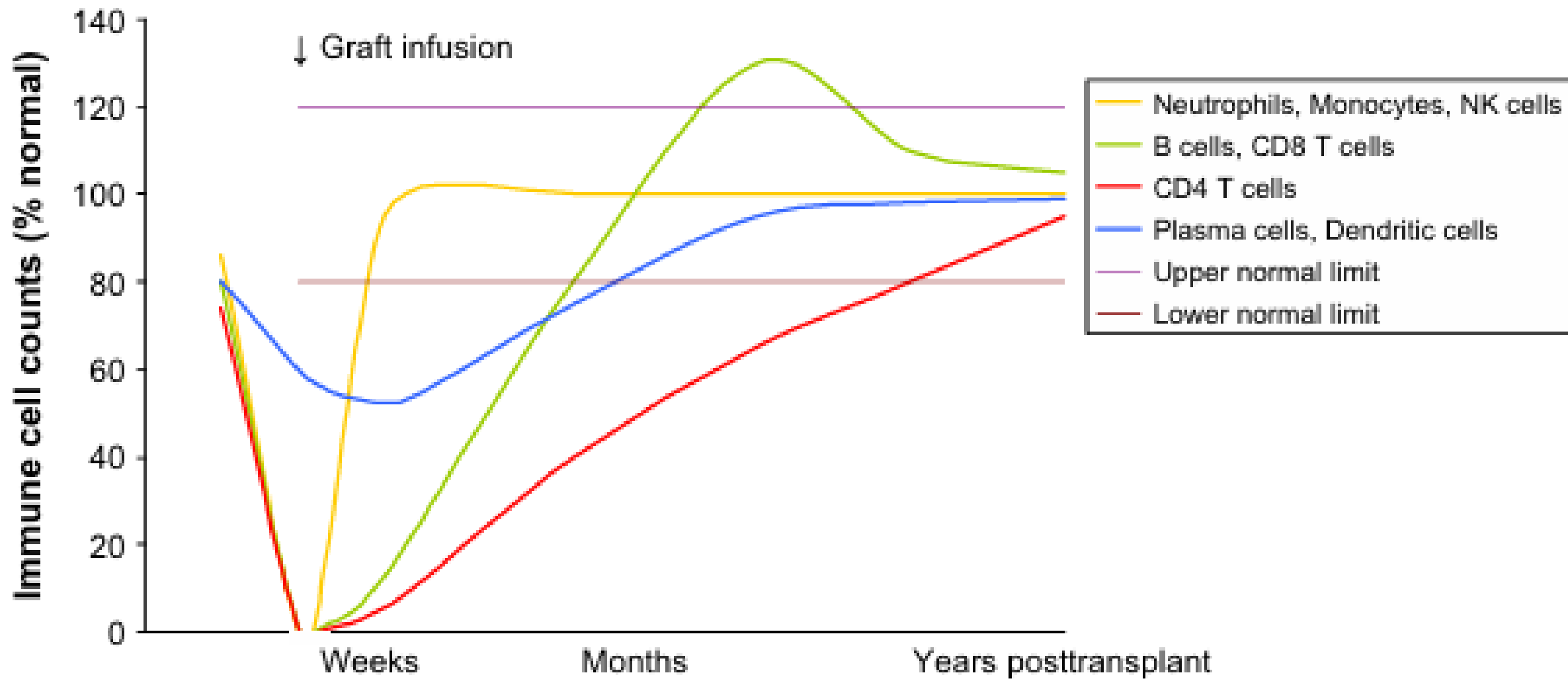


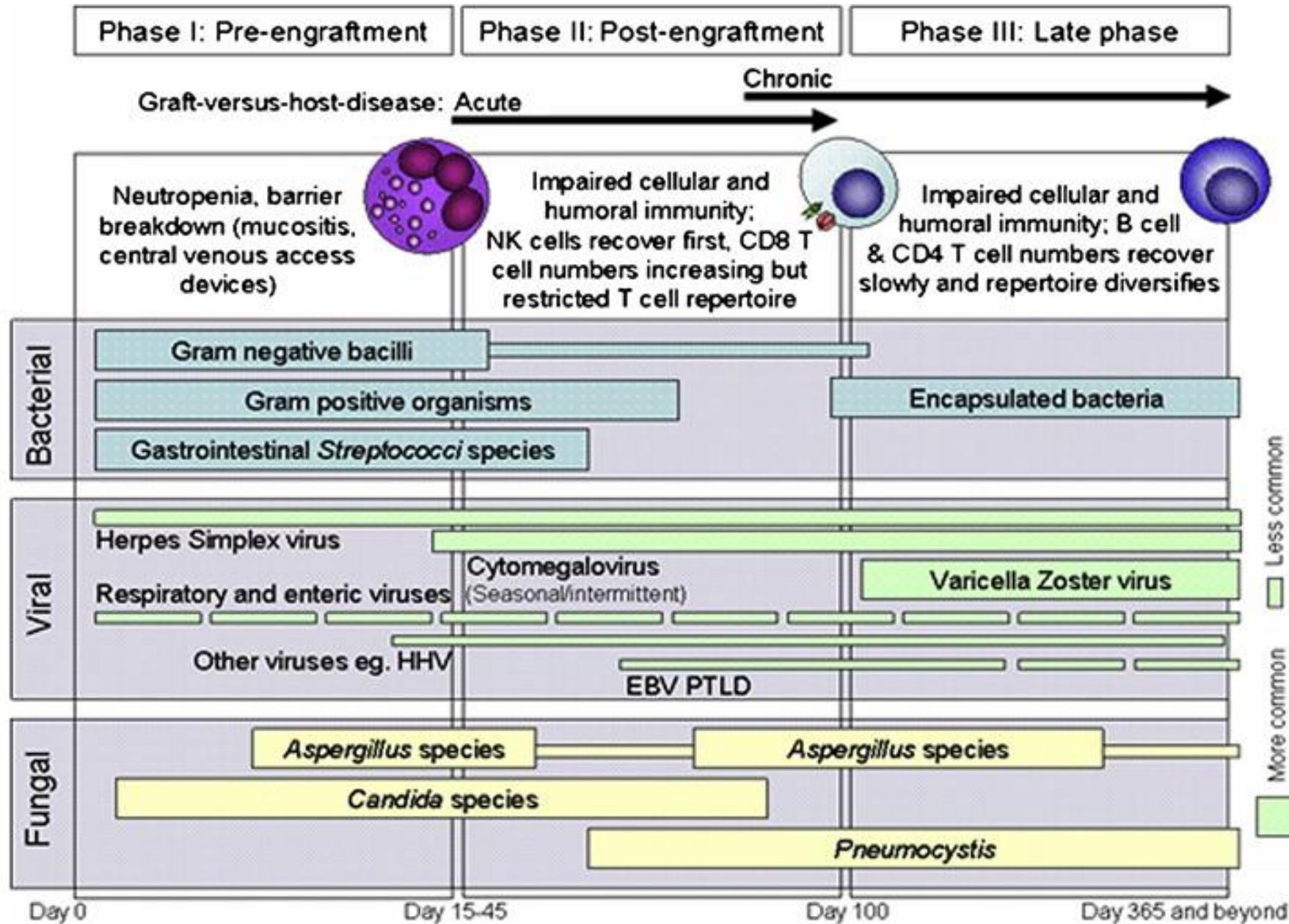


Viral infections

Uday Kulkarni MD, DM
Professor,
Department of Haematology,
Christian Medical College Vellore,
Tamil Nadu, India



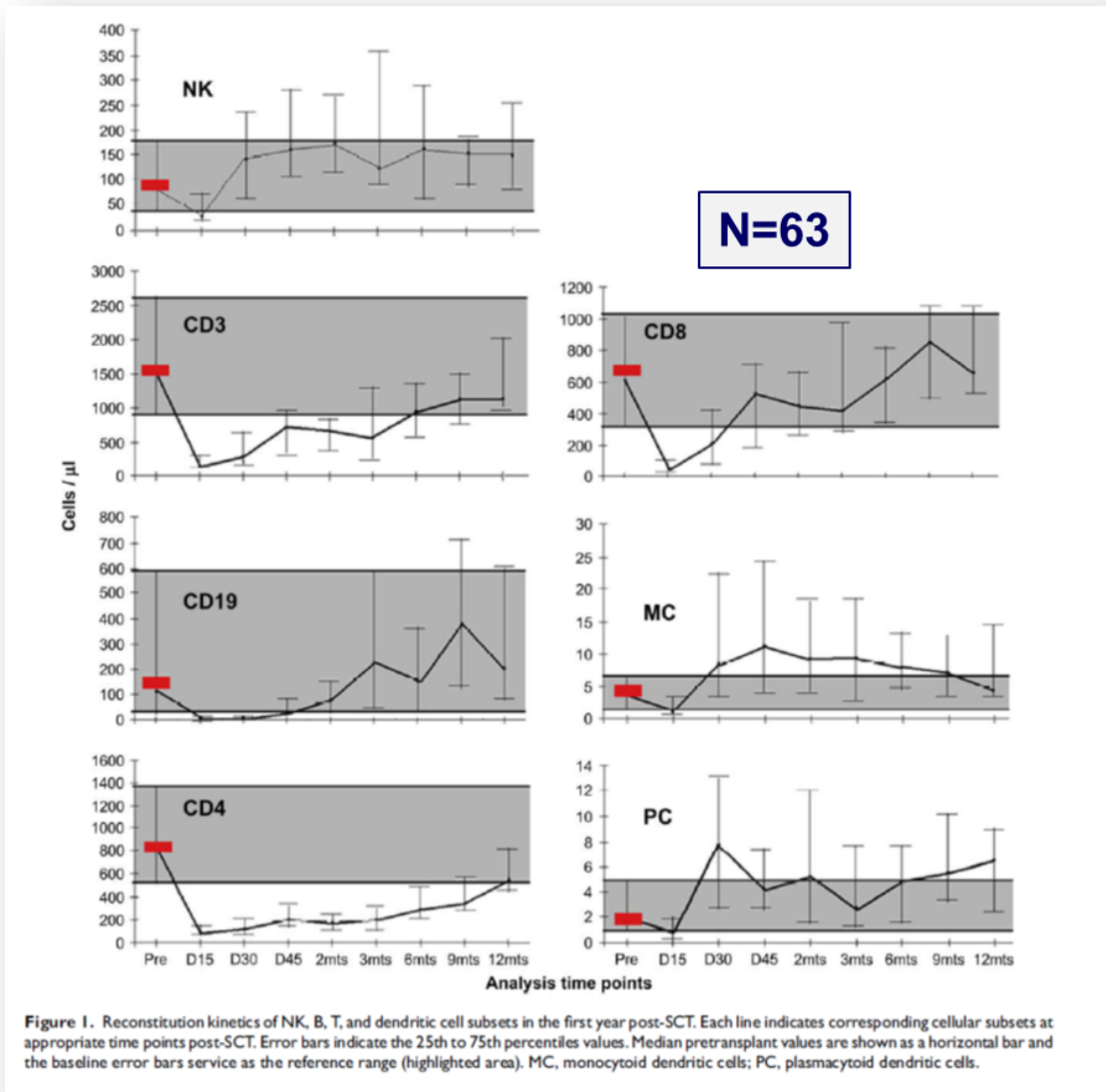
Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant*. 2009;15(10):1143-1238.



Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant.* 2009;15(10):1143-1238.

Figure 2. Phases of opportunistic infections among allogeneic HCT recipients Abbreviations: EBV, Epstein-Barr virus; HHV6, human herpesvirus 6; PTLD, posttransplant lymphoproliferative disease.

