td>Osteoporosis</td><td>• Recommend calcium 1200 mg daily (based on elemental calcium dosing)
• Recommend vitamin D 2000 units daily
• For patients that are on an early steroid withdrawal maintenance immunosuppression regimen, calcium and vitamin D supplementation are not required</td></tr>
</table>

Tacrolimus – renal transplant

<table>
<tr><th></th><th colspan="2">Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">Post-operative day 1</td><td rowspan="3">• Initiation of tacrolimus should start before or at the time of transplant, rather than delayed until the onset of graft function (UW Health, Very Low, Conditional)
• Capsules and suspension may be taken with or without food. Since the presence of food affects the bioavailability of tacrolimus, if taken with food, it should be taken consistently the same way each time. (UW Health, Very Low, Conditional)
• Tacrolimus may be given sublingually in patients unable to adequately absorb enteral formulations or in those unable to take oral. If a patient is being transitioned to tacrolimus sublingual from tacrolimus IR, each dose should be divided by 2 and given sublingually. (UW Health, Very Low, Conditional)
• Use of IV tacrolimus is reasonable for patients unable to adequately absorb enteral formulations, and conversion from IV to oral tacrolimus is recommended as soon as enteral therapy can be tolerated to minimize risk of anaphylactic reactions that occur with injectables containing castor oil derivatives. (UW Health, Very Low, Conditional)
• Tacrolimus ER may be utilized in patients with documented intolerable adverse effects with tacrolimus IR or who are unable to obtain a therapeutic drug concentration with the IR formulation. If a patient is being transitioned to tacrolimus ER (Envarsus®) from tacrolimus IR, the total daily dose should be multiplied by 0.8, then rounded to the nearest capsule size. (UW Health, Very Low, Conditional)</td></tr>
<tr><td>Dosing (initial)</td><td>Decreased sensitivity (African-American, >80kg)</td><td>0.1 mg/kg/day (use ABW), by mouth divided in 2 doses twice daily, rounded to nearest capsule size</td></tr>
<tr><td></td><td>Increased sensitivity (NPO, <80kg)</td><td>Fixed dose 2 mg by mouth twice daily</td></tr>
<tr><td>Drug-drug Interactions (not an all-inclusive list)</td><td>Increases tacrolimus concentration
Check Lexicomp for dose adjustments
<u>Adjust tacrolimus dose empirically:</u>
• Fluconazole
• Posaconazole
• Voriconazole
• Ritonavir
• Letermovir
<u>Monitor tacrolimus levels and adjust as needed:</u>
• Clarithromycin
• Erythromycin</td><td>Decreases tacrolimus concentration
Check Lexicomp for dose adjustments
<u>Monitor tacrolimus levels and adjust as needed:</u>
• Rifampin
• Phenytoin
• Carbamazepine
• Phenobarbital</td></tr>
<tr><td>Target levels

Dose Adjustments

Labs</td><td>Concurrent use of mycophenolate +/- prednisone

Tacrolimus goals may differ if patient is not on mycophenolate +/- prednisone regimen. Goal level should be discussed with provider.

<table><tr><th></th><th>Target TAC Trough Level</th></tr><tr><td>DGF</td><td>7-9 ng/mL</td></tr><tr><td>0-3 months:</td><td>8-11 ng/mL</td></tr><tr><td>3-6 months:</td><td>7-9 ng/mL</td></tr><tr><td>6-12 months:</td><td>6-8 ng/mL</td></tr><tr><td>>12 months:</td><td>5-7 ng/mL</td></tr></table>
<table><tr><td>Below/Above Target</td><td></td></tr><tr><td><u>≥</u>50%</td><td>Adjust dose by 25-50%</td></tr><tr><td><50%</td><td>Adjust dose by 25%</td></tr></table>*Holding doses may be necessary</td><td><u>Laboratory Monitoring:</u>
Tacrolimus (trough), potassium, and creatinine
Inpatient: Daily
Post-Discharge:<table><tr><th>Day</th><th>Frequency</th></tr><tr><td>0-90</td><td>Not less than weekly</td></tr><tr><td>91-180</td><td>Not less than twice monthly</td></tr><tr><td>181-2 years</td><td>Not less than once monthly</td></tr><tr><td>>2 years</td><td>Not less than quarterly</td></tr></table>As Needed:
• Change in medication formulation, patient status, or creatinine increase <u>≥</u>0.3 mg/dL above baseline
• 3 to 7 days (ideally 4 days) following dose adjustment</td></tr>
</table>

