UW Medicine

UNIVERSITY OF WASHINGTON
MEDICAL CENTER

Liver, Kidney, Pancreas, Intestinal Transplant Medication Guidelines

Resident's Handbook

#22 Revised 2/5/14
(for staff use only)

Disclaimer: The following Handbook is a summary of some UWMC Division of Transplantation guidelines. It is provided as a general guide and not the ultimate source of information or standard of care upon which to base clinical decisions. Transplant is a rapidly changing area of medicine. These guidelines may undergo frequent modification post-publication as dictated by current and changing clinical thought.

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I. Kidney Transplantation Induction Immunosuppression Guideline 4-13

Induction: Basiliximab (Simulect®) (IL-2 blockade) or rabbit anti-thymocyte globulin (rATG) (Thymoglobulin®) (polyclonal antibody) will be selected based on the immunologic risk factors of the patient. Risks and benefits of each therapy with regard to donor and recipient risk factors are considered. **Basiliximab** has increased tolerability compared to **rATG**; however, rejection rates are lower with rATG in higher immunologic risk populations. rATG increases the risk of infections and malignancy compared to basiliximab. rATG may also reduce ischemia-reperfusion injury, while basiliximab has not been shown to have this benefit. rATG's duration of effect and potency of immunosuppression is dose related.

Considerations for determining intensity of induction approach:

Low Intensity:

- Infectious disease issues: HIV, HCV, HBV, recurrent infections
- Age >65 years (>55 if diabetic)
- No delayed graft function observed or expected
- Living donor- well matched HLA
- Deceased donor- 0 mismatch HLA and no DGF expected
- Severe cardiovascular or pulmonary disease
- History of cancer

Standard Intensity:

- Autoimmune disease
- Delayed graft function expected (CIT >24h, DCD)
- African American

High Intensity:

- PRA >20%
- ABO incompatible
- Positive flow crossmatch
- Severe recurrent autoimmune disease
- Re-transplant

Standard deceased donor recipient maintenance immunosuppression: Tacrolimus (Prograf®) will be started post-operatively 0.025mg/kg PO q12h with a target level goal of 8-12 ng/ml by the time the induction agent course is completed. **Myfortic®** (mycophenolate acid) will be given 1080mg po pre-op then 720mg PO bid unless the patient develops severe neutropenia or GI disturbances. An alternative to Myfortic® is Cellcept®(mycophenolate mofetil) which is used in the event the patient requires IV therapy (Cellcept 1gm = Myfortic 720mg).

Standard living donor recipient maintenance immunosuppression: Tacrolimus 0.025mg/kg PO q12h and Myfortic 720mg PO bid will be started pre-operatively on POD -2 and continued without interruption peri-operatively. Post-operative tacrolimus dosing will be determined via therapeutic drug monitoring with a goal of 8-12 ng/ml as with deceased donor recipients.

Steroids: All patients will receive methylprednisolone intra-op for prevention of reperfusion injury and post-op as a pre-med for rATG (see induction specific tables). Steroid-free regimens have demonstrated reasonable patient and graft survival, but with higher rejection rates than steroid maintenance. Steroid-free regimens reduce fracture risk and may reduce risk factors for cardiovascular disease. **Patients assigned to high intensity induction or with autoimmune disorders are ineligible for steroid-free maintenance**.

Delayed Graft Function (patient requiring dialysis within first week after transplant): see DGF guideline

Ia. Kidney Induction Guideline: Low Intensity

Day Post-Op	Steroid Taper	Basiliximab (Simulect®)	Mycophenolate (Myfortic®, MPA)	Tacrolimus (Prograf®, FK506)
Clinic Day -2			720mg PO bid	0.025mg/kg po q12h (rounded to nearest 0.5mg)
Pre-Op 4SE (Day 0)			1080mg PO (omit if living donor)	Continue tacrolimus if started pre-op
Intra-op Day 0	Methylprednisolone 500mg IV	20mg IV	720mg PO bid	Start at 0800 or 2000 after returning to floor at 0.025mg/kg po q12h (rounded to nearest 0.5mg)
Day 1	MP 250mg IV		same	Monitor daily tacrolimus level, adjust for goal level: 8-12 ng/ml
Day 2	MP 125mg IV		same	same
Day 3	Prednisone 50mg PO qd		same	same
Day 4	Prednisone 25mg PO qd (last dose if steroid free)	20mg IV POD 4 or day of 1st clinic visit	same	same
Day 5+	Prednisone 10mg PO qd		same	Per Tx Nephrology

If living donor, start tacrolimus and Myfortic on POD -2, omit pre-op Myfortic 1080mg
If steroid free, omit steroids after day 4. If continuing steroids, they will be tapered by nephrologist as outpatient to 5mg po qday.

Ib. Kidney Induction Guideline: Standard Intensity

	Steroid Taper	rATG (Thymoglobulin®)	Mycophenolate (Myfortic, MPA®)	Tacrolimus (Prograf®,FK506)
Clinic Day -2			720mg PO bid	0.025mg/kg po q12h (rounded to nearest 0.5mg)
Pre-Op 4SE (Day 0)			1080mg PO (omit if living donor)	Continue tacrolimus if started pre-op
Intra-op Day 0	Methylprednisolone 500mg IV (give 60 min pre-rATG)	Dose #1: Start 1mg/kg IV (round to nearest 25mg) infused over 12 hours. May be given by peripheral vein	720mg PO bid	Continue tacrolimus if started pre-op
Day 1	MP 250mg IV (rATG today – order this dose 60 min pre-rATG)	Dose #2: 1mg/kg IV infused over 6 hours	same	Start when signs of renal recovery evident (check with attending) at 0.025mg/kg po q12h (rounded to nearest 0.5mg)
Day 2	MP 125mg IV	Dose #3: 1mg/kg IV Infused over 6 hours	same	Monitor daily tacrolimus level, adjust for goal level: 8-12 ng/ml
Day 3	Prednisone 50mg PO qd	May prolong rATG course for DGF in consideration of delaying CNI start. To be decided in rounds.	same	same
Day 4	Prednisone 25mg PO qd (last dose if steroid free)		same	same
Day 5+	Prednisone 10mg PO qd		same	Per Tx Nephrology

If living donor, start tacrolimus and Myfortic on POD -2, omit pre-op Myfortic 1080mg
If steroid free, omit steroids after day 4 except pre-rATG methylprednisolone. If continuing steroids, they will be tapered by nephrologist as outpatient to 5mg po qday.

Ic. Kidney Induction Guideline: High Intensity

	Steroid Taper	rATG (Thymoglobulin®)	Mycophenolate (Myfortic, MPA®)	Tacrolimus (Prograf®,FK506)
Clinic Day -2			720mg PO bid	0.025mg/kg po q12h (rounded to nearest 0.5mg)
Pre-Op 4SE (Day 0)			1080mg PO (omit if living donor)	Continue tacrolimus if started pre-op
Intra-op Day 0	Methylprednisolone 500mg IV (give 60 min pre-rATG)	Dose #1: Start 1.5mg/kg IV (round to nearest 25mg) infused over 12 hours. May be given by peripheral vein	720mg PO bid	Continue tacrolimus if started pre-op
Day 1	MP 250mg IV (rATG today – order this dose 60 min pre-rATG)	Dose #2: 1.5mg/kg IV infused over 6 hours	same	Start when signs of renal recovery evident (check with attending) at 0.025mg/kg po q12h (rounded to nearest 0.5mg)
Day 2	MP 125mg IV (rATG today –order this dose 60 min pre-ATG)	Dose #3: 1.5mg/kg IV infused over 4-6 hours	same	Monitor daily tacrolimus level, adjust for goal level: 8-12 ng/ml
Day 3	Prednisone 50mg PO qd	(Optional) Dose #4 1.5mg/kg IV infused over 4-6 hours	same	same
Day 4	Prednisone 25mg PO qd	Further rATG to be decided on rounds.	same	same
Day 5+	Prednisone 10mg PO qd (to be tapered further by nephrologist as outpatient)		same	Per Tx Nephrology

If living donor, start tacrolimus and Myfortic on POD -2, omit pre-op Myfortic 1080mg

II. Simultaneous Kidney-Pancreas, Pancreas alone Transplantation Induction Guideline 4-13

Induction: rATG

Recipient Immunologic Risk: patients receiving pancreas transplants are considered to be in the **high intensity** category

Standard maintenance immunosuppression: All patients will receive triple immunosuppression maintenance with tacrolimus, and mycophenolate (Myfortic) and prednisone. **Tacrolimus (Prograf®)** will be started post-operatively 0.025mg/kg PO q12h with a target level goal of 8-12 ng/ml by the time the induction agent course is completed. **Myfortic®** (mycophenolate acid) will be given 1080mg po pre-op then 720mg PO bid unless the patient develops severe neutropenia or GI disturbances. An alternative to Myfortic® is Cellcept®(mycophenolate moffetil) which is used in the event the patient requires IV therapy due to prolonged NGT or nausea/vomiting. (Cellcept 1gm = Myfortic 720mg).

Steroids: All patients will receive methylprednisolone intra-op for prevention of reperfusion injury and post-op as a pre-med for rATG. After a short oral taper to 10mg by POD 5, patients will be tapered to 5-10mg by post-op day 30 and maintained indefinetly. Steroid-free regimens will not be attempted.

Delayed Kidney Graft Function (patient requiring dialysis within first week after transplant): see DGF guideline

II. Simultaneous Kidney-Pancreas, Pancreas alone Transplantation Induction Guideline

	Steroid Taper	rATG (Thymoglobulin®)	Mycophenolate (Myfortic, MPA®)	Tacrolimus (Prograf®,FK506)
Pre-Op 4SE (Day 0)			1080mg PO	
Intra-op Day 0	Methylprednisolone 500mg IV (give 60 min pre-rATG)	Dose #1: **1.5 mg/kg** IV (round to nearest 25mg) infused over 12 hours. May be given by peripheral vein	720mg PO bid	
Day 1	MP 250mg IV (rATG today – order this dose 60 min pre-rATG)	Dose #2: **1.5 mg/kg** IV infused over 6 hours	same	Start when signs of renal recovery evident (check with attending) at 0.025mg/kg po q12h (rounded to nearest 0.5mg)
Day 2	MP 125mg IV (rATG today –order this dose 60 min pre-rATG)	Dose #3: **1.5 mg/kg** IV infused over 4-6 hours	same	Monitor daily tacrolimus level, adjust for goal level: 8-12 ng/ml
Day 3	Prednisone 50mg PO qd	Optional for highly sensitized patients: Dose #4 **1.5 mg/kg** IV infused over 4-6 hours	same	same
Day 4	Prednisone 25mg PO qd		same	same
Day 5+	Prednisone 10mg PO qd (to be tapered further by nephrologist as outpatient)		same	Per Tx Nephrology

III. Delayed Kidney Graft Function Guideline 3-13

Delayed Graft Function:
Delayed graft function is occasionally an unpredicted occurrence during the induction period and may alter the original plan for induction.
Definition of DGF: Patient requiring dialysis within the first week after transplant.
Diagnostic approach: consider transplant imaging to rule out technical defect. Check for donor specific antibodies. Biopsy at POD#7 may be performed at clinical discretion of nephrologist
Induction Immunosuppression: Induction with rATG should continue and conversion from basiliximab to rATG should be considered. rATG should be continued until a maximum dose of 6mg/kg has been given or therapeutic tacrolimus levels have been attained. rATG may be given every other day to further delay tacrolimus initiation. CD3 counts may useful to help guide dose and interval of administration. Attending physician will determine the dosing and schedule.
Maintenance immuno: Tacrolimus dosing initiation may be delayed. It is generally begun when SCr < 3.0 or 6mg/kg of rATG has been exceeded (or the maximum dose set by the attending). If renal function has not returned, the rATG must be stopped and targeted tacrolimus levels attained. Graft biopsy may help determine the next course of immunosuppressive therapy.