Immune reconstitution - - -



Delayed IR

- T cell replete haploidentical HCT
- Use of PTCy
- T cell depleted haploidentical HCT
- Mismatched HCT

Burden of viral infections post-transplant

CMV

- 97.5% recipients – seropositive
- **Reactivation before day 100 – 36.6%**
- Response to therapy – 90%; **42% had a second reactivation**
- CMV disease – 1.68%
- Higher risk of reactivation with male donor, HLA mismatch, acute GVHD, steroid refractory acute GVHD
- CMV reactivation associated with worse overall survival

BKV

- BK hemorrhagic cystitis in 8% of all HSCT recipients
- Risk factors – acute GVHD, bacterial UTI and residual disease at transplant

Incidence of viral infections post-HCT - -

Post haplo-HCT n = 269 (up to June 2020)

- Documented Bacterial infections seen in 44.2%
- 86% were gram negative infections – 31.2% were carbapenem resistant
- **Viral infections very common and seen in 71%**
- **CMV viremia seen in 62.8% and BK virus in the urine (34.2%).**
- Fungal infections 38.2% (proven only in 13.1%)

Burden of viral infections post-transplant

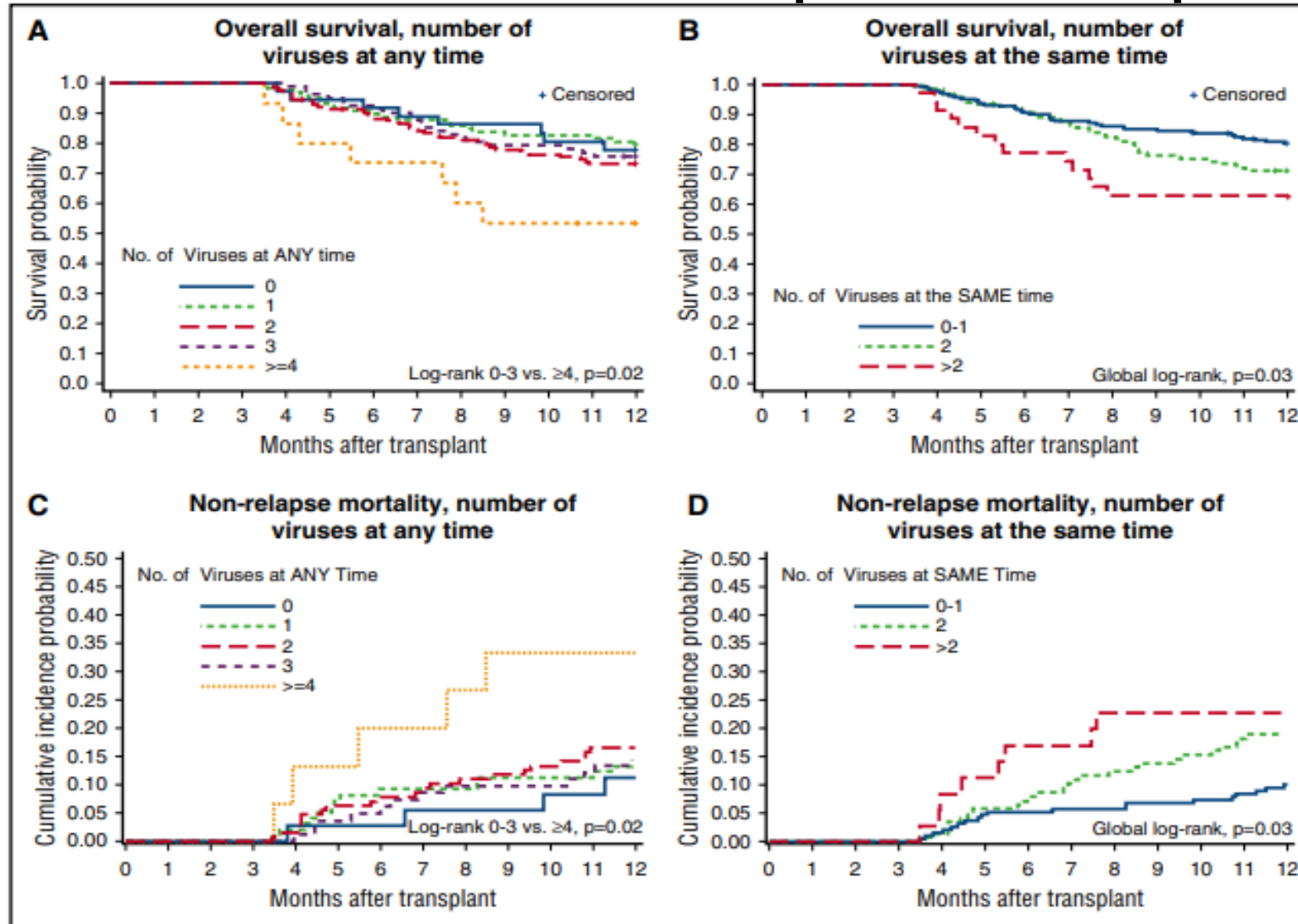


Figure 4. Plots of time to overall mortality and NRM through day 365 post-HCT among day-100 survivors (n = 358). Kaplan-Meier plots of overall mortality stratified by the cumulative number of different viruses detected at any time by day 100 (A) and cumulative maximum number of viruses detected at the same time by day 100 (B). Cumulative incidence curves of NRM stratified by the cumulative number of different viruses detected at any time by day 100 (C) and cumulative maximum number of viruses detected at the same time by day 100 (D).

Hill JA, Mayer BT, Xie H, Leisenring WM, Huang ML, Stevens-Ayers T, Milano F, Delaney C, Sorrow ML, Sandmaier BM, Nichols G, Zerr DM, Jerome KR, Schiffer JT, Boeckh M. The cumulative burden of double-stranded DNA virus detection after allogeneic HCT is associated with increased mortality. *Blood*. 2017 Apr 20;129(16):2316-2325.

