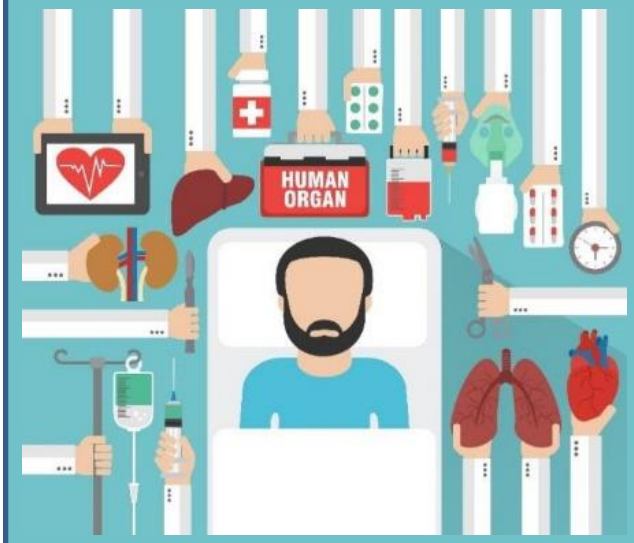

Solid Organ Transplant Infection Prophylaxis Handbook

Transplant Infectious Diseases

Ajmera Transplant Program
Toronto General Hospital

Approved by the UHN Pharmacy & Therapeutic Committee in Dec. 9, 2022
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Transplant Infectious Diseases

Solid Organ Transplant Infection Prophylaxis Handbook

THE TORONTO TRANSPLANT ID PROGRAM *for infection-free transplantation*

UHN Soham & Shaila Ajmera Family Transplant Centre

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TABLE 1. INFECTIOUS DISEASE SCREENING FOR CANDIDATES AND DONORS PRIOR TO TRANSPLANTATION

TEST	CANDIDATE	DECEASED DONOR	LIVING DONOR
Viral			
HIV			
Human immunodeficiency virus (HIV) antibody/antigen (fourth Generation HIV screening test)	X	X	X
HIV nucleic acid amplification testing (NAT) (High Risk Only)		X	X
Cytomegalovirus (CMV) IgG antibody	X	X	X
Hepatitis B virus (HBV)			
HBV surface antigen (HBsAg)	X	X	X
HBV core antibody (HBcAb-IgM and IgG, or total core antibody)	X	X	X
HBV surface antibody (HBsAb) (High Risk Only)	X		
HBV NAT (High Risk Only)	X	X	X
Hepatitis C virus (HCV)			
HCV antibody (High Risk Only)	X	X	X
HCV NAT (High Risk Only)	X	X	X
Epstein-Barr virus (EBV) antibody (EBV, VCA IgG, IgM)	X	X	X
West Nile virus serology (April – October)			X
VZV IgG	X	X	X
Measles IgG	X	X	X
Parasitic			
Toxoplasma IgG antibody	X	X	X
Strongyloides IgG (Tropics, subtropics, warm temperate regions)	X	X	X
Trypanosma cruzi serology (Latin America)	X	X	X
Fungal			
Coccidiodes serology (Southern California, Arizona,. 2019)	X	X	X
Bacterial			
Syphilis	X	X	X
Rapid plasma reagin (RPR)			
Tuberculosis	X		X
Purified protein derivative (PPD) or Interferon gamma release assay (IGRA)			
Urine culture		X	
Blood culture		X	

(Modified from Malinis et al, Clinical Transplantation. 2019;33:e13548.)

TABLE 2. SUMMARY OF 2012 CSA INCREASED-RISK DONOR CRITERIA

CSA CRITERIA FOR INCREASED-RISK DONORS[A]
Nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years.
Men who have had sex with another man in the preceding 5 years.
Persons who have engaged in sex in exchange for money or drugs in the preceding five years.
Persons who have had sex in the preceding 12 mo with any of the above persons or a person known or suspected to have HIV, HCV, or HBV infection.
Exposure in preceding 12 mo through percutaneous inoculation or open wound.
Prison, lock up, jail or juvenile detention >72 hr in the past 12 mo.
Nonsterile tattooing, piercings in the past 12 mo.
Close contact with anyone with clinically active viral hepatitis (living in the same house where kitchen and bathroom are shared) in the past 12 mo.

CSA, Canadian Standards Association; HIV, human immunodeficiency virus; HCV, hepatitis C virus; HBV, hepatitis B virus.
[A]Adapted from CSA standards 2012, Annex E.

TABLE 3. RISK PER 10,000 DONORS OF AN HIV INFECTION OCCURRING DURING THE WINDOW PERIOD, BY ELISA AND NAT. ASSUMES A WP OF 21 DAYS FOR ELISA AND 7 DAYS FOR NAT

RISK CATEGORY	ELISA PER 10,000	NAT + ELISA PER 10,000	RISK OF WINDOW PERIOD INFECTION FOR NAT AND ELISA EXPRESSED AS RATIO
MEN WHO HAVE SEX WITH MEN	5.8 (5.2-6.6)	2.4 (2.1-2.7)	1:4167
INTRAVENOUS DRUG USE	6.6 (6.1-7.2)	2.7 (2.5-3.0)	1:3704
COMMERCIAL SEX WORKER	3.7 (3.0-4.8)	1.5 (1.2-2.0)	1:6667
SEX WITH A PARTNER IN ABOVE CATEGORIES	0.7 (0.5-0.9)	0.3 (0.2-0.4)	1:33,333
PERCUTANEOUS INJURY RESULTING IN HIV EXPOSURE THROUGH BLOOD	1.5 (0.8-2.4)	0.6 (0.4-1.0)	1:16,667
INCARCERATED	1.0 (0.8-1.2)	0.4 (0.3-0.5)	1:25,000

ELISA, enzyme-linked immunosorbent assay; HIV, human immunodeficiency virus; NAT, nucleic acid testing; WP, window period.

TABLE 4. RISK PER 10,000 DONORS OF AN HIV INFECTION OCCURRING DURING THE WINDOW PERIOD, BY ELISA AND NAT

RISK CATEGORY	ELISA PER 10,000	NAT AND ELISA PER 10,000	RISK OF WINDOW PERIOD INFECTION FOR NAT AND ELISA EXPRESSED AS RATIO
MEN WHO HAVE SEX WITH MEN	14.3 (10.7 - 17.3)	1.5 (1.1 - 1.8)	1:6667
INTRAVENOUS DRUG USE	377.4 (346.0 - 412.1)	40.8 (37.4 - 44.6)	1:245
COMMERCIAL SEX WORKER	270.8 (242.6 - 298.9)	29.1 (26.1 - 32.2)	1:344
SEX WITH A PARTNER IN ABOVE CATEGORIES	168.3 (157.7 - 191.4)	18.0 (16.9 - 20.5)	1:556
PERCUTANEOUS INJURY RESULTING IN HIV EXPOSURE THROUGH BLOOD	13.9 (2.9 - 44.6)	1.4 (0.3 - 4.3)	1:7143
INCARCERATED	107.8 (102.4 - 116.7)	11.5 (10.9 - 12.5)	1:870

Assumes a WP of 70 days for ELISA and 7 days for NAT.

WP, window period; HCV, hepatitis C virus; ELISA, enzyme-linked immunosorbent assay; NAT, nucleic acid testing.

TABLE 5. INITIAL PROPHYLAXIS CONSIDERATIONS IN SOLID ORGAN TRANSPLANT RECIPIENTS

ORGAN	USUAL BACTERIAL PRE-OP PROPHYLAXIS	VIRAL CMV[1]	PJP	FUNGAL
KIDNEY	Cefazolin 2g IV push (60 minutes prior to incision)	Valganciclovir (VGCV) -D+/ R- -R+ with ATG	TMP-SMX, SS 1 tablet M/ W/ F	Nystatin 100,000 units swish and swallow qid x3 months
KIDNEY/ PANCREAS	Cefazolin 2g IV push (60 minutes prior to incision)	VGCV -D+/ R- -R+ with ATG	TMP-SMX, SS 1 tablet M/ W/ F	Fluconazole 400mg IV x1 pre-op for SPK 800mg IV x1 pre-op for PTA and PAK Nystatin 500,000 units swish and swallow qid x3 months
HEART	Cefazolin 2g IV push (60 minutes prior to incision)	VGCV -D+/ R- -R+ with ATG	TMP-SMX, SS 1 tablet M/ W/ F	Caspofungin 70mg IV loading dose followed by 50mg daily IV during initial hospital stay. Then switch to Nystatin 100,000 units swish and swallow qid x3 months at discharge
LIVER	Cefazolin 2g IV (60 minutes prior to incision)	CMV D+/ R- High risk of VGCV	TMP-SMX, SS 1 tablet M/ W/ F 1 year	Nystatin 100,000 units swish and swallow qid x3 months. Consider systemic antifungal prophylaxis if risk factors are present (Table 13)
INTESTINE	Piperacillin-Tazobactam 4.5g IV q8h x 72hrs	VGCV -D+/ R- -R+	TMP-SMX, SS 1 tablet M/ W/ F	Fluconazole 400mg IV on day 0 post- op; or if previous exposure or resistance to azoles start caspofungin 70mg IV loading dose followed by 50mg IV daily
LUNG	Piperacillin-Tazobactam 4.5g IV q8h x 72hrs Please follow the recommendations for Cystic Fibrosis patients	VGCV -D+/ R- -R+	TMP-SMX, SS 1 tablet M/ W/ F	Consider systemic antifungal prophylaxis based on the history of pre-transplant colonization or IFI (pg 24) If systemic antifungal not indicated, Nystatin 500,000 units swish and swallow qid for 3 months at discharge