III. Kidney DGF Guideline: extended rATG (example, exact dose and schedule to be determined by attending)

	Steroid Taper	rATG (Thymoglobulin®)	Mycophenolate (Myfortic, MPA®)	Tacrolimus (Prograf®,FK506)
Day 1	MP 250mg IV (rATG today – order this dose 60 min pre-rATG)	Dose #2: **1.5 mg/kg** IV infused over 6 hours	720mg PO bid	Start when signs of renal recovery evident (check with attending) at 0.025mg/kg po q12h (rounded to nearest 0.5mg)
Day 2	MP 125mg IV		same	Monitor daily tacrolimus level, adjust for goal level: 8-12 ng/ml
Day 3	Prednisone 50mg PO qd (methylpred 1 mg/kg IV 60min pre-rATG if ATG today)	Dose #3: **1mg/kg** IV infused over 4-6 hours	same	same
Day 4	Prednisone 25mg PO qd		same	same
Day 5	Prednisone 10mg PO qd (methylpred 1 mg/kg IV 60min pre-rATG if rATG today)	Dose #4 **1 mg/kg** IV infused over 4-6 hours	same	same
Day 6	Prednisone 10mg PO qd		same	same
Day 7	Prednisone 10mg PO qd (methylpred 1 mg/kg IV 60min pre-rATG if rATG today)	Dose #5 **1 mg/kg** IV infused over 4-6 hours PRN	same	same
Day >7	Prednisone tapered per attending discretion		same	Per Tx Nephrology

IV. Liver Transplantation Induction Immunosuppression Guideline 7-12

Induction Immunosuppression

The primary induction agent used will be r**ATG** (**Thymoglobulin®)**, a polyclonal anti-thymocyte globulin. Contraindications to rATG use include factors associated with significant perioperative pulmonary or cardiovascular instability such as significant bleeding, hypotension, pulmonary hypertension or dysfunction. ATG should not be held for platelets < 10,000; platelet infusions should be given instead. Filgrastim (GCSF) will be given to support ANC and maintain ANC >1000. **Basiliximab (Simulect®),** an interleukin-2 receptor antagonist monoclonal antibody, will used as a second line agent in the event of pulmonary or cardiovascular instability.

rATG Guideline: r**ATG (Thymoglobulin®)** 1.5 mg/kg will be ordered no later than 6 hours post-op, for a total of 3 doses on post-op day 0, 1, and 2. Methylprednisolone 1gm IV will be given as an induction agent intraoperatively, then 500mg IV post-op with first dose of rATG, and 1mg/kg as pre-med for dose 2 and 3. **Tacrolimus (Prograf®),** a calcineurin-inhibitor, will be initiated on post-op day 4-5 (after the last dose of rATG).

Basiliximab Guideline: **Basiliximab (Simulect®)** 20 mg will be ordered no later than 6 hours post-op and again on POD 4. In addition, methylprednisolone 1 gm IV will be given intra-operatively and 500mg IV on POD 1**. Tacrolimus (Prograf®),** a calcineurin-inhibitor, will be initiated on post-op day 4 (after the last dose of basiliximab).

Steroid Guideline: When steroids are desired as an alternative induction immunosuppression agent due to rATG or basiliximab intolerance, the following schedule may be applied. After day 31, a further taper to lower maintenance doses or off can be considered. If the patient was taking prednisone prior to transplant or prednisone is being added after receiving induction, resume maintenance dose; no taper required.

Day Post-OP	Steroid	Day Post-OP	Steroid
0	Methylpred 1gm IV x1 (OR)	6	Prednisone 30mg po **QDay**
1	Methylpred 500mg IV x1	7-9	Prednisone 25mg po QDay
2	Methylpred 50mg IV bid	10-16	Prednisone 20mg po QDay
3	Methylpred 40mg IV bid	17-23	Prednisone 15mg po QDay
4	Prednisone 30mg po bid	24-30	Prednisone 12.5 mg po QDay
5	Prednisone 20mg po bid	≥31	Prednisone 10mg po QDay

Maintenance Immunosuppression

Standard/Monotherapy Immunosuppression: Tacrolimus monotherapy will be initiated at 0.025mg/kg orally every 12 hours on POD 4-5 for rATG induction and POD 4 for Basiliximab induction with an initial target level of 5-8 ng/ml. Maintenance immunosuppression will consist of tacrolimus monotherapy in the majority of patients.

Dual therapy Immunosuppression: Some patients may benefit from the addition of a second agent for maintenance immunosuppression. These adjuncts can be started immediately post-op or later as the situation dictates.

- **Autoimmune hepatitis (AIH) and Inflammatory bowel disease (IBD**): Liver transplant patients with AIH or IBD should be initiated on dual immunosuppressive therapy with tacrolimus and azathioprine (Imuran®) 1mg/kg orally daily to prevent recurrent disease.
- **Alternative primary immunosuppressive agent used:** If tacrolimus cannot be given and is changed to an alternative primary agent (i.e. cyclosporine or sirolimus), dual immunosuppression with mycophenolate mofetil (Cellcept®) 1g orally every 12 hours is recommended due to the higher risk of rejection with agents other than tacrolimus.
- **Acute rejection:** Patients with acute rejection may be maintained on multiple agents to prevent future episodes of rejection (i.e. MMF 1g po q12h).
- **Lower tacrolimus exposure:** Some patients may have tacrolimus levels maintained lower than the stated goal range (i.e. <5 ng/ml) at the discretion of the physician i.e. patients where goal levels are difficult to achieve (variable pharmacokinetics), patients in renal failure (see RIFLE criteria), or patients not tolerating the usual goal range. In such patients, dual therapy can be considered to reduce rejection risk. Azathioprine (1mg/kg po daily), MMF (1g po q12h), or prednisone (10-20mg po daily) could be considered for use in this role.

IV. Liver Transplantation Induction Guidelines

Day Post-Op	Steroids	rATG (Thymoglobulin®)	Basiliximab (Simulect®)	Tacrolimus (Prograf®, FK506)	Mycophenolate (Cellcept®) Or Azathioprine
Day 0 **Intra-Op (OR)**	1gm IV intraop (1gm IV repeated **if** op > 12 hours or if > 10 units blood transfused)				
Day 0 **Within 6 hours post-op (ICU)**	**rATG induction:** 500 mg IV 60min pre-rATG **Simulect induction:** 500mg IV on POD1, no further doses	1.5 mg/kg IV infused over 12 hours	20mg IV		**AIH or IBD:** add AZA **Alternative primary immuno:** add MMF
Day 1	1 mg/kg IV 60min pre-rATG **OR** If steroid induction, see taper page 5	1.5 mg/kg IV infused over 6 hours	Possible re-dose if > 10 units of blood transfused		
Day 2	1 mg/kg IV 60min pre-rATG **OR** If steroid induction, see taper page 5	1.5 mg/kg IV infused over 6 hours			
Day 3	If steroid induction, see taper page 5				
Day 4 and beyond	If steroid induction, see taper page 5 If maintenance steroids are added: see Steroid Guideline		20mg IV	**rATG induction:** start POD 4-5 **Simulect induction:** start POD 4 FK 0.025 mg/kg po q12 hours Target level 5-8 ng/mL	**If tacrolimus <5** consider adding AZA, MMF, or pred

V. Liver-Kidney Transplantation Induction Immunosuppression Guideline 3-08

Background

Although kidney transplants placed in the setting of liver transplantation have a decreased early rejection rate compared to kidney only transplants, longer term outcome is not as well established. The uncertain survival may be due to recipient survival or to immunologic injury. Based upon this information, the following immunosuppressive guideline will be the starting point for each patient realizing that individual needs based upon type of liver disease, liver allograft status, infectious complications, medication tolerance and renal biopsy results will result in modification of the medication regimen.

Immunosuppression

Kidney/Liver recipients will receive tacrolimus and mycophenolate without steroid maintenance except for the sensitized recipient. Kidney/Liver recipients should not be on tacrolimus monotherapy. Monotherapy with calcineurin inhibitor therapy may increase toxic renal fibrosis. If allograft biopsies remain stable over one year and fibrosis is not extensive then reconsideration of monotherapy may be undertaken but only with close follow-up by nephrology. In the event of delayed kidney graft function, consult Transplant Nephrology attending.

Tacrolimus target levels

Months 0-3 months = 12-15 ng/ml; 3-6 months = 10-12 ng/ml; 6-12 months = 8-12 ng/ml; then as indicated per guideline biopsy.

V. Liver-Kidney Transplantation Standard Induction Guideline

rATG Guideline ↓ **Simulect® Guideline** ↓

Day Post-Op	Steroid	Antithymocyte globulin (rATG, Thymoglobulin®)	Basiliximab (Simulect®)	Tacrolimus (Prograf®, FK506)	Mycophenolate (Myfortic®)
Day 0 Intra-Op (OR)	Methylpred 1gm IV intra-op (repeat **if** op > 12 hrs or >10 units blood tx)		20mg IV intraop or immediately post-op		
Day 0 (ICU) – Day 1	MP 500 mg IV post-op If giving ATG: give 60 min pre-rATG	To begin ASAP if patient stable as directed by Tx attending 1.5 mg/kg IV infused over 12 hours	Possible re-dose of 20mg IV if > 10 units of blood transfused)	Check with Tx attding. Begin w/in 0-24 hours. Usual initial dose: 1mg PO q12h-attending	720mg PO bid
Day 2	MP 1mg/kg IV 60min pre-rATG	1.5 mg/kg IV infused over 6 hours		Target Level: 12-15 ng/ml	same
Day 3		none		same	same
Day 4	MP 1mg/kg IV 60 min pre-rATG	1.5 mg/kg IV infused over 6 hours	20mg IV	same	same
Day >4		none		same	same

V. Liver-Kidney Transplantation Induction Guideline: Sensitized Recipient 3-08

Day Post-Op	Steroid	rATG (Thymo-globulin®)	Tacrolimus (Prograf®, FK506)	Myco-phenolate (Myfortic®)	Rituximab (Rituxan®)	IVIG (non-sucrose)
Pre-Op (ICU/ 4SE)				1080mg PO		Plasma-pheresis followed by IVIG 400mg/kg
Day 0 Intra-Op (OR)	Methylpred 1gm IV intra-op (repeated if op > 12 hrs or > 10 units blood tx)					
Day 1	MP 500 mg IV post-op Give 60 min pre-rATG	1.5 mg/kg IV infused over 12 hours	To begin within 48 hours. Check with Tx attending Start at 1mg PO q12h-verify with Tx attending (0800\2000) Target Level: 12-15 ng/ml	720mg PO bid		Plasma-pheresis followed by IVIG 400mg/kg
Day 2	MP 50mg IV bid	none	same	Same		Plasma-pheresis followed by IVIG 400mg/kg
Day 3	MP 40mg IV bid **(and 1mg/kg IV pre-rATG)**	1.5 mg/kg IV infused over 6 hours	same	Same	1gm IV if crossmatch + or DSA detected	
Day 4	Pred 30mg po bid	none	same	Same		
Day 5	Pred 20mg po bid **(and 1mg/kg IV pre-rATG)**	1.5 mg/kg IV infused over 6 hours	same	Same		
Day >=6	▶See: Liver tx oral steroid taper guideline page 5	none	▶See: Tacrolimus target level table L/K	Same	Further doses per Nephrology attending	

VI. Liver Transplantation ABO Incompatible Induction Immunosuppression Guideline 8-06

Background

Standard Immunosuppression will include induction with rATG and maintenance with tacrolimus, mycophenolate, and steroids. Fluconazole will replace clotrimazole for antifungal prophyaxis. Plasmapheresis will be performed daily for the first 3 days or until anti-ABO titers < 8, then schedule based on anti-ABO titers. IVIgG (immune globulin) is replaced post-PP at 100mg/kg. Rituximab (Rituxan®) is given after third PP (or sooner if titers are rising) at 375mg/m^2. This may be repeated if IgG or IgM titers rise 4 fold.