CMV

- Pre-transplant donor and recipient serology testing – risk of reactivation highest if donor is CMV seronegative and recipient is CMV seropositive.
- Reactivations are detected on routine qPCR monitoring
- Monitoring for CMV in alternate donor transplants (Haploidentical or unrelated donor) is standard practice.
- Log 3 and above: threshold for pre-emptive treatment
- Disease can present as fever, colitis, pneumonitis, retinitis

	ESCMID grade
CMV risk status determination	
All patients and donors should be tested for CMV IgG antibodies	Allu
CMV serology in allogeneic HCT candidates should be done at two timepoints	
At diagnosis of an underlying disease, which might be an indication for an allogeneic HCT, and before any blood transfusion is administered	Allu
If no CMV serology result is available at the time of diagnosis, any available stored pre-transfusion samples should be tested	BII
Before HCT, close to the transplant	Allu
CMV PCR before HCT is recommended	BIIu
Clinical judgement should be used to decide on whether to administer anti-CMV prophylaxis in patients with unclear CMV status; these patients need to be monitored as patients who are CMV seropositive	BII
Screening and monitoring	
All CMV D+/R+, D-/R+, and D+/R- allogeneic HCT recipients should be monitored for CMV DNA load in plasma or whole blood by QNAT	All
Monitoring for CMV DNAemia is recommended for allogeneic HCT recipients receiving letermovir prophylaxis	AI
Less frequent monitoring can be considered, especially in CMV D-/R- allogeneic HCT recipients undergoing low or standard risk HCT because the risk of primary infection and the incidence of end-organ disease are low if the administration of CMV-safe blood products can be assured	CII
Monitoring of CMV DNAemia should be done at least once a week for the first 100 days after the transplant	Allu
Extended monitoring for CMV DNAemia is recommended for at least another 3 months in patients at higher risk, such as those having undergone mismatched, cord blood, or haploidentical HCT, T-cell depleted patients, patients on steroids, patients with ongoing GVHD, and patients with previous episodes of CMV DNAemia	BII
Monitoring should be extended in patients with chronic GVHD requiring more intensive systemic immunosuppression, or in those with persistent immunodeficiency according to the perceived clinical risk for CMV reactivation and disease	BII
Monitoring of CMV DNA load for a given patient should be done with the same specimen type (plasma or whole blood) and QNAT platform	Alltu
CMV DNA load values for initiating pre-emptive antiviral therapy should take into account the QNAT platform used, the matrix chosen for CMV DNA quantification, the associated risk of CMV-disease, and the presence or absence of antiviral prophylaxis	Allu
For a given patient and transplant centre, screening and monitoring of CMV DNA loads should be done with the same QNAT platform and type of specimen unless there are specific reasons to suspect underperformance of a given matrix indicating comparison of both plasma and whole blood	Allu
Changes in CMV DNA load in plasma or whole blood ($>0.5 \log_{10}$) can assist in making decisions as to when to initiate pre-emptive antiviral treatment	BIIu

Ljungman P, Alain S, Chemaly RF, et al. Recommendations from the 10th European Conference on Infections in Leukaemia for the management of cytomegalovirus in patients after allogeneic haematopoietic cell transplantation and other T-cell-engaging therapies. *Lancet Infect Dis.* 2025;25(8):e451-e462.

	ESCMID grade	
	Adults	Children
Letermovir is recommended as the strategy of choice for preventing CMV for CMV primary prophylaxis for CMV seropositive allogeneic HCT recipients	AI	BIIa
Letermovir prophylaxis should be started as early as feasible after allogeneic HCT to reduce the risk of early reactivations	BII	No data
Letermovir should be started no later than day 28 after transplantation	AI	No data
Prophylaxis should be continued for at least 100 days after HCT	AI	Allu
Extended prophylaxis should be considered in patients at high risk for CMV disease and can continue to at least 200 days after transplantation	BI	CIII
For some individuals, prophylaxis for longer than 200 days after transplantation can be considered if the treating physician's judgement is that the benefit is stronger than the risk	CII	CIII
Drug-drug interactions should be considered when giving letermovir prophylaxis	BII	CIIIt
Letermovir blips (single test low-level DNA positivity in plasma or whole blood samples occurring especially early during letermovir prophylaxis) are common; interruption of letermovir prophylaxis is not recommended unless there are repeated positive samples showing increased viral load	BII	CIIIt
Primary letermovir prophylaxis in patients with CMV negative status, regardless of the donor serostatus, is not recommended	DII	DIII
After discontinuation of letermovir prophylaxis, secondary prophylaxis with letermovir can be considered		
After successful treatment (negative QNAT test) of a CMV reactivation in patients perceived to be at increased risk for CMV disease	BII	CIII
In patients who, for some reason, have not received primary prophylaxis and have reactivated CMV that has been successfully treated	BII	CIII
Prophylactic valganciclovir could be used if letermovir prophylaxis is not used as primary prophylaxis for CMV seropositive allogeneic HCT recipients	CI	CIIIt
The use of valganciclovir, ganciclovir, intravenous immunoglobulin, or foscarnet as prophylaxis against CMV reactivation is generally not recommended	DII	CIIIt (GCV), DIIIt (FOS), DIII (IVIG)

ESCMID=European Society for Clinical Microbiology and Infectious Diseases. CMV=cytomegalovirus. HCT=haematopoietic cell transplant. QNAT=quantitative nucleic acid testing. GCV=ganciclovir. FOS=foscarnet. IVIG=intravenous immunoglobulin.

Table 2: Recommendations for antiviral prophylaxis in adults and children

Ljungman P, Alain S, Chemaly RF, et al. Recommendations from the 10th European Conference on Infections in Leukaemia for the management of cytomegalovirus in patients after allogeneic haematopoietic cell transplantation and other T-cell-engaging therapies. *Lancet Infect Dis.* 2025;25(8):e451-e462.

