GUIDANCE FOR PREVENTION AND TREATMENT OF CYTOMEGALOVIRUS (CMV)
for Stem Cell Transplant Recipients at
Atrium Health Wake Forest Baptist
Updated: Spring 2022

CMV PREVENTION

1. PROPHYLAXIS

a. Start letermovir in all high-risk recipients of allogeneic stem cell transplant patients between day zero to day 8; high risk defined below.
    1. **High risk patients include:**
        i. All CMV R+ patients and CMV mismatch pairs (R+/D- or R-/D+)
        ii. At least 1 HLA mismatch from related/unrelated donor
        iii. Haploidentical donor
        iv. Graft vs Host Disease (GVHD) grade 2 or greater requiring systemic corticosteroids (>0.5mg/kg of prednisone equivalent daily)
        v. T cell depleted SCT (in vivo or ex vivo) which will include CD34 selected products
    2. For high-risk CMV R- patients, letermovir use is preferred, but valganciclovir may be used as an alternative based on insurance approval.

b. Letermovir dose: 480mg PO or IV daily
For detailed dosing recommendations, see table below

c. Continue prophylaxis with letermovir until Day 100

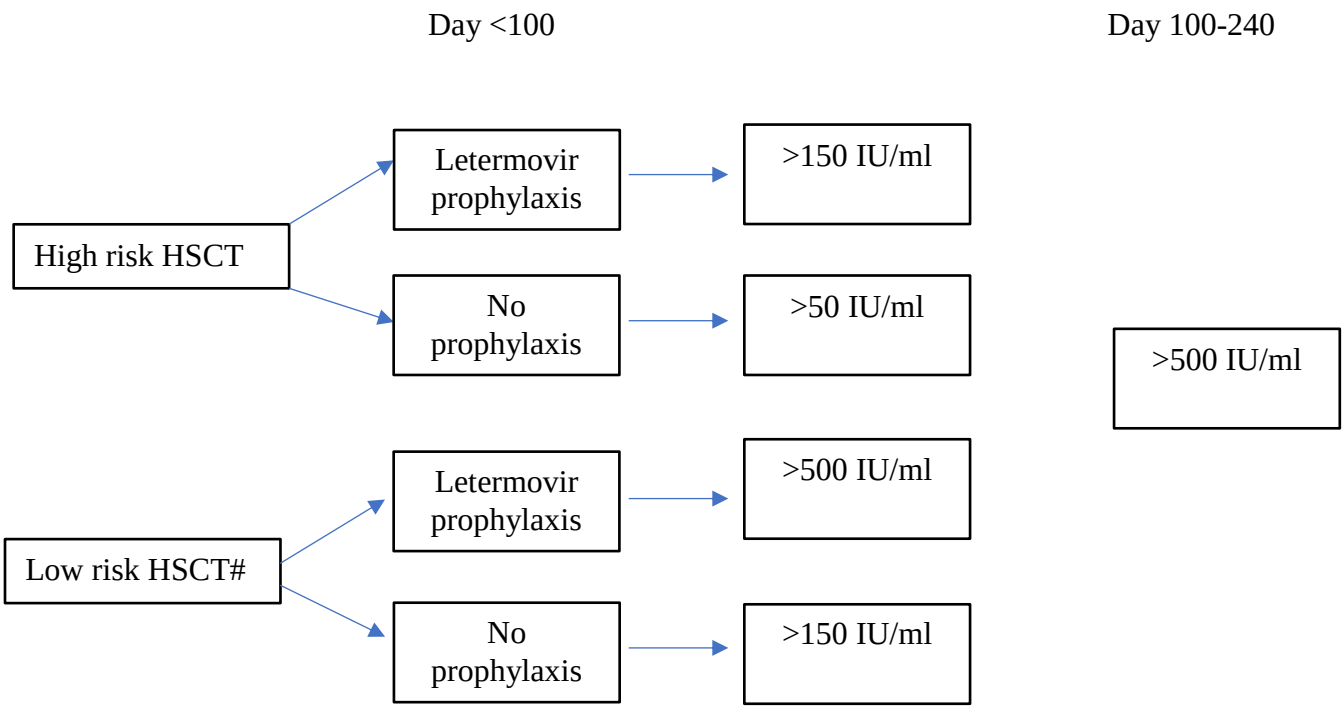
2. Secondary prophylaxis

a. Consider extending prophylaxis beyond Day 100 for high risk patients, especially with GVHD and on high dose steroids or systemic immunosuppressants (IST).