Day Post-Op	Steroid	rATG (Thymoglobulin®)	Tacrolimus (Prograf®, FK506)	Mycophenolate (Cellcept®, Myfortic®)
Day 0 Intra-Op (OR)	Methylpred 1gm IV upon induction MP 500mg IV after HA if >= 15u RBC transfused			1gm (Cellcept®)IV after HA
Day 0 (ICU)	MP 1.5mg/kg IV @8pm if pt arrives in ICU 12mn-4am			600 mg/m^2 (max dose 1gm) IV @8pm if pt arrives in ICU 12mn-4am
Day 1	MP 500 mg IV give 60 min pre-rATG	1.5 mg/kg IV after PP (16 hr infusion)		1gm IV bid (8am/8pm) Adjust for WBC
Day 2	MP 250 mg IV		0.05mg/kg PO bid Goal level: 10-15 ng/ml	1gm IV bid (8am/8pm)
Day 3	MP 250 mg IV give 60 min per-rATG	1.5 mg/kg IV after PP (16 hr infusion)	same	same
Day 4	MP 1mg/kg IV bid		same	same
Day 5	MP 1mg/kg IV bid	1.5 mg/kg IV after PP (16 hr infusion)	same	same
Day 6-10	MP 0.5mg/kg IV bid **or** Pred 0.5mg/kg PO bid		same	1gm IV bid (8am/8pm) Adjust for WBC
Day 11-15	Pred 0.4mg/kg PO bid		same	720mg PO bid (Myfortic®)
Day 16-30	Pred 0.3mg/kg PO bid		same	same
Day 31-60	Pred 0.25mg/kg PO bid		same	same
Day 61-90	Pred 0.4mg/kg PO qd		same	same
Day 91-120	Pred 0.2mg/kg PO qd		Goal level: 8-12 ng/ml	same
Day 121-180	Pred 0.1mg/kg PO qd		same	same
Day 181-365	Pred 0.1mg/kg PO qod		Adjust to goal level 5-8 ng/ml	same
Day >365	Pred 0.1mg/kg PO qod		Adjust to goal level ~5 ng/ml	same

VII. Intestine Transplantation Induction Immunosuppression Guideline 3-08

Standard Immunosuppression

The primary induction agent used will be Thymoglobulin®, a polyclonal antithymocyte globulin or rATG. rATG will be given intra-operatively at 1.5mg/kg and continued for 4 doses total (given on post-op days 0, 1, 2, and 4). One gram of methylprednisolone will be given intra-operatively as an induction agent and pre-medication for the rATG along with acetaminophen and diphenhydramine. rATG should not be held for platelets < 10,000; platelet infusions should be given instead. Filgrastim (GCSF) will be given for WBC < 2. Tacrolimus (Prograf®), a calcineurin-inhibitor, will be initiated within 24-48 hours post-op with an initial target level of ~15 ng/ml. Maintenance immunosuppression will consist of tacrolimus and prednisone (see taper).

Renal Failure Guideline

Definition of RF: CrCl <=50 ml\min or SCr>=2.0
Includes patients that have renal failure pre-transplant or develop renal failure perioperatively. The following approach will be taken:

Standard Approach: Tacrolimus and prednisone will be initiated as maintenance immunosuppression but tacrolimus may be delayed until at least POD 4. Target levels will be reduced to10 ng/ml. To further reduce the risk of renal toxicity from tacrolimus, mycophenolate at 2gm/day will started immediately post-op. In addition, rATG doses will be given at 1mg/kg and course extended to 6 doses (POD 0, 2, 4, 6, 8, 10). Mycophenolate will continue until renal failure resolves and may be discontinued with resumption of tacrolimus standard target levels.

Steroid taper guideline

Day Post-OP	Steroid
0	Methylpred 1gm IV x1 (OR)
1	Methylpred 500mg IV x1
2	Methylpred 250mg IV x1
3	Methylpred 125mg IV x1
4	Methylpred 80mg IV x1
5	Methylpred 40mg IV x1
6-15	Prednisone 20mg po QDay
16-30	Prednisone 15mg po QDay
≥31	Prednisone 10mg po QDay

Further taper to lower maintenance or off per assessment by attending

VII. Intestine Transplantation Standard Induction Guideline

Day Post-Op	Steroid	Antithymocyte globulin (rATG, Thymoglobulin®)	Tacrolimus (Prograf®, FK506)
Day 0 Intra-Op (OR)	MP 1gm IV (1gm IV repeated **if** op > 12 hours or if > 10 units blood transfused)	1.5 mg/kg IV infused over 12 hours	
Day 1	MP 500 mg IV give 60min pre-rATG	1.5 mg/kg IV infused over 6 hours	To begin within 24-48 hours. Check with Tx attending. Dose: 0.05mg/kg/day (0.025mg/kg PO q12h) (0800/2000) Target Level: 15 ng/ml
Day 2	MP 250mg IV give 60min pre-rATG	1.5 mg/kg IV infused over 6 hours	same
Day 3	MP 125mg IV	None	same
Day 4	MP 80mg IV give 60min pre-rATG	1.5 mg/kg IV infused over 6 hours	same
Day 5	MP 40mg IV	None	same
Day 6-15	Prednisone 20mg qd		same
Day 16-30	Prednisone 15mg qd		same
Day ≥ 31	Prednisone 10mg qd		

VII. Intestine Transplantation Induction Guideline: Renal Failure

Day Post-Op	Steroid	rATG (Thymoglobulin ®)	Tacrolimus (Prograf®, FK506)	Mycophenolate
Day 0 Intra-Op (OR)	Methylpred 1gm IV (MP 1gm IV repeated **if** operation > 12 hours or if > 10 units blood transfused)	1 mg/kg IV infused over 12 hours		
Day 1	MP 500mg IV			1gm PFT/IV bid
Day 2	MP 250mg IV given 60 min pre-rATG	1mg/kg IV infused over 6 hours		same
Day 3	MP 125 IV	none		same
Day 4	MP 80mg IV given 60 min pre-rATG)	1mg/kg IV infused over 6 hours	Check with transplant attending in regard to starting. Dose: 0.05mg/kg/day (0.025mg/kg PO q12h) (0800/2000) Target Level: 7-10 ng/ml	same
Day 5	MP 40mg IV	none	Same	same
Day 6	Pred 20mg PO qd (and MP 1mg/kg IV given 60 min pre-rATG)	1mg/kg IV infused over 6 hours	Same	same
Day 7	Pred 20mg PO qd	none	same	same
Day 8	Pred 20mg PO qd (and MP 1mg/kg IV given 60 min pre-rATG)	1mg/kg IV infused over 6 hours	same	same
Day 9	Pred 20mg PO qd	none	same	same
Day 10	Pred 20mg PO qd (and MP 1mg/kg IV given 60 min pre-rATG)	1mg/kg IV infused over 6 hours	same	same
Day >11	▶See: Intestine tx oral steroid taper guideline		same	May discontinue if renal failure resolves

VIII. Acute Rejection Guidelines: K/P Transplantation 3-08

Kidney or Pancreas Rejection Treatment Algorithm

Biopsy Findings	Transplant Type	Rejection treatment	Maintenance Immuno
Focal mild w\o lab changes	KTA or SPK	Re-biopsy	Escalate oral
	PA	MP IV pulse	Same
Focal mild w\lab changes	KTA or SPK	MP IV pulse	Escalate oral
	PA	rATG 7-10 dose course	Escalate oral
Mild	KTA or SPK	MP IV pulse	Escalate oral
Mild	PA	rATG 7-10 dose course	Same
Moderate	KTA or SPK or PA	rATG 7-10 dose course	Same
Severe or humoral or vascular or C4d (+)	KTA or SPK or PA	Per attending; consider rATG, IVIG, plasmapheresis, Rituxan, Campath, cyclophosphamide	Escalate oral and push to high target levels
Recurrent rejection	KTA or SPK	Per bx findings; may be candidate for IVIG or XRT	Escalate oral; convert maintenance tx; push to high target levels
	PA	Per bx findings; may be candidate for IVIG or XRT	Same

Kidney or Pancreas Rejection Steroid Pulse

Steroid treatment for rejection will consist of 3-5 days of IV treatment and then an oral taper to a target of choice over 3 weeks depending upon the time of the rejection and severity and number of recurrences

High Dose Methylprednisolone Pulse**:**
MP 500mg IV qd x 3 days
MP 250mg IV qd x 2 days
Then oral taper

High Dose Oral taper
Pred 60mg po qd x 3 days
Pred 40mg po qd x 3 days
Pred 30mg PO qd x 5 days
Pred 20mg PO qd x 5 days
Pred 15mg PO qd x 7 days
Pred 10mg PO qd indef

Low Dose Methylprednisolone Pulse:
MP 500mg IV qd x 2 days
MP 250mg IV qd x 1 day
Then oral taper

Low Dose Oral taper
Pred 30mg PO qd x 7 days
Pred 20mg PO qd x 7 days
Pred 15mg PO qd x 7 days
Pred 10mg PO qd indef

Kidney or Pancreas Humoral Rejection Treatment

Humoral rejection will be diagnosed based upon renal transplant histology showing C4d staining and peritubular capillary congestion with PMNs or transplant glomerulitis. Additionally, anti-donor anti-HLA antibodies or anti-endothelial antibodies should be detected as measured by the HLA laboratory at PSBC. Treatment will include pheresis which will be performed two days in a row with immediate post-pheresis treatment including IVIG (sucrose-free) of 400mg/kg. Pheresis will then be performed every other day checking the anti-donor antibody titers until they are not dectectable. Rituxan will be given at 1000mg on day 3 (a non-pheresis day) and repeated on day 14. rATG may also be considered to help decrease T cell help in the process of increasing the number of B cells with an antibody product that is directed against the allograft. The goal of treatment is a negative anti-donor antibody titer and histologic resolution of C4d staining that may take up to 2-3 weeks.

VIII. Acute Rejection Guidelines: Liver Transplantation 3-08

Liver Rejection Treatment Algorithm

Biopsy Findings	LFT's	Rejection Treatment
Non-specific changes	N/A	None
Focal/Mild	Normal	None; Re-bx
Mild	Normal	None; Re-bx
Mild	Abnormal	*__Steroid Pulse__: MP 1gm IV qd x 1 day; no taper except HCV\HBV (see below)
Moderate	N/A	*__Steroid Pulse__: MP 1gm IV qd x 1 day, 500mg IV qd x 1 day, then taper (see below)
Severe	N/A	__rATG (Thymoglobulin)__ 1.5mg/kg IV qd x 7 days minimum

***If enzymes are not resolving, may continue IV pulse.**

Liver Rejection Steroid Pulse

Moderate Cellular Rejection Non HCV\HBV steroid taper	Mild or Moderate Cellular Rejection HCV\HBV steroid taper
MP 1gm IV x 1 , then MP 500mg IV x 1 Pred 50mg po bid x 2 days Pred 30mg po bid x 2 days Pred 20mg po bid x 2 days Pred 20mg po qd x 2 days Pred 10mg po qd **Taper to off over 2 days or continue as maintenance dose per assessment of attending.**	Mild: MP 1gm x 1 Moderate: MP 1gm x 1, then 500mg IV x 1 Pred 50mg po bid x 2 days Pred 40mg po bid x 2 days Pred 30mg po bid x 2 days Pred 20mg po bid x 2 days Pred 20mg po qd x 5 days Pred 15mg po qd x 5 days Pred 10mg po qd **Taper to off over 2 days or continue as maintenance dose per assessment of attending.**

VIII. Acute Rejection Guidelines: Intestine Transplantation 3-08

Intestine Rejection Treatment Algorithm

Biopsy Findings	Rejection Treatment
Non-specific changes	None
Mild/Moderate	*__Steroid Pulse__: MP 1gm IV qd x 3 days, then taper (see below)
Severe or steroid resistant	__rATG (Thymoglobulin)__ 1.5mg/kg IV qd-qod x 4-7 days minimum

Intestine Rejection Steroid Pulse

Mild/Moderate Cellular Rejection
MP 1gm IV x 3 days Pred 50mg po bid x 2 days Pred 30mg po bid x 2 days Pred 20mg po bid x 2 days Pred 20mg po qd x 2 days Pred 10mg po qd

VIII. Acute Rejection Guidelines: Prophylactic Meds Post Rejection 7-13

Type of Prophylaxis	Steroids only	Antibody therapy[1]
CMV	None	If donor or recipient (+), valganciclovir 900mg po qd x1 month
HSV	If recipient HSV 1 or 2 (+) Acyclovir 400mg po bid x1 month	If recipient is not on valganciclovir, then acyclovir 400mg po bid x1 month (Regardless of serostatus)
Candida	Fluconazole 200mg po weekly or clotrimazole 10mg po qid x1 month	Fluconazole 200mg po weekly or clotrimazole 10mg po qid x1 month
Pneumocystis	Trim/sulfa single strength po qhs x1 month (except intestine- indef)	Trim/sulfa single strength po qhs x1 month (except intestine- indef)
Ulcer	H2 antagonist or PPI x1 month	H2 antagonist or PPI x1 month

The durations above may be individualized according to the patient's specific clinical situation. If the rejection episode occurs within the period of routine post-transplant prophylaxis (i.e. 3-6 months), the patient should remain on the prophylaxis indicated for their transplant (See VIII. Infectious Disease Prophylaxis Guidelines). If the guideline above would add or extend their prophylaxis beyond what is routine, the start date for the above timeframes is from the initial dose of antirejection therapy.