Adverse effects	Acute kidney injury	• Assess tacrolimus trough level for correlation with elevated creatinine • If trough level is above goal and creatinine has increased ≥ 0.3 mg/dL above baseline: o Decrease tacrolimus dose if trough is <4 ng/mL above goal o Hold tacrolimus if trough ≥5 ng/mL above goal and consider increasing current prednisone dose
	Neurological symptoms (tremor, headache)	• Assess tacrolimus trough level for correlation with tremors or headache • If trough level is above goal, adjust tacrolimus dose and follow up with patient • if trough level within target range, no dose adjustment is recommended, follow-up with patient in 1 week • If adverse effects are intolerable or interacting with daily activities and there is no other known cause of symptom: o Consult the transplant physician to consider converting the patient to tacrolimus ER, belatacept, cyclosporine, or refer to primary care provider for supportive therapy, such as addition of low dose beta blocker (propranolol)
	New onset diabetes after transplantation (NODAT) *Diagnosis* • Sx of DM + casual PG concentrations ≥200 mg/dL • FPG ≥126 mg/dL • 2-hr PG ≥200 mg/dL during an oral glucose tolerance test	• No tacrolimus dose adjustment is recommended • Consider consulting diabetes management & nutrition services • Diagnosis of new onset diabetes after transplant (NODAT) is defined by the World Health Organization (WHO) and American Diabetes Association (ADA) that develops for the first time after transplantation • If there is no improvement in glucose control 6 months after transplant (NODAT requiring insulin OR A1c >7% with glucose lowering agent) and there have been 3 months of minimal glucocorticoid doses o Consult transplant physician and consider converting the patient to cyclosporine

Cyclosporine – renal transplant

<table>
<tr><th></th><th colspan="2">Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">Post-operative day 1</td><td>• The initiation of cyclosporine should start before or at the time of transplantation, rather than delayed until the onset of graft function (UW Health, Very Low, Conditional)</td></tr>
<tr><td rowspan="2">Dosing (initial)</td><td>Decreased sensitivity (African-American, >80kg)</td><td>Fixed dose 150 mg by mouth twice daily</td><td rowspan="3">• Neoral/Gengraf (cyclosporine modified) and Sandimmune (cyclosporine non-modified) are not bioequivalent and cannot be used interchangeably (UW Health, Very Low, Conditional)
• Capsules and suspension may be taken with or without food. However, since the presence of food affects the bioavailability of cyclosporine, if taken with food, it should be taken consistently the same way each time. (UW Health, Very Low, Conditional)</td></tr>
<tr><td>Increased sensitivity (NPO, <80kg)</td><td>Fixed dose 100 mg by mouth twice daily</td></tr>
<tr><td>Drug-Drug Interactions (not an all-inclusive list)</td><td>Increases cyclosporine concentration
Check Lexicomp for dose adjustments
<u>Adjust cyclosporine dose empirically:</u>
• Fluconazole
• Posaconazole
• Voriconazole
• Ritonavir
• Letermovir
<u>Monitor cyclosporine levels and adjust as needed:</u>
• Clarithromycin
• Erythromycin</td><td>Decreases cyclosporine concentration
Check Lexicomp for dose adjustments
<u>Monitor cyclosporine levels and adjust as needed:</u>
• Rifampin
• Phenytoin
• Carbamazepine
• Phenobarbital</td></tr>
<tr><td>Target levels