3. PRE-EMPTIVE THERAPY

a. Monitor all the allogeneic stem cell transplant patients with weekly CMV PCR from post-engraftment until Day 100, lesser interval until Day 180, and longer if GVHD or immunosuppression is continued until > D+240 and off IST.

b. Viral thresholds for starting pre-emptive therapy

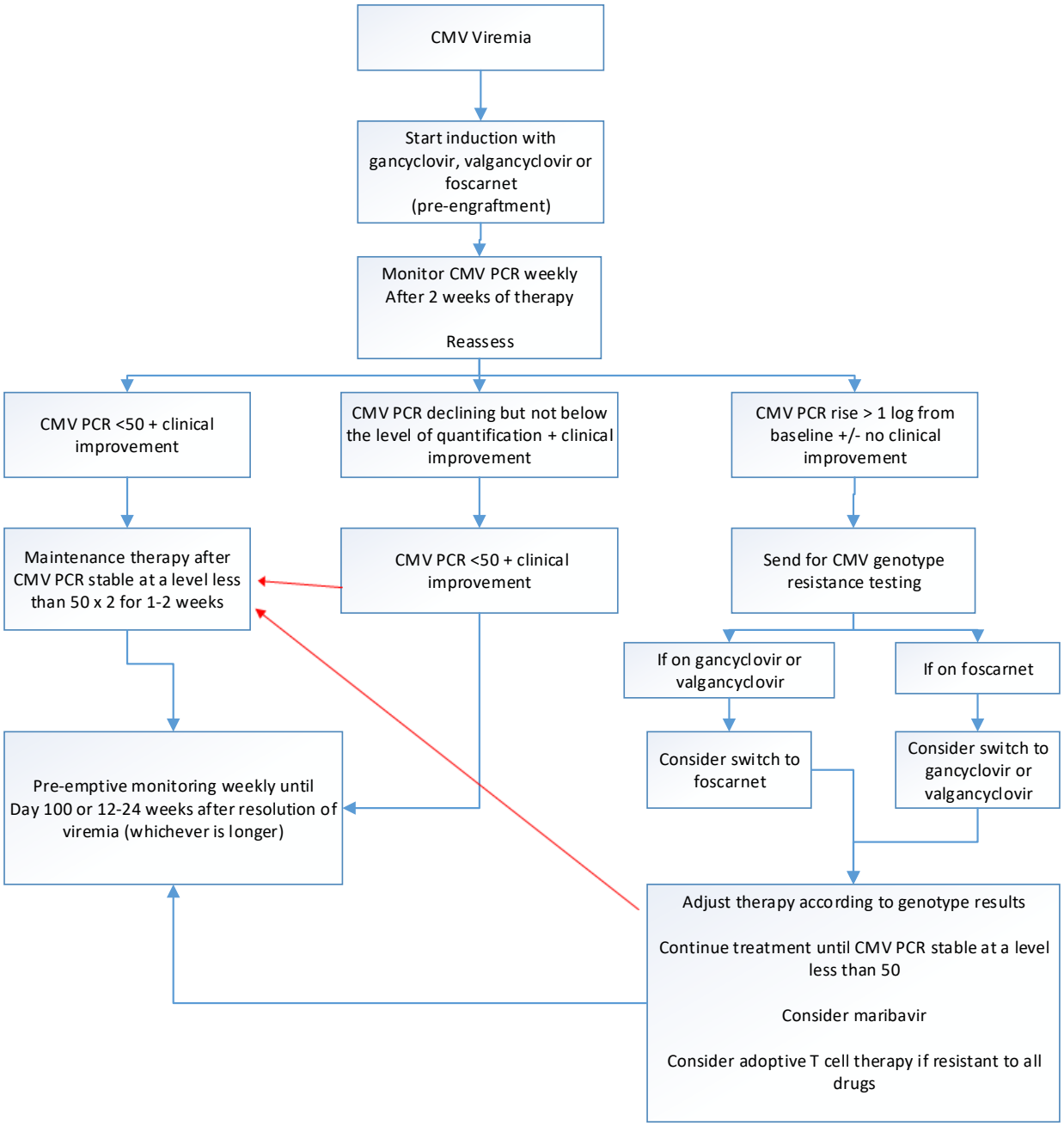


[#]Low risk patients defined as CMV neg/neg or GVHD prophylaxis not including ATG or post-transplant cyclophosphamide (PTCy)
*For patients with active GVHD and on high dose steroids (> 0.5 mg/kg/day), use lower thresholds as listed for Day < 100

4. Treatment options for CMV viremia and disease

	Induction dosing	Maintenance dosing
Pre- engraftment	IV Foscarnet 90 mg/kg q12h	IV Foscarnet 90mg/kg daily
Post-engraftment (ANC >1000 for 3 days)	IV Ganciclovir 5 mg/kg q12h *or* PO Valganciclovir 900 mg q12h (if no issues with GI absorption)	IV Ganciclovir 5mg/kg q24h *or* PO Valganciclovir 900 mg q24h