[1]CMV low and intermediate risk, please consult full table

TABLE 6. BACTERIAL PROPHYLAXIS IN SOT

ORGAN	USUAL PRE-OPERATIVE PROPHYLAXIS[1]	CONSIDERATIONS
KIDNEY	Cefazolin 2g IV push (30 minutes prior to incision)	If documented anaphylaxis to beta- lactam or MRSA positive patient: Vancomycin 1g[3] IV infused over at least one hour
KIDNEY/ PANCREAS	Cefazolin 2g IV push (30 minutes prior to incision)	If documented anaphylaxis to beta- lactam or MRSA positive patient: Vancomycin 1g[3] IV infused over at least one hour
ALLO ISLET CELL TRANSPLANT AND TOTAL PANCREATECTOMY WITH AUTO-ISLET (TPIAT)	Piperacillin-Tazobactam 4.5g IV q8 hr x 72h	
HEART	Cefazolin 2g[2] IV push just before the procedure	If documented anaphylaxis to beta- lactam or MRSA positive patient: Vancomycin 1g[3] IV infused over at least one hour
LIVER	Cefazolin 2g[2] IV push (60 minutes prior to incision)	If documented anaphylaxis to beta- lactam or MRSA positive patient: Vancomycin 1g[3] IV infused over at least one hour
INTESTINE	Pre-op dose is pip-tazo 4.5g IV x1 pre-op (60 minutes prior to incision) Post-op regimen is q8h for 72 hours	Ciprofloxacin 400mg IV and Metronidazole 500mg IV OR For MRSA positive patients give Vancomycin 1g[3] IV infused over at least one hour (90 min prior to incision)
	NON-CYSTIC FIBROSIS PATIENT -Piperacillin-Tazobactam 4.5g IV q8h x 72hrs CYSTIC FIBROSIS PATIENT (*B cepacia* +ve and –ve) Please follow the recommendations below	

[1] Please adapt according to renal function if applicable
[2] 3g IV for patient weight ≥120 kg
[3] Vancomycin dosing according to patient weight: <80kg 1g, 80-120kg 1.5g, >120kg 2g

LUNG TRANSPLANT BACTERIAL PROPHYLAXIS

NON-CYSTIC FIBROSIS PATIENT

POST-OP PROPHYLAXIS:

- **Piperacillin-Tazobactam** 4.5g IV q8h x 72hrs →Stop.

If clinical concern after 72h, switch to culture-directed antibiotic or de-escalate to one of the following:

- **Ceftriaxone** 1g IV q24h.
- **Amoxicillin-Clavulanate** 875mg PO q12h.
- **Moxifloxacin** 400mg PO/ IV q24h (if penicillin/ cephalosporin allergy).

If cultured organism is not sensitive to de-escalation antibiotics, continue pipercillin/tazobactam for severe infections.

If penicillin allergic → use: Ciprofloxacin 400mg IV q12h and Vancomycin 1g IV q12h.

Review donor bronchoalveolar lavage (BAL) and blood cultures done at donor site at 24h, 48h, 72h and 7 days post retrieval.

CYSTIC FIBROSIS PATIENT (B. cepacia +ve and –ve)

If patient was receiving antibiotics for an exacerbation immediately prior to transplant, continue the same antibiotics during and following surgery.

If patient was not receiving antibiotics, check patient's chart for antibiotic protocol combination based on prior standard sputum cultures.

If none of these data are available, use default regimen consisting of (take allergies into account):

Burkholderia cepacia NEGATIVE:

- **Ceftazidime**: 3g IV q8h x 14 days.
- **Meropenem**: 2g IV q8h x 14 days.
- **Tobramycin** inhaled 160mg bid {or TOBI podhaler 112mg bid (4 capsules) if available} or Colisitin inhaled 75mg bid x 3 months (use whichever inhaled drug patient was receiving pre-transplant).

Burkholderia cepacia POSITIVE:

- **Meropenem**: 2g IV q8h x 21 days.
- **Ceftazidime**: 3g IV q8h x 21 days.
- **Azithromycin:** 500mg IV daily x 21 days.
- **Tobramycin:** inhaled 160mg bid OR Colistin 75mg by inhalation bid.

We suggest considering previous colonization in patients in whom the transplant requires abdominal manipulation, consult transplant infectious diseases.

Once discharged, continue Tobramycin inhaled 160mg bid (or TOBI podhaler inh 112mg bid if available) or Colistin inhaled 75mg bid for 3 months.[1]

[1]Colistin inhaled only covered for CF patients, EAP for non CF. (Tobramycin should be first line for non-CF).

Pneumocystis jirovecii PROPHYLAXIS

- Starting by week two (2).

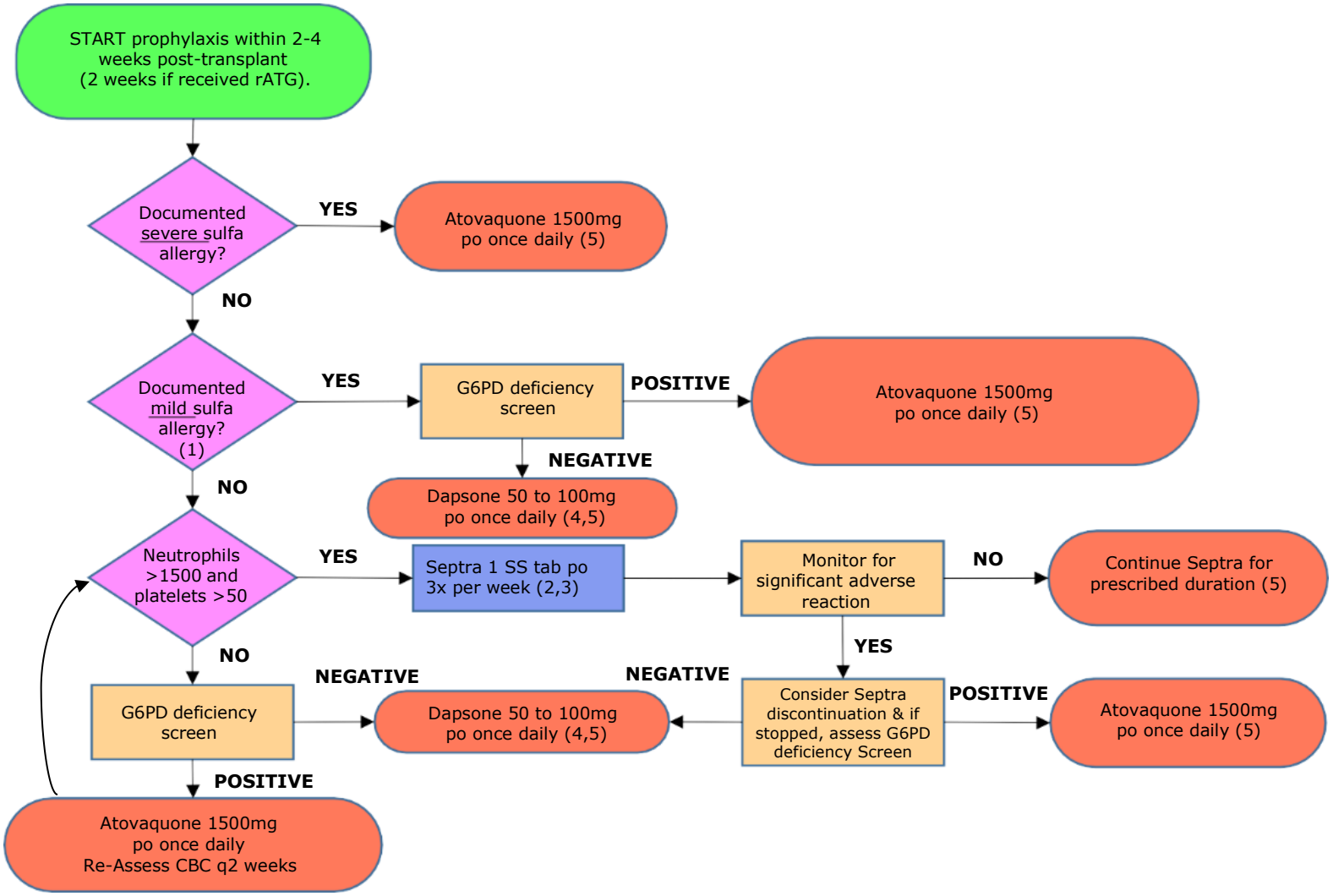
- For duration and dose of trimethoprim/sulfamethoxazole (TMP-SMX, Septra) prophylaxis, see table 7 below:

Table 7. DURATION AND DOSE OF TMP-SMX PROPHYLAXIS

TYPE OF TRANSPLANT	DOSE	DURATION
HEART	TMP-SMX, 1 single strength tablet daily If toxo mismatch: TPM-SMX 1 double strength tablet daily	Lifelong
LIVER	TMP-SMX, 1 single strength tablet M/ W/ F	1 year
KIDNEY	TMP-SMX, 1 single strength tablet M/ W/ F	Lifelong
INTESTINE	TMP-SMX, 1 single strength tablet M/ W/ F	Lifelong
LUNG	-Non-CF patients: TMP-SMX, 1 single strength tablet M/ W/ F -CF patients: TMP-SMX, 1 double strength tablet M/ W/ F	Lifelong

TMP-SMX, single strength tablet: 80/400 mg
TMP-SMX, double strength tablet: 160/800 mg

FIGURE 1. ALGORITHM FOR PRIMARY *Pneumocystis jirovecii* (PJP) PROPHYLAXIS IN SOLID ORGAN TRANSPLANT RECIPIENTS



FOOTNOTES

1) A thorough allergy history should be performed to avoid unnecessary use of second, third, or fourth line agents. Severe allergic reactions include anaphylaxis or desquamation (e.g. Stevens Johnson syndrome). Mild allergic reactions include maculopapular rash or pruritis.
2) Septra is the drug of choice as it is the most efficacious and least expensive.
3) For Cystic Fibrosis lung transplant recipients, use Septra 1 DS tab po 3 times per week.
4) Although not supported by published literature, other regimens such as dapsone 100 mg po Mon to Fri have been used.
5) Duration of prophylaxis is indefinite for most cases. Liver transplant recipients not on corticosteroids may receive 12 months.
6) Inhaled pentamidine 300 mg q4weeks is less efficacious, more costly, and logistically burdensome compared to other alternatives. This should be reserved as a fourth line option for patients intolerant to atovaquone.
7) Elevated liver enzymes are not a contraindication to starting Septra. If liver enzymes increase by 3 times baseline during Septra therapy, discontinue Septra. Perform G6PD deficiency screen and if negative, start dapsone; if positive, start atovaquone. Consider switching back to Septra once liver enzymes normalize.

