

**Lung Transplant Program  
UCSF Medical Center**

**LUNG TRANSPLANT  
MANUAL**

**2005**

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## INTRODUCTION

Lung transplantation has become accepted therapy for the treatment of carefully chosen patients with end stage lung disease who have not benefited from available therapies. The treatment is highly successful, with more than 80 percent of patients surviving the first year and greater than 50% of patients surviving beyond five years. The quality of life of long-term survivors is excellent, with the majority returning to productive activities. These results are possible because of the development of specialized care teams and the application of rigorous patient-care protocols, both in the hospital and for the long term. Full integration of community physicians and pulmonologists is essential for long-term success. Also crucial is the availability of a consistent array of patient data and an aggressive response to deviations from expected outcomes. This leads to early diagnosis and management of rejection and other complications.

The lung transplant service performs 30-35 transplants every year. The postoperative patients are cared for in 10 ICC and 10 Long, whereas patients who are admitted for medical complications are cared for on 14 Long. The patient population is primarily adult. The service currently follows approximately 100 outpatients, with 20 pre-patient and post-patient clinic visits per week.

## LUNG TRANSPLANT PROGRAM PERSONNEL

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## IMMUNOSUPPRESSION GUIDELINES FOR LUNG AND HEART-LUNG TRANSPLANT RECIPIENTS

### Induction Immunosuppression Therapy

The role of induction therapy in solid organ transplantation is to prevent acute allograft rejection. The use of induction therapy allows for the delay in initiating calcineurin inhibitor therapy, thereby preventing potential for nephrotoxicity. Induction therapy most commonly consists of a monoclonal antibody (e.g., basiliximab) along with high dose steroids. Antithymocyte globulin (e.g., Thymoglobulin®) is not routinely used for induction therapy in the lung and heart-lung population due to the higher risk and incidence of infection.

Drug	Dose
Simulect® (Basiliximab)	POD #0: 20 mg IV POD #4: 20 mg IV
Solumedrol® (Methylprednisolone)	POD #0: 500 mg IV per lung POD #1-2: 125 mg IV q 12 hours x 4 doses

### MONOCLONAL ANTIBODY

#### ***Basiliximab (Simulect®)***

- Simulect will be held for patients who have received long-term immunosuppression prior to transplantation or who have active sepsis.
- Two doses of 20 mg IV: 1<sup>st</sup> dose during implantation, 2<sup>nd</sup> dose on POD #4.

### CORTICOSTEROID

#### ***Methylprednisolone (Solumedrol®)***

- 500 mg IV per lung during implantation, followed by 125 mg IV q 12 hours x 4 doses

### Maintenance Immunosuppression Therapy

The role of maintenance therapy in solid organ transplantation is to prevent allograft rejection. The most common maintenance regimen is a triple-drug regimen that includes a steroid, a calcineurin inhibitor and an antiproliferative agent. Currently, UCSF lung and heart-lung transplant recipients are initiated on a regimen consisting of prednisone, tacrolimus and mycophenolate mofetil.

### CORTICOSTEROID

#### ***Prednisone (Deltasone®)***

- Prednisone is available in tablet and liquid formulations

**Dose**

- POD #3: 20 mg po daily
- 1 Month: 0.2 mg/kg po daily if negative surveillance biopsies at 2 weeks and 4 weeks, continue dose indefinitely

**CALCINEURIN INHIBITORS (CI)**

- Tacrolimus or Cyclosporine will be started on POD #1
- Exception: patients with acute renal insufficiency – start CI's with renal recovery
- Trough levels for tacrolimus and cyclosporine should be checked q AM before patient's receive AM dose
- Tacrolimus and cyclosporine dosages are adjusted based on daily trough levels and patient's renal function
- Tacrolimus and cyclosporine is available in capsule, liquid, and IV formulations

	<b><i>Tacrolimus (Prograf®, FK506, TAC)</i></b>	<b><i>Cyclosporine (Neoral®, Gengraf®, Sandimmune®, CSA)</i></b>
<b>Starting Dose</b>	<ul style="list-style-type: none"> <li>• 1 mg PO bid</li> <li>• Initiate SL route in CF patients, switch to PO once trough therapeutic</li> <li>• Sublingual route has nearly twice the absorption, therefore use lower dose</li> </ul>	<ul style="list-style-type: none"> <li>• 2.5-5 mg/kg PO bid</li> </ul>
<b>Target Trough</b>	<ul style="list-style-type: none"> <li>• 0-3 months: 12-14 ng/ml</li> <li>• &gt; 3 months: 10-12 ng/ml</li> </ul>	<ul style="list-style-type: none"> <li>• 0-3 months: 300-350 ng/ml</li> <li>• &gt; 3 months: 250-300 ng/ml</li> </ul>
<b>Dosage Adjustment</b>	<ul style="list-style-type: none"> <li>• Increase dose with concomitant medications that ↓ tacrolimus levels: Antiepileptics: carbamazepine, phenobarbital, phenytoin Antimicrobials: rifabutin, rifampin</li> <li>• Decrease dose with concomitant medications that ↑ tacrolimus levels: Azole antifungals: fluconazole, itraconazole, ketoconazole, voriconazole Macrolide antibiotics: clarithromycin, erythromycin (**Not azithromycin) CCB: diltiazem, verapamil</li> </ul>	

**ANTIPROLIFERATIVE AGENTS**

- Cellcept will be initiated in patients receiving an orthotopic lung or heart-lung transplant
- Cellcept will be given intravenously during the immediate post-operative period and switched to PO once the patient is extubated and tolerating PO's (IV dose = PO dose).
- May switch to Imuran if patient is intolerant to Cellcept (diarrhea, neutropenia)
- Cellcept is available in capsule, liquid, and IV formulations
- Imuran is available in tablet and IV formulations

	<b><i>Mycophenolate mofetil</i></b> <b>(Cellcept®, MMF)</b>	<b><i>Azathioprine</i></b> <b>(Imuran®, AZA)</b>
<b>Starting Dose</b>	<ul style="list-style-type: none"> <li>• POD #0 1000 mg PO preoperatively</li> <li>• POD #1 1000 mg IV/PO bid, continue indefinitely</li> </ul>	<ul style="list-style-type: none"> <li>• 2 mg/kg PO daily</li> <li>• 1 mg/kg IV daily</li> </ul>
<b>Dosage Adjustment</b>	<ul style="list-style-type: none"> <li>• Increase dose Early rejection (max 1.5 gm bid)</li> <li>• Decrease dose GI irritation (N/V/D) Leukopenia: WBC &lt; 5000, ↓ dose 50% WBC &lt; 2500, HOLD</li> </ul>	<ul style="list-style-type: none"> <li>• Decrease dose Leukopenia: WBC &lt; 5000, ↓ dose 50% WBC &lt; 2500, HOLD Renal Insufficiency: CrCl 10-50 ml/min, ↓ dose 25% CrCl &lt; 10 ml/min, ↓ dose 50%</li> </ul>