Dose Adjustments

Labs</td><td>
<table>
<tr><th></th><th>Goal CSA Level</th></tr>
<tr><td>0-3 months:</td><td>200-300 ng/mL</td></tr>
<tr><td>3-6 months:</td><td>150-250 ng/mL</td></tr>
<tr><td>6-12 months:</td><td>100-200 ng/mL</td></tr>
<tr><td>>12 months:</td><td>50-100 ng/mL</td></tr>
</table>
<table>
<tr><td>Below/Above Target</td><td></td></tr>
<tr><td>≥50%</td><td>Adjust dose 25% to 50%</td></tr>
<tr><td>≤50%</td><td>Adjust dose by 25%</td></tr>
</table>
*Holding doses may be necessary</td><td><u>Laboratory Monitoring:</u>
Cyclosporine (trough), potassium, and creatinine
Inpatient: Daily
Post-Discharge:
<table>
<tr><td>Day</td><td>Frequency</td></tr>
<tr><td>0-90</td><td>Not less than weekly</td></tr>
<tr><td>91-180</td><td>Not less than twice monthly</td></tr>
<tr><td>181-2 years</td><td>Not less than once monthly</td></tr>
<tr><td>>2 years</td><td>Not less than quarterly</td></tr>
</table>
As Needed:
• Change in medication formulation, patient status, or creatinine increase ≥0.3 mg/dL above baseline
• 3 to 7 days (ideally 4 days) following dose adjustment</td></tr>
</table>

Adverse effects	Acute kidney injury	• Assess cyclosporine trough level for correlation with elevated creatinine • If trough level is above goal and creatinine has increased ≥ 0.3 mg/dL above baseline: o Decrease cyclosporine dose if trough is <50 ng/mL above goal o Hold cyclosporine if trough ≥50 ng/mL above goal and consider increasing current prednisone dose
	Neurological symptoms (tremor, headache)	• Assess cyclosporine trough level for correlation with tremors or headache • If trough level is above goal, adjust cyclosporine dose and follow up with patient • if trough level within target range, no dose adjustment is recommended, follow-up with patient in 1 week • If adverse effects are intolerable or interacting with daily activities and there is no other known cause of symptom: o Consult the transplant physician to consider converting the patient to tacrolimus ER, belatacept, or refer to primary care provider for supportive therapy, such as addition of low dose beta blocker (propranolol)
	New onset diabetes after transplantation (NODAT) *Diagnosis* • Sx of DM + casual PG concentrations ≥200 mg/dL • FPG ≥126 mg/dL • 2-hr PG ≥200 mg/dL during an oral glucose tolerance test	• No cyclosporine dose adjustment is recommended • Consider consulting diabetes management & nutrition services • Diagnosis of new onset diabetes after transplant (NODAT) is defined by the World Health Organization (WHO) and American Diabetes Association (ADA) that develops for the first time after transplantation • If there is no improvement in glucose control 6 months after transplant (NODAT requiring insulin OR A1c >7% with glucose lowering agent) and there have been 3 months of minimal glucocorticoid doses: o Consult transplant physician

Belatacept – renal transplant

	Recommendation		Notes/Evidence
Dosing	Induction dosing (starting post-transplant or converting from CNI <6 months from transplant)	Day 0, day 4: 10 mg/kg/dose Ends of weeks 2, 4, 8, 12: 10 mg/kg/dose 5 mg/kg/dose every 4 weeks (±3 days) starting at week 16	• Indicated for use in patients who are EBV seropositive as a replacement for CNIs or to allow for CNI minimization (UW Health, Very Low, Conditional) • EBV serostatus should be evaluated prior to initiation of belatacept (UW Health, Very Low, Strong)
	Conversion dosing w/ CNI taper (converting from CNI to belatacept >6 months from transplant)	Initial phase: - Day 0: 5 mg/kg/dose - End of weeks 2, 4, 6, and 8: 5 mg/kg/dose Maintenance phase: - 5 mg/kg/dose every 4 weeks (±3 days) starting end of week 12 CNI taper: - 100% of previous dose on days 1-14 - 50% of previous dose on days 15-28 - 25% of previous dose on days 29-41 - Discontinue CNI on day 42	
	Conversion dosing with no CNI taper (converting from CNI to belatacept >6 months from transplant)	Initial phase: - Day 0: 10 mg/kg/dose - End of weeks 2, 4, 6, and 8: 10 mg/kg/dose Maintenance phase: - 5 mg/kg/dose every 4 weeks (±3 days) starting end of week 12	
Labs	<u>Laboratory Monitoring:</u> **Prior to initiation**: EBV serostatus		
Adverse effects	Post-transplant lymphoproliferative disorder (PTLD)	• Consult transplant provider if concerns for PTLD (weight loss, fatigue, unexplained anemia/thrombocytopenia/leukopenia, hypercalcemia)	