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iii. Fishman, JA. Prevention of infection caused by pneumocystis carinii in transplant recipients. Clin Infect Dis 2001;33:1397-1405.
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ANTIVIRAL PROPHYLAXIS

HERPES VIRUS PROPHYLAXIS (HSV/ HZV)

- If the patient is currently receiving therapy with valganciclovir **(VGCV)** or ganciclovir **(GCV)** there is no necessity to add another antiviral.

- If the patient is NOT currently receiving therapy with valganciclovir or ganciclovir, add acyclovir 400mg PO q12h for 1 month post-transplant especially in liver transplant.

CYTOMEGALOVIRUS (CMV) PROPHYLAXIS

CURRENT DEFINITIONS:

- CMV INFECTION: Evidence of CMV replication regardless of symptoms (differs from latent CMV) defined as virus isolation or detection of viral proteins or nucleic acid in any body fluid or tissue specimen.

- CMV DISEASE: Evidence of CMV infection with attributable symptoms. CMV disease can be further categorized as a viral syndrome (i.e. fever, malaise, leukopenia, and/or thrombocytopenia), or as tissue invasive ("end organ") disease.

- **DNAemia:** Will be used instead of viremia, to reflect the detection of CMV DNA in blood or plasma (whether actively replicating virus or not).

PRE-TRANSPLANT TESTING:

- Perform donor and recipient CMV IgG serology for risk stratification.

- Repeat serologic testing at the time of transplant if pre-transplantation serology is negative.

- An equivocal serologic assay result in the donor should assume that it is positive. In the recipient, this result should be interpreted to assign the recipient to the highest appropriate CMV risk group for post-transplantation management decisions.

POST-TRANSPLANT MANAGEMENT:

- Universal prophylaxis and pre-emptive therapy are the main approaches for prevention of CMV in SOT.

- Universal prophylaxis entails the administration of antiviral medication to all patients or a subset of "at risk" patients and pre-emptive therapy involves monitoring for CMV in blood at regular intervals to detect early viral replication.

TABLE 8. COMPARISON OF PROPHYLAXIS VERSUS PREEMPTIVE THERAPY

	PROPHYLAXIS	PREEMPTIVE THERAPY
EARLY CMV DNAEMIA/ INFECTION	Rare	Common
PREVENTION OF CMV DISEASE	Good efficacy	Good efficacy
LATE CMV (INFECTION/ DISEASE)	Common	Rare
RESISTANCE	Uncommon	Uncommon (with weekly testing)
EASE OF IMPLEMENTATION	Relatively easy	More difficult
PREVENTION OF OTHER HERPES VIRUSES	Prevents HSV, VZV	Does not prevent
OTHER OPPORTUNISTIC INFECTIONS	May prevent	Unknown
COSTS	Drug costs	Monitoring costs
SAFETY	Drug side effects	Less drug toxicity
PREVENTION OF REJECTION	May prevent	Unknown
GRAFT SURVIVAL	May improve	May improve

-Start within the first 10-14 days post-transplant and continue for 6-9 months depending on the type of transplant and the risk of the recipient. The following table presents the recommended approaches to CMV prevention.

TABLE 9. CYTOMEGALOVIRUS PREVENTION IN SOLID ORGAN TRANSPLANT RECIPIENTS

ORGAN	SEROSTATUS	RISK LEVEL	RECOMMENDED
ALL	D-/R-	Low	Monitoring for clinical symptoms, prophylaxis against other herpes infections
KIDNEY	D+/R-	High	6 months of VGCV
	R+ with ATG	Intermediate	3 months of VGCV
LIVER	D+/R-	High	3 months of VGCV
	R+	Intermediate	Pre-emptive treatment
	R+ with ATG	Intermediate	3 months of VGCV
KIDNEY/PANCREAS	D+/R-	High	6 months of VGCV
	R+ with ATG	Intermediate	3 months of VGCV
HEART	D+/R-	High	6 months of VGCV
	R+ with ATG	Intermediate	3 months of VGCV
LUNG	D+/R-	High	9 months of VGCV
	R+	Intermediate	6 months of VGCV
INTESTINAL	D+/R-	High	6 months of GCV/VGCV + - surveillance after prophylaxis
	R+	Intermediate	3 months GCV/VGCV ± surveillance after prophylaxis

**All patients not on VGCV/GCV should receive Acyclovir 400mg BID po prophylaxis for 1 month.

ANTIVIRAL TREATMENT

-Viral load thresholds for triggering therapy in asymptomatic patients:

a) D+R-: ≥ 500 IU/mL
b) R+: ≥ 1000 IU/mL
c) D-R-: ≥ 500 IU/mL

TABLE 10. DOSAGE RECOMMENDATIONS FOR ANTIVIRALS FOR CMV

ANTIVIRAL	CRCL (ML/MIN) COCKROFT-GAULT FORMULA	MAINTENANCE/ PREVENTION DOSE	TREATMENT DOSE
GANCICLOVIR	>70 50-69 25-49 10-24 <10	5.0mg/ kg q24 h 2.5mg/kg q24 h 1.25mg/kg q24 h 0.625mg/kg q24 H 0.625mg/kg 3 times a week after hemodialysis	5.0mg/ kg q12 h 2.5mg/kg q12 h 2.5mg/kg q24 h 1.25mg/kg q24 h 1.25mg/kg 3 times a week after hemodialysis
VALGANCICLOVIR	>60 40-59 25-39 10-24 <10	900mg PO once daily 450mg PO once daily 450mg PO every 2 d 450mg twice weekly 100mg 3 times a week after hemodialysis (use valganciclovir solution)	900mg PO every 12h 450mg PO every 12h 450mg once daily 450mg every 2 d 200mg 3 times a week after hemodialysis (use valganciclovir solution)

Adapted from: Kotton CN, Kumar D, Caliendo AM, Huprikar S, Chou S, Danziger-Isakov L, Humar A; The Transplantation Society International CMV Consensus Group. The Third International Consensus Guidelines on the Management of Cytomegalovirus in Solid-organ Transplantation. Transplantation. 2018 Jun;102(6):900-931.

CMV MONITORING:

-If at any time ganciclovir/valganciclovir is stopped early, switch to weekly CMV PCR monitoring.

-Surveillance after prophylaxis may be considered in patients at increased risk for post-prophylaxis CMV disease weekly for 8 to 12 weeks after the end of prophylaxis.

1) CMV IgG or IgM testing is not routinely recommended post-transplant.

2) CMV PCR more than once a week is rarely indicated.

3) Life-long CMV monitoring is also rarely necessary.

4) CMV PCR monitoring while on antiviral prophylaxis should NOT be done unless there is a specific concern.

5) Post CMV infection or disease after the completion of therapy.

   a. Repeat CMV PCR every other week for two-three months.

6) Recipient positive (R+) for 8 weeks and Recipient negative (R-) for 12 weeks.

EPSTEIN-BARR VIRUS (EBV) MONITORING

1) EBV PCR monitoring is recommended in high-risk EBV D+/R- patients.
2) The frequency of monitoring should not exceed more than once a month (Suggested 1, 2, 3, 4, 5, 6, 9 and 12 months post-transplant).
3) Routine EBV testing or monitoring in asymptomatic R+ patients is NOT recommended.
4) EBV PCR testing should be only in patients with a strong suspicion of PTLD or EBV relatedsymptomatic disease.
5) EBV serology post-transplant should not be done.

BK VIRUS MONITORING

1) Screening for BKV by plasma PCR should be performed monthly until month 9, then every three months until two years post-transplant in renal transplant recipients.
2) Urine BKV PCR should not be used in screening for BK nephropathy.
3) BKV PCR testing is NOT routinely recommended in non-renal organ transplant recipients and should only be done if high suspicion of BK nephropathy.
4) BKV plasma PCR values >3 log 10 units should be followed by monthly monitoring to determinewhether the value is sustained or increasing.
5) Following intervention (i.e., reduction of immunosuppression), BKV viral load should be monitored every 2-4 weeks.
6) Immunosuppression reduction is associated with 10-15% risk of allograft rejection. Thus, allograft function should be closely monitored following immunosuppression reduction.
7) All renal transplant patients with unexplained allograft dysfunction should be tested for plasma BK viral load.
8) All histologic specimens of renal allograft biopsies should be tested for BKV or SV40 immunohistochemical (IHC) staining.