***Sirolimus (Rapamune®, RAPA, SIR)***

- Not routinely used as a first line antiproliferative agent
- Interferes with wound healing therefore not given for two months after surgery
- Add in patients with marginal renal function in whom higher doses of tacrolimus or cyclosporine would be undesirable (adjust TAC or CSA to target lower trough levels)
- Add therapy in patients who are intolerant to calcineurin inhibitors
- Add therapy in patient who have recurrent rejection on standard immunosuppression
- Sirolimus is available in tablet (1 mg, 2 mg and 5 mg) and liquid (1 mg/ml) formulations

<b>Starting Dose</b>	<ul style="list-style-type: none"> <li>• If not on voriconazole (Vfend®) 4 mg PO q day X 2 doses, then 2 mg PO q day</li> <li>• If on voriconazole (Vfend®) 2 mg PO q day X 2 doses, then 1 mg PO q day</li> </ul>
<b>Target Trough</b>	<ul style="list-style-type: none"> <li>• Sirolimus: 6-12 ng/ml Check trough levels before the 4<sup>th</sup> dose when initiating or altering dose **Troughs are send out labs, takes 3-4 days for results to be in STOR</li> <li>• TAC or CSA (if on combination therapy with a calcineurin inhibitor): TAC 8-10 ng/ml CSA 100-150 ng/ml</li> </ul>
<b>Dosage Adjustment</b>	<ul style="list-style-type: none"> <li>• Increase dose with concomitant medications that ↓ sirolimus levels Antiepileptics: carbamazepine, phenobarbital, phenytoin Antimicrobials: rifabutin, rifampin</li> <li>• Decrease dose with concomitant medications that ↑ sirolimus levels Azole antifungals: fluconazole, itraconazole, ketoconazole, voriconazole Macrolide antibiotics: clarithromycin, erythromycin (***)Not azithromycin)</li> </ul>

CCB: diltiazem, verapamil

- Decrease dose with bone marrow suppression: ↓ WBC, ↓ PLT

## Treatment of Allograft Rejection

### Acute Rejection

*During first 3 months post transplant:*

- A2 rejection
  - Solumedrol 500 mg iv q day X 3 days
  - Prednisone 50 mg po BID X 3 days
  - Taper prednisone by 5 mg per dose (10 mg per day) until baseline dose
- Recurrent A2 rejection
  - Solumedrol 1000 mg iv q day X 3 days
  - Taper as above

*After 3 months post transplant:*

- A2 rejection

**If no decline in FEF 25-75 or FEV1, no symptoms and no CT changes:** Repeat CT, PFTs and bronchoscopy in 1 month

**If 20% or greater decline in FEF 25-75 or FEV1:**

- Solumedrol 500 mg iv q day X 3 days
- Prednisone 50 mg po BID X 3 days
- Taper prednisone by 5 mg per dose (10 mg per day) until baseline dose

### Intractable Rejection

Anti-thymocyte globulin protocol (see Index)

### Chronic Rejection

aka Obliterative Bronchiolitis

- Add Sirolimus (Rapamune®) to current immunosuppression regimen
  - 4 mg q day x 2 doses, then 2 mg q day (if pt not on voriconazole)
  - 2 mg q day x 2 doses, then 1 mg q day (if pt on voriconazole)
  - Check sirolimus trough levels in 4-5 days
- Add Azithromycin (Zithromax®) 250 mg MWF

# LUNG TRANSPLANT EVALUATION GUIDELINES

## Eligibility Criteria for Lung Transplant

Evaluation and selection of patients for transplantation is the result of a coordinated process, which looks at the whole patient. While outside information can be screened for basic eligibility, a comprehensive evaluation will require a visit to the UCSF. Patients with end stage lung disease requiring life support may be considered for inpatient transfer for urgent evaluation and listing, however this is an exceptional circumstance.

Evaluation is conducted in stages and is customized to efficiently address key issues that might preclude transplantation in a particular patient. After the evaluation is completed, patients are discussed in the multidisciplinary transplantation-evaluation conference. A complete presentation is made and opinions welcomed from all participants in the program. Decisions about selection are made by consensus.

## Evaluation goals

The comprehensive transplant evaluation seeks to determine the ability of the patient to benefit from transplantation and to enjoy a successful outcome with long-term good health.

## Requirements for candidacy

1. The patient has a progressive, potentially fatal lung disease that substantially impairs the quality of life and daily function, and for which all alternative medical and surgical treatments short of lung transplantation have been exhausted.
2. The patient's lung disease is not expected to recur and cause disability within five years.
3. The patient is not moribund and the lung transplant is likely to prolong life for at least five years (with a better-than-50-percent chance of five-year survival) and the lung transplant will restore the patient to a range of physical and social function suitable for the activities of daily living.
4. The patient does not have involvement of a major system (e.g., cardiovascular or neurological) that would preclude surgery or indicate a poor potential for rehabilitation.
5. The patient's psychological assessment, social arrangement and family support indicate reasonable expectation that the patient will adhere strictly to the difficult long-term medical regimen that will be required post-transplant.
6. The patient has no active alcohol or substance-abuse problems and has signed a contract, has completed at least six months of documented rehabilitation and sobriety, and has psychological clearance.
7. The patient has a severity of illness meeting minimum listing criteria and does not have any absolute contraindication.
8. The patient undergoes a comprehensive assessment, which is reviewed by the multidisciplinary transplantation committee.

In general we consider lung transplantation in persons with end stage lung disease who are less than 60 years of age for a double lung or heart-lung transplant, and less than 65 for a single lung transplant. However, there is no absolute age contraindication and we consider patients based on his/her physiologic age rather than strict chronologic age. Long-term survival does favor younger patients as co-morbid illnesses increase with the ageing process.

## **The Following Lung Conditions Will Be Considered**

### **OBSTRUCTIVE Lung Disease**

- Emphysema
- Alpha-1 Antitrypsin deficiency
- Obliterative Bronchiolitis

### **SUPPURATIVE Lung Disease**

- Cystic Fibrosis
- Bronchiectasis

### **INTERSTITIAL Lung Disease**

- Idiopathic pulmonary fibrosis
- Sarcoidosis
- Eosinophilic granulomatosis
- Occupational lung disease
- Hypersensitivity pneumonitis
- Drug toxicity
- Lymphangioleiomyomatosis

### **VASCULAR Lung Disease**

- Primary pulmonary hypertension
- Eisenmenger's pulmonary hypertension
- Chronic pulmonary emboli

## **Contraindications to Lung and Heart-Lung Transplantation**

### **Absolute Contraindications**

- Malignancy – within two years. For extracapsular renal, breast stage 2 or higher, colon Duke stage B or higher, or melanoma stage III or higher, wait 5 years
- Irreversible secondary organ failure unless considered for a combined transplant
- Severe right heart failure. Consider heart/lung transplantation
- Septicemia
- HIV infection (though currently under re consideration)
- Hepatitis B/C- if antigen positive and histological evidence of disease
- Continued abuse of alcohol, tobacco or other drugs
- Psychiatric history likely to result in non-compliance and or persistent non-compliance with medical therapy.