Mycophenolate – renal transplant

<table>
<tr><th></th><th colspan="2">Recommendation</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">Post-operative day 1</td><td rowspan="3">• Full dose mycophenolic acid is the preferred anti-proliferative medication used for renal transplant patients (UW Health, Very Low, Conditional)
• IV mycophenolate mofetil is indicated if the patient has an acute condition that affects gastrointestinal absorption (i.e., GI bleed or obstruction, malabsorption syndromes, severe diarrhea or severe vomiting) (UW Health, Very Low, Conditional)
• Mycophenolate mofetil suspension is utilized for patients receiving medications via nasogastric or orogastric tube</td></tr>
<tr><td>Dosing (initial)</td><td>Mycophenolate sodium (Myfortic)
Mycophenolate mofetil (Cellcept)</td><td>720 mg by mouth twice daily
1000 mg by mouth twice daily</td></tr>
<tr><td>Drug-drug interactions (not an all-inclusive list)</td><td colspan="2">Decreases mycophenolate concentration
Check Lexicomp for dose adjustments
• Cyclosporine</td></tr>
<tr><td>Target levels

Labs</td><td><table><tr><th></th><th>Goal MPA Trough</th></tr><tr><td>CsA based regimens:</td><td>1.3-2.8 mg/L</td></tr><tr><td>TAC based regimens:</td><td>1.9-2.8 mg/L</td></tr></table></td><td><u>Laboratory Monitoring:</u>
• Lab monitoring of MPA levels is not recommended to assess for toxicity or efficacy
• If levels are requested, they are only appropriate for mycophenolate mofetil and should be drawn as a trough</td><td>• MPA AUC is a better predictor of clinical events than MPA trough. Trough levels are poorly correlated with AUC and are not recommended (UW Health, Very Low, Conditional)</td></tr>
<tr><td rowspan="2">Adverse effects</td><td>Diarrhea

If a patient has ≥50% increase in their frequency of daily bowel movements for ≥ 5-7 days
• 0-3 months post-transplant:
o C. difficile, C. difficile toxin B PCR
o CMV PCR
• ≥3 months post-transplant:
o CMV PCR
o Complete blood count
o Clostridium difficile toxin B PCR
o Cryptosporidium
o Giardia PCR
o Norovirus PCR
o Rotavirus AG
o Stool culture, with E. Coli (Shiga) toxin
o Stool O&P (parasitology, isospora, cyclospora, pinworm)
o Consider colonoscopy if diarrhea persists and all stool studies are negative</td><td colspan="2">• If diarrhea work-up is negative for an infectious cause of diarrhea and it is affecting activities of daily living or the patient is having limited and/or decreased oral intake:
o Decrease mycophenolate by 25% and increase dosing frequency (ex. 720 mg BID → 360 mg TID)
▪ If fails, decrease mycophenolate by 50%
o Follow up with patient in 1 week
o If dose is decreased to 180 mg twice daily (MYF) or 250 mg twice daily (MMF) consult provider to determine if other immunosuppression needs to be adjusted
o Consider adding the following:
▪ Add loperamide (Imodium®) 2 mg as needed after each loose stool (max dose: 16 mg daily)
▪ Diphenoxylate/atropine (Lomotil®) 5 mg four times daily as needed (max dose: 20 mg/day)
▪ Psyllium fiber (Metamucil®) 3.4 g daily as needed</td></tr>
<tr><td>Heartburn/nausea</td><td colspan="2">• Counsel patient on taking MYF or MMF with food if not already doing so
• Convert from MMF to MYF if only upper GI complaints (heartburn, nausea)
• Add calcium carbonate as needed, or the addition of an H2RA or PPI if not already on
• If symptoms continue following 1 week of daily therapy increase H2RA or PPI dose to twice daily, reassess in 1 week
• If symptoms persist for ≥1 week, consider EGD to rule out infection vs. ulceration</td></tr>
</table>