TABLE 11. PROTOCOL FOR HIV-INFECTED RECIPIENTS[1]

	Kidney Transplant	Liver Transplant	Heart Transplant	Lung Transplant	Kidney-Pancreas Transplant
Meet centre-specific inclusion Criteria	X	X	X	X	x
CD4 count >100 cells/µL (without history of OI)	NR[B]	X[C]	NR	NR	NR
CD4 count >200 cells/µL during 3mo prior to transplantation	X	X	X	X	X
Undetectable HIV viral load while receiving antiretroviral therapy	X	X	X	X	X
Detectable HIV viral load due to intolerance of HAART, HIV can be suppressed post-tx	NR	X	NR	NR	NR
Documented compliance with a stable antiretroviral regimen	X	X	X	X	X
Absence of active opportunistic infection and malignancy[d]	X	X	X	X	X
Absence of chronic wasting or severe malnutrition	X	X[E]	X	X	X
History of hepatitis B or C with lack of evidence of advanced fibrosis or cirrhosis	[F]	X[E]	[F]	[F]	[F]
Appropriate follow-up with providers experienced in the management of HIV	X	X	X	X	X
Ready access to immunosuppressive Medication therapeutic drug monitoring	X	X	X	X	X

All recommendations are strong, moderate for kidney and liver transplantation but strong, low for all others given the more limited experience with these populations.

NR, not recommended; NA, not applicable.
[b]There are currently insufficient data upon which to base recommendations regarding transplantation of non-liver recipients with lower CD4 counts but no history of OIs.
[c]With no history of AIDs defining illness such as opportunistic infection or malignancy.
[d]Patients with a previous history of progressive multifocal leukoencephalopathy, chronic interstitial cryptosporidiosis, primary central nervous system lymphoma, and visceral Kaposi's sarcoma were excluded from the original HIV-TR study. Patients with hepatocellular cancer can be considered for liver transplantation if they meet center-specific criteria. Data on the safety of transplantation in patients with HPV-related anal carcinoma in situ are insufficient to determine definitive guidance for patients with this malignancy.
[e]BMI > 21 kg/m2 (weak, low)
[f]Absence of data in current era of DAAs and in setting of non-liver HBV co-infected recipients. Patients with controlled hepatitis B on therapy may be considered. Caution for hepatitis C-infected patients, in whom DAA therapy has not been initiated.

[1]*Clinical Transplantation. 2019;33:e13499. doi.org/10.1111/ctr.13499*

TABLE 12. POTENTIAL PHARMACOKINETIC (PK) AND PHARMACODYNAMIC (PD) DRUG INTERACTIONS BETWEEN ANTIRETROVIRALS AND IMMUNOSUPPRESSANTS (CONSULT PHARMACY)[1]

	Glucocorticoids	Calcineurin inhibitors	mTOR inhibitors	Antimetabolites
NNRTI's				
PK	↓	↓	↓	NI
PD		RPV, EFV: QTc prolongation		
	EFV: ↑ TG, LDL, HDL Psychiatric AE's—depression, psychosis, suicidal ideation	RPV: ↑ Scr (no change in GFR)		
NRTI's				
PK	NE	NI	NE	NI
PD	TDF > TAF: Loss of BMD	TDF > TAF: Renal dysfunction, proteinuria, ↓phos		ZDV: Anemia and neutropenia 3TC, ABC—↑ lactic acidosis and mitochondrial toxicity ZDV/D4T—avoid with MMF—antagonistic
	d4T > ZDV > ABC: ↑ TG and LDL TAF:↑ TG, LDL, HDL			
Unboosted protease inhibitors (PI)[a]				
PK	↑↑	↑↑	↑↑	NI
PD		SQV/r: QTc prolongation ATV and LPV/r: ↑ risk CKD		GI intolerance
Boosted protease inhibitors (PIs)[a]				
PK	↑↑	↑↑↑	↑↑↑	NI
PD	DRV, FPV,IDV, LPV/r: Increased risk CV events IDV, LPV/r: Increase risk of diabetes COBI and r boosted PIs: ↑ TG, LDL, HDL			
Integrase inhibitors[b]				
PK	NE	NI	NI	NE
PD		RAL,DTG: ↑CPK and rhabdo DTG: ↑ Scr (no change in GFR)		
Pharmacokinetic boosters (cobicistat)				
PK	↑↑	↑↑↑	↑↑↑	NI
PD		COBI: ↑ Scr (no change in GFR)		
CCR5-antagonists				
PK	NE	NE	NE	NE
PD				
Fusion inhibitors				
PK	NE	NE	NE	NE
PD	NE	NE	NE	NE

↑↑, known significant drug interaction resulting in increased exposure due to CYP inhibition; ↑↑↑, known severe drug interaction resulting in increased exposure due to CYP inhibition; ↓, slight potential for decreased exposure due to CYP induction; NE, no interaction expected based on theoretical considerations; NI, no interaction found in clinical studies.

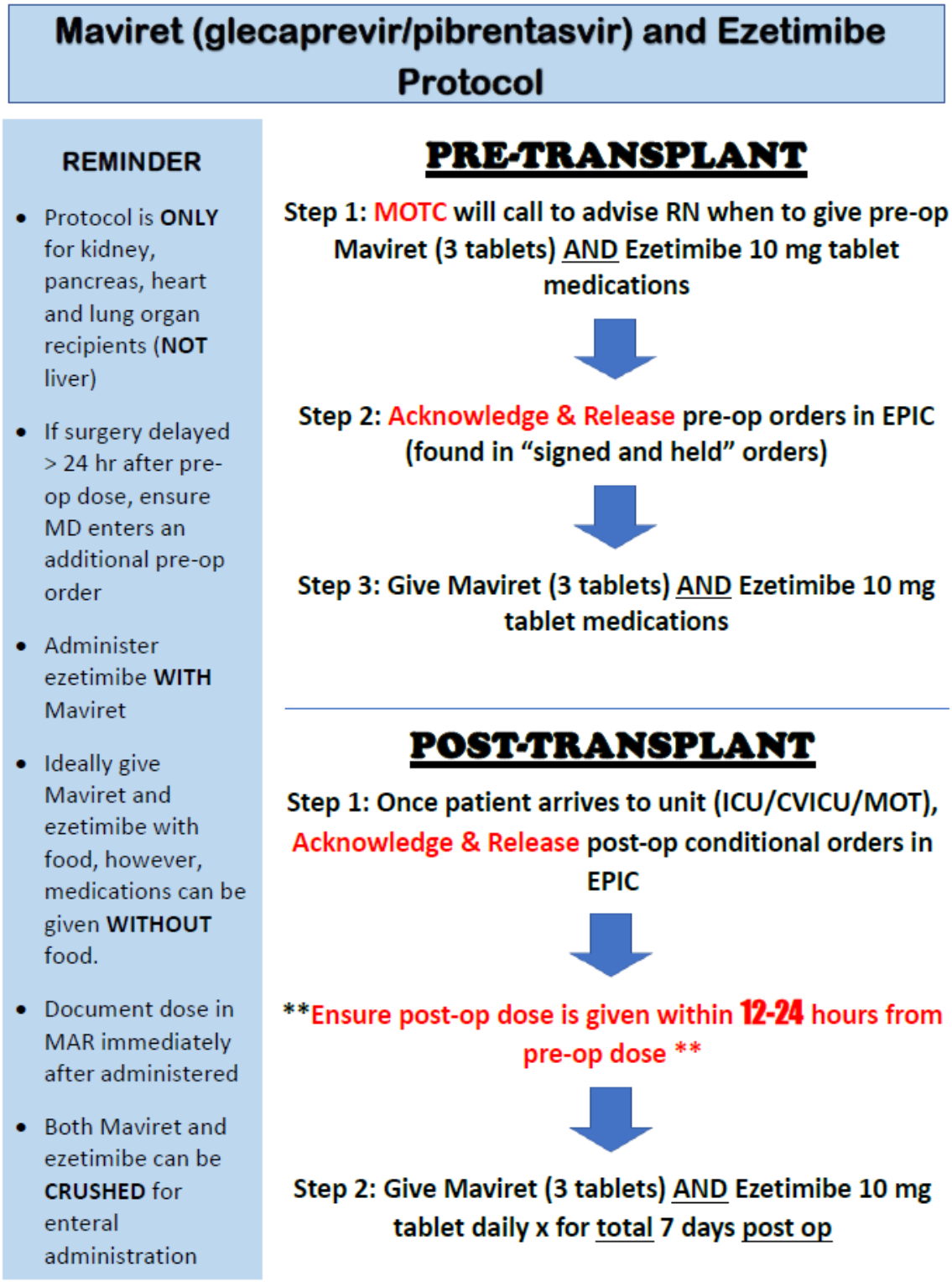
Drug name abbreviations: 3TC Lamivudine; ABC Abacavir; ATV Atazanavir; COBI Cobicistat'; D4T Stavudine; DDI Didanosine; DRV Darunavir; DTG Dolutegravir; EFV Efavirenz; FPV Fosamprenavir; IDV Indinavir; LPV Lopinavir; r Ritonavir; RAL Raltegravir; RPV Rilpivirine; SQV Saquinavir; TAF Tenofovir alafenamide; TDF Tenofovir disoproxil fumarate; ZDV Zidovudine.

[a]The degree of CYP inhibition may vary across the class of protease inhibitors.

[b]Integrase inhibitors combined with pharmacokinetic boosters such as cobicistat will result in increased exposure of glucocorticoids, calcineurin inhibitors, and mTOR inhibitors.

[1]Clinical Transplantation. 2019;33:e13499. doi.org/10.1111/ctr.13499

Figure 2: HCV prophylaxis in Non Liver SOT Recipients



ANTIFUNGAL PROPHYLAXIS
CANDIDA PROPHYLAXIS

Kidney Transplant:

-Nystatin 100,000 units swish and swallow qid x3 months.