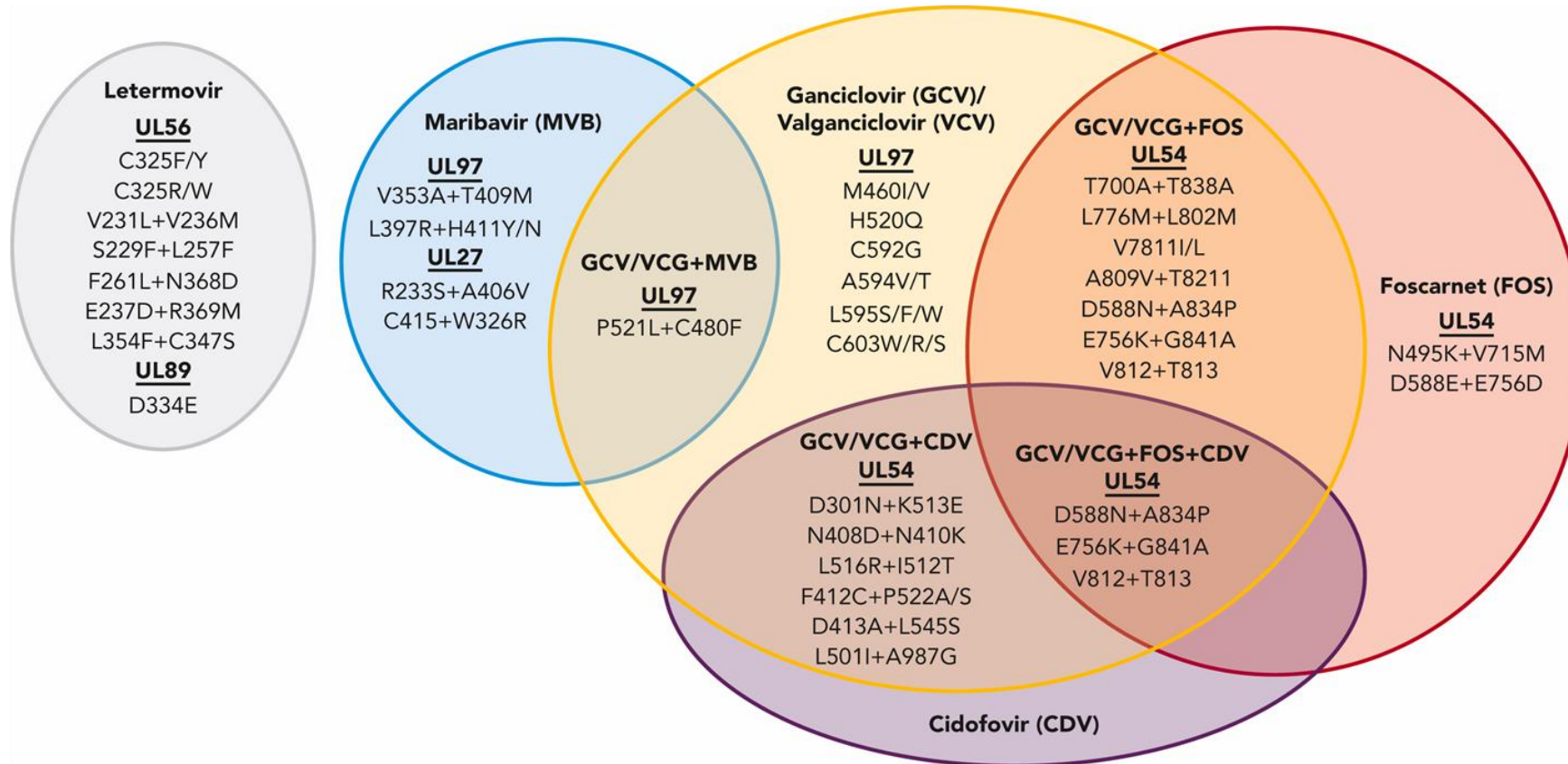
	ESCMID grade	
	Adults	Children
Maribavir is effective for treatment of resistant or refractory CMV infection and disease and is associated with lower risk for side-effects than the other alternatives	A1	B1It*
Maribavir is not indicated for CMV disease involving the CNS and the eyes	D1It	D1It
If resistance is suspected, it should be documented by genotyping	A1I	A1I
Change of therapy is recommended before having results of resistance testing available	B1I	B1I
Foscarnet is an alternative therapy for resistant or refractory CMV infections, in particular in the CNS and eyes, but is associated with clinically significant toxicity	B1I	A1I
Cidofovir is an option for the treatment of CMV retinitis	B1I	B1I
CMV-specific T cells are an option for treatment of resistant or refractory CMV infection or disease, if available	B1I	C1Iu
Combination therapy for resistant or refractory CMV infections could be considered	B1I	C1I
The combination of maribavir with valganciclovir or ganciclovir should not be used	D1It	C1II
Letermovir is not indicated for pre-emptive therapy of CMV infection or treatment of CMV end-organ disease including resistant or refractory infections	D1II	D1It

CMV=cytomegalovirus. ESCMID=European Society for Clinical Microbiology and Infectious Diseases. *Can be considered when the patient is older than 12 years. However, it is not approved by the European Medical Association for individuals younger than 18 years.

Table 3: Treatment of resistant or refractory CMV

Ljungman P, Alain S, Chemaly RF, et al. Recommendations from the 10th European Conference on Infections in Leukaemia for the management of cytomegalovirus in patients after allogeneic haematopoietic cell transplantation and other T-cell-engaging therapies. *Lancet Infect Dis.* 2025;25(8):e451-e462.

How I prevent viral reactivation in high-risk patients



Sanjeet S. Dadwal, Genovefa A. Papanicolaou, Michael Boeckh, How I prevent viral reactivation in high-risk patients, *Blood*, 2023, Figure 3.