### **Relative Contraindications**

- Coronary artery disease-must be able to revascularize, if for lung transplant only
- Intubated and ventilator dependent-if unable to ambulate
- Obesity BMI >30
- Chronic renal impairment with GFR <50ml/min, unless candidate for combined renal transplant
- Diabetes with end organ damage
- Severe osteoporosis (bone mineral density > 2 sd's less than predicted for age)
- Active peptic ulcer or diverticulitis

# THE LUNG TRANSPLANT ASSESSMENT

## Stages of assessment

1. Preliminary assessment clinic
2. Secondary assessment
3. Decision
4. Waiting List

## PRELIMINARY ASSESSMENT CLINIC

The preliminary assessment outpatient clinic appointment should be conducted within one month of referral unless the patient is clearly unsuitable and a Consultant Physician or Surgeon has made this decision. Prior to arrival to clinic, the pertinent medical records will be obtained and reviewed by the nurse coordinator. If after review of these tests and a phone interview, the patient is deemed a good candidate he/she is scheduled for a Preliminary Assessment Clinic visit. The general principle of this assessment is to carefully review the medical history and data, perform a careful physical exam, begin education regarding lung transplantation and perform psychosocial screen. This initial visit allows the avoidance of more detailed studies and blood tests if the patient is clearly unsuitable for transplantation.

## SECONDARY ASSESSMENT

Following the initial visit, patients will undergo secondary studies to evaluate for underlying, undiagnosed disease. If possible, these tests will be performed at UCSF over a 3-4 day period. (see below for the list of tests) These tests are ordered based on the person's primary disease, age, and individual needs. At all stages of the assessment the patient and family are involved in any discussions and encouraged to ask any questions.

## Objectives of Assessment Procedures

- To assess the patient's clinical, social and psychological suitability as a transplant recipient
- To impart factual information to the patient and his/her family concerning all aspects of transplantation
- To meet Hospital staff and transplant patients
- To provide an opportunity for the patient, and his or her family, to begin to come to terms with the prospect of transplantation, and to be informed about the procedure and its aftermath

## Investigations Conducted

The importance of the multidisciplinary involvement in the assessment of the patient and care received is paramount. The assessment should involve a whole spectrum of healthcare professionals, including Pulmonologists, Surgeons, Radiologists, Nurses, Transplant Coordinators, Pharmacists, Occupational Therapists, Dieticians, Physiotherapists, Social Workers, Psychologists (if indicated Psychiatrists) - everyone has a key role to play.

## Clinical Assessment

- Lung Condition
- Cause
- Previous thoracic surgery
- Current therapy

## **Social History**

- Marital status
- Housing
- Employment
- Smoking
- Drugs/alcohol abuse

## **Past/Concurrent History**

- Unresolved pulmonary process
- Malignancy
- Diabetes
- Hypertension
- Renal disease
- Liver disease
- Peripheral or cerebrovascular disease
- Peptic Ulceration, GI bleeding
- Diverticular disease, GI sepsis
- Unresolved sepsis in any site
- Herpes virus infection
- Previous blood transfusion

## **Routine Observations**

- Temperature
- Blood pressure
- Heart rate
- Height
- Weight

## **Radiology**

- Chest x-ray
- CT Scan of the Chest

## **Cardiac Assessment**

- ECG
- Echocardiogram
- 6 minute exercise walk and/or metabolic exercise test (if capable of doing)
- Ejection Fraction assessment
- Cardiac Catheterization & Coronary angiogram if over the age of 50

## **Pulmonary Assessment**

- Pulmonary function tests
- 6 minute walk test with oxymetry
- Arterial blood gases
- Sputum culture

## **Microbiology Assessment**

- MSU and urine test
- Nose swab

- MRSA screen

### **Dental Assessment**

- Full dental examination
- Advice on dental hygiene
- Restorative work and extractions as necessary

### **Hematology Blood Tests**

- Blood group
- Panel Reactive Antibody screen
- Complete blood count
- Reticulocytes
- APTT, PT, INR, Fibrinogen

### **Biochemistry Test**

- Urea & electrolytes
- Creatinine
- Uric acid
- Calcium phosphate
- Liver function tests
- Cardiac enzymes
- Amylase
- Thyroid function tests
- Fasting blood glucose
- Fasting blood lipids.

### **Serology Blood Sample**

- Hepatitis B/C
- HIV
- Syphilis
- Rubella
- Epstein Barr Virus
- Toxoplasma
- Varicella-Zoster
- Herpes simplex
- Cytomegalovirus

### **Immunology Blood Tests**

- Auto-immune (including ANF, DNA, SCAT/LATEX)
- HLA typing
- Lymphocytotoxic antibody screen

### **Psychosocial Assessment**

- Letter from GP confirming compliance with past therapy
- Interview with Social Worker

### **Other**

- Creatinine Clearance or GFR
- Dietician (after discussion with transplant team)

- Physiotherapy assessment

## **FINAL DECISION**

The decision to place a patient on the waiting list is a multidisciplinary one. Following completion of the testing, the patient is presented at the Lung Transplant Listing Meeting, held weekly. The patient and relatives will be informed of the outcome and given the opportunity to discuss it with a representative of the transplant team.

The multidisciplinary transplant meeting is made up of a wide selection of healthcare professionals. These include:

- Cardiothoracic Surgeons
- Pulmonologists
- Cardiologist
- Transplant Coordinators
- Transplant Nurses
- Dieticians
- Pharmacists
- Financial Counselors
- Social Workers

If the patient decides to go forward with transplantation, he or she is then registered with UNOS and placed on the waiting list. If the patient is not deemed suitable and/or declines the option of transplantation the Clinician explains to the patient and their family the options available to them. The GP and referring Clinicians are informed of the outcome of the assessment.

## **THE WAITING LIST**

The patient receives detailed explanations that are consistent and key information pertaining to the waiting period for transplantation is recorded appropriately in accordance with UNOS

At all stages the patient is encouraged to ask questions and an information booklet should be provided. The following key areas must be discussed with the patient as appropriate:

- Provision of a cell phone or pager and explanation of its use.
- The patient's responsibility to make him/herself available to be contacted by the Transplant Unit at anytime. This is discussed with the Transplant Co-ordinator
- Patients are requested to inform the Transplant Unit of any changes in their circumstances i.e.,
  - If they become unwell
  - If they are admitted to hospital
  - Any changes in medication
  - Vacations

An information booklet will be given to the patient. This will explain:

- Preparation for admission for surgery
- Maintenance of regular contact
- Reporting changes in circumstances
- What to do when called for surgery
- The operation
- Accommodation for partners
- Publicity and the media
- Wards and departments after the operation.