Lung Transplant:

For any lung transplant recipient meeting 2 or more of the following criteria;

- ✓ Placement of ECMO (pre or post-op)
- ✓ Pre-transplant chest tube
- ✓ Immediate post-transplantation re-exploration of the thoracic cavity
- ✓ Donor or Recipient peri-operative positive BAL culture with *Candida* spp $>10^6$
- ✓ Antifungal Agent
- ✓ Fluconazole 400mg empirically (Pending speciation and susceptibility)
- ✓ If positive GM, then switch to voriconazole. Voriconazole recommended (Caspofungin may be used as second line in case of toxicity)
- ✓ Duration 4 weeks

Heart Transplant:

-Start**:** Caspofungin 70mg IV once, followed by 50mg IV daily during initial transplant hospital stay, then switch to Nystatin 100,000 units swish and swallow qid x3 months at discharge. CT chest 3, 6, and 9 months after the transplant.

Intestinal Transplant:

-Start: Fluconazole 200mg IV q24h x7 days.

Pancreas Transplant:

-Simultaneous Pancreas Kidney transplant: Fluconazole 400 mg x1 peri-operatively.

-Pancreas after kidney transplant (Normal Renal Function) Fluconazole 800mg IV x1 peri-operatively.

Liver Transplant:

-Nystatin 100,000 units swish and swallow qid x3 months or stop when prednisone dose is <10 mg daily.

-Consider systemic antifungal prophylaxis if any of the risk factors noted in Table 13 occur.

TABLE 13. RISK FACTORS FOR INVASIVE FUNGAL INFECTION (IFI) IN LIVER TRANSPLANT RECIPIENTS.

HIGH-RISK CRITERIA FOR IFI IN LIVER TRANSPLANT RECIPIENTS
Choledochojejunostomy anastomosis
Re-transplantation
Intraoperative use of >40 units of blood products
Pre-op Cr>177micro mol/L or any dialysis 48h pre-op
Candida colonization in the perioperative period
Return to the OR within 5 days post OLT

Pappas PG, Alexander BD, Andes DR, et al. Invasive fungal infections among organ transplant recipients: results of the Transplant-Associated Infection Surveillance Network (TRANSNET). Clin Infect Dis. 2010 Apr 15;50(8):1101-11.

More than one risk factor will require systemic antifungal prophylaxis:

- Fluconazole 400mg PO q24h for 21 days.
- If the patient has previous exposure or resistance to azoles start: caspofungin 70mg IV once, followed by 50mg IV q24h for 21 days.

Comments:

- A meta-analysis demonstrated that routine prophylaxis with fluconazole or lipid formulation of amphotericin B reduced the incidence of IFI following liver transplantation with comparable efficacy.

Evans JD, Morris PJ, Knight SR. Antifungal prophylaxis in liver transplantation: a systematic review and network meta-analysis. Am J Transplant. 2014;14(12):2765-2776.

- Comparisons between echinocandins and fluconazole for targeted fungal prophylaxis in liver transplant recipients note similar reductions in IFI though echinocandin use is associated with less *Aspergillus* colonization/infection.

-Winston DJ, Limaye AP, Pelletier S, et al. Randomized, double-blind trial of anidulafungin versus fluconazole for prophylaxis of invasive fungal infections in high-risk liver transplant recipients. Am J Transplant. 2014 Dec;14(12):2758-64.
-Saliba F, Pascher A, Cointault O, et al. TENPIN (Liver Transplant European Study Into the Prevention of Fungal Infection) Investigators; TENPIN Liver Transplant European Study Into the Prevention of Fungal Infection Investigators. Randomized trial of micafungin for the prevention of invasive fungal infection in high-risk liver transplant recipients. Clin Infect Dis. 2015 Apr 1;60(7):997-1006.

ASPERGILLUS PROPHYLAXIS

HEART TRANSPLANT

-Start prophylaxis with Caspofungin 70mg IV once, followed by 50mg IV daily during initial transplant hospital stay. For long and complicated hospital stays, consider continuing IV or switch to po voriconazole on a case to case basis.

-Low dose CT chest (NB: radiation exposure similar to plain CXR film) for screening at 1, 2 and 3 months, then stop.

-Screening low-dose CT scan of chest 3 months then q3 months until 1-year post-transplant.

LUNG TRANSPLANT

Aspergillus Protocol

Definitions

Diagnosis involves radiology, host factors/clinical picture, micro and histology.

Categories of Diagnosis

- **Probable IA** is diagnosed in the presence of radiological changes (nodule, cavitation or air crescent) if micro is positive from 2 or more contaminated sites (sputum) OR 1 BAL OR if Galactomannan (GM) is positive (>1) on BAL or serum with negative cultures.
- **Proven IA** is diagnosed if there is positive histology or culture from sterile tissue.

Clinical Syndromes

1. **Colonization**: Positive BAL culture or GM in the absence of symptoms or any change on CT scan of the chest.
2. **Tracheobronchitis**: Positive BAL culture or GM in the presence of abnormal respiratory secretions and airways AND absence of any change on CT scan of the chest.
3. **Bronchial anastomotic infection:** Positive BAL culture or GM with abnormal bronchial anastomotic site with relatively normal looking airways AND absence of any change on CT scan of the chest.
4. **Pulmonary IA**: Positive BAL culture or GM in the presence of symptoms or new radiological findings on CT scan of chest.
5. **Disseminated IA**: Positive blood culture or GM in the presence of symptoms or new radiological findings in two noncontiguous parts of the body.

Risk Factors for invasive Aspergillosis include;

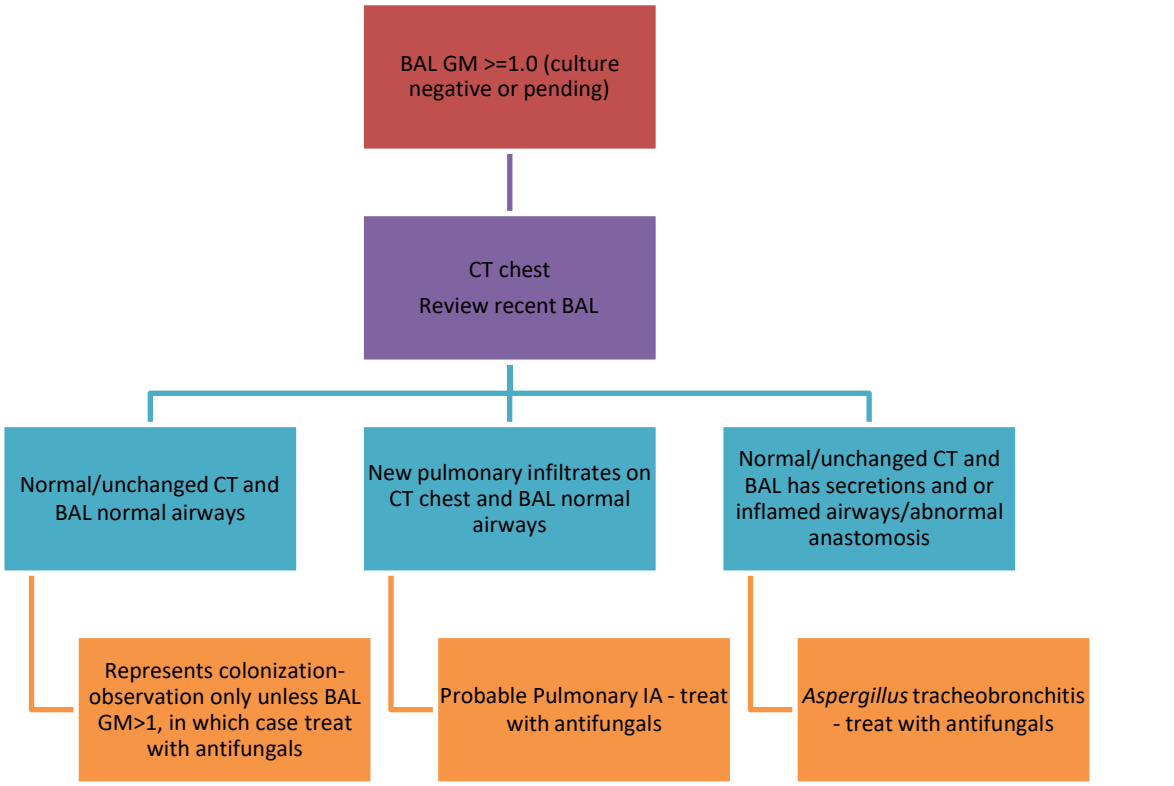
- Pre or Post Transplant *Aspergillus* colonization.
- Only 30% of IA cases are in these patients.
- 20-25% of lung transplant patients will be colonized with *Aspergillus.*
- Growth within 6 months before transplant confers greatest risk.
- Growth within 1 year post transplant confers increased risk.
- Administration of Solumedrol/Thymoglobulin.
- Single lung transplant.
- Bronchial stents.
- Anastomotic dehiscence.
- Acquired hypogammaglobulinemia (<400mg/dl).

Prophylaxis and Monitoring

Order GM in BAL in **ALL** lung transplant recipients undergoing bronchoscopy during first year of transplant ("BAL plus galactomannan" in standard transplant bronchoscopy order set). Also order GM in BAL in patient suspected of infection irrespective of duration of time from transplant.

- Start prophylaxis with voriconazole in lung transplant recipients with a history of pre-transplant colonization or history of invasive aspergillosis within six months prior to transplantwith concomitant pre-transplant immunosuppression (steroids, MMF, Calcineurin inhibitors).
- Voriconazole 6mg/kg PO q12h for 2 doses then 4mg/kg PO q12h thereafter. Alternatives in cases of suspected toxicities to voriconazole include:
    - Amphotericin B inhaled 10mg or 20mg bid in patients with negative cultures and GM index value less than one (colonization).
    - Caspofungin 70mg IV once, followed by 50mg IV daily.
    - Posaconazole: 300mg PO/IV (three 100 mg delayed-release tablets) two times a day on the first day, then 300mg once a day.
    - Isavuconazole: 200mg PO (two capsules) every 8hr for 6 doses followed by 200mg/day.
- Consult Transplant ID prior to initiating alternatives to azoles.
- Duration 6 weeks if week 6 BAL (GM, culture) is negative.
- Repeat CT scan of the chest at 6 weeks; if week 2 and 6 BAL are not done. If negative, can stop voriconazole.
- Persistently positive culture for Aspergillus or GM, continue prophylaxis or call Transplant ID.
- Consult Transplant ID if hepatotoxicity (increased liver function tests >3x normal) or significant worsening if abnormal initially.