Azathioprine – renal transplant

<table>
<tr><th></th><th colspan="2">Recommendation</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">Failure to tolerate mycophenolate</td><td></td></tr>
<tr><td>Dosing (initial)</td><td colspan="2">1-2 mg/kg by mouth daily</td><td rowspan="3">• Azathioprine is recommended for use in patients unable to tolerate adverse effects of mycophenolate (UW Health, Very Low, Conditional)
• Azathioprine is considered to be less effective than MPA in preventing rejection. Prior to initiating azathioprine, consider the total immunosuppression for the patient and timing out from transplant</td></tr>
<tr><td>Drug-drug interactions (not an all-inclusive list)</td><td colspan="2">Increases azathioprine concentration:
Check Lexicomp for dose adjustments
<u>Avoid concurrent use:</u>
• Febuxostat
<u>Adjust azathioprine dose empirically:</u>
• Allopurinol</td></tr>
<tr><td>Labs</td><td colspan="2"><u>Laboratory Monitoring:</u>
• There is no recommended azathioprine level for monitoring purposes. However, if toxicity is suspected, check thiopurine methyltransferase (TPMT)</td></tr>
<tr><td rowspan="2">Adverse effects</td><td>Leukopenia</td><td>• Consult transplant provider if WBC <3</td><td rowspan="2"></td></tr>
<tr><td>Gastrointestinal

If a patient has ≥50% increase in their frequency of daily bowel movements for ≥ 5-7 days
• 0-3 months post-transplant:
o C. difficile, C. difficile toxin B PCR
o CMV PCR
• ≥3 months post-transplant:
o CMV PCR
o Complete blood count
o Clostridium difficile toxin B PCR
o Cryptosporidium
o Giardia PCR
o Norovirus PCR
o Rotavirus AG
o Stool culture, with E. Coli (Shiga) toxin
o Stool O&P (parasitology, isospora, cyclospora, pinworm)
Consider colonoscopy if diarrhea persists and all stool studies are negative</td><td>• See diarrhea work-up algorithm</td></tr>
</table>

Sirolimus/everolimus – renal transplant

<table>
<tr><th></th><th colspan="2">Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">For use in patients with:
CNI toxicity
Skin cancer
Quadruple therapy</td><td>Sirolimus/everolimus may impair or delay wound healing, and should be used with caution in the peri-surgical period (UW Health, Very Low, Conditional)
Indicated for use in patients with recurrent skin cancers as a replacement for azathioprine, MPA, or CNIs (UW Health, Very Low, Conditional)</td></tr>
<tr><td rowspan="2">Dosing (initial)</td><td>Sirolimus</td><td>6 mg load on day 1, followed by 2 mg by mouth once daily</td><td rowspan="3"></td></tr>
<tr><td>Everolimus</td><td>0.75 mg by mouth twice daily</td></tr>
<tr><td>Drug-drug interactions (not an all-inclusive list)</td><td>Increase mTOR concentration (not an all-inclusive list):
Check Lexicomp for dose adjustments
<u>Avoid concurrent use:</u>
Posaconazole
Voriconazole
Ritonavir
<u>Monitor mTOR levels and adjust as needed:</u>
Fluconazole
Ritonavir
Letermovir
Clarithromycin
Erythromycin</td><td>Decrease mTOR concentration (not an all-inclusive list)
Check Lexicomp for dose adjustments
<u>Monitor mTOR levels and adjust as needed:</u>
Rifampin
Phenytoin
Carbamazepine
Phenobarbital</td></tr>
<tr><td>Target levels