[1] Includes rabbit anti-thymocyte globulin (rATG), alemtuzumab (Campath)

IX. Acute Rejection Drug Information 7-13

Pulse Steroid

Action: Corticosteroids block numerous cytokine synthesis including IL-1 which activates T-cells.
When: First line agent used to treat mild-moderate cellular rejection
Dose/Administration: Doses <=125mg are given IVP; doses >125mg are diluted in 50ml of D5W and infused over 30 minutes.
Monitoring: VS, wt, BS,
Other immuno: Continue maintenance or escalate doses; adjust to higher target levels
Blood glucose management: Type 1 & 2 diabetics: insulin infusion guideline; non-diabetics: hospital standard high dose lispro sliding scale

Cost: 1000mg = $100

rATG (Thymoglobulin®)

Action: Polyclonal anti-thymocyte globulin derived from rabbits immunized with human thymocytes. Interacts with peripheral lymphocytes resulting in the blockade of T-cell functions and selective depletion of T-cells. Indicated for treatment of acute renal graft rejection
When: First line agent used to treat severe cellular and humoral rejection; also used as induction agent
Dose/Administration: 1-1.5mg/kg/dose IV x 5-10 doses. May be administered on alternate days if needed due to low WBC counts. Infuse over 4-12 hours. A central line is preferred for administration but may be given peripherally mixed in 500ml NS + hydrocortisone 20mg and Heparin 1000u. Doses are stable for 24 hours stored in the refrigerator. Administer with a 0.22 micron filter separately from other drugs and IV fluids including D5W. Infuse first dose over 12 hours, then 4-6 hours thereafter. Doses are on call from inpatient pharmacy due to expense ($1000-2000). Premeds of antihistamine, acetaminophen and methyprednisolone are given 60 minutes pre-dose.
Premeds: **Tylenol®:** 650mg PO/PR 60 min pre & q4h prn fever, HA.
Benadryl®: 25-50mg PO/IV 60 min pre & q4h prn chills, itching
Methylprednisolone: First dose: 250-500mg or 1mg/kg IV 60 min pre (for induction: see specific guideline)
Monitoring: O2 saturation measured pre-infusion. Weight is measured daily. VS: First dose: monitored pre and every 30 minutes x 2 hours, then hourly x 4 hours. Subsequent doses: pre and at 30 minutes, then q4h. Monitor for s/s of anaphylaxis (SOB, face swelling, hives, hypotension), rash, infusion-related reactions. Notify physician for T>37.8;BP>160/95 or <90/50, respiratory distress, pain in chest or abdomen, s/s of infection. Maintain CD3 lymphocyte count <0.1; WBC > 3.0; PLTs > 10k (liver) and >100k (kidney, pancreas).
Major Adverse Effects: Infusion related 25-70% (chills, fever, dyspnea, hypertension, tachycardia); Hematologic 35-60% (neutropenia, thrombocytopenia); Other (30-40%): N/V/D, peripheral edema, infection, myalgia/arthralgia, serum sickness.
Other immuno: Continue maintenance or escalate doses; adjust to higher target levels
Blood glucose management: Hospital standard low dose lispro sliding scale

Cost: 100 mg = $2000

IV Immune Globulin (IVIG, Gamunex®, Flebogamma®)

Action: Immune modulator. Polyclonal antibodies derived from human plasma. Has been shown to inhibit anti-HLA alloantibodies and has been used to treat rejection in antibody mediated rejection and reduce PRA in highly sensitized patients.
When: First or second or rescue rejection; especially antibody mediated rejection; bx results should be available; plasmapheresis may be required if post-transplant flow crossmatch is positive.
Dose/Administration: Polyimmune globulin, preferred non-sucrose containing (Gamunex®) (10%): To treat rejection: 2gm/kg IV x 1 (may be divided 1gm/kg IV qd x 2 or 500mg/kg IV qd x 4) or 400-500mg/kg post plasmapheresis; dose may be repeated in 1 month; typical volume is 400-1500ml infused over 4-12hours; In conjuction with plasmapheresis: 100-400mg/kg post PP
Alternate: **Flebogamma®** 2gm/kg IV as 5% solution (150gm/3000ml) (sorbitol-based
Premeds: Tylenol 650mg PO/PR and Benadryl 25-50mg IV/PO 30min pre-IV IgG
Monitoring: VS, hypersensitivity reactions, infusion-related reactions
Other immunosuppression: Continue maintenance or escalate doses: adjust to high target levels

Cost: Gamumex® 70gm = $10,300; Flebogamma® 70gm = $9200

Rituximab (Rituxan®)

Action: Chimeric (mouse) monoclonal antibody directed against CD20 antigen found on normal and malignant B lymphocytes. After binding, B cell lysis occurs. Indicated for CD20 (+) B-cell non-Hodgkins lymphoma. Off label solid organ transplant uses include preconditioning treatment ABO incompatible or high HLA antibody transplants, treatment of PTLD, and treatment of severe, humoral or resistant rejection.

When: Second line agent used to treat severe antibody-mediated (humoral) or resistant rejection

Dose/Administration: 375mg/m2 or 1gm IV infusion x 1; may repeat in 7-14 days; infusion over 2-4 hours via central or peripheral line; subsequent doses given days-weeks apart. Often given in combination with other rejection treatments: plasmapheresis, IV immune globulin, rATG, and steroids. Diluted in 500ml (250ml if concentrated) NS and infused starting at 50mg/hr, increased by 50mg/hr every 30 minutes to maximum of 400mg/hr. Stable for 12 hours at room temp or 24 hours refrigerated. Administered separately from other drugs and IV fluids. Doses on call from Oncology satellite pharmacy. Premeds of antihistamine, acetaminophen, and -+/- methylprednisolone are given 60 minutes pre-dose.

Premeds: **Tylenol®:** 650mg PO/PR 60 min pre & q4h prn fever, HA.
Benadryl®: 25-50mg PO/IV 60 min pre & q4h prn chills, itching
+/- Methylprednisolone: 1mg/kg IV

Monitoring: O2 saturation measured pre-infusion. VS: monitored pre and every 30 minutes x 2 hours, then hourly x 4 hours. Monitor for s/s of anaphylaxis (SOB, face swelling, hives, hypotension), rash, infusion-related reactions. Non-life threatening hypersensitivity reactions may respond to adjustments in infusion rate. Interrupt infusions for severe reactions; may be able to resume at 50% rate if reactions have completely resolved. Precaution is advised I patients who have significant cardiovascular risk factors. It is advised to hold blood pressure meds prior to infusion. Patients who develop clinically significant cardiopulmonary events should have infusion discontinued. Notify physician for T>37.8;BP>160/95 or <90/50, respiratory distress, pain in chest or abdomen, s/s of infection. Maintain WBC > 3.0; PLTs > 200K

Major Adverse Effects: Infusion related events: chills (33%), fever (5%), rash (15%), dyspnea (7%), bronchospasm (8%), hypotension (10%). Hematologic: lymphopenia (48%), neutropenia (14%), thrombocytopenia (12%), anemia (8%). Other: nausea (23%), infection (31%), HA (19%), myalgia/arthalgia (10%), angioedema (11%)

Other immuno: Continue maintenance or escalate doses: adjust to high target levels; often given in combination with other rejection treatments: plasmapheresis, IVIG, rATG, steroids

Blood glucose management: Hospital standard low dose lispro sliding scale.

Cost: 1gm = $8000

Alemtuzumab (Campath®)

Action: Immunosuppressant. Recombinant DNA-derived humanized monoclonal antibody directed against the cell surface glycoprotein, CD52. After binding to CD52(+) peripheral B & T lymphocytes, monocytes, macrophages, NK cells, an antibody-dependent lysis occurs. The mechanism of action includes complement-mediated lysis, cell mediated cytotoxicity, and induction of apoptosis of targeted cells. Indicated for treatment of B-cell chronic lymphocytic leukemia. Off label solid organ transplant uses include treatment of GVHD, induction immunosuppression, and treatment of rejection, treatment of autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, vasculitis, ITP and scleroderma. Depression of CD4 and CD8 cell types lasts for 2 to >12 months.

When: Used for induction therapy, 2nd or 3rd line agent for severe or vascular (C4D+) rejection, or GVHD

Dose/Administration: (For non-SCCA patient)

Usual dosage range 10-30mg or 0.3mg/kg IV. Doses may be x 1 repeated to keep absolute lymphocyte counts<200 cells/μL. Dose escalation as with tx of B-CLL is not used. Standard dilution: 10-30 mg in 100 ml 0.9% NS (also compatible w/D5W). Infusion rate: over 2 hours via central or peripheral line. Stability: within 8 hours of dilution. Storage: may be stored at room temp or refrigerated; protect from light. Compatibilities: administer separately from other drugs and IV fluids. Doses on call from inpatient pharmacy. Drug is non-formulary as of 2/06.

Premeds of antihistamine, acetaminophen, and methylprednisolone are given 60 minutes pre-dose.

Premeds:
Tylenol®: 650mg PO/PR 60 min pre & q4h prn fever, HA. `
Benadryl®: 25-50mg PO/IV 60 min pre & q4h prn chills, itching
Methylprednisolone: 1st dose: 500mg IV; 2nd dose: 250mg IV; 3rd and subsequent doses: 125mg IV

Monitoring: Monitor VS every 30 minutes for the first 2 hours, then hourly for 4 hours. Monitor for signs and symptoms of anaphylaxis (shortness of breath, swelling in face, hives, red skin, low blood pressure, syncope). Measure weight qd. Notify Physician for: Temp>37.8;BP>160/95 or <90/50; respiratory distress, pain in chest or abdomen, or signs and symptoms of infection. Hold for platelets < 25; ANC < 250. **Laboratory monitoring:** CBC with diff, platelet counts qd during tx; CD4 lymphocyte counts assessed regularly after tx completed until recovery to >=200 cells/μL

Major Adverse Events: (incidence based on patients tx for B-CLL)

Because of the humanization of alemtuzumab, the first-dose effect is relatively mild. First infusion reactions (fever, rash, nausea, vomiting, headache and rigors) due to cytokine release syndrome can be limited with steroid pre-treatment. Infusion related: rigors (89%), fever (83%), rash (33%), dyspnea (28%), hypotension (15%); Hematologic: neutropenia (70%), thrombocytopenia (62%), anemia (47%), pancytopenia (5%) (higher risk for doses >90mg/week). Other: N/V (41-54%), infections (37%), fatigue (34%), diarrhea (22%)

Other immuno: Continue maintenance or escalate doses: adjust to high target levels when used for rejection

Blood glucose management: Hospital standard low dose lispro sliding scale.