FIGURE 3. ANTIFUNGAL PROPHYLACTIC STRATEGY IN LUNG TRANSPLANT RECIPIENTS

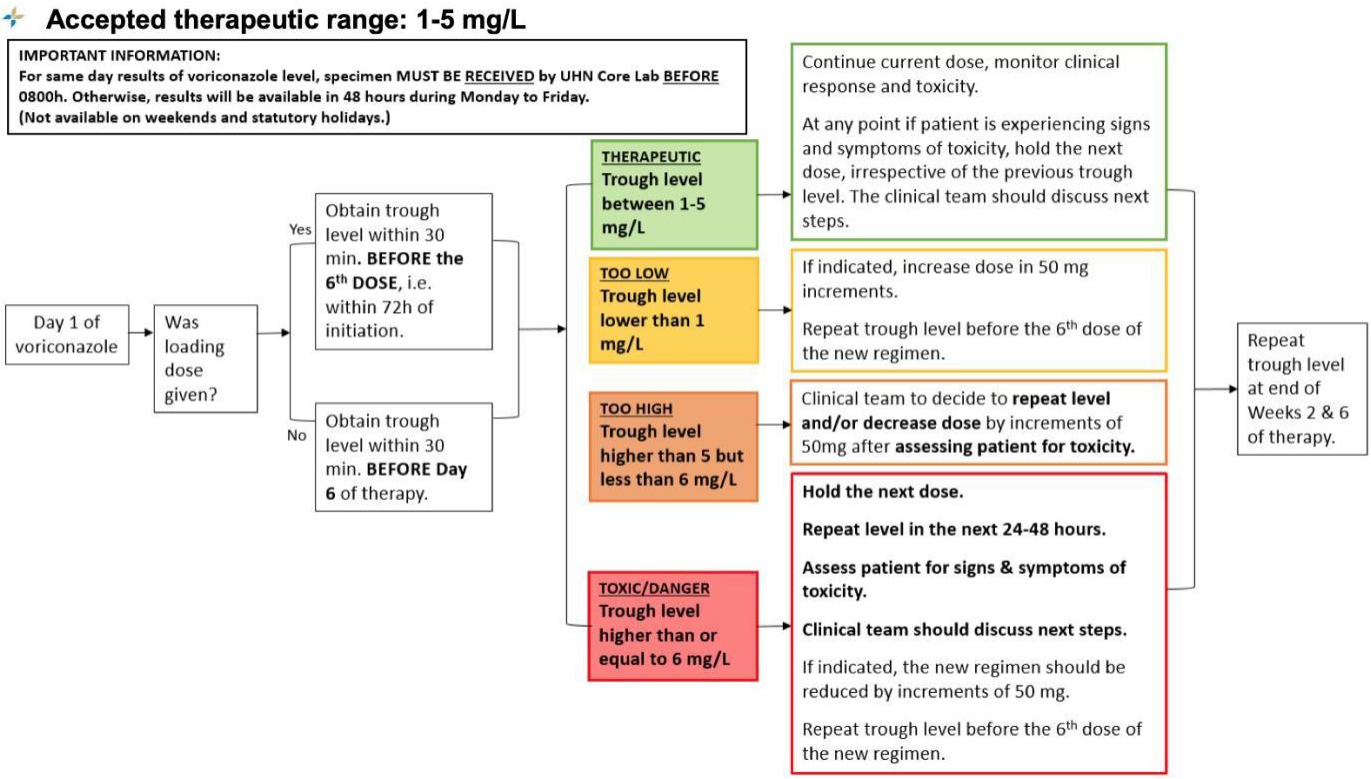


VORICONAZOLE DOSING RECOMMENDATIONS:

Dose:

-Invasive aspergillosis: 6 mg/kg IV or PO q12h x 2 doses, followed by 4mg/kg IV or PO q12h.

FIGURE 4. THERAPEUTIC DRUG MONITORING FOR VORICONAZOLE



-For more information on Voriconazole monitoring and adjustment visit:

https://www.antimicrobialstewardship.com/antimicrobials

TABLE 14. ADVERSE DRUG REACTIONS OF VORICONAZOLE

COMMON	Visual disturbances: “abnormal vision”, blurriness, color changes, enhanced vision, seen in 20.6% of patients but less than 1% required discontinuation, duration of abnormality usually less than 30 minutes, typically starting 30 minutesafter dosing.
OCCASIONAL	Increased transaminases (13%) and alkaline phosphatase, discontinuation requiredin 4-8%, rash 6%, hallucinations 4.3%, nausea and vomiting, increase in total bilirubin, encephalopathy (>5.5 mcg/ mL), osteitis, peripheral neuropathy
RARE	Squamous cell carcinoma

TABLE 15. COMMON DRUG INTERACTIONS WITH VORICONAZOLE

DRUG	INTERACTION	DOSING INFORMATION
TACROLIMUS	Tacrolimus AUC increased by 300%	When voriconazole is started, decrease tac dose by 1/3 to 2/3, monitor levels *Consult pharmacy for further dosing considerations and recommendations*
CYCLOSPORINE	Cyclosporine AUC increased by 70%	Decrease cyclosporine by ½ *Consult pharmacy for further dosing considerations and recommendations*
SIROLIMUS	Sirolimus serum concentrations are significantly increased; combination NOT recommended.	*Consult pharmacy for further dosing considerations and recommendations*

Review the rest of the medications that the patient is taking to avoid or manage interactions.

SCEDOSPORIUM AND Mucorales PROPHYLAXIS

- Assessment of microbial colonization patterns can also be used to guide peri-transplant prophylaxis.

- Any report of *Scedosporium* requires species identification.

- Start voriconazole therapy for 3 months if *Scedosporium apiospermum*.

- You can consider using Isavuconazole for prophylaxis in lung transplant recipients colonized with Mucorales. Consider consulting Transplant ID for management.

TUBERCULOSIS PROPHYLAXIS

- Pre-transplant or Post-transplant anti-tuberculous prophylaxis or therapy should be provided for SOT candidates/recipients with the following specific indications:

TABLE 16. INDICATIONS PRE-TRANSPLANT or POST-TRANSPLANT ANTI-TUBERCULOUS PROPHYLAXIS/ THERAPY

INDICATION
Tuberculin reactivity of ≥5mm before transplantationPositive interferon-gamma release assays (IGRAs)
History of tuberculin reactivity/positive IGRA without adequate prophylaxis
Recent conversion of tuberculin skin test or IGRA to positive
Radiographic evidence of old TB without prior prophylaxis; a chest CT scan should be performed in these patients to look for disseminated disease and to serve as a baseline study
History of inadequately treated active TB
Close contact with an individual with active pulmonary TB
Receipt of an allograft from a donor with latent TB or with a remote history of untreated or inadequately treated active TB

TABLE 17. TREATMENT OF LATENT TUBERCULOSIS

-The first step in treatment of latent TB is to exclude active TB. Patients with relevant symptoms such as cough >2 weeks, fevers, night sweats, weight loss and/or abnormal chest X-ray should be tested for acid-fast bacilli (smear, mycobacterial culture, and nucleic acid amplification testing).

-Sputum specimens (via cough or induction at least 8 hours apart and including at least one early-morning specimen).

	DRUGS	DURATION	SCHEDULE
STANDARD REGIMEN			
	INH	9 Months	Daily
ACCEPTABLE ALTERNATIVE REGIMENS			
	INH	6 Months	Daily
	INH/RMP	3 Months	Daily
	RMP	4 Months	Daily
	INH/RPT	3 Months	Once Weekly

INH= isoniazid, RMP=rifampin, RPT=rifapentine

- Dose Isoniazid: 5mg/kg (300mg max) PO daily.
- Dose Rifampin: 10mg/kg (600mg max) PO daily.
- Add Pyridoxine (vitamin B6) 50mg with Isoniazid PO every day may decrease neuropathy risk.

Daily use of levofloxacin or moxifloxacin for 9 months (*conditional recommendation, based on very weak evidence*) **is recommended**, based on evidence that later generation FQN are generally well tolerated and can adequately replace INH in active TB therapy. However, the tolerability and safety of long-term use of FQN are not well known; patients should be advised of this and monitored closely for adverse events including tendinitis. Consider consulting Transplant ID for management.

Monitoring liver function test:

- Age <35: only if needed or if there is clinical suspicion of liver disease.
- Age 35-50: month 1, 2 and 9.
- Age >50: monthly.

If liver transaminases increase beyond 5 times the upper limit of normal (or 3 times in the presence of symptoms) the LTBI regimen should be stopped.

- Pre-transplant liver candidates with latent tuberculosis, we suggest to wait until post-op to treat.
- Donor diagnosed with latent tuberculosis → give treatment to the recipient if it's a lung transplant.