Dose Adjustments

Labs</td><td colspan="2"><table><tr><th></th><th>Goal Trough Levels (SIRO/EVR+TAC)</th><th>Goal Sirolimus Level (SIRO/EVR+MPA)</th></tr><tr><td>0-3 months:</td><td>TAC: 5-7 ng/mL
SIRO/EVR: 4-7 ng/mL</td><td>SIRO/EVR: 8-10 ng/mL</td></tr><tr><td>3-6 months:</td><td>TAC: 5-7 ng/mL
SIRO/EVR: 4-7 ng/mL</td><td>SIRO/EVR: 8-10 ng/mL</td></tr><tr><td>6-12 months:</td><td>TAC: 3-5 ng/mL
SIRO/EVR: 3-5 ng/mL</td><td>SIRO/EVR: 5-8 ng/mL</td></tr><tr><td>>12 months:</td><td>TAC: 3-5 ng/mL
SIRO/EVR: 3-5 ng/mL</td><td>SIRO/EVR: 5-8 ng/mL</td></tr></table><u>Laboratory Monitoring:</u>
Recommended once weekly upon initiation and with any dose changes
When the target trough level has been attained, recommend monitoring levels once monthly</td><td></td></tr>
</table>

Adverse effects	Proteinuria	• Monitor at 6 months and then annually post-transplant per standard lab monitoring • Consider administration of angiotensin-converting enzyme (ACE)-inhibitors and angiotensin II receptor antagonists and reducing mTOR levels
	Mouth ulcers	• Development of mouth ulcers also seems to be dose-related, because they usually appear after the loading dose and often improve after a dose reduction • Addition of a high-potency topical steroid may be considered
	Hyperlipidemia	• Monitor cholesterol and lipids • If hyperlipidemia occurs, follow current guidelines for management (diet, exercise, lipid lowering agents) • Immunosuppressive strategies minimizing doses of mTORs, CNIs, or corticosteroids may help in controlling hyperlipidemia
	Thrombocytopenia	• Consider dose reduction or temporary drug suspension if appropriate