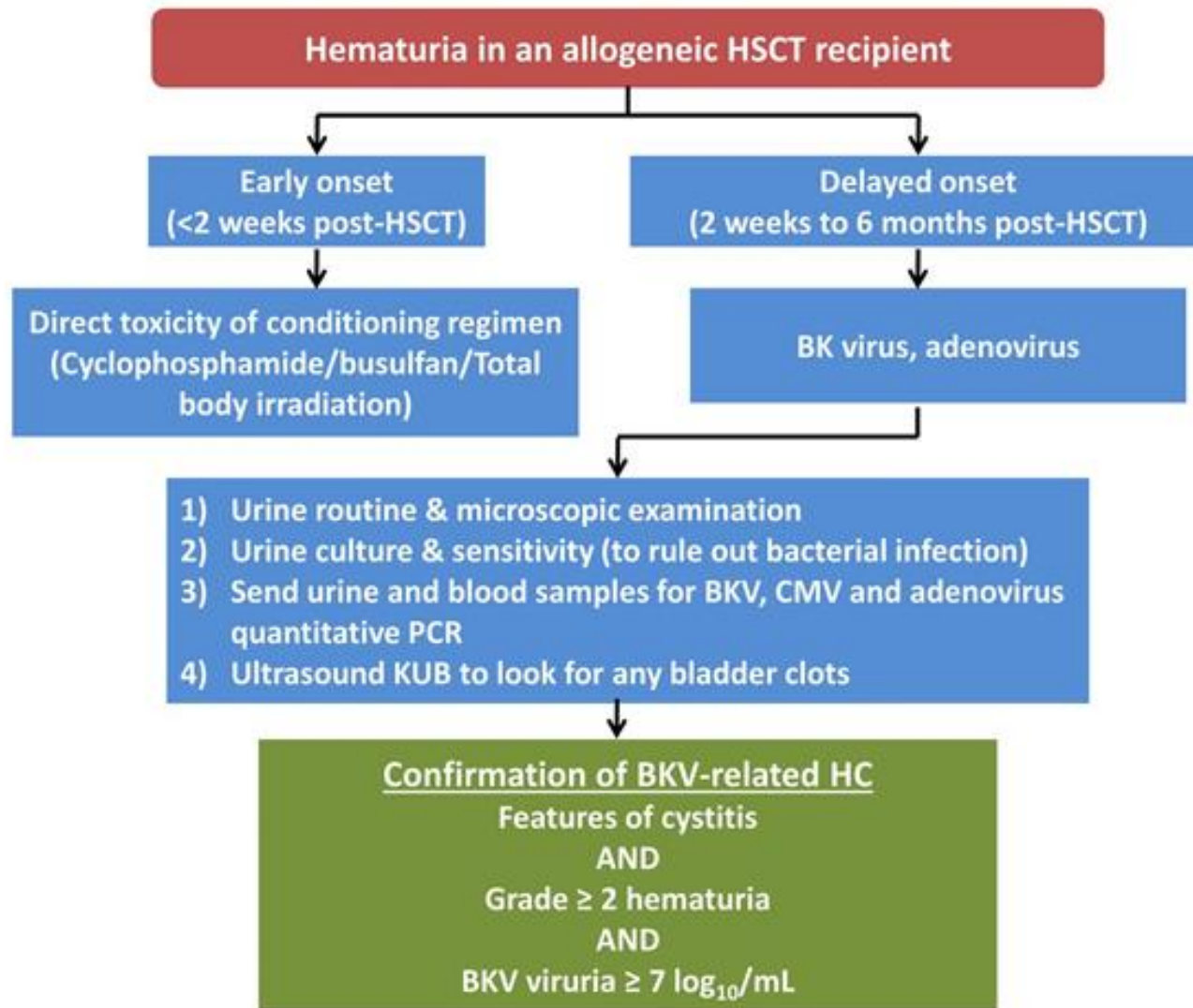


Figure 1. Approach to haematuria in an allogeneic HSCT recipient while considering BK virus-related cystitis.