TABLE 18. CRITERIA FOR THE DIAGNOSIS OF NON TUBERCULOUS MYCOBACTERIAL DISEASE

CLINICAL	PULMONARY OR SYSTEMIC SYMPTOMS	BOTH REQUIRED
RADIOLOGIC	Nodular or cavitary opacities on chest radiograph, or a high-resolution computed tomography scan that shows bronchiectasis with multiple small nodules.	
MICROBIOLOGIC	1. Positive culture results from at least two separate expectorated sputum samples. If the results are nondiagnostic, consider repeat sputum AFB smears and cultures or, 2. Positive culture results from at least one bronchial wash or lavage or, 3. Transbronchial or other lung biopsy with mycobacterial histologic features (granulomatous inflammation or AFB) and positive culture for NTM or biopsy showing mycobacterial histologic features (granulomatous inflammation or AFB) and one or more sputum or bronchial washings that are culture positive for NTM	

FIGURE 5. NTM Management In Lung Transplant Recipients with Positive Sputum for NTM Pre-Transplant

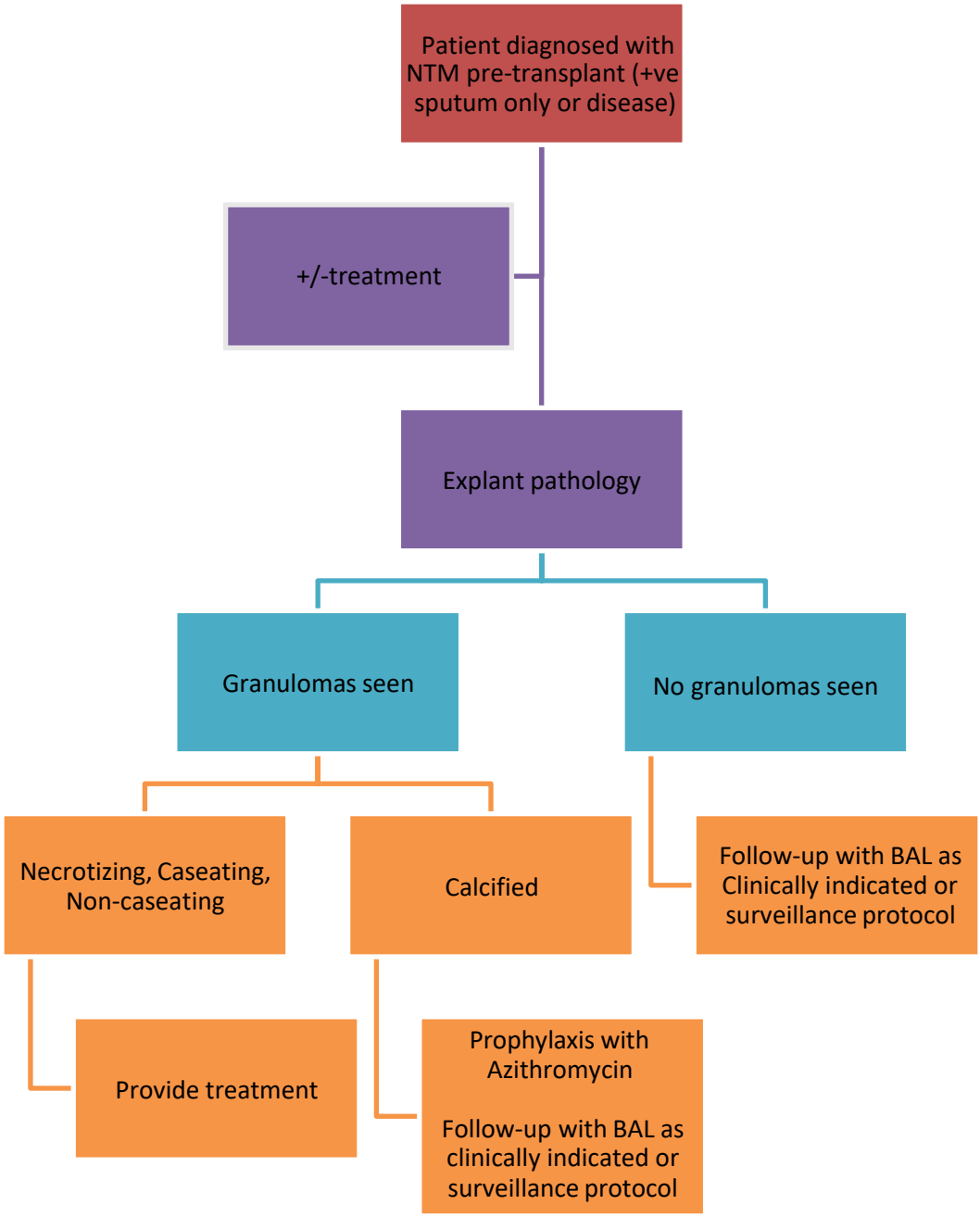


TABLE 19. RECOMMENDED TREATMENT REGIMENS FOR MYCOBACTERIUM AVIUM COMPLEX

ORGANISM	NO. OF DRUGS	PREFERRED DRUG REGIMEN	DOSING FREQUENCY
M. AVIUM COMPLEX			
NODULAR-BRONCHIECTATIC	3	Azithromycin is strongly preferred over clarithromycin in transplant patients (due to drug interaction between CNI's and clarithromycin) Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol	3 times weekly
CAVITARY	≥3	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol Amikacin IV (streptomycin)[b]	Daily (3 times weekly may be used with aminoglycosides)
REFRACTORY[C]	≥4	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol Amikacin inhalation or Amikacin IV (streptomycin)[b]	Daily (3 times weekly may be used with aminoglycosides)

[b]Consider for cavitary, extensive nodular/bronchiectatic disease or macrolide-resistant MAC. Amikacin or streptomycin may be given 3 times a week.
[c]Refractory disease is defined as remaining sputum culture positive after 6 months of guideline-based therapy.

TABLE 20. DOSING GUIDELINES FOR DRUGS USED IN THE MANAGEMENT OF NONTUBERCULOUS MYCOBACTERIAL PULMONARY DISEASE

Drug	Daily Dosing	Thrice Weekly Dosing	Hepatic Impairment	Renal Impairment
Oral				
Azithromycin	250–500 mg per day	500 mg per day	N/A	N/A
Ciprofloxacin	500–750 mg twice per day	N/A	N/A	250–500 mg dosed at intervals according to CrCl
Clarithromycin	500 mg twice per day	500 mg twice per day	N/A	Reduce dose by 50% if CrCl < 30 mL/min
Clofazimine[a]	100–200 mg per day	N/A	Caution in severe hepatic impairment	N/A
Doxycycline	100 mg once to twice a day	N/A	N/A	N/A
Ethambutol	15 mg/kg per day	25 mg/kg per day	N/A	Increase dosing interval (eg, 15–25 mg/kg, 3 times per week)
Isoniazid	5 mg/kg up to 300 mg per day	N/A	Caution	N/A
Linezolid	600 mg once or twice per day[b]	N/A	N/A	N/A
Moxifloxacin	400 mg per day	N/A	N/A	N/A
Rifabutin	150–300 mg per day (150 mg per day with clarithromycin)	300 mg per day	Caution	Reduce dose by 50% if CrCl < 30 mL/min
Rifampicin (rifampin)	10 mg/kg (450 mg or 600 mg) per day	600 mg per day	Caution	N/A
Trimethoprim/sulfamethoxazole	800 mg/160 mg tab twice daily	N/A	Caution	Reduce dose by 50% if CrCl15–30 mL/min
Parenteral				
Amikacin (IV)	10–15 mg/kg per day[c], adjusted according to drug level monitoring[d]	15–25 mg/kg per day[c], adjusted according to drug level monitoring[d]	N/A	Reduce dose or increase dosing interval (eg, 15 mg/kg, 2–3 times per week)
Cefoxitin (IV)	2–4 g 2–3 times daily (maximum daily dose is 12 g/day)	N/A	N/A	Reduce dose or increase dosing interval
Imipenem (IV)	500–1000 mg, 2–3 times per day	N/A	N/A	Reduce dose or increase dosing interval
Streptomycin (IV or IM)	10–15 mg/kg per day, adjusted according to drug level monitoring	15–25 mg/kg per day, adjusted according to drug level monitoring	N/A	Reduce dose or increase dosing interval (eg, 15 mg/kg, 2–3 times per week)
Tigecycline (IV)	25–50 mg once or twice per day[b]	N/A	25 mg once or twice daily per day in severe hepatic impairment	N/A
Inhalation				
Amikacin liposome inhalation suspension	590 mg per day	N/A	N/A	N/A
Amikacin, parenteral formulation	250–500 mg per day	N/A	N/A	N/A

Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline.Daley CL, Iaccarino JM, Lange C, Cambau E, Wallace RJ Jr, Andrejak C, Böttger EC, Brozek J,Griffith DE, Guglielmetti L, Huitt GA, Knight SL, Leitman P, Marras TK, Olivier KN, Santin M, Stout JE, Tortoli E, van Ingen J, Wagner D, Winthrop KL. Clin Infect Dis. 2020 Aug 14;71(4):e1-e36. doi: 10.1093/cid/ciaa241.

Amikacin liposome inhalation suspension is available by SAP only.

Mycobacterium abscessus

- Detection of *M. abscessus* prior to lung transplantation is a relative contraindication; however, this is controversial because local control and infection clearance is possible in patients with recurrent disease.

- Experts recommend eradication of NTM infection should be attempted prior to lung transplantation and all foreign bodies should be removed at the time of lung transplant, including lines and breast implants.

- Ideally, Pre-transplant patients with *M.abscessus* should have three sputum samples negative for AFB stain and preferably mycobacteria cultures for more than three months with stable radiological disease.

- Patients with *M.abscessus* disease on treatment with negative AFB and stable radiological disease can be listed after 6-8 weeks of therapy.

- These patients should be considered candidates for bilateral lung transplantation.

- In patients with *M. abscessus* colonization before transplant consider induction regimens other than anti-thymocyte globulin if possible, reducing the serum levels of tacrolimus and cyclosporine, treatment with immunoglobulin G if hypogammaglobulinemia exists. These patients would be treated with drugs at least 6-8 weeks prior to transplant.