Cost: 30mg = $5000

X. Infectious Disease Prophylaxis Guidelines 7-13

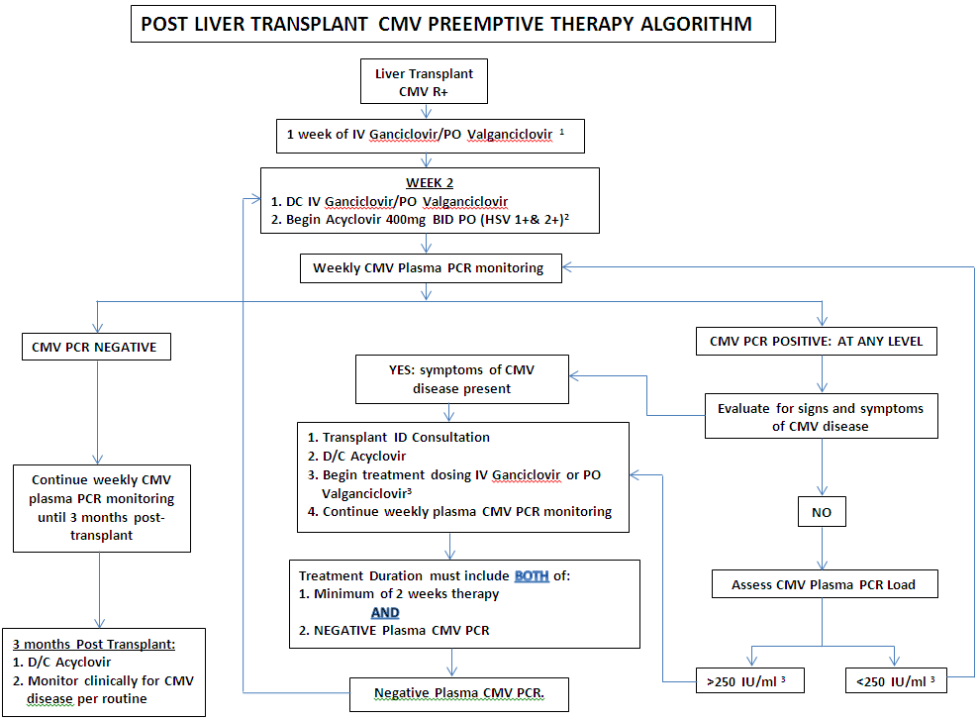
	Liver, L-K	Intestine	Kidney	Kidney-Pancreas
Peri-Operative				
Standard	Ceftriaxone 2gm IV intraop	Ertapenem 1g IV intra-op then q24h x 48 hr p/o **and** Vancomycin IV x 1 intraop; repeat q6h intraop, then IV q12h x 48h postop Dose: 50-70kg = 1g 71-100kg = 1.5g >100kg = 2g	Cefazolin 2gm IV intraop If >120kg, give 3gm IV	Cefazolin 2gm IV intraop then 1gm IV q12h x 24h p/o If >120kg, give 3gm IV intraop
PCN allergy (hives/ anaphylaxis)	Levofloxacin 750mg IV intraop	Levofloxacin 750mg IV intraop, then 750mg IV q24h x 48h p/o **and** Metronidazole 1gm IV x 1 redose 500mg in 8h intraop, then 500mg IV q8h x 48h p/o	Levofloxacin 750mg IV intraop	Levofloxacin 750mg IV intraop, then 500mg IV q24h x 1 p/o
H/o MRSA (colonization or infection)	Add Vancomycin IV x 1 intraop; repeat q6h intraop (except L/K tx) Dose: 50-70kg = 1g 71-100kg = 1.5g >100kg = 2g		Add Vancomycin IV intraop Dose: 50-70kg = 1g 71-100kg = 1.5g >100kg = 2g	Add Vancomycin IV intraop Dose: 50-70kg = 1g 71-100kg = 1.5g >100kg = 2g
Pneumocystis (and UTI for K, K-P)				
Standard	Trim/Sulfa 80/400 (ss) po qhs (6 mo)	Trim/Sulfa 80/400 (ss) po qhs (indef)	Trim/Sulfa 80/400 (ss) po qhs (6 mo) (HIV+: indef)	Trim/Sulfa 80/400 (ss) po qhs (6-12 mo)
Sulfa allergy or Neutropenia	1. Dapsone 100mg po qd (6 mo) check G6PD or 2. Pentamidine 300mg inhaled qmonth x 6 L-K: consider nitrofurantoin	1. Dapsone 100mg po qd (indef) check G6PD or 2. Pentamidine 300mg inhaled qmonth (indef)	1. Dapsone 100mg po qd (6 mo) check G6PD or 2. Pentamidine 300mg inhaled qmonth (6 mo) Consider nitrofurantoin	1. Dapsone 100mg po qd (6 mo) check G6PD or 2. Pentamidine 300mg inhaled qmonth (6 mo) Consider nitrofurantoin
Fungal				
Standard	Fluconazole 200mg po qweek or Clotrimazole 10mg po qid (3 mo)	Fluconazole 400mg IV/po qd x 1 month, then Nystatin 5ml s/s q6h or Clotrimazole 10mg po qid (2 mo or longer)	Clotrimazole 10mg po qid or Fluconazole 200mg po qweek (3 mo)	Fluconazole 100mg po qd (3 mo)
Guideline for Liver Tx at high risk	**Criteria for liver transplant patients at high risk for invasive candidiasis post-tx (IDSA):** **At time of tx:** Fulminant hepatic failure; hospitalized at time of tx; requires HD/UF; re-transplant **Post-tx:** Requires HD/UF; requires re-operation **Other considerations: Patients with >=2 of the following risk factors :**Choledochojejunostomy, SCr >2.0, intraop use of >40 units of blood products **Fluconazole 400mg IV on call to OR then continue or start 400mg PO qd x minimum of 14 days OR until hospitalization, whichever is longer, then clotrimazole (or weekly fluconazole) x 2 months.** **Renal Dosing:** 400mg po qd for CrCl >= 50);200mg po qd for CrCl < 50' HD/UF = 400mg postHD			

X. Infectious Disease Prophylaxis Guidelines 7-13

	Liver, L-K	Intestine	Kidney	Kidney-Pancreas
CMV / HSV (antiviral doses may need adjustment based on renal function)				
CMV: D(+)R(-)	Ganciclovir 5mg/kg IV q24h while NPO, then Valganciclovir 900mg po qd (3 mo)	Ganciclovir 5mg/kg IV q12h x 14 days, then Valganciclovir 900mg po qd (3 mo)	Valganciclovir 450-900mg po qd (3-6 mo)	Ganciclovir 5mg/kg IV q24h while NPO, then Valganciclovir 900mg po qd (3-6 mo)
CMV: D(+) R(+) D(-) R(+)	Ganciclovir 5mg/kg IV q24h while NPO, then Valganciclovir 900mg po qd through POD#7, then pre-emptive therapy (see guideline) (3 mo)	Ganciclovir 5mg/kg IV q12h x 14 days, then Valganciclovir 900mg po qd (3 mo)	Valganciclovir 450-900mg po qd (3 mo)	Ganciclovir 5mg/kg IV q24h while NPO, then Valganciclovir 900mg po qd (3 mo)
CMV: D(-) R(-)	Acyclovir 5mg/kg IV q8h while NPO then 400mg po bid (1 mo)	Acyclovir 5mg/kg IV q8h until demonstrates adequate absorption, then 400mg po bid (1 mo)	Acyclovir 400mg po bid (1 mo)	Acyclovir 400mg po bid (1 mo)
Hepatitis B (antiviral doses may need adjustment based on renal function)				
Recipient HBV: sAg(+)	Hepatitis B immune globulin (HBIG) 10,000 u IV qd x 7 doses (POD 0-6) Then, HBIG 10,000 u IV qmonth x 1 year If HBV DNA PCR (+) and taking anti-HBV drugs pre-tx, continue antiviral (adefovir, lamivudine, entecavir, or tenofovir)		See Hepatitis and Kidney transplant" post-tx guideline	See Hepatitis and Kidney transplant" post-tx guideline
Donor HBV: cAb (+),sAg (-) **Recipient:** cAb (+), sAg(-)	Lamivudine 100mg po qd x 2 years			
Donor HBV: cAb(+),sAg(-) **Recipient:** cAb (-), sAg (-), sAb (+)	Entecavir 0.5mg po qd or Tenofovir 300mg po qd x 2 years			
Donor HBV: cAb (+),sAg (-) **Recipient:** cAb (-). sAg (-), sAb (-)	Entecavir 0.5mg po qd Or Tenofovir 300mg po qd indefintely			
Hepatitis C	See HCV post-tx guideline		See Hepatitis and Kidney transplant post-tx guideline	See Hepatitis and Kidney transplant" post-tx guideline
HIV (+)			See Clinical Management Guideline for HIV+ Kidney Tx Recipients	

XI. Preemptive Therapy (PET) Guideline for CMV Prevention in Liver Transplant Recipients 7-13

- The PET protocol will apply to post-OLT patients who are CMV seropositive [R+] regardless of donor serostatus (ie. donor can be either CMV seropositive or seronegative)
- Patients who receive rATG induction therapy will receive either IV ganciclovir (5mg/kg daily) or po valganciclovir (900mg daily) for 7 days post-transplant, then IV ganciclovir or po valganciclovir will be discontinued and restarted only if:
  - Symptoms of CMV disease develop
    OR
  - Patient develops viremia (positive CMV PCR) at >250 IU/mL
- Patients who are HSV 1 or 2 seropositive will begin po acyclovir on day 8 post-transplant at a dose of 400mg BID for 3 months post-transplant (see algorithm)
  - acyclovir will be held during ganciclovir therapy
- Beginning day 8, patients will be monitored weekly with CMV plasma PCR for 3 months post-transplant and IV ganciclovir or po valganciclovir will be given according to the attached algorithm



[1] 1 week of IV/PO Ganciclovir given only to patients who receive rATG or ALA post-transplant.
[2] Acyclovir 400mg PO BID only given to patients who are HSV 1+ and/or HSV 2+.
[3] Threshold of 1000 copies/ml=NEW THRESHOLD OF 250 IU/ml. A conversion factor of 4 copies to 1 IU/ml can be used to compare results with previous test results from our laboratory. The limit of quantitative detection (the minimum virus level that gives a positive result in 95% of replicates) is 20 IU/mL (1.3 log IU/mL). Quantitative results less than 20 IU/mL are described as very low positive. The clinical significance of very low positive results is uncertain and should be individualized. This in-house developed PCR uses primers specific for the UL123 and gB genes. Reference: Boeckh, M. et al, J Clin Micro. 2004:42:1142-8

XI. Ganciclovir and Valganciclovir Renal Dosing 7-13

CrCl (mL/min)	Ganciclovir Treatment Dose*	Ganciclovir Prevention Dose*
≥ 70	5mg/kg every 12 hours	5mg/kg every 24 hours
50-69	2.5mg/kg every 12 hours	2.5mg/kg every 24 hours
25-49	2.5mg/kg every 24 hours	1.25mg/kg every 24 hours
10-24	1.25mg/kg every 24 hours	0.625mg/kg every 24 hours
<10 (on hemodialysis)	1.25mg/kg post dialysis on dialysis days	0.625mg/kg post dialysis on dialysis days

* Use Total Body Weight (Adapted from Package Insert)

CrCl (mL/min)	Vanganciclovir Treatment Dose	Valganciclovir Prevention Dose
≥ 60	900mg twice daily	900mg once daily
40-59	450mg twice daily	450mg once daily
25-39	450mg once daily	450mg every 2 days[1]
10-24	450mg every 2 days[1]	450mg twice weekly
<10 (on hemodialysis)	Not recommended[2] See text below	Not recommended[2] See text below

[1] For patients with CrCl 10-24 requiring Valganciclovir Treatment dosing, or for patients with CrCl 25-39 requiring Valganciclovir Prophylaxis dosing (for patients requiring every 2 days dosing) MWF dosing may be used if every 2 days dosing is considered a threat to treatment adherence

[2] For pts with CrCl <10 (i.e. where Valganciclovir is not recommended):

1. Preferred option
   a. Prophylactic dosing
      i. IV ganciclovir 0.625mg/kg IV post dialysis on dialysis days
      ii. if available: Oral ganciclovir 500mg po post dialysis on dialysis days
   b. Treatment
      i. IV ganciclovir 1.25mg/kg IV post dialysis on dialysis days
2. Secondary option (alternative if ganciclovir unavailable/unfeasible)
   a. Replace prophylaxis with preemptive therapy (weekly monitoring with plasma CMV PCR & institution of antiviral therapy)
      i. Any positive PCR for D+R-
      ii. ≥250 IU/mL for R+
   b. If antiviral therapy instituted, the **treatment** (not prophylaxis) dosing regimen should be used
3. Tertiary option (if oral ganciclovir and pre-emptive strategy unavailable/unfeasible)
   a. Prophylaxis or Treatment
      i. Oral valganciclovir dosed based on best available evidence from pharmacokinetic studies in renal disease: valganciclovir 450mg po twice weekly. This should give blood concentrations of ganciclovir similar to 1.25mg/kg iv 3x/week post-HD (treatment dose). For prophylaxis the same dose should be used to avoid sub-therapeutic concentrations caused by dialysis removal (valganciclovir 450mg po once weekly is NOT recommended).

For alternative renal replacement therapy (i.e. CVVH, SLED, SCUF) please contact clinical pharmacist for recommendations

Product Information: Cytovene(R), ganciclovir injection and capsules. Roche Laboratories, Inc., Nutley NJ, 2000.
Product Information: Valcyte™, valganciclovir. Roche Pharmaceuticals, Nutley, New Jersey, 2001.
Czock, D; Scholle C; Rasche, FM, et al. Pharmacokinetics of valganciclovir and ganciclovir in renal impairment. Clinical Pharmacology& Therapeutics 2002 Aug;72(2):142-50.

XII. Post-Liver Transplant HCC Guideline (Sirolimus) 2-13

Candidates: Patients with a pre-tx diagnosis of HCC and those patients transplanted under the down-staging protocol will have their explant liver tumors evaluated and scored based on **PCRS** (predicting cancer recurrence score) point system. Those with a score ≥1 will have sirolimus added to their immune regimen at 4-8 weeks post- transplant.

Dosing: Loading dose is 5mg po x 1, then 2mg po qday. Blood levels are checked on day 3-4 after loading dose, then once weekly until steady state.

Sirolimus Goal Level: 5-8ng/ml for 3 months then 5ng/ml thereafter.

Duration: Continued for minimum of 2 years.