Prednisone – renal transplant

<table>
<tr><th></th><th colspan="2">Recommendations</th><th>Notes/Evidence</th></tr>
<tr><td>Initiation</td><td colspan="2">Post-operative day 4 following dexamethasone taper</td><td>• Prednisone 30 mg once daily will be started on POD 4 following dexamethasone taper and may be continued on discharge</td></tr>
<tr><td rowspan="3">Dosing (initial)</td><td>Standard steroid taper
• Prednisone taper should occur following POD4
• Factors that may influence the duration of prednisone taper:
o Current and historical CNI levels
o Current MPA dose
o Current renal function
o Episodes of rejection</td><td><table>
<tr><td rowspan="2">Dexamethasone</td><td>100 mg</td><td>POD0</td></tr>
<tr><td>50 mg</td><td>POD1</td></tr>
<tr><td rowspan="2">Dexamethasone or Prednisone</td><td>18 mg (dex) or 90 mg (pred)</td><td>POD2</td></tr>
<tr><td>12 mg (dex) or 60 mg (pred)</td><td>POD3</td></tr>
<tr><td rowspan="2">Prednisone</td><td>30 mg</td><td>POD4</td></tr>
<tr><td colspan="2">Discharge on 30 mg and decrease dose by 5 mg each week to a target dose of 10 mg daily</td></tr>
</table></td><td rowspan="3">• Steroid withdrawal can be considered for patients who receive alemtuzumab for induction (UW Health, Very Low, Conditional)
• Rapid steroid taper can be considered for patients who receive alemtuzumab or thymoglobulin for induction (UW Health, Very Low, Conditional)
• Prednisone doses should be split to twice daily dosing for patients requiring insulin for glucose control (UW Health, Very Low, Conditional)</td></tr>
<tr><td>Rapid steroid taper</td><td><table>
<tr><td rowspan="2">Dexamethasone</td><td>100 mg</td><td>POD0</td></tr>
<tr><td>50 mg</td><td>POD1</td></tr>
<tr><td rowspan="2">Dexamethasone or Prednisone</td><td>18 mg (dex) or 90 mg (pred)</td><td>POD2</td></tr>
<tr><td>12 mg (dex) or 60 mg (pred)</td><td>POD3</td></tr>
<tr><td rowspan="3">Prednisone</td><td>30 mg</td><td>POD4</td></tr>
<tr><td>10 mg</td><td>POD5</td></tr>
<tr><td colspan="2">Discharge on 10 mg and consider reduction to 5 mg at week 3 to target dose of 5 mg daily</td></tr>
</table></td></tr>
<tr><td>Early steroid withdrawal</td><td><table>
<tr><td rowspan="2">Dexamethasone</td><td>100 mg</td><td>POD0</td></tr>
<tr><td>50 mg</td><td>POD1</td></tr>
<tr><td rowspan="2">Dexamethasone or Prednisone</td><td>18 mg (dex) or 90 mg (pred)</td><td>POD2</td></tr>
<tr><td>12 mg (dex) or 60 mg (pred)</td><td>POD3</td></tr>
<tr><td rowspan="2">Prednisone</td><td>30 mg</td><td>POD4</td></tr>
<tr><td colspan="2">Steroid withdrawal on POD5</td></tr>
</table></td></tr>
<tr><td>Labs</td><td colspan="3"><u>Laboratory Monitoring:</u>
Glucose, bone mineral density</td></tr>
<tr><td rowspan="3">Adverse effects</td><td>Hyperglycemia</td><td colspan="2">• Prednisone doses should be split to twice daily dosing for patients requiring insulin for glucose control</td></tr>
<tr><td>Heartburn/reflux</td><td colspan="2">• Start a proton pump inhibitor (PPI) at time of transplant
• If a patient complains of heartburn on daily dosing of the PPI, frequency may be increased to twice daily (pending renal function)
• Discontinue PPI in patients with no history of heartburn/gastroesophageal reflux disease (GERD) prior to transplant if prednisone is discontinued</td></tr>
<tr><td>Osteoporosis</td><td colspan="2">• Recommend calcium 2000 mg daily (based on elemental calcium dosing)
• Recommend vitamin D 2000 units daily
• For patients that are on an early steroid withdrawal maintenance immunosuppression regimen, calcium and vitamin D supplementation are not required</td></tr>
</table>

UW Health Kidney Transplant Induction and Desensitization Protocols

Donor Status	Protocol	Virtual XM	Sum MFI	PE + IVIG (100mg/kg after each PE); MPA / TAC Desensitization	Induction Regimen	Prednisone Taper
Live	D0	Negative	-	-	ESW: Alemtuzumab 30mg x1 OR Thymoglobulin 1.5mg/kg daily x3-4	• Discontinue POD5
				-	Non-ESW: Basiliximab 20mg x1	• Discharge on 10mg/day[1] • Consider reduction to 5mg at week 3 • Target dose 5mg/day
	D1	Weak positive	<1000	MPA/TAC:d(-7)	Alemtuzumab 30mg x1 OR Thymoglobulin 1.5mg/kg daily x3-4	• Discharge on 30mg/day • Reduce daily dose by 5mg each week • Target dose 10mg/day
	D2	Positive	1,000 - 4,000	PE/IVIG: 2-3 pre-Tx and post-Tx; MPA/TAC:d(-7)	Thymoglobulin 1.5mg/kg daily x 4 OR Thymoglobulin 1.5mg/kg daily x3-4	
Deceased	D5a	Negative	-	-	ESW: Alemtuzumab 30mg x1 OR Thymoglobulin 1.5mg/kg daily x3-4	• Discontinue POD5
				-	Non-ESW: Basiliximab 20mg x1	• Discharge on 10mg/day[1] • Consider reduction to 5 mg at week 3 • Target dose 5mg/day
				-	Non-ESW + High DGF Risk: Alemtuzumab 30mg x1 OR Thymoglobulin 1.5mg/kg daily x3-4	
	D5b	Weak positive	<1000	-	Alemtuzumab 30mg x1 OR Thymoglobulin 1.5mg/kg daily x3-4	• Discharge on 30mg/day • Reduce daily dose by 5mg each week • Target dose 10mg/day
	D5c	Positive	1,000 - 4,000	PE/IVIG: Pre-Tx: 1 Post-Tx: 2-3	Thymoglobulin 1.5mg/kg daily x 4	