During the waiting period the Transplant Unit will maintain contact with the patient and his/her family to offer support, information and guidance according to their needs. Clinical review of patients on the waiting list will be as clinically indicated.

## LUNG TRANSPLANT SERVICE

### Rounds & Meetings

Surveillance bronchoscopies in Radiology 3<sup>rd</sup> Floor are scheduled daily at 7a.m. and 8a.m. Following bronchoscopy, radiology rounds are performed from 9:30-10:00 a.m. Inpatient hospital rounds are from 10am-Noon and are conducted by the lung transplant service, which consists of the transplant attending, the transplant fellow, the inpatient nurse coordinator, the transplant pharmacist and social worker. Every member of the team participates on rounds. The lung transplant service is responsible for the management of all patients who are status post lung transplant. Patients who are immediately post-op or who are re-admitted with surgical complications are under the primary care of the thoracic surgery team, with consultation of the lung transplant medical service. All other patients are admitted to the internal medicine service with active consultation by the lung transplant medical service. There are frequently urgent bronchoscopies and interventional procedures scheduled from 12-3:00 p.m. The transplant fellow along with the transplant attending is responsible for reviewing outpatient charts daily at 3-4:00 p.m. to review labs and test results and make medication changes. The post lung transplant clinic is on Tuesdays from 9-12. The pre lung transplant clinic is on Thursdays from 9-12. The lung transplant listing meeting is on Wednesday, from 3-4 p.m. and multi-disciplinary rounds/clinical conference is from 4-5p.m.

	Monday	Tuesday	Wednesday	Thursday	Friday
7:30	Bronchoscopy in 3 <sup>rd</sup> Floor Radiology 7:30 to 9:30				
8:30					
9:30	X-Ray Rounds	Post Tx Clinic 9-12	X-Ray Rounds	Pre Tx Clinic 9-12	X-Ray Rounds
10	Inpatient Rounds		Inpatient Rounds		Inpatient Rounds
11					
12					
1	Urgent Bronchoscopy and OP Chart Review	Inpatient Rounds	OP Chart Review	Inpatient Rounds	Urgent Bronchoscopy and OP Chart Review
2					
3		Urgent Bronchscopy and OP Chart Review	LTx Listing Meeting	Urgent Bronchsopy and OP Chart Review	
4					
5					

# SOLID ORGAN TRANSPLANT IMMUNOSUPPRESSANTS

## General Principles About Immunosuppression

Allograft rejection is a major barrier to long-term graft and patient survival. Transplant recipients must take immunosuppressive drugs for life to prevent allograft rejection. A triple regimen, typically consisting of a calcineurin inhibitor, an antiproliferative agent and a corticosteroid is the most common immunosuppression regimen used to prevent allograft rejection. Immunosuppressive drugs with different mechanisms of action and adverse effects are used in combination to maximize immunosuppression and minimize dose-related toxicities.

The specific combination of drugs and target drug levels will vary according to the patient. It is best to check with the attending physician as to the particular regimen and doses to be used.

## Immunosuppressants are classified into one of five categories:

1. Interleukin-2 receptor antagonists
  - Basiliximab (Simulect®)
  - Daclizumab (Zenapax®)
2. Corticosteroids
  - Methylprednisolone (SoluMedrol®)
  - Prednisone (Deltasone®)
3. Calcineurin inhibitors
  - Tacrolimus (Prograf®)
  - Cyclosporine (Sandimmune®, Neoral®, and Gengraf®)
4. Antiproliferative agents
  - Mycophenolate mofetil (CellCept®)
  - Azathioprine (Imuran®)
  - Sirolimus (Rapamune®)
5. Antilymphocyte antibodies
  - Antithymocyte globulin (Atgam®, Thymoglobulin®)
  - Muromonab-CD3 (Orthoclone OKT3®)

## INTERLEUKIN-2 RECEPTOR ANTAGONISTS (IL-2 RA)

IL-2 RA's are monoclonal antibodies used for induction therapy at the time of transplantation to prevent acute rejection.

### **BASILIXIMAB (Simulect®):**

- Chimeric monoclonal antibody
- Use: induction therapy in lung and heart-lung transplant recipients at UCSF
- Dose: 20 mg IV at time of transplantation and on POD#4

**DACLIZUMAB (Zenapax®):**

- Humanized monoclonal antibody
- Use: induction therapy in heart transplant recipients at UCSF
- Dose: 1 mg/kg IV at time of transplantation, on POD#7 and every 14 days thereafter for a total of 5 cumulative doses (Doses should be rounded to the nearest 25 mg increment)

**Mechanism of action:**

- Blocks  $\alpha$ -subunit of IL-2 receptor, inhibits binding of IL-2 to the receptor, prevents T-cell activation

**Adverse effects:**

- Similar to placebo in clinical trials

fever	HTN
pain	N/V/D
anaphylaxis	dyspepsia
headache	abdominal pain
tremor	constipation
dyspnea	infection

**Drug interactions:**

- None reported, additive immunosuppressive effect with concomitant immunosuppressants

**Clinical Pearls:**

- The use of induction therapy in organ transplantation allows for the delay in initiating calcineurin inhibitor therapy, thereby preventing potential for nephrotoxicity.
- Induction therapy with IL-2R antagonists may be withheld in patients who have been treated with immunosuppressant medication for their underlying pulmonary disease prior to transplant.

**CORTICOSTEROIDS**

Corticosteroids are used to prevent allograft rejection. However, high dose steroids can be used to treat rejection.

**METHYLPREDNISOLONE (Solu-Medrol®):**

- Prevention dose: 500 mg IV per organ at time of transplantation, followed by IV Solu-medrol taper of 125 mg q 12 hrs x 4 doses
- Treatment dose: 250-500 mg IV once daily x 3 doses, followed by oral prednisone taper

**PREDNISONE (Deltasone®):**

- Maintenance dose: range 10-20 mg once daily
- The maintenance dose will initially be 20 mg once daily post IV Solu-Medrol taper
- Dose will be tapered to 0.2 mg/kg once daily if surveillance lung biopsies are negative for rejection

**Mechanism of Action:**

- Inhibits IL-1 production by suppression of IL-1 gene transcription

## Adverse effects:

**P** sychosis  
**R** ound face (Cushing's)  
**E** dema  
**D** iabetes/hyperglycemia, **D**ermatologic changes (acne, hirsutism)  
**N** eurologic/CNS changes  
**I** nfection, **I**nsomnia, **I**ncrease appetite (weight gain)  
**S** tomach upset/ulcer  
**O** steoporosis  
**N** ervousness  
**E** ye changes (cataracts, glaucoma)

## Drug Interactions:

- Decrease steroid effect: rifampin, phenytoin
- Additive toxicity: NSAIDs (may increase risk of GI ulceration)
- Steroids may decrease effectiveness of vaccines

## Clinical Pearls:

- GI/ulcer prophylaxis: initiate proton pump inhibitor (PPI) or H<sub>2</sub>-blocker

**PPI:** Pantoprazole 40 mg daily

- Pantoprazole (Protonix®) is on UCSF formulary and is available for PO & IV administration.
- CAUTION: tablets CANNOT be crushed for NGT administration!