- For detailed renal dosing, refer to the table below
- If the patient develops leukopenia and/or neutropenia, would recommend switching valgancylovir/gancyclovir to IV foscarnet.
- Consider maribavir for treatment failure or intolerance/ resistance



Important Notes:
* Increase in CMV PCR early (< 2 weeks) in to therapy does not indicate failure
* Consider ID consult for CMV viremia/disease, particularly for symptomatic disease
* Pre-emptive monitoring must be done weekly through day 100, then decrease until Day 180, and longer if GVHD or immunosuppression is continued.
* Oral valganciclovir should be used only if the patient has good oral intake, GI GVHD Stage 1-2, no severe diarrhea or liver disease.
* To order CMV genotype testing, quantitative CMV PCR must be > 500 IU/ml

Drugs for CMV infection

Prophylaxis				
Drug Name	**Dosing**	**Side effects**	**Important Interactions**	**Notes**
Letermovir	Cr Cl > 10ml/min: 480mg IV or PO daily CrCl <10ml/min: No data	GI: Nausea, vomiting or diarrhea Headache, peripheral edema	1. Cyclosporine increases concentrations of letermovir and letermovir increases cyclosporine concentrations. Use 240 mg daily dose of letermovir when co-administering with cyclosporine. 2. Voriconazole: Letermovir may decrease voriconazole concentrations. Monitor serum concentrations of voriconazole. (No interactions described with posaconazole and isavuconazole.)	No activity against HSV or VZV

Treatment					
Drug Name	**Dosing**			**Side effects**	**Notes**
	Renal Function (ml/min)	Induction	Maintenance	1.Bone marrow suppression (leukopenia and neutropenia) 2. Nausea, vomiting, diarrhea 3. Confusion, headache	If there is leukopenia or neutropenia, consider foscarnet, and consider G-CSF when feasible
Ganciclovir IV	CrCl >70	5mg/kg q12h	5mg/kg q24h		
	CrCl 50-69	2.5mg/kg q12h	2.5mg/kg q24h		
	CrCl 25-49	2.5mg/kg q 24h	1.25mg/kg q24h		
	CrCl 10-24	1.25mg/kg q24h	0.625mg/kg q24h		
	CrCl<10/HD	1.25mg/kg 3 x week (dose AD)	0.625mg/kg 3 x week (dose AD)		
	CVVHD	2.5mg/kg q24h	1.25 mg/kg q24h		
Valganciclovir PO	CrCl ≥ 60	900 mg q12h	900mg q24h	1.Bone marrow suppression (leukopenia and neutropenia) 2. Nausea, vomiting, diarrhea 3. Confusion, headache	If there is leukopenia or neutropenia, consider foscarnet, and where feasible consider G-CSF
	CrCl 40-59	450mg q12h	450mg q24h		
	CrCl 25-39	450mg q24h	450mg every 2d		
	CrCl 10-24	450mg every 2d	450mg 2 x week		
	Cr Cl <10 /HD	Use not recommended			
Foscarnet IV	CrCl/kg (>1.4)	90mg/kg q12h	90mg/kg q24h	1.Nephrotoxicity (damage to tubular cells) 2. Hypomagnesemia and hypocalcemia 3. Genital ulcers	Give with IVF bolus +/- IV magnesium and IV calcium as premeds before each dose
	CrCl/kg >1-1.4	70 mg/kg q12h	70 mg/kg q24h		
	CrCl/kg >0.8-1	50 mg/kg q12h	50 mg/kg q24h		
	CrCl/kg >0.6-0.8	80 mg/kg q24h	80 mg/kg q48h		

	CrCl/kg >0.5-0.6	60 mg/kg q24h	60 mg/kg q48h	4. Seizures	
	CrCl/kg ≥0.4-0.5	50 mg/kg q24h	50 mg/kg q48h		
	CrCl/kg <0.4	Use not recommended			
Maribavir PO	400 mg BID	Not adjusted for renal dysfunction		1. nausea, vomiting, diarrhea 2. decreased hemoglobin and platelets 3. taste disturbances 4. increased SCr	May increase tacrolimus and sirolimus concentrations

References:

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3. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for Preventing Infectious Complications among Hematopoietic Cell Transplantation Recipients: A Global Perspective. Biology of Blood and Marrow Transplantation. 2009;15:1143-1238.
4. Einsele H, Ljungman P, Boeckh M. How I treat CMV reactivation after allogeneic hematopoietic stem cell transplantation. Blood. 2020;135:1619-1629.
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