Immunosuppression Regimen Adjustments:

Current Regimen	Sirolimus Containing Regimen
Tacrolimus monotherapy	Add Sirolimus
TAC + (MMF or AZA)	Add Sirolimus AND d/c MMF or AZA
TAC + Steroids	Add Sirolimus AND wean steroids by 3 months. IF HCV/HBV then wean steroids by 6 month.
TAC + (MMF or AZA) + Steroids	Add Sirolimus AND d/c MMF or AZA; wean steroids by 3 months (or 6 months HCV/HBV)
CSA + MMF	Add Sirolimus AND keep MMF till sirolimus level >5ng/ml.

Monitoring: CBC, lipids, sirolimus levels, U/A for proteinuria, physical exam for edema, wound healing, pulmonary function. Women of childbearing potential will be counseled to use appropriate contraception.

Infectious Disease Prophylaxis: No changes to standard regimen.

Risk Evaluation and Mitigation Strategy (REMS): The transplant pharmacist will counsel patients, provide them with the FDA approved Medication Guide and document the counseling session in ORCA.

Note: "(Patient name) will begin using Sirolimus (Rapamune®) as part of their immunosuppressive regimen following their OLT for (dx). Regimens containing Sirolimus have been shown to decrease HCC recurrence and improve patient survival. [1-7] In addition to the FDA approved Medication Guide, we discussed the following issues:

- Sirolimus is an immunosupresssant and can increase the risk of infections and certain cancers.
- Sirolimus may cause allergic reactions, edema, poor wound healing, mouth ulcers, increased cholesterol or triglycerides, decreased kidney function, viral infections, lung or breathing problems, blood clotting problems including hepatic artery thrombosis, anemia, low WBC, and low platelets.

After reviewing this information, all questions were answered and the patient states understanding of the risks and benefits associated with using Sirolimus.

PCRS Score (Predicting Cancer Recurrent Score) System:

Explant pathology:	**Points**
Tumor ≥ 4.5cm	1
Tumor in both liver lobes	2
Macroinvasion	3
Only well-differentiated tumor grade	-3

PCRS≤0 = No extra tumor follow-up

PCRS≥1 = Standard tumor follow-up

References:

1. Schnitzbauer AA, Zuelke C, Graeb C et al. A prospective randomized, open-labeled, trial comparing sirolimus-containng versus mTOR-inhibitor-free immunosuppression in patients undergoing liver transplantation for hepatocellular carcinoma. BMC Cancer 2010;10:190.
2. Liang W, Wang D, Ling X et al. Sirolimus-based immunosuppression in liver transplantation for hepatocellular carcinoma: A meta-analysis. Liver Transplantation 2012;18:62-69.
3. Vivarelli M, Dazzi A, Zanello M et al. Effect of different immunosuppressive schedules on recurrence-free survival after liver transplantation for hepatocellular carcinoma. Transplantation 2010;89:227-231.
4. Zimmerman MA, Trotter JF, Wachs M et al. Sirolimus-based immunosuppression following liver transplantation for hepatocellular carcinoma. Liver Transplantation 2008;14:633-638.
5. Toso C, Merani S, Bigam DL et al. Sirolimus-based immunosuppression is associated with increased survival after liver transplantation for hepatocellular carcinoma. Hepatology 2010;51:1237-1243
6. Chinnakotla S, Davis GL, Vasani S et al. Impact of sirolimus on the recurrence of hepatocellular carcinoma after liver transplantation. Liver Transplant 2009;15:L1834-1842
7. Zhou J, Wang Z, WuZ, et al. Sirolimus-based immunosuppression therapy in liver transplantation for patients with hepotcellular carcinoma exceeding the Milan criteria. Transplant Proc 2008;40:3548-3553.

XIII. Other Prophylactic Medication Guidelines 7-13

	Liver, L-K	Intestine	Kidney	Kidney-Pancreas
Ulcer/GERD	Ranitidine 50mg IV q8h (when NPO) then 150mg po qhs (3 mo) Alternative/GERD: Omeprazole 20mg po qd	Ranitidine 50mg IV q8h (if on TPN, add to bag) then 150mg po bid (3 mo) Alternative/GERD: Omeprazole 20mg po qd or lansoprazole 30mg qd for NGT/JT	Ranitidine 50mg IV q24h (when NPO) then 150mg po qhs (3mo) Alternative/GERD: Omeprazole 20mg po qd	Ranitidine 50mg IV q24h (when NPO) then 150mg po qhs (3mo) Alternative/GERD: Omeprazole 20mg po qd
Thrombosis	Per attending directive	Per attending directive	ASA-EC 81mg po qd (indef)	ASA-EC 81mg po qd (indef)
Vitamins	Multivitamin po qd (indef)	Multivitamin po qd (indef)	Multivitamin po qd (indef)	Multivitamin po qd (indef)
Anemia	Ferrous sulfate 325mg po tid (3mo)	Ferrous sulfate 325mg po tid (3mo)	EPO/Fe when indicated	EPO/Fe when indicated
Osteoporosis	Cholecalciferol 1000u po qd (1400u total/day) (indef.) Calcium carbonate 1gm po bid Ca2+ intake to = 1200-1500mg/day total intake	Cholecalciferol 1000u po qd (1400u total/day) (indef.) Calcium carbonate 1gm po bid Ca2+ supp to = 1200-1500mg/day total intake	Calcitriol 0.25mcg po qd (+ cholecalciferol 400u in multivit) (indef) Calcium carbonate 1gm po bid Ca2+ intake to = 1200-1500mg/day total intake	Calcitriol 0.25mcg po qd (+ cholecalciferol 400u in multivit) (indef) Calcium carbonate 1gm po bid Ca2+ intake to = 1200-1500mg/day total intake
Bowel Program	Docusate 250mg po bid (3mo) Bisacodyl 10mg PR PRN MOM 30ml po bid PRN	PRN	Docusate 250mg po bid (3 mo) Bisacodyl 10mg PR PRN Use of MOM, Mag citrate- check Mg	Docusate 250mg po bid (3 mo) Bisacodyl 10mg PR PRN Use of MOM, Mag citrate- check Mg
Alprostadil	Per attending directive	Start 0.2mcg/kg/hr; titrate to 0.6 mcg/kg/hr x 48-72hrs		

XIV. Miscellaneous Medication Management Guidelines 3-08

	Liver, L-K	Intestine	Kidney	Kidney-Pancreas
Blood Pressure	1. Amlodpine 2.5-20mg po qd 2. Metoprolol 25-200mg bid or Atenolol 25-100mg qd	same as liver	same as liver	same as liver
Sleep	Diphenhydramine 25-50mg po hs PRN **Avoid benzodiazepines**	same as liver	same as for liver	same as for liver
Bladder Spasm			Oxybutinin 5mg po q8h PRN	same as for kidney
Diarrhea		Loperamide PRN		
Nausea	Metoclopramide 10mg po/IV q6h prn Alternatives: scopalamine, ondansetron	same as for liver Alternatives: same as for liver	same as for liver Alternatives: same as for liver	same as for liver Alternatives: same as for liver
Acidosis				Sodium Bicarbonate 2.6gm po qid for those with bladder drainage; adjust to CO_2 = 25 (indef)
Phosphate Supplement	Sodium Phosphate (**K-Phos Neutral®**) 250mg -500mg po bid-tid (PRN) **Avoid Neutraphos® products** (contain potassium)	same as for liver	same as for liver	same as for liver
Magnesium Supplement	Magnesium oxide 400mg (241mg Mg) po tid-qid (PRN) Alternative if having diarrhea: Mg 133mg/Protein tabs; 2 tid-qid	PRN	PRN	PRN
Potassium Supplement	**Avoid**	**PRN**	**Avoid**	**Avoid**
Hyperkalemia	Acute: Kayexalate 15-30gm po	Acute: Kayexalate 15-30gm po Chronic: Fludrocortisone 0.1mg po qd, Lasix	Acute: Kayexalate 15-30gm po Chronic: Fludrocortisone 0.1mg po qd, Lasix	same as for kidney

XIV. Miscellaneous Medication Management Guidelines 3-08

	Liver, L-K	Intestine	Kidney	Kidney-Pancreas
Pain management	Hydromorphone (Dilaudid) PCA, then oxycodone or hydromorphone po **Avoid** excess acetaminophen (Vicodin, Percocet), Demerol **Do not use NSAIDs**	same as for liver	same as for liver	same as for liver
Lipid management (smooth muscle effects)	PRN Pravachol preferred statin	PRN Pravachol preferred statin	Reduce usual maintenance statin by 1/2 or start Pravachol 5-10mg po qhs (may start in clinic) Reduce ezetimibe (Zetia)from 10mg to 5mg/day	Reduce usual maintenance statin by 1/2 or start Pravachol 5-10mg po qhs (may start in clinic) Reduct ezetimibe (Zetia) from 10mg to 5mg/day
Hyperparathyroidism /Vitamin D deficiency			Calcitriol 0.25mcg po qd Calcium carbonate 1gm po bid Sensipar PRN See Evaluation and Treatment protocol	Calcitriol 0.25mcg po qd Calcium carbonate 1gm po bid Sensipar PRN See Evaluation and Treatment protocol
Anemia			Darbepoetin PRN See Evaluation and Treatment Protocol	Darbepoetin PRN See Evaluation and Treatment Protocol
Neutropenia	See guideline Page 26	See guideline Page 26	See guideline Page 26	See guideline Page 26
Neurotoxicitiy	See guideline Page 26	See guideline Page 26		
Mycophenolate intolerance	See below	See below		

Mycophenolate Intolerance Management Guidelines liver, intestine 8-06

Definition of Intolerance: Persistent WBC below 3.0; chronic diarrhea or nausea/vomiting

Approach for GI intolerance: If patient develops diarrhea or nausea/vomiting, switching from Cellcept® to Myfortic® may be trialed. Dividing the dose may also be trialed (720gm po bid→360mg po qid (Myfortic®); 1gm po bi→500mg po qid (MMF, Cellcept®)). An MPA level should be assessed for toxicity, especially in renal insufficiency or renal failure. If MPA >5mcg/ml adjust dose downward. If patient has persistent N/V/D after dose adjustment, discontinue mycophenolate and begin or azathioprine.

Approach for Neutropenia: If patient develops persistent neutropenia, an MPA level should be assessed for toxicity, especially in renal insufficiency or renal failure. If MPA >5mcg/ml adjust dose downward. Consider performing an Immunknow® (Cylex) study. If patient has persistent neutropenia after dose adjustment, follow guidelines for neutropenia in liver transplant patients.

XV. Neurotoxicity Management Guidelines

Liver or Intestine Transplantation 5-12

Definition of Neurotoxicity: seizure, expressive aphasia, severe tremor, and/or brain MRI findings consistent with calcineurin inhibitor toxicity

Approach: If clinical and brain MRI findings are consistent with calcineurin inhibitor toxicity, and patient is taking tacrolimus (FK506), discontinue tacrolimus and begin mycophenolate mofetil at 1000mg po bid. After FK 506 level has decreased to < 5 ng/ml, begin cyclosporine and target cyclosporine level to 150-200 ng/ml for liver and ~200ng/ml for intestine.

XV. Neutropenia Management Guidelines

Liver or Intestine Transplantation 7-12

The following are a suggested approach to neutropenia management. Approach may differ between transplant clinicians. Other guidelines may exist for patients receiving cytotoxic chemotherapy or hepatitis C treatment.

Definition of Neutropenia: ANC <1000 (all patients after OLT should receive CBCs with differential)

Approach: If ANC falls to <1.5, check marrow suppressive meds: ensure **Ganciclovir/Valganciclovir** dose appropriate for renal function and decrease **Azathioprine, Mycophenolate, or Sirolimus** to 1/2 dose.

If ANC <= 1000, give **filgrastim (GCSF**) at 5mcg/kg (round to nearest 300mcg or 480mcg) SQ x 1; evaluate ANC daily and repeat dose if ANC < 1000. Continue **AZA/MMF/Rapa** at 1/2 dose.

If ANC falls to <500, hold Ganciclovir/Valganciclovir prophylaxis (continue if being used for treatment) and **Bactrim®/Septra®.** Add acyclovir 400mg po bid while CMV prophylaxis held, consider pre-emptive CMV treatment strategy (see PET guideline). Give dose of **Pentamidine** 300mg nebulized. **Hold AZA/MMF/Rapa**. Continue or start **GCSF** at 5mcg/kg SQ qday with evaluation of ANC daily until ANC >1000

If no response in ANC after 4 doses of GCSF, continue GCSF; consider increasing dose to 10mcg/kg.

Kidney or Pancreas Transplantation 4-13

The following are a suggested approach to neutropenia management. Approach may differ between transplant clinicians.