Omeprazole 20 mg daily

- Omeprazole (Prilosec®) suspension is available at UCSF for NGT administration

**H<sub>2</sub>-blocker:** Famotidine 20 mg PO/IV bid

- Osteoporosis prophylaxis: initiate calcium supplement & bisphosphonate

**Calcium Supplements:** Oscal-D 500 mg tid (provides 500 mg elemental calcium per dose)

- Daily calcium supplementation should equal 1500 mg ELEMENTAL calcium, given in divided doses (500 mg tid)
- Calcium carbonate contains 40% elemental calcium
- Calcium carbonate 500 mg (i.e., TUMS®) provides 200 mg elemental calcium
- Calcium carbonate 1250 mg (i.e., Oscal®) provides 500 mg elemental calcium
- Calcium absorption requires Vitamin D & is increased when taken with food

**Bisphosphonate:** Alendronate (Fosamax®) 70 mg q week  
Risedronate (Actonel®) 35 mg q week

- Administration
  - Dose should be given first thing in the morning on an empty stomach
  - Dose should be given with at least 8 oz. plain water only (no milk, juice, coffee, or sparkling water)
  - Patient should wait 30 minutes before having any food, drinks or other medications
  - Patient should avoid lying down for 30 minutes to prevent reflux

## **CALCINEURIN INHIBITORS (CI)**

Calcineurin inhibitors are used to prevent allograft rejection

## **TACROLIMUS (Prograf®, FK506, TAC)**

### **Mechanism of action:**

- Binds to FK binding protein; prevents IL-2, IL-3, and gamma-interferon production thereby, prevents lymphocyte proliferation

### **Dose:**

- Should be individualized based upon patient's tacrolimus levels, rejection status and drug side effects and toxicity
- Tacrolimus dose should be started at 1 mg PO bid (SL in cystic fibrosis patients)
- Dosage adjustments are made by 0.5 – 1 mg increments
- Average dose ranges from 2-8 mg twice daily (0.5-2 mg twice daily in patients on concomitant voriconazole therapy, or other drugs that inhibit tacrolimus metabolism)

### **Tacrolimus levels:**

- Drawn as troughs before AM dose (about 10-12 hours after previous dose)
- Measured using a whole-blood IMX assay
- Should be checked q AM while patients are in house

**Target troughs:** 12-14 ng/ml (months 0-3 post transplant)  
 10-12 ng/ml (> 3 months post transplant without evidence of allograft rejection)  
 5-10 ng/ml (if on concomitant sirolimus therapy)

### **Formulation & routes of administration:**

- Capsules are available in 0.5 mg, 1 mg or 5 mg strengths for oral or sublingual (SL) administration.
- Suspension is available for NGT administration (prepared by inpatient pharmacy, not commercially available).
- IV formulation is available; however, is reserved for patients unable to tolerate oral meds or for patients who are NPO.
- SL route can be used in patients who do not tolerate oral meds due to nausea/vomiting or in patients who are NPO. Drug absorption via the SL route is greater than PO/NGT route and will result in higher drug levels. When switching from PO/NGT to SL route, it is necessary to adjust tacrolimus dose.

**Clinical Pearls:**

- Tacrolimus dosing and target trough levels are patient specific, such that patients with rejection problems may have their levels maintained higher than the usual target range, and patients with adverse reaction problems may have their levels maintained lower than the usual target range
- IV tacrolimus is rarely used. If it is necessary to give IV tacrolimus, doses start at 0.03-0.05 mg/kg/day as a continuous infusion over 12 hours. IV therapy should only be continued until the patient can tolerate oral medications. When switching the patient from IV to PO tacrolimus, start PO meds 12 hours after the end of IV infusion. Caution: anaphylaxis has been reported with the use of IV tacrolimus.

**CYCLOSPORINE (Sandimmune®, Neoral®, Gengraf®, CSA)**

- There are 3 different cyclosporine brand products, none of which are equivalent to each other and one product cannot be substituted for another product.
- When writing chart orders, it is necessary to write for the brand product (i.e., "Neoral"), do not write "cyclosporine" or "CSA"

**Mechanism of action:**

- Prevents IL-2, IL-3, and gamma-interferon production thereby, prevents lymphocyte proliferation

**Dose:**

- Should be individualized based upon patient's cyclosporine levels, rejection status and drug side effects and toxicity
- Cyclosporine doses should be started at 2.5-5 mg/kg PO bid
- Dosage adjustments are made by 25 mg increments
- Average dose ranges from 100-250 mg twice daily

**Cyclosporine levels:**

- Drawn as troughs before AM dose (about 10-12 hours after previous dose)
- Should be checked q AM while patients are in house

**Target troughs:**      300-350 ng/ml (months 0-3 post transplant)  
                                 250-300 ng/ml (> 3 months post transplant without evidence of allograft rejection)  
                                 100-150 ng/ml (if on concomitant sirolimus therapy)

**Formulation & routes of administration:**

- Sandimmune®, Neoral®, and Gengraf® is available in 25 mg and 100 mg capsules, and 100 mg/ml oral solution.
- Sandimmune® is available in an IV formulation.

**Clinical Pearls:**

- Cyclosporine dosing and target trough levels are patient specific, such that patients with rejection problems may have their levels maintained higher than the usual target range, and patients with adverse reaction problems may have their levels maintained lower than the usual target range

- IV cyclosporine is rarely used. If it is necessary to give IV cyclosporine, give 1/3 of the oral dose as a continuous infusion over 24 hours. IV therapy should only be continued until the patient can tolerate oral medications.

