

**Maine Medical Center
Transplant Program
Policies and Procedures
Antimicrobial Prophylaxis Policy**

Purpose

Infection after kidney transplantation is the most common complication within the first year and develops in up to 50% of recipients. The mainstay of antimicrobial management after solid organ transplantation is the prevention and treatment of such infections. Transplant recipients are at greatest infection risk within the first 3 months when immunosuppression is most intense and again after rejection rescue therapy. Post-transplant infections derive from exogenous (allograft itself, blood transfusions, environment), and endogenous sources (reactivation of latent infection).

Policy

In order to prevent infection in patients receiving immunosuppressive therapy post-transplantation, the following steps will be taken:

1. The donor's medical history is carefully reviewed, with respect to vaccinations, and unusual exposures to infections (e.g. travel to endemic areas, drug abuse, risky sexual behavior).
2. The patient will be risk stratified for post transplant infection by examining donor and recipient serologies.
3. Pharmacologic measures are taken to prevent infection and include the following:
 - Administration of prophylactic antimicrobial therapy during the first few months post transplant when immunosuppression of the patient is highest.
 - Administration of antibiotic prophylaxis against infective endocarditis and PCP.
 - Period vaccinations per Centers for Disease Control and Prevention guidelines regarding administration of vaccines in immunosuppressed persons.

Procedures

All patients who receive immunosuppressive therapy will also receive infection prophylaxis per the following:

Cytomegalovirus

CMV is a most important pathogen post-transplantation. Both the direct and indirect effects of CMV infection can have profound results on long term patient and graft survival. Pharmacological treatment for prevention of CMV is based on the serostatus of the donor and the recipient, immunosuppressive regimen and blood transfusions the kidney donor may have received during time of recovery. Prophylaxis will be administered as follows:

- Oral valganciclovir is the drug of choice for preventing CMV infection in at risk patients (CMV D+/R-, CMV D+/R+, CMV D-/R+)
- The duration of valganciclovir prophylaxis depends on the at risk group
 - 12 weeks for CMV D+/R+, CMV D-/R+
 - 24 weeks for CMV D+/R-
- For patients with an eGFR >60mls/min, the target daily valganciclovir dose is 900mg QD
- For patients with an eGFR 60-40mls/min, the target daily valganciclovir dose is 450mg QD
- For patients with an eGFR 25-39mls/min, the target valganciclovir dose is 450mg QOD
- For patients with an eGFR 10-24mls/min, the target valganciclovir dose is 450mg twice weekly
- For patients with an eGFR <10mls/min, valganciclovir is used with caution (no more than once per week).

Required post discontinuation CMV PCR Surveillance

1. Negligible risk CMV D-/R-: CMV PCR is not required
2. Intermediate risk CMV D-/R+ and D+/R+ Check CMV PCR at 4 month visit
3. High Risk CMV D+/R-: CMV PCR Required at months 7, 8, 9, 10, 11 and 12

If the kidney donor and recipient are both CMV seronegative (CMV D-/R-), a 3-month course of Acyclovir is used. The rationale is to prevent non-CMV herpes virus infections. The dose of acyclovir is titrated according to the recipients GFR (see SCM order set (Transplant Antimicrobial Prophylaxis).

Epstein Barr Virus

EBV is a member of the herpes virus family to which most adults have been exposed during adolescence. Seronegative recipients of seropositive grafts (usually children and young adults) are at significant risk of developing Epstein Barr viremia with consequent risk of developing post transplant lymphoproliferative disorder (PTLD), a life threatening complication. Such patients (EBV D+/R-) need prolonged antiviral prophylaxis. Clinical trial data to guide such therapy is not available. Discussions have been held and the following policy has been agreed upon for high risk patients:

- All EBV D+/R- patients will receive 6 months prophylaxis
- The optimal agent remains unclear. Both acyclovir and valganciclovir are effective. If the patient is also at risk of CMV, the latter agent should be chosen
- The value of routine EBV PCR testing is unclear and is no longer routinely recommended. EBV PCR testing continues to be of value in the evaluation of PTLD however
- The presence of viremia after discontinuation of prophylaxis necessitates reintroduction of antiviral medication and consideration of reducing immunosuppression.