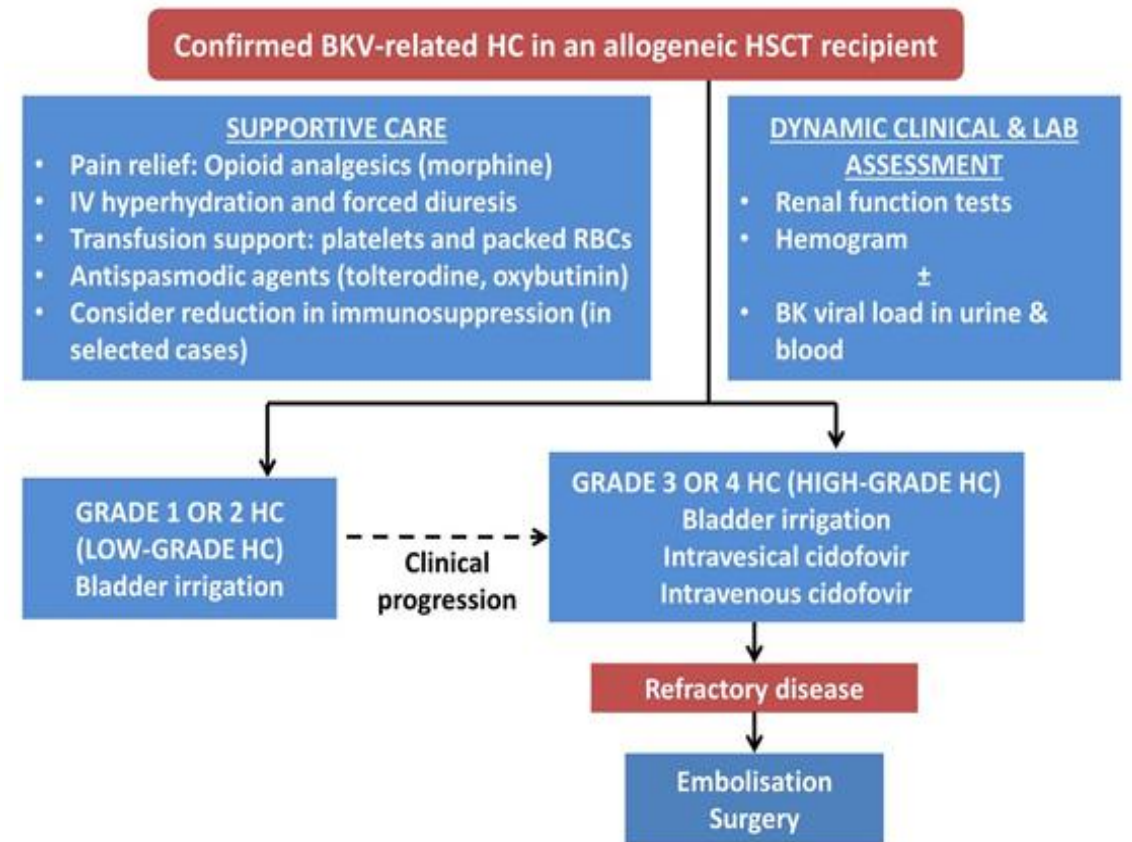


Figure 2. Approach to a confirmed BKV-related HC in an allogeneic HSCT recipient.

Jandial A, Mishra K, Sandal R, Kant Sahu K. Management of BK virus-associated haemorrhagic cystitis in allogeneic stem cell transplant recipients. Ther Adv Infect Dis. 2021 Feb

EBV

- Usually suspected with lymphocytosis with or without adenopathy
- Reactivations: around 100 days post transplant
- Can present as post-transplant lymphoproliferative disease
- Commoner with alternate donor transplants, T deplete transplants, use of ATG
- Reduced risk with administration of rituximab on day -1

Pathogen: Epstein-Barr virus

Indication	First Choice	Alternatives
Prevention of Epstein-Barr virus-related posttransplant lymphoproliferative disease in high-risk patients (BII)	Rituximab, 375 mg/m ² Note: Number and frequency of doses is undefined. Consider administration weekly until the indicator test is negative (CIII)	None

Pathogen: Herpes simplex virus

Indication	First Choice	Alternatives
Prevention of <u>early</u> reactivation among seropositive HCT recipients (regardless of donor HSV serostatus) Note: Start prophylaxis at the beginning of conditioning therapy and continue until engraftment or until mucositis resolves	Acyclovir Adults/Adolescents (≥ 40 kg): <ul style="list-style-type: none">• 400-800 mg orally twice daily; or• 250 mg/m²/dose i.v. every 12 hours (AI); Pediatrics (<40 kg): <ul style="list-style-type: none">• 250 mg/m²/dose i.v. every 8 hours (BIII); or• 125 mg/m²/dose i.v. every 6 hours• Maximum dose, 80 mg/kg/day	Adults/Adolescents (≥ 40 kg): Valacyclovir, 500 mg orally daily (CIII); or 500 mg orally twice daily in highly immune suppressed patients (eg, T cell depletion, anti-T cell antibodies, high-dose steroids) (BIII) Pediatrics (<40 kg): Acyclovir 60 - 90 mg/kg/24 hours orally, divided in 2-3 doses/day; or Valacyclovir 250 mg orally twice daily
Prevention of <u>late</u> reactivation among seropositive HCT recipients	Acyclovir Adults/Adolescents (≥ 40 kg): 800 mg orally twice daily during the first year after HCT (BIII)* Pediatrics (<40 kg): 60-90 mg/kg orally divided in 2-3 doses daily (not to exceed 800 mg twice daily)	Valacyclovir, oral dosing throughout the first year after HCT (BIII) Adults: 500 mg twice daily Pediatrics: 250 mg twice daily

Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant.* 2009;15(10):1143-1238.

Pathogen: Varicella-zoster virus

Indication	First Choice	Alternatives
<p><u>Postexposure prophylaxis</u> HCT recipients who are exposed to varicella (All) or zoster (All) or exposed to a VZV vaccinee who develops a rash (BIII):</p> <ul style="list-style-type: none">• <24 months after HCT; or• >24 months after HCT and on immune suppressive therapy or have chronic GVHD <p>Note: Ideally, administer prophylaxis within 96 hours (preferably, within 48 hours) after close contact with a person who has chickenpox or shingles</p>	<p>Varicella-zoster immunoglobulin, if available</p> <p>Adult/Adolescents (≥ 40 kg): 5 vials (125 units each or 625 units total) intramuscularly (All)</p> <p>Pediatrics (<40 kg): 125 units (1.25 mL)/10 kg body weight administered intramuscularly (All), maximum dose of 625 units</p>	<p>Note: For drug therapy, continue until 22 days from exposure</p> <p>Adults/Adolescents (≥ 40 kg): Valacyclovir 1g 3 times per day, day 3-22 after exposure (CII)</p> <p>Pediatrics (<40 kg): Valacyclovir 500 mg 3 times daily orally; or 600 mg/m² orally 4 times daily (CIII)</p>
<p><u>Prophylaxis of disease reactivation</u> in adults or adolescents following:</p> <ul style="list-style-type: none">• Allogeneic HCT (BI)• Autologous HCT (CII)	<p>Acyclovir*</p> <p>Adults/Adolescents (≥ 40 kg): 800 mg orally twice daily for 1 year (BI)</p> <p>Pediatric (<40 kg): 60-80 mg/kg orally divided in 2-3 doses daily</p>	<p>Adult/Adolescent (≥ 40 kg): Valacyclovir 500 mg orally twice daily (BII)</p> <p>Pediatric (<40 kg): Valacyclovir 250 mg orally twice daily (BII)</p>

Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant*. 2009;15(10):1143-1238.