### Tacrolimus & Cyclosporine Adverse effects:

tremors	nephrotoxicity	N/V/D
headaches	hyperkalemia	seizure (rare)
nightmares	hypomagnesemia	alopecia (TAC)
flushing	hypertension	hirsutism (CSA)
anxiety	hyperglycemia	gingival hyperplasia (CSA)
depression	hyperuricemia	Increased risk of cancer
confusion	hyperlipidemia	Increased risk of infections

**Tacrolimus & Cyclosporine-induced hypomagnesemia** can be treated with magnesium oxide 400 mg bid to start and titrated to Mg<sup>2+</sup> level and diarrhea

### Tacrolimus & Cyclosporine Drug Interactions:

- Both tacrolimus and cyclosporine are metabolized by the liver via cytochrome P450 3A4 enzyme

Drugs that ↑ TAC/CSA levels  
(e.g., CYP3A4 inhibitors)

- voriconazole, fluconazole, itraconazole, ketoconazole
- erythromycin, clarithromycin (not azithromycin)
- diltiazem, verapamil
- grapefruit juice

Drugs that ↓ TAC/CSA levels  
(e.g., CYP3A4 inducers)

- rifampin, rifabutin
- phenytoin, phenobarbital, carbamazepine

Concomitant nephrotoxic agents

- gentamicin, tobramycin
- amphotericin B
- NSAIDs

## ANTIPROLIFERATIVE AGENTS

Antiproliferative agents are used to prevent allograft rejection

### MYCOPHENOLATE MOFETIL (Cellcept®, MMF)

#### Mechanism of action:

- Inhibits de novo purine synthesis thereby inhibiting the proliferation of lymphocytes

#### Dose:

- 1000 mg bid
- Dose may be adjusted due to leukopenia or GI intolerance

#### Adverse effects:

Gastrointestinal:

Bone Marrow:

Others side effects:

nausea  
vomiting  
ulceration  
gastritis  
abdominal pain  
pancreatitis

anemia  
leukopenia  
pancytopenia

dizziness  
weakness  
joint pain  
rash  
fever  
muscle cramps  
increased risk of infection

**Drug interactions:**

- Aluminum or Mag-containing antacids (e.g., Maalox, Mylanta, Alternagel) decreases the absorption of MMF
- Cholestyramine decreases the absorption of MMF
- Probenecid increases MMF levels by competing for renal elimination

**Clinical Pearls:**

- Mycophenolate mofetil can cause GI ulceration, therefore, peptic ulcer disease is a relative contraindication.
- Due to the potential for GI ulceration, all patients on mycophenolate mofetil should be on PPI or H<sub>2</sub>-blocker for ulcer prophylaxis.

**AZATHIOPRINE (Imuran®, AZA)**

**Mechanism of action:**

- Azathioprine is converted to 6-mercaptoprine and acts as an antimetabolite, blocking mRNA and DNA synthesis, thereby inhibiting the differentiation & proliferation of T- and B-cells

**Dose:**

- Loading dose: 2-5 mg/kg once daily
- Maintenance dose: 1-2 mg/kg once daily
- Doses should be rounded to the nearest 25 mg increment (AZA is available as a 50 mg scored tablet)
- Azathioprine is available in IV formulation, IV dose = 50% PO dose

**Adverse effects:**

\*\*Most common side effect is leukopenia

N/V/D/A	pulmonary edema	generalized erythematous, maculopapular rash
alopecia	cough	hepatotoxicity: within 6 months post-tx
arthralgia	dyspnea	veno-occlusive disease: rare, occurs with chronic tx 1-2 years
myalgia	hypotension	Bone-marrow suppression (dose-related)
retinopathy	hypersensitivity	-leukopenia
fever	serum sickness	-macrocytic anemia
rigors	Raynaud's	-pancytopenia
		-thrombocytopenia

**Drug interactions:**

- Allopurinol blocks the AZA metabolism; ↓ azathioprine dose by 25-33%

## **SIROLIMUS (Rapamune®, RAPA, SIR)**

### **Mechanism of action:**

- Macrolide antibiotic (structurally related to tacrolimus) that binds mTOR (mammalian target of rapamycin), resulting in inhibition of IL-2 driven lymphocyte proliferation. It is also believed to have antitumor effects.

### **Dose:**

- Should be individualized based upon patient's sirolimus levels, rejection status and drug side effects and toxicity.
- Sirolimus has a long half-life (approximately 60 hours). In order to achieve therapeutic drug levels quickly, a loading dose can be given when initiating a patient on sirolimus, followed by the maintenance dose.
- The loading dose is typically 3 times the maintenance dose (5-10 mg x 1). Maintenance doses are approximately 2-5 mg daily. For lung and heart-lung transplant recipients starting on sirolimus, loading doses of 2-4 mg will be given.
- Dosage adjustments are made by 0.5-1 mg increments.

### **Formulations:**

- Sirolimus is available in 1 mg, 2 mg and 5 mg tablets, and 1 mg/ml oral solution.

### **Sirolimus levels:**

- Drawn as a trough just before sirolimus dose.
- Sirolimus levels are sent out labs at UCSF, results are usually available in 3-4 days.

### **Adverse effects:**

hypertension	leukopenia	peripheral edema
hypertriglyceridemia	thrombocytopenia	poor wound healing
hyperlipidemia	anemia	interstitial lung disease (rare)

### **Drug interactions:**

- Sirolimus is metabolized in the gut and liver by cytochrome P450-3A4.

Drugs that ↑ SIR levels  
(e.g., CYP3A4 inhibitors)

- voriconazole, fluconazole, itraconazole, ketoconazole
- erythromycin, clarithromycin (not azithromycin)
- diltiazem, verapamil
- grapefruit juice
- cyclosporine (?compete for liver metabolism)

Drugs that ↓ SIR levels  
(e.g., CYP3A4 inducers)

- rifampin, rifabutin
- phenytoin, phenobarbital, carbamazepine

### **Clinical Pearls:**

- Sirolimus interferes with wound healing, therefore, is not given for two months after transplant surgery.
- Cyclosporine can increase blood sirolimus levels when given together. In patients on concomitant cyclosporine therapy, it is recommended that sirolimus be given 4 hours after cyclosporine to minimize this interaction.

## **ANTILYMPHOCYTE ANTIBODY (ALA)**

### **ANTITHYMOCYTE GLOBULIN (Thymoglobulin®, Atgam®)**

Antithymocyte globulin is used for the treatment of rejection episodes resistant to conventional (corticosteroids) treatment or to prevent acute rejection as part of an induction regimen in patients at high immunologic risk for rejection.

#### **Mechanism of action:**

- Antithymocyte globulin is a polyclonal IgG antibody that is derived from rabbits (Thymoglobulin®) or horses (Atgam®, rarely used). The antibody binds to lymphocytes that express CD2, CD3, CD4, CD8, CD11a, CD18 and others, inactivates them and depletes them from the circulation.

#### **Dose:**

- Dosing regimen is the same for prevention and treatment of rejection
- The usual starting dose is 1.5 mg/kg/day IV for the first dose, then 1 mg/kg/day thereafter
- Doses should be rounded off to the nearest 25 mg increment
- Dose may be adjusted for thrombocytopenia
- Inpatient orders are to be written on a daily basis by housestaff

#### **Adverse effects:**

- Flu-like symptoms: fever, chills, arthralgias, myalgias, headache, rigors
- Bone marrow suppression: leukopenia, thrombocytopenia
- Others: opportunistic infections, predisposition for malignancies

### **MUROMONAB-CD3 (Orthoclone OKT®3, OKT3)**

OKT3 is used for the treatment of rejection episodes resistant to conventional (corticosteroids) treatment.