Definition of Neutropenia:

a. Mild leukopenia (WBC < 3.5 and ANC > 1500)
b. Moderate leucopenia (ANC 1000-1500)
c. Severe leucopenia (ANC < 1000)

Approach:

1. CBC with differential to evaluate ANC
2. Rule-out infection
3. CMV serum PCR
4. Revise/adjust medications: anti-virals, antibiotics, immunosuppressants (rATG)
5. Consider MPA level (consider decrease if level >4 ng/ml)
6. Other causes

Treatment:
Patients with ANC <1000 should receive GCSF (Neupogen®) therapy at 5mcg/kg subcutaneoulsy (rounded to 300mcg or 480mcg). Doses should be ordered only after daily assessment.

Consider repeat initial evaluation or Hematology referral for non-responders (ANC < 1000 after 3 doses)

XVI. DVT prophylaxis Guidelines 7-13

Patients undergoing solid organ transplantation often have increased risks of bleeding but also comorbidities that make them at increased risk for DVT. The benefits of standard primary prophylaxis must be weighed against the risks and relative contraindications. Refer to UW Medicine: Guidelines for Prevention of Venous Thromboembolism (based on Geerts WH et al. Chest 2008; 133 (suppl 6): 381-453 (Link in Powerplan)). Pharmacologic thromboprophylaxis should be used for SOT patients w/o contraindications to anticoagulation and patients should be considered medical/surgical moderate to high risk. Note: Severe liver disease (elevated coagulation tests) does not assure "auto-anticoagulation"; thrombosis risk may outweigh bleeding risk. The information below is intended as a reference and should not supersede clinical judgment.

Typical Indications in transplant patients:

- Limited mobility or prolonged bed rest plus 1 or more other risk factors
- Surgery
- Immobility
- Erythropoesis-stimulating agents
- Inflammatory bowel disease
- Nephrotic syndrome
- Obesity
- Central venous catheters
- Thrombophilia (Factor V Leiden, Factor II mutation, antiphospholipid antibodies)
- Prior h/o of VTE
- Other risks: h/o TIPS, use of venovenous bypass, use of hemostatic agents, infectious complications, greater number of comorbidities, prolonged pre-transplant hospitalization

Risk Assessment: Patients are considered at "At Risk" to "High Risk"

Approach:
Pre-op patients:
Liver: (TED stockings and SCD's); no pharmacologic therapy
Kidney/Pancreas: TED stockings and SCD's; no pharmacologic therapy
Living donors: TED stocking and SCD's; heparin 5000 units subq x1

Post-op patients:
Liver: days 0-7 – TEDs/SCDs, no routine pharmacologic prophylaxis, may start heparin 5000 units subq q8h per clinician discretion
Days >7 – start heparin 5000 units subq q8h unless contraindicated (see below)
All other: Launch "VTE for Transplant Services" sub Power Plan:
At risk: Heparin 5000 units subq q8h to start on POD # 1
High risk: Heparin 5000 units subq q8h to start on POD #1 and SCD's
Heparin contraindicated (see below): SCD's only

Pharmacologic Prophylaxis Contraindications:

- Active bleeding within 48-72 hours
- HIT
- Fully anticoagulated

Peri- procedure: (bx, non-tx surgery, ERCP, etc.) Hold heparin pre-procedure and x 24 hours after procedure

Heparin contraindicated: SCDs only

Re-admissions / medical admits: Follow standard UWMC guidelines for DVT prophylaxis – vast majority of patients should be considered at risk given hospital risk stratification:
http://depts.washington.edu/anticoag/home/sites/default/files/VTE%20prophylaxis%20guidelines.pdf

XVII. Cylex Immuknow™ Assay 7-13

The **Cylex Immuknow™ Assay** may be used to test the level of cell-mediated immunity, reduce the risk of toxicity, and allow a more individualized approach to managing immunosuppression. The assay will be used to monitor overall level of immune function as a tool to adjust immunosuppressive drug therapy. It does not accurately predict ongoing or absence of rejection. It will be used in patients who have prolonged complicated post-op courses or patients who develop severe multiple infectious episodes or as a guide in long-term follow-up patients.

ATP Level (ng/ml)	Result
<=225	Low Immune Cell Response
226-524	Moderate Immune Cell Response
>=525	Strong Immune Cell Response

XVIII. Immunosuppression Target Blood Levels Guideline*

Liver: Target Blood Levels 7-12

Time post-transplant	Immuno	0-3 mo	3-6 mo	6-12 mo	12-24 mo	>24 mo
FK506 (Tacrolimus) (whole blood LCMSMS)	**FK**	5-8 ng/ml			5 ng/ml	3-5 ng/ml
	FK - MMF or AZA +/- Pred	≤8 ng/ml (<5 ng/ml per clinician discretion)			5 ng/ml	3-5 ng/ml
	FK - Rapa	5-8 ng/ml			5 ng/ml	3-5 ng/ml
CSA (Cyclosporine) (whole blood LCMSMS)	**CSA - MMF or AZA - Pred**	150-200 ng/ml	150 ng/ml	100 ng/ml	80-100 ng/ml	60-80 ng/ml
Rapa (Sirolimus) (LCMSMS)	**Rapa - MMF-Pred**	5-10 ng/ml				
	Rapa - FK	5-8 ng/ml			5 ng/ml	3-5 ng/ml

Liver-Kidney: Target Blood Levels 3-08

Time post-transplant	Immuno	0-3 mo	3-6 mo	6-12 mo	12-24 mo	>24 mo
FK50-6 (Tacrolimus) (whole blood LCMSMS)	**FK - MMF +/- Pred**	12-15 ng/ml	10-12 ng/ml	8-12 ng/ml	8-12 ng/ml	

Intestine: Target Blood Levels 3-08

Time post-transplant	Immuno	0-1 mo	1-3 mo	3-12 mo	>12 mo
FK50-6 (Tacrolimus) (whole blood LCMSMS)	**FK - Pred**	15 ng/ml	12-15 ng/ml	8-10 ng/ml	5-8 ng/ml
	FK – MMF - Pred	10-12 ng/ml	10 ng/ml	7-8 ng/ml	5-7 ng/ml
CSA (Cyclosporine) (whole blood LCMSMS)	**CSA – MMF - Pred**	200 ng/ml	180-200 ng/ml	150 ng/ml	100 ng/ml
Rapa (Sirolimus) (LCMSMS)	**Rapa – MMF - Pred**	8-10 ng/ml	8-10 ng/ml	8-10 ng/ml	8-10 ng/ml

***Target levels may vary depending upon function of organ, biopsy, presence of infection and/or combination of immunosuppressive drugs used for maintenance therapy.**

XVIII. Immunosuppression Target Blood Levels Guideline*

Kidney or Pancreas: Target Blood Levels 4-13

Time post-transplant	Immuno	0-1 mo	1-3 mo	3-12 mo	>12 mo
Tacrolimus (trough, whole blood LCMSMS)	**Tac-MPA+/-Pred**	8-12 ng/ml	5-10 ng/ml	5-10 ng/ml	4-7 ng/ml
	Tac-mTOR-Pred	5-7 ng/ml	3-7 ng/ml	3-7 ng/ml	3-5 ng/ml
CSA (Cyclosporine) (trough, whole blood LCMSMS)	**Alternate to Tac**	200-250 ng/ml	175-225 ng/ml	150-200 ng/ml	125-175 ng/ml
CSA (2 hr peak, C2, whole blood LCMSMS)	**Alternate to Tac**	800-1000 ng/ml	700-900 ng/ml	600-800 ng/ml	500-700 ng/ml
MPA (trough, plasma CEDIA)	**Tac-MPA+/-Pred**	No target		<4 ng/ml if clinical signs of toxicity	
Sirolimus (trough, whole blood LCMSMS)	**Alternative to MPA (with CNI)**	5-8 ng/ml			
Sirolimus (trough, whole blood LCMSMS	**CNI free regimen**	6-10 ng/ml			
Everolimus (trough, whole blood LCMSMS)	**Tac-mTOR-Pred**	5-6 ng/ml			

***Target levels may vary depending upon function of organ, biopsy, presence of infection and/or combination of immunosuppressive drugs used for maintenance therapy.**

XIX. Kidney Recipient Laboratory Follow Up Guideline 7-13

Inpatients will generally have daily labs including a complete metabolic panel with phos and mg (CMP, Chem10), CBC, and calcinurin inhibitor level. Once discharged, suggested lab schedule is as follows, with additional/repeat labs ordered as clinically indicated:

Test	Time from transplant (Weeks)								
	1 (first clinic)	2	3	4	8	12	24	36	48
CMP	2x/wk	2x/wk	2x/wk	2x/wk	q1wk	q2wks	q2-4 wks	q2-4 wks	q4wks
CBC/ DIFF	2x/wk	2x/wk	2x/wk	2x/wk	q1wk	q2wks	q2-4 wks	q2-4 wks	q4wks
CNI lvl	2x/wk	2x/wk	2x/wk	2x/wk	q1wk	q2wks	q2-4 wks	q2-4 wks	q4wks
LFTs	√			√		√	√	√	√
Iron stores	√								
PTH	√					√			√
25OH vitD	√					√			√
UA	√	√	√	√	√	√	√	√	√
P/Cr ratio	√			√	√	√	√	√	√
Lipids						√			√
Uric Acid						√			√
HbgA1c						√			√
BK urine				√	√	√	√	√	√
BK serum				Check if urine screening + (up trending)					
MPA	No routine monitoring – consider if cytopenias, BK reactivation, GI toxicity								
CMV PCR	No routine monitoring – consider if symptomatic for CMV syndrome/disease (unexplained leukopenia, GI symptoms, malaise, fever)								
CDC High Risk Labs*				√		√			√

*CDC High Risk labs include HIV screen and RNA quant, HCV Ab and RNA quant, HBV surface Ag, surface Ab, and core Ab

XX. UWMC HIV+ Kidney Transplant Recipients Clinical Management Guideline 2-14

Evaluation and Inclusion/Exclusion Criteria for Patient Selection:

General Criteria: As with non-HIV transplant candidates, the candidate must have an anticipated life expectancy of at least 5 years and otherwise conform to criteria for listing for non-HIV kidney transplant recipients (See standard protocol for acceptance into UWMC kidney transplant program). In addition the following must be true:

- Female patients of childbearing age must practice contraception and have a negative B-HCG pregnancy test.
- Willing to use PCP, herpes/CMV and fungal prophylaxis as indicated.
- If co-infected with Hepatitis B, must have undetectable HBV RNA at the time of transplant.

HIV Criteria: The patient must have well-established follow up with an ID HIV specialist. The patient must also undergo evaluation by the UWMC Transplant Infectious Diseases specialist*. The specialist must find the patient strictly adherent with HAART therapy and to be on a stable regimen for at least 6 months. Other HIV treatment criteria that must be met include:

- HIV RNA levels undetectable for at least 6 months prior to transplant (Less than 40 copies/ml).
- At time of organ availability the most recent HIV RNA must be within 16 weeks prior to transplant.
- CD4 T-cell counts greater than or equal to 200/microliter for at least 6 months.
- HIV RNA and CD4 count shall be performed every 3 months.

OI Criteria: If there is a history of opportunistic infections (OIs), there should be no active disease after completing treatment for at least 1 year. The UWMC Transplant HIV consultant will make recommendations regarding the risks and advisability of immunosuppression in the setting of previous OI, as well as for secondary prophylaxis after transplantation. The patient must meet the following criteria for specific OIs:

- CMV retinitis: no active disease on ophthalmologic exam.
- Histoplasmosis, disseminated or extrapulmonary: must be on secondary prophylaxis.
- CNS toxoplasmosis: completed therapy and MRI without active disease.
- Cutaneous Kaposi's sarcoma: complete remission with immune reconstitution and no active/vascular residual cutaneous lesions on physical exam and negative chest CT scan.
- Extrapulmonary Cryptococcus: negative serum cryptococcal antigen.
- HIV-related encephalopathy:
  - Diagnosed prior to HAART
  - Resolved on HAART with marked improvement in mental status with increased CD4+ T-cell count
  - No evidence of progression of CNS disease
  - Otherwise considered eligible from a functional standpoint.

Other pre-transplant evaluations: Work up should follow the standard UWMC kidney transplant guidelines. This includes serologic testing (HSV, CMV, VZV, EBV, syphilis, Hepatitis A, B, and C, measles, mumps, and rubella), evaluation for latent TB (IGRA – e.g. Quantiferon), consideration for testing based on other exposures (e.g. strongyloides, endemic fungi), and updated vaccinations (Tdap, Pneumovax/Prevnar, Influenza, Hepatitis A and B, VZV, and HPV, as appropriate). In addition, Hepatitis B and Hepatitis C nucleic acid testing should be performed, along with serologies for HHV-8 and toxoplasma.