Post-reperfusion biopsy recommended for all patients • Patients with GN should receive Thymoglobulin and steroid continuation
Patients receiving an A2 to B Transplant with anti-A titer ≥1:16 receive Thymoglobulin ≤1:8 receive 2 doses of Basiliximab

[1] - Rapid Steroid Taper: Dex 100mg IVx1, Dex 50mg IVx1, Pred 90mg POx1, Pred 60mg POx1, Pred 30 mg POx1, Pred 10 mg PO daily

UW Health Kidney Rejection Treatment Protocols

Type	TCMR						ABMR	Mixed
Banff	Suspicious	IA	IB	IIA	IIB	III	Banff 2019	-
Protocol #	R1	R2		R3			R4	R5

Start CMV, thrush, PJP, PUD prophylaxis
Follow-up biopsy recommended at 12 weeks (± 1 week) for all patients
DSA Monitoring: Monthly x 3 months, 6 months, 12 months, annually

Rejection Protocols

R1 Inpatient: Dex 50mg IV x 1, Dex 44mg IV x 1 (omit for outpatients), then prednisone taper[2]; Outpatient: Dex 50mg IV x 1, then prednisone taper[2]
R2 Dex 100mg IV x1, Dex 50mg IV x1, Dex 44mg IV x1 (omit for outpatients), followed by prednisone taper[2]
R3 R2 + Thymo (1.5mg/kg daily x 4-7)
R4a Early ABMR[4]: R2 + PE/IVIG (100mg/kg) x 4-6 then IVIG (500 mg/kg/week) x4 ± Ritux[3] 375 mg/m2 x1
R4b Late ABMR[4]: R2 + IVIG (500mg/kg/week) x 4 ± Ritux[3] 375 mg/m^2 x 1
R5 R2 + PE/IVIG (early only[4]) x 4-6 + Thymo (1.5mg/kg daily x 5-7) + IVIG (500 mg/kg/week) x 4 ± Ritux[3] 375 mg/m^2 x1

[2] Standard Prednisone Taper: 180mg x1, 150mg x1, 120mg x1, 90mg x1, 60mg x1, 30mg daily x 7 days, then 20mg daily x 7 days, then 10 mg daily until clinic appointment. Dexamethasone dosed daily, prednisone total daily dose split BID
[3] Ritux use not recommended if ABMR injury is minimal (focal C4d, without microcirculation inflammation); following PE if concurrent
[4] Early is defined as 0-6 months following transplant, late is > 6 months following transplant
All weight-based medication dosing should use IBW unless other weight is specified

Abbreviations
A2B=ABO B recipient of an A donor; ABMR=Antibody mediated rejection; CMV=Cytomegalovirus, d=Day; Dex=Dexamethasone IV; DGF=Delayed Graft Function; DSA=Donor Specific Antibody; ESW=Early Steroid Withdrawal; GN=Glomerulonephritis; IBW=Ideal Body Weight; IVIG=Intravenous Immune Globulin; MFI=Mean Fluorescent Intensity; MPA=Mycophenolic Acid; PE=Plasma Exchange; POD=Post-Op Day; PJP=Pneumocystis Jiroveci Pneumonia; PUD=Peptic Ulcer Disease; Ritux=Rituximab; TAC=Tacrolimus; TCMR=T-cell Mediated Rejection; Thymo=Thymoglobulin; XM=Cross match

Contact for Content	Contact for Content	Contact for Changes
Aji Djamali, MD - Nephrology (608) 262-7330 • axd@medicine.wisc.edu	Didier Mandelbrot, MD - Nephrology (608) 262-4352 • damandel@medicine.wisc.edu	David Hager, PharmD – Pharmacy (608) 890-8993 • dhager@uwhealth.org

UWHealth
uwhealth.org/transplant

PH-453294-19 Updated (03/2021)