#### **Mechanism of action:**

- OKT3 is a murine monoclonal antibody that reacts against 95% of peripheral T lymphocytes but does not react against B lymphocytes, NK cells, granulocytes or monocytes. OKT3 acts by coating the circulating T lymphocytes, subjecting them to opsonization by the reticuloendothelial system. OKT3 modulates the T lymphocytes' antigen-receptor CD3 complex, which results in the removal of all CD3 molecules from the cell surface so that the cell lacks the ability to function as a T lymphocyte.

#### **Dose:**

- 5 mg IV once daily for 7-14 days
- Inpatient orders are to be written on a daily basis by housestaff

**Precautions/Warnings:**

- Pulmonary edema: severe pulmonary edema has occurred in patients with fluid overload. Prior to initiation of OKT3, it is imperative that there be no clinical evidence of volume overload, uncontrolled hypertension or uncompensated heart failure. To minimize the risk of OKT3-induced pulmonary edema, the following must be observed:
  1. Chest X-ray must be obtained and cleared within 24 hours of first dose
  2. Assessment of patient for signs and symptoms of volume overload
- First-dose effect: the first and/or second dose of OKT3 may be associated with flu-like symptoms (fevers, rigors, headache). These symptoms may occur within 30 minutes to 6 hours and up to 24 hours after the first dose. To minimize symptoms, refer to "Pretreatment" guidelines.
- Anaphylaxis: < 1% of patients may experience an anaphylactic reaction. Due to this risk, the patient should be observed for at least 10 minutes after the injection. The following medications must be at bedside:
  1. epinephrine (1:1000 dilution)
  2. hydrocortisone injection
  3. diphenhydramine injection
- Infection: use of OKT3 may increase the patient's susceptibility to infection. All patients should be on PCP, CMV, and thrush prophylaxis.

**Adverse effects:**

- 10%: tachycardia, dizziness, trembling, shortness of breath, nausea/vomiting
- 1-10%: headache, stiff neck, photophobia, pulmonary edema
- 1%: aseptic meningitis, seizures, chest pain/tightness, hyper-/hypotension, arthralgia, tremor, dyspnea, wheezing, anaphylactic reactions

**Clinical Pearls:**

- All patients receiving Thymo or OKT3 should be given premedications 30 minutes prior to dose to prevent infusion-related reactions:
  - Steroid: Solu-medrol, hydrocortisone or prednisone
  - Acetaminophen 650 mg
  - Diphenhydramine 25 mg
- All patients receiving Thymo or OKT3 must receive prophylaxis for opportunistic infections including:
  - PCP prophylaxis
  - CMV prophylaxis
  - Thrush prophylaxis

## DONOR MICROBIAL CULTURES

Donor cultures are obtained on every transplanted lung intra-operatively. ...

### Prophylactic Therapy against Bacterial Infections

All lung and heart-lung transplant recipients will receive initial surgical prophylaxis for 5 days, which will empirically cover gram-positive and gram-negative organisms. Antibiotics may be modified initially based on known microbial colonization of the patient (i.e., cystic fibrosis patients with pseudomonas colonization). The duration of antibiotic therapy may be extended as appropriate pending intra-operative microbial cultures. In addition, inhaled tobramycin will be initiated in all patients for a total of 3 months post transplant on a regimen of 28 days on and 28 days off therapy.

### Intra-operative Donor Microbial Cultures

- If negative growth, discontinue antibiotics on POD #5. If the patient has chest tubes in place, order Kefzol 1 gm IV q 8 hr until chest tubes out (choose alternative antibiotic if patient has penicillin/cephalosporin allergy).
- If positive growth, continue antibiotics for a total of 10-14 days. Modify antibiotic regimen as appropriate based upon culture results and susceptibility data.

### Coverage of Gram-Positive Organisms

#### *Vancomycin (Vancocin®)*

- Dose: 10-15 mg/kg IV q 12 hr (usually 1 gm IV q 12 hr)
- Renal dosing:

CrCl	40–60 ml/min	Vancomycin	10-15 mg/kg q 12-24 hr
	20–40		10-15 mg/kg q 24-48 hr
	10–20		10-15 mg/kg q 48-72 hr
	< 10		10-15 mg/kg q 4-7 days
CRRT			7.5-15 mg/kg q 24 hr
HD			15-20 mg/kg x 1, then 500 mg post HD
- Check vancomycin trough before 4<sup>th</sup> dose

If patient has a documented vancomycin allergy, Linezolid 600 mg IV/PO bid

- Call ID pharmacy (719-9421) for approval of linezolid
- Monitor platelets, linezolid can cause thrombocytopenia, which usually occurs in 7-10 days
- If donor cultures are negative for MRSA/MRSE, D/C linezolid on POD#5!
- If donor cultures are positive for MSSA/MSSE, switch antibiotics!

#### *Cefazolin (Kefzol®)*

- Start cefazolin IF chest tubes are still in place after vancomycin/Zosyn has been d/c'd
- Dose: 1 gm IV q 8 hr
- Renal dosing:

CrCl	10–50 ml/min	Cefazolin	1 gm q 12 hr
	< 10		1 gm q 12 hr
CRRT			1 gm q 12 hr
HD			2 gm post HD

## Coverage of Gram-Negative Organisms

### *Piperacillin/Tazobactam (Zosyn®)*

- Dose: 4.5 gm IV q 8 hr or 3.375 gm IV q 6 hr
- Dose for Pseudomonas coverage: 4.5 gm IV q 6 hr (for CrCl > 20 ml/min)
- Renal dosing:

CrCl	< 10 ml/min	Zosyn 2.25-3.375 gm q 8 hr
	CRRT	3.375 gm q 6 hr
	HD	2.25 gm q 8 hr

### *Ciprofloxacin (Cipro®)* – for patients with documented penicillin allergy

- Dose: 400 mg IV q 12 hr (if CrCl < 10 ml/min, dose 200 mg IV q 12 hr)
- Renal dosing:

CrCl	< 10 ml/min	Cipro 200 mg q 12 hr (or 250 mg PO bid)
	CRRT	400 mg q 12 hr (or 500 mg PO bid)
	HD	200 mg q 12 hr (or 250 mg PO bid)

## Inhaled Tobramycin

- Prophylaxis for a total of 3 months post transplant, 1<sup>st</sup> and 3<sup>rd</sup> month on therapy, 2<sup>nd</sup> month off therapy.
- Dose: Tobramycin 80 mg inhaled bid
- Patients are discharged on TOBI® (brand tobramycin) 300 mg inhaled bid

## OPPORTUNISTIC INFECTIONS

Opportunistic infections are a common cause of morbidity and mortality in lung transplant recipients. Common opportunistic infections seen in transplant recipients include cytomegalovirus (CMV), herpes simplex virus (HSV), varicella zoster virus (VZV), pneumocystis carinii pneumonia (PCP), invasive aspergillosis, and mucocutaneous candidiasis (thrush).