Fungal Disease

Fungal disease is an important source of morbidity and mortality post-transplant. Candidiasis is the most common fungal infection. Except for the effective prevention of oral thrush with clotrimazole lozenges or oral nystatin solution, there is no current antimicrobial prophylactic regimen to utilize during the initial hospitalization to lessen later fungal disease.

Bacterial Infections

Bacterial infections occur in approximately 47% of kidney transplant recipients. Urinary tract infections are the most common bacterial infection. Bacterial infection is the most common cause of infection in all types of transplant recipients. All recipients receive in the Post transplant period Bactrim SS for one year. If patient is sulfa allergic, atovaquone, pentamidine or dapsone may be used for prevention of PCP.

Dental Prophylaxis

Transplant recipients historically have been advised to take prophylactic antibiotics before dental work is performed. The evidence basis for this recommendation has been reviewed and has been found to lack rigor. Therefore, Maine Transplant Program no longer recommends prophylactic antibiotics for patients whose sole indication is immunosuppression after kidney transplantation

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Revised 10/31/07, 6/10/09, 5/26/11, 10/26/11, 2/12/13, 3/26/14, 1/19/16, 2/12/16, 12/6/16, 6/5/17, 7/8/19, 6/28/22

Antimicrobial Prophylaxis Schedule and Dosing

Cytomegalovirus:

Valganciclovir PO indicated for all patients, unless donor and recipient are both CMV negative.
Administered for 3 months post txn and 1 month post use of antilymphocyte preparations.

Dose based on estimated GFR

<u>Estimated GFR</u>	<u>Valganciclovir Dose:</u>
> 60 ml/min	900 mg daily PO
40 - 60 ml/min	450mg qd PO
25 – 39 ml/min	450mg QOD PO
10 – 24 ml/min	450mg twice weekly PO
< 10 ml/min	Use with caution. Dose after dialysis

D(+)/R(-) recipients will receive prophylaxis for 6 months after transplantation

Herpes Virus:

CMV D-R-

Receive Acyclovir according to GFR

<u>eGFR</u>	<u>Acyclovir Dose</u>
>10 ml/min	400mg bid
<10 ml/min	400mg daily

Duration: 12 weeks

Pneumocystis:

Indications: All patients

Initiated at the same time as calcineurin inhibitor therapy and continued for the first year post transplant

1st line: TMP/SMX (cotrimoxazole, Bactrim) 1 single strength tablet PO qd.

2nd line:

- Aerosolized Pentamidine 300mg Neb q month is 2nd line treatment of choice
- Atovaquone 1500mg PO qd may also be used

3rd line: Dapsone 100mg PO once weekly. Check G6PD and do not use if deficient.

Candidiasis:

Administered during the first month post txn and during subsequent treatment of rejection with either methylprednisolone or antilymphocyte preparations

1st line: clotrimazole troche 10 mg, PO, TID for 1 month

2nd Line: fluconazole 50mg, PO, qd for 1 month (NB Pharmacokinetic drug interactions with CI, mTORi)

Urinary Tract Infections:

Covered by the Bactrim prophylaxis for pneumocystis.

For patients not on Bactrim who are high risk for UTI:

Cephalexin 250 mg PO qhs

Amoxicillin 500mg/d

Ciprofloxacin 250mg po daily only recommended if there are no other options

Gamma Globulin Treatment

Background

Gamma globulin deficiency is common after kidney transplantation

- Approximately 40% within first year post transplantation
- Is severe (defined <400mg/dl) in 15%
- Associates with significant risk of infection
- Associates with markedly increased mortality risk (RR~21)

IVIg Treatment

- No data on IVIg treatment for hypogammaglobulinemia post kidney transplant
- Pros: May reduce risk of recurrent infection
- Cons:
 - Expense
 - Risk of AKI/Hemolysis/Allergy

Protocol

1. Check total Ig level when post transplant patients are experiencing multiple infections (defined as >3 infections in 12 months)
2. Consider treating when IgG<400mg/dl
3. Rx Privigen start at lowest dose of 300mg/kg every 3 weeks
4. Prehydrate with NS 10 to 20 mL/kg to mitigate AKI risk
 - Premedication not required on initial dose unless pt experiences SAEs
 - Monitor kidney function
5. Repeat 21 day trough Ig levels after 3 months with goal to maintain level >400mg/dl