***UWMC Transplant HIV consultants:** Robert Rakita, MD, Erika Lease, MD, Ajit Limaye, MD, Elizabeth Ann Misch, MD, John Scott, MD, Geoffrey Gottlieb, MD

UWMC HIV pharmacist: Rupali Jain, Pharm. D.

Relative contraindications: The following are generally considered contraindications to kidney transplant for HIV+ recipients, but should be evaluated on a case by case basis:

- Significant wasting due to HIV.
- Demonstrated non-compliance with medical treatment.
- Documented history of progressive multifocal leukoencephalopathy, extracutaneous Kaposi's sarcoma, EBV and HHV8 related lymphoproliferative disorders, or primary CNS lymphoma.
- History of other neoplasia is an exclusion except for the following: cutaneous Kaposi's sarcoma as outlined above, in situ anogenital carcinoma, treated basal or squamous cell carcinoma of the skin, solid tumors treated with curative therapy and disease free for duration as outlined in UWMC standard transplant inclusion criteria (more than 2 to greater than 5 year disease free depending on type of primary tumor).
- Concurrent chronic infection with Hepatitis C or HTLV-1.
- Presence of cirrhosis. *[These patients may in future be considered for liver transplantation]*
- Elevated immunologic risk (prior transplant, peak PRA greater than 20%, positive crossmatch, or other immunologic factors*) [Rationale: Higher immunologic risk patients have a greater risk of subsequent rejection on top of the already increased rejection risk associated with HIV]. Such patients could be considered on a case by case basis, if the benefits are deemed to outweigh the risks.*
- Significant cardiovascular, pulmonary disease, urologic abnormalities or psychosocial issues that may exclude a patient are as outlined in standard UWMC transplant acceptance criteria.
- Donor kidneys with high likelihood of delayed graft function to avoid the need for rATG induction

Interaction management:
There are significant interactions between the drugs used to treat HIV (HAART) and immunosuppressive drugs, in particular calcineurin inhibitors and mTOR inhibitors. Other transplant pharmacotherapy can also interact with HAART (i.e. ranitidine/PPI's and atazanavir). Check with the clinical pharmacist to discuss medication interaction issues. Monitoring of immunosuppressive drug levels is essential to managing these interactions.

- Drug levels shall be obtained daily during inpatient stay until stabilization, then 2-3 times per week.
- More intensive monitoring may be required, particularly if HAART regimen is modified later in life after transplant (HAART regimen should not be changed peri-transplant)
- See target trough blood levels of standard protocol.

Drugs used for HAART include: protease inhibitors (PIs), nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), integrase inhibitors, fusion inhibitors, and CCR5 antagonists.

The basic treatment structure for HAART is: 2 NRTI + boosted PI or NNRTI or integrase inhibitor. Alternate treatment structure may be used with more advanced patients**. It is essential the patient continues on their home HAART regimen peri-transplant without interruption. The HAART regimen should not be changed in the peri-transplant period.** In the case of life-threatening toxicity, discuss any deviation from HAART therapy with the UWMC Transplant HIV consultants. See HIV+ Kidney HAART Therapy Appendix for the list of individual drugs and drug interaction issues (see also *Transplantation Proceedings,* 41, 3796–3799 (2009)**,** and http://www.aidsinfo.nih.gov/guidelines/, go to Adult and Adolescent Guidelines).

Treatment of Rejection:
Treated rejection should always be documented by renal biopsy if possible. Acute rejection should be treated with pulse steroid protocol according to the standard guideline for Kidney Rejection. Use of anti-thymocyte globulin may be considered for treatment of severe rejection or as rescue therapy after careful discussion with the patient weighing the risks of infection and malignancy versus risk of graft loss. See standard protocol for steroid pulse doses and prednisone tapers.

XX. HIV+ Kidney Recipient Induction Immunosuppression Guideline 2-14

Induction: Basiliximab (Simulect®) (IL-2 blockade) is the usual induction agent. The use of alternative induction agents may be considered on a case-by-case basis. Basiliximab is given in 2 doses on POD 0 intra-operatively and POD 4.

Maintenance immunosuppression: For deceased donor recipients: **Tacrolimus (Prograf®)** will be started on POD 0 or 1. For living donor recipients, **Tacrolimus and Mycophenolate** will be started 2 days prior to transplant on POD -2 and continued without interruption peri-operatively. The appropriate tacrolimus dosing regimen shall be determined in consultation with Transplant Nephrology, Transplant ID and the Transplant Clinical Pharmacist in anticipation of clinically significant drug-drug interactions between HAART and CNI (See Appendix). Cyclosporine modified shall be reserved as a second-line calcineurin inhibitor used when the patient has intolerance or allergy to tacrolimus.

Tacrolimus Dosing:

- PI-containing regimen, or patients on Stribild® (Elvitegravir/cobicistat/emtricitabine/tenofovir): Give a "mini" loading dose 1-2mg PO x 1. Then check the tacrolimus blood level QAM and re-dose with 0.5mg PO x1 when level < 8ng/ml (or as directed by attending), typically in 3-5 days. Maintenance dosing is typically 1 to 2 times **per week**.
- Non-PI regimens: 0.025mg/kg (rounded to nearest 0.5mg) PO q12h, adjust dose normally.
- Tacrolimus level goal for all patients is 8-12ng/ml for months 0-3.

Cyclosporine Dosing (2nd line if unable to tolerate tacrolimus)**:**

- PI-containing regimen or patients on Stribild® (Elvitegravir/cobcistat/emtricitabine/tenofovir): Cyclosporine modified 25mg PO q12h, adjust dose normally.
- NNRTI-containing regimen without PI: 5mg/kg (rounded to the nearest 25mg) PO q12h, adjust dose normally.
- Non-PI, non-NNRTI regimen: no change from standard.
- Check with attending for goal cyclosporine level and monitoring strategy.

Mycophenolate (MPA) Dosing:

- For deceased donor recipients, **mycophenolate sodium (Myfortic®)** shall be started pre-op, 1080mg po x 1 dose, then 720mg PO bid thereafter. For living donor recipients, **mycophenolate** will begin on POD -2 at 720mg PO bid and continued without interruption peri-operatively (no loading dose). The regimen may be adjusted if toxicity occurs.
- An alternative to **Myfortic®** is **Cellcept® (mycophenolate mofetil)**, used in the event the patient requires IV or feeding-tube route of administration (Mycophenolate mofetil (Cellcept®) 1000mg = Mycophenolate sodium (Myfortic®) 720mg).
- Drug level monitoring (MPA level) is generally not performed unless toxicity is suspected.

Corticosteroid Dosing: All kidney transplant recipients will receive methylprednisolone intra-op for prevention of reperfusion injury. Corticosteroids will continue post-operatively on a tapering schedule as part of the maintenance immunosuppression regimen (see chart for dosing regimen). Steroid free regimens will generally not be used given the increased risk for rejection in HIV+ kidney recipients.

Delayed Graft Function: In the case of delayed graft function, the attending nephrologist and surgeon should weigh the risks and benefits of changing induction regimen to anti-thymocyte globulin. Tacrolimus initiation may be delayed. If the decision is made to change to rATG, see regular Delayed Kidney Graft Function Guideline for dose suggestions.

XX. HIV+ Kidney Recipient Induction Guideline

Day Post-Op	Steroid Taper	Basiliximab (Simulect®)	Mycophenolate (Myfortic®, MPA)	Tacrolimus (Prograf®, FK506)
Clinic Day -2			720mg PO bid	PI containing HAART regimen: 1-2mg PO x 1 Non-PI HAART regimen: 0.025mg/kg po bid
Pre-Op 4SE (Day 0)			1080mg PO (omit if living donor)	PI containing HAART regimen: Check level pre-op, redose post-op 0.5mg po x1 for level <8 Non-PI HAART regimen: Continue pre-op regimen.
Intra-op Day 0	Methylprednisolone 500mg IV	20mg IV	720mg PO bid	PI containing HAART regimen: 1-2mg PO x 1 if not given pre-op Non-PI HAART regimen: start at 0800 or 2000 after returning to floor 0.025mg/kg po bid (round to nearest 0.5mg)
Day 1	MP 250mg IV		same	Monitor daily tacrolimus level, adjust for goal level: 8-12 ng/ml PI containing HAART regimen: single dose of 0.5-1mg when level <8 Non-PI HAART regimen: Adjust dose similar to non-HIV patient
Day 2	MP 125mg IV		same	same
Day 3	Prednisone 50mg PO x 1 day		same	same
Day 4	Prednisone 25mg PO x 1 day	20mg IV POD 4 or day of 1st clinic visit	same	same
Day 5+	Prednisone 10mg PO qd		same	Per Tx Nephrology

If living donor, start tacrolimus and Myfortic on POD -2, omit pre-op Myfortic 1080mg

XX. HIV+ Kidney Recipient Infection Prophylaxis Guideline 2-14

Primary Prophylaxis (no history of infection): Patients will receive standard antimicrobial prophylaxis for prevention of surgical infection, non-invasive candida, and primary prophylaxis of CMV or HSV similar to non-HIV+ kidney recipients. Patients may require additional primary prophylaxis for other infections based on CD4 count or other recipient/donor risk factors (see table below).
Secondary Prophylaxis (patient with history of opportunistic infection): Patients with a history of the following OIs may require additional, prolonged or different prophylaxis after transplant (see table below).

	Primary Prophylaxis	Secondary Prophylaxis
CMV	**See standard protocol.**	**Prolong normal prophylaxis if CD4 ≤ 100 DC when CD4 > 200 x 6 mo.** Valganciclovir 900mg po qday (dose adjusted for renal impairment)
HSV	**See standard protocol.**	*Consult transplant ID if history of recurrent or severe outbreak*
Pneumocystis pneumonia	**Lifelong for all patients** Trim/Sulfa 80/400mg(ss) po qhs OR Dapsone 100mg po qday (check G6PD) OR Pentamidine 300mg inhaled qmonth *For sulfa allergy consider desensitization to sulfa to enable use of Trim/Sulfa. Consider nitrofurantoin for UTI Px if not using Trim/Sulfa. Discuss length of UTI px with nephrology.*	Same as primary prophylaxis
Toxoplasma gondii	**If D (+)or R(+) lifelong** Bactrim DS 1 tab po qhs OR Bactrim SS qhs OR Dapsone 50mg po qday + Pyrimethamine 50mg po qweek + Leucovorin 25mg po qweek OR Atovaquone 1500mg po daily	**Lifelong as secondary prophylaxis** Pyrimethamine 25-50mg po qday + Sulfadiazine 500-1000mg po qid + Leucovorin 25mg po qday *(covers PCP as well so can d/c PCP px)* OR Pyrimethamine 25mg po qday + Clindamycin 600mg po qid + Leucovorin 25mg po qday *(does NOT cover PCP)*
Mycobacterium Avium Complex (MAC)	**If CD4 ≤ 50. DC when CD4 >100 x 6 mo.** Azithromycin 1200mg po qweek OR Clarithromycin 500mg po bid *(CYP 3A4 inhibitor can ↑ CNI levels)*	**Indication: post-tx or rejection treatment or if CD4≤ 50. DC when CD4 >100 x 6 mo.** Azithromycin 600mg po qday + Ethambutol 15mg/kg/day OR Clarithromycin 500mg po bid + Ethambutol 15mg/kg/day
Cryptococcus (extrapulmonary)	**None**	**Indication: post-tx or rejection treatment or if CD4≤200. DC when CD4>200 x 6 mo.** Fluconazole 200mg po qday
Histoplasmosis	**While CD4 count <150 and at high risk due to occupational exposure or residing in endemic area.** Itraconazole 200mg po qday with food *Consider monitoring itraconazole levels. Oral solution has improved bioavailability(taken without food)* OR Fluconazole 400mg po qday	**Indication: post-tx or rejection treatment or if CD4≤150. DC when CD4>150 x 6 mo.** Itraconazole 200mg po qday with food *Consider monitoring itraconazole levels. Oral solution has improved bioavailability(taken without food)* OR Fluconazole 400mg po qday
Coccidioides	**Potentially lifelong if IgG+ or IgM+ in pts from high risk area.** **Lifelong for recipient of organ from donor with hx of coccidioides.** Fluconazole 400mg po qday OR Itraconazole 200mg po bid	**Lifelong as secondary prophylaxis** Fluconazole 400mg po qday lifelong. OR Itraconazole 200mg po bid lifelong