All lung and heart-lung transplant recipients must receive antimicrobial prophylaxis to prevent opportunistic infections:

- CMV (and HSV, VZV) prophylaxis
- PCP prophylaxis
- Aspergillus prophylaxis
- Thrush prophylaxis
- Toxoplasma prophylaxis

### Cytomegalovirus (CMV) Infection

CMV is the most common opportunistic infection in transplant recipients with the risk being highest 1-4 months post transplant. The risk of infection is dependent upon prior CMV exposure in the donor and recipient. CMV disease is associated with increased morbidity and mortality, risk of other opportunistic infections, risk of allograft dysfunction, and risk of acute and/or chronic allograft rejection.

- Symptoms of CMV infection: fever, malaise, leukopenia, GI symptoms
- Potential organ involvement: lung (pneumonitis), eye (retinitis), GI (esophagitis, gastritis, colitis)
- Diagnosis: CMV antigen, buffy coat or “shell viral assay”, viral culture or histochemical stain on biopsy

### *Patient Risk Stratification*

	<b>Donor CMV Ab</b>	<b>Recipient CMV Ab</b>
High risk (aka “CMV mismatch”)	+	-
Moderate risk	+	+
	-	+
Low risk	-	-

### CMV Prophylaxis

- Patients at high risk of developing CMV infection will receive prophylaxis for 12 months post transplant. These patients will also receive Cytogam® therapy.
- Patient at moderate risk of developing CMV infection will receive prophylaxis for 6 months post transplant.
- Patients at low risk of developing CMV infection will not receive prophylaxis.
- Patients who have received therapy for treatment of allograft rejection will receive prophylaxis for 6 months.

- Patients who have been treated for CMV infection/disease will receive additional 6 months of maintenance therapy.
- Patients who are immediately post-transplant will receive IV ganciclovir while intubated or NPO. Patients will be transitioned to PO valganciclovir when tolerating PO's.

**Ganciclovir (Cytovene®) – IV**

*For CMV prophylaxis or treatment*

- Dose: 5 mg/kg IV q 12 hours
- Renal dosing:
 

Creatinine Clearance (ml/min)	50–79	2.5 mg/kg q 12 hr
	10–50	1.25–2.5 mg/kg q 12-24 hr
	< 10	1.25 mg/kg q 24 hr
	CRRT	2.5–5 mg/kg q 24 hr
	HD	1.25 mg/kg post HD

**Valganciclovir (Valcyte®) – PO**

- When treating CMV infection, give treatment doses for 14-21 days, then change to prophylaxis doses
- Dose:

	<u>For CMV treatment</u>	<u>For CMV prophylaxis</u>
CrCl ≥ 60 ml/min	900 mg bid	900 mg q day
CrCl 40–59	450 mg bid	450 mg q day
25–39	450 mg q day	450 mg q 48 hr
10–24	450 mg q 48 hr	450 mg biw
CRRT	450 mg q day	450 mg q 48 hr
HD	450 mg post HD	450 mg biw post HD

**Cytomegalovirus Immune Globulin (Cytogam®, CMV-IGIV)**

*For CMV mismatched patients ONLY*

- NF (non-formulary) form is required, fill one out indicating patient is CMV mismatch, at high risk of CMV infection

Week Post-transplant	Dose (round to nearest 2.5 gram)
Week 0	150 mg/kg
Week 2	100 mg/kg
Week 4	100 mg/kg
Week 6	100 mg/kg
Week 8	100 mg/kg
Week 12	50 mg/kg
Week 16	50 mg/kg

**CMV Quantitative PCR (CMV QPCR)**

- Transplant recipients who are not on ganciclovir/valganciclovir are potentially at risk for developing CMV infection. CMV QPCR provides....
- After valganciclovir is discontinued, CMV QPCR should be checked every month for 1 year, then every 3 months.

## Pneumocystic Carinii Pneumonia (PCP) Prophylaxis

- All patients will receive PCP prophylaxis for life

	Drug	Adverse Effects
Agent of Choice	Trimethoprim/sulfamethoxazole (TMP/SMX, Septra®, Bactrim®, Cotrim®) <ul style="list-style-type: none"> <li>1 double-strength (DS) tab PO MWF</li> <li>1 DS tab PO bid Sat/Sun only</li> </ul>	GI upset (N/V, anorexia) Rash, urticaria Thrombocytopenia Nephrotoxicity
Alternatives (if sulfa allergy)	Dapsone <ul style="list-style-type: none"> <li>&lt; 70 kg: 50 mg PO MWF</li> <li>≥ 70 kg: 100 mg PO MWF</li> </ul>	Hemolytic anemia (check for G6PD deficiency) Methemoglobinemia
	Pentamidine (Nebupent®) <ul style="list-style-type: none"> <li>300 mg q Month</li> </ul>	Cough, dyspnea, wheezing

## Aspergillus Prophylaxis

- All patients will receive prophylaxis with voriconazole for 3 months post transplant
- All patients will receive prophylaxis with inhaled amphotericin B for \_\_\_ months post transplant

Drug	Adverse Effects	Drug Interaction
Voriconazole (Vfend®) <ul style="list-style-type: none"> <li>200 mg IV/PO bid</li> </ul>	Visual changes (photophobia, color changes, blurred vision)	Can increase Prograf, Neoral and Rapamune levels.
Amphotericin B (conventional) <ul style="list-style-type: none"> <li>20 mg inh bid</li> </ul>	Wheezing, cough, SOB, taste perversion, nausea, vomiting	

## Thrush Prophylaxis

- All patients will receive prophylaxis for life

	Drug	Adverse Effects
Agent of Choice	Clotrimazole (Mycelex®) Troche <ul style="list-style-type: none"> <li>10 mg PO tid</li> </ul>	Nausea/vomiting
Alternatives	Nystatin (Mycostatin®) <ul style="list-style-type: none"> <li>5 ml swish/swallow tid</li> </ul>	Nausea/vomiting/diarrhea Abdominal pain

## Toxoplasma Prophylaxis

- Transplant patients who are at high risk [donor toxo ab (+) and recipient toxo (-)] for developing toxoplasma infection will receive prophylaxis with pyrimethamine and folic acid for 6 weeks.

Drug	Adverse Effects
Pyrimethamine (Daraprim®) 25 mg PO daily	Pancytopenia, GI upset
Folic acid 1 mg daily	Flushing, rash