- Empiric therapy consists of three drug regimens:

    - In *M. abscessus*, subspecies *abscessus* and *bolletii:* most isolates have active *erm* genes. In that case, the following drugs could be used: amikacin, cefoxitin, tigecycline, imipenem and linezolid.

    - In *M. abscessus*, subspecies massiliense: most isolates usually do not have active erm genes; therefore macrolides (azithromycin, clarithromycin) could be used along with two drugs from following: amikacin, cefoxitin, tigecycline, imipenem, and linezolid.

- Multidrug regimen could be continued in the post-transplant phase for minimal of weeks or more while the surveillance for *M. abscessus* isolation should continue with BAL, sputum and wound cultures.

- These patients should be considered for bilateral lung transplantation (as opposed to single lung transplant) to decrease disease burden and prevent reinfection of the graft.

- Cleaning of clinic, equipment and isolation procedures. Consider placing patients with *M. abscessus* disease in negative pressure rooms. Anyone who touches or cares for the infected sites such as wounds should wash their hands carefully with soap and water.

- The duration of treatment is at least 12 months of negative sputum cultures while on multidrug antibiotic therapy has been proposed.

- Consider consulting Transplant ID for management.

IMMUNIZATION

- The following table has the recommendations for vaccines in solid organ transplant recipients:

TABLE 21. VACCINE RECOMMENDATIONS IN SOT RECIPIENTS

VACCINE	PRE-TRANSPLANT	POST-TRANSPLANT	TIMING
MMR	+	-	**4 weeks before transplant**
ZOSTER RECOMBINANT INACTIVATED	>=50 y/o	+ for >=50 y/o	
INFLUENZA	+	+	**1 month post-transplant**
HEPATITIS B	+	+	
PCV13	+	+	
PPSV23	+	+	
HPV	+	+	
HIB	+	+	
COVID-19 MRNA	**+**	**+**	

- Wait at least 3-6 months post-transplant to restart vaccination.

- Live vaccines wait 4 weeks to transplant.

INFLUENZA VACCINE

- Recommended annually, high dose (60 µg per strain)

PNEUMOCOCCAL VACCINES

- There are two options of vaccines:

a) Pneumococcal polysaccharide 23-valent vaccine (PPSV 23)
b) Pneumococcal conjugate 13-valent vaccine (PCV 13)

- Patient with no previous vaccination: Administer 1 dose of PCV13, then at least 8 weeks later 1 dose of PPSV 23. This should be followed by another dose 5 years later of PPSV23.

HEPATITIS B VIRUS

- Better to vaccinate pre-transplant.
- Usual schedule: 0, 1, and 6 months.

Accelerated schedule: 3 doses 0, 1, 2 months or 0, 7, 21 days then 4th dose 6-12 months after the first dose.

- There are three options of vaccines:

a) Recombivax:
    a. 10mcg (1ml)-> Immunocompetent, pre-lung and pre-heart.
    b. 40mcg (1ml) -> Post-transplant, pre-kidney and pre-liver.

b) Engerix-B
    a. 20mcg (1ml): Immunocompetent, pre-lung and pre-heart.
    b. 40mcg (2ml): Post-transplant, pre-kidney and pre-liver.

c) Twinrix (combined HAV and HBV vaccine) can be used if additional immunity for HAV is desired (e.g. for travel or underlying liver disease).

HERPES ZOSTER

- Recommended pre- or post-transplant in patients >=50 years old: 2-dose series of Recombinant ZosterVaccine (RZV), 2-6 months apart.

MEASLES, MUMPS, and RUBELLA (MMR)

- Pre-transplant: Wait 4 weeks to transplant.
- Post-transplant: Consult Transplant ID to evaluate each individual case.

HUMAN PAPILLOMAVIRUS (HPV)

- 9-valent vaccine (HPV 9) is recommended.
- Pre-transplant: 3 doses (0, 1-2, and 6 months) aged 9-45 years, men and women.
- Post-transplant: If patient has not received a complete course of pre-transplant HPV vaccination, additional doses could be given 3-6 months after transplant.

Meningococcal vaccine

Only post-transplant patients who;

- Receives eculizumab.
- Has functional or anatomical asplenia.
- Travels to meningitis belt countries or Hajjmilitary personnel during recruit training.
- Laboratory workers who are routinely exposed to N. meningitidis.

Vaccination includes

1. Quadrivalent meningitis vaccine (2 doses at least 8 weeks apart and if the risk exists another dose q5 years);
    - Should be given at least 4 weeks after PCV13.
2. Serogroup B (MenB-4C, Bexsero): 2 doses, 1 month apart.

Haemophilus influenzae type B (HiB)

Only in patients with a history of total/partial splenectomy or functional asplenia (e.g., thalassemia, sickle cell disease, cirrhosis, chronic viral hepatitis, primary biliary cirrhosis, inflammatory boweldisease, celiac disease, etc.).

If an SOT patient undergoes splenectomy, vaccine should be given 14 days before surgery.

COVID-19 Vaccine

- Primary series: A 3-dose primary series of mRNA COVID-19 vaccines (8 weeks between doses).
- 1st booster dose: A dose of an mRNA vaccine **≥5 months (140 days),** and at a minimum of three months (84 days).
- 2nd booster dose: A dose of an mRNA vaccine **≥5 months (140 days)**, and at a minimum of 3 months (84 days), after their first booster dose.
- Moderna: 100 mcg dose.
- Pfizer: 30 mcg dose.

Cholera

Only for travelers;

- Dukoral (oral inactivated vaccine): could be used but protection is achieved in <50% of immunocompromised patients.

Typhoid Vaccine

Only for travelers;

- T21a (Oral, Vivatif Berna, Swiss serum and Vaccine Institute): contraindicated ViCPS (injection, Typhim Vi) can be used.

- Immunization (1 dose) should be completed 2 weeks before travel. Booster is needed if travels again after 2 years.

Sustained Low Efficiency Dialysis (SLED) Dosing Guidelines

- For use when SLED runs <12h.

- For antibiotics given q24h, give dose post-SLED if a patient is on 8 – 12 hours of SLED.

- For 24 hour SLED, dose medications at full dosing for normal renal function.

TABLE 22. DOSING RECOMMENDATIONS IN SLED

DRUG	DOSING	REFERENCE
ACYCLOVIR	10mg/kg IV q24h	
AMIKACIN	4mg/kg IV q24h (trough <2) Consider loading dose of 10mg/kg IV	
AMPICILLIN	1g IV q8h Consider 2g 8h for *Enterococcus* endocarditis or *Listeria* meningitis	
ANIDULAFUNGIN	100mg IV q24h	*Int J AntimicrobChemother 2009;34:282-283.*
CEFAZOLIN	1g IV q8h Consider 2g q8h for MSSAendocarditis/ bacteremia	
CEFTAZIDIME	1g IV q8h or 2g IV q12h	*J Antimicrob Chemother 2017;72:1433-1440*
CIPROFLOXACIN	400mg IV q24h Consider 400mg IV q12h for *Pseudomonas* infections	
COLISTIN	200mg IV colistin loading dose, then 100mg q8h IV	*J Antimicrob Chemother 2014;69:2008-2010*
TMP/ SMX	15mg/kg/d divided IV q12h of TMP component	*BMC Pharmacol Toxicol 2013; 14:19(weak evidence)*
DAPTOMYCIN	6mg/kg q24h	*J Antimicrob Chemother 2007;60:224-25.* *Nephrol Dial Transplant 2010;25:1537-1541*

ERTAPENEM	1g IV q24h	*Nephrol Dial Transplant 2009; 24: 267-271.*
FLUCONAZOLE	400mg IV q24h	
FOSCARNET	45-90 mg/kg IV q24h	
GANCICLOVIR	2.5 mg/kg IV q24h	
GENTAMICIN	2-2.5 mg/ kg IV q24h (trough <2)	*Kidney int 2003;63: 1072-1078 (weak evidence)*
LEVOFLOXACIN	500mg IV q24h	*Int J Clin Pharm 2016;38:127-134 (weak)*
LINEZOLID	600mg IV q12h	*Crit Care Med 2004;32:2437-2442 (weak)*
MEROPENEM	1g IV q8h	*Crit Care Med 2006;34: 51-56*
MOXIFLOXACIN	400mg IV q24h	*Clin J Am Soc Nephrol 2006;1:1263-1268*
OSELTAMIVIR	30mg PO daily (prophylaxis) 75mg PO daily (treatment)	As recommended by: www.antimicrobialstewardship.com
PENICILLIN G	3 MU IV q6h	
PIPERACILLIN/ TAZOBACTAM	3.375g IV q8h Consider 3.375g IV q6h for Pseudomonas infections	*Annals of Pharmacotherapy 2018;52(10):965-973*
TENOFOVIR DISOPROXIL FUMARATE[1]	300mg PO q48h	
TOBRAMYCIN	2-2.5mg/ kg q24h (trough <2) Consider loading dose of 5mg/kg IV	*Antimicrob Agents Chemother. 2010;54(9):3635-40.*
VANCOMYCIN	1g IV q24h or 15 mg/kg IV q24h	*Criti Care Med 2006;34: 51-56.* *Hosp Pharm 2004; 39: 138-143.*
VALGANCICLOVIR	No SLED info; change to ganciclovir	
VORICONAZOLE	Can give IV formulation despite theoretical concern of cyclodextrin accumulation (loading dose of 6mg/kg x 2 IV q12h, then 4mg/kg IV q12h)	

[1] In case of using tenofovir alafenamide, the dose of 25 mg once daily is not needed to bemodified in patients using SLED.

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Your comments on the usefulness of the resources contained in the Handbook are welcomed and may be forwarded to Shahid Husain, Transplant Infectious Diseases at Ajmera Transplant Centre (**Shahid.husain@uhn.ca**).