Pathogen: Adenovirus

Indication	First Choice	Alternatives
Preemptive therapy among high-risk seropositive HCT recipients (CII)	Cidofovir, i.v. (BII) All Ages 5mg/kg once weekly or 1 mg/kg 3 times per week† for 2-4 weeks or until immune recovery, if tolerated and effective	Ribavirin (CIII) All Ages 15 mg/kg ^b 3 times daily for 4 days followed by 8 mg/kg‡ 3 times daily for up to 10 days

HCT indicates hematopoietic cell transplant.

*Data on optimal dosing of oral ribavirin for adenovirus infection are very limited and based on maximum tolerated doses [837,838]; dose reduction may be required when hemolytic anemia occurs.

†The 1 mg/kg 3 times a week dose may cause less renal toxicity, but it is insufficient to treat concomitant CMV infection; if concomitant CMV infection is present, the 5 mg/kg/week is recommended.

‡Dose may be rounded to nearest dose that can be divided by 200 (capsule size); an oral suspension is available.

Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant*. 2009;15(10):1143-1238.

Pathogen: Respiratory syncytial virus

Indication	First Choice	Alternatives
Prophylaxis for respiratory syncytial virus (RSV) lower respiratory infection among hypogammaglobulinemic <i>pediatric</i> HCT recipients at risk for primary RSV disease during RSV season	RSV monoclonal antibody (palivizumab) 15 mg/kg intramuscularly once per month (CIII) <i>Note:</i> Use of palivizumab does not eliminate the need to administer pooled IVIG that may be required to maintain serum IgG >400 mg/dL. RSV IVIG, if available, may be administered instead of pooled IVIG	None
Preemptive treatment of RSV upper respiratory infection in the presence of lymphopenia	Aerosolized ribavirin, [319] 6 g/300 mL sterile water to make a concentration of 20 mg/mL; administer 2 g for 2 hours every 8 hours or 6 g over 18 hours/day for 7-10 days in a tent (CIII); use small-particle aerosol generator model SPAG-2	

IVIG indicates intravenous immunoglobulin; HCT, hematopoietic cell transplant.

Notes: Persons with IgA deficiency should not receive standard immunoglobulin products (DIII). Researchers have reported that use of IgA-depleted immunoglobulin preparations can be used with caution among these persons [834-836].

Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant*. 2009;15(10):1143-1238.

Pathogen: Influenza

Indication	First Choice	Alternatives															
Prevention of influenza A or B	<p>Life-long annual seasonal influenza vaccination, starting before HCT and restarting 6 months after HCT (All)</p> <p><i>Adult/Adolescents:</i> Whole- or split-virus influenza vaccine, 0.5 mL/dose intramuscularly or deeply subcutaneously</p> <p>Pediatrics: Type of influenza</p> <table border="1"> <thead> <tr> <th>Age</th> <th>Dose</th> <th>vaccine</th> </tr> </thead> <tbody> <tr> <td>6-35 months</td> <td>0.25 mL</td> <td>Split-virus*</td> </tr> <tr> <td>3-8 years</td> <td>0.5 mL</td> <td>Split-virus₊</td> </tr> <tr> <td>9-12 years</td> <td>0.5 mL</td> <td>Split-virus₊</td> </tr> <tr> <td>> 12 years</td> <td>0.5 mL</td> <td>Whole- or split-virus₊</td> </tr> </tbody> </table>	Age	Dose	vaccine	6-35 months	0.25 mL	Split-virus*	3-8 years	0.5 mL	Split-virus ₊	9-12 years	0.5 mL	Split-virus ₊	> 12 years	0.5 mL	Whole- or split-virus ₊	None
Age	Dose	vaccine															
6-35 months	0.25 mL	Split-virus*															
3-8 years	0.5 mL	Split-virus ₊															
9-12 years	0.5 mL	Split-virus ₊															
> 12 years	0.5 mL	Whole- or split-virus ₊															
<p>Prophylaxis and preemptive treatment during community and nosocomial outbreaks of influenza A (BII) for HCT recipients (regardless of prior vaccination status) who are:</p> <ul style="list-style-type: none"> • <24 months post-HCT; or • >24 months post-HCT and are on immunosuppression or have cGVHD <p>Note: Choice of drug depends on susceptibility of the circulating strain</p> <p>Note: Longer treatment courses may be required in HCT recipients because of prolonged shedding and slow clinical recovery</p>	<p>Adult/Adolescents: Oseltamivir, 75 mg orally 2 times/day for 5 days (treatment); or Oseltamivir, 75 mg orally daily (prophylaxis) Rimantadine, 100 mg orally 2 times/day (CIII) Zanamivir: For prevention, 5 mg inhaled twice daily for 10-28 days, with duration depending on type of exposure; for treatment, 10mg inhaled twice daily for 5 days</p> <p>Pediatrics: Rimantadine Children 1-9 years old, 5 mg/kg/day once daily or divided in 2 doses (CIII); maximum daily dose, 150 mg; Children ≥ 10 years old (weight, <40 kg), 5 mg/kg/day orally, divided in 2 doses; children ≥ 10 years old (weight, ≥40 kg), 100 mg orally 2 times/day Oseltamivir, 2 mg/kg (rounded for convenient dosing) orally 2 times/day for 5 days Zanamivir For prevention in children ≥5 years old, 5 mg inhaled twice daily for 10-28 days For treatment in children ≥7 years old, 10 mg inhaled twice daily for 5 days</p>	<p>Adult/Adolescents: Amantadine, 100 mg orally 2 times/day (CIII)</p> <p>Pediatrics: Amantadine Children 1-9 years old, 5 mg/kg/day; maximum daily dose, 150 mg; Children ≥ 10 years old (weight, <40 kg), 5 mg/kg/day orally, divided in 2 doses; Children ≥ 10 years old (weight, ≥40 kg), 100 mg orally 2 times/day</p>															

Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant.* 2009;15(10):1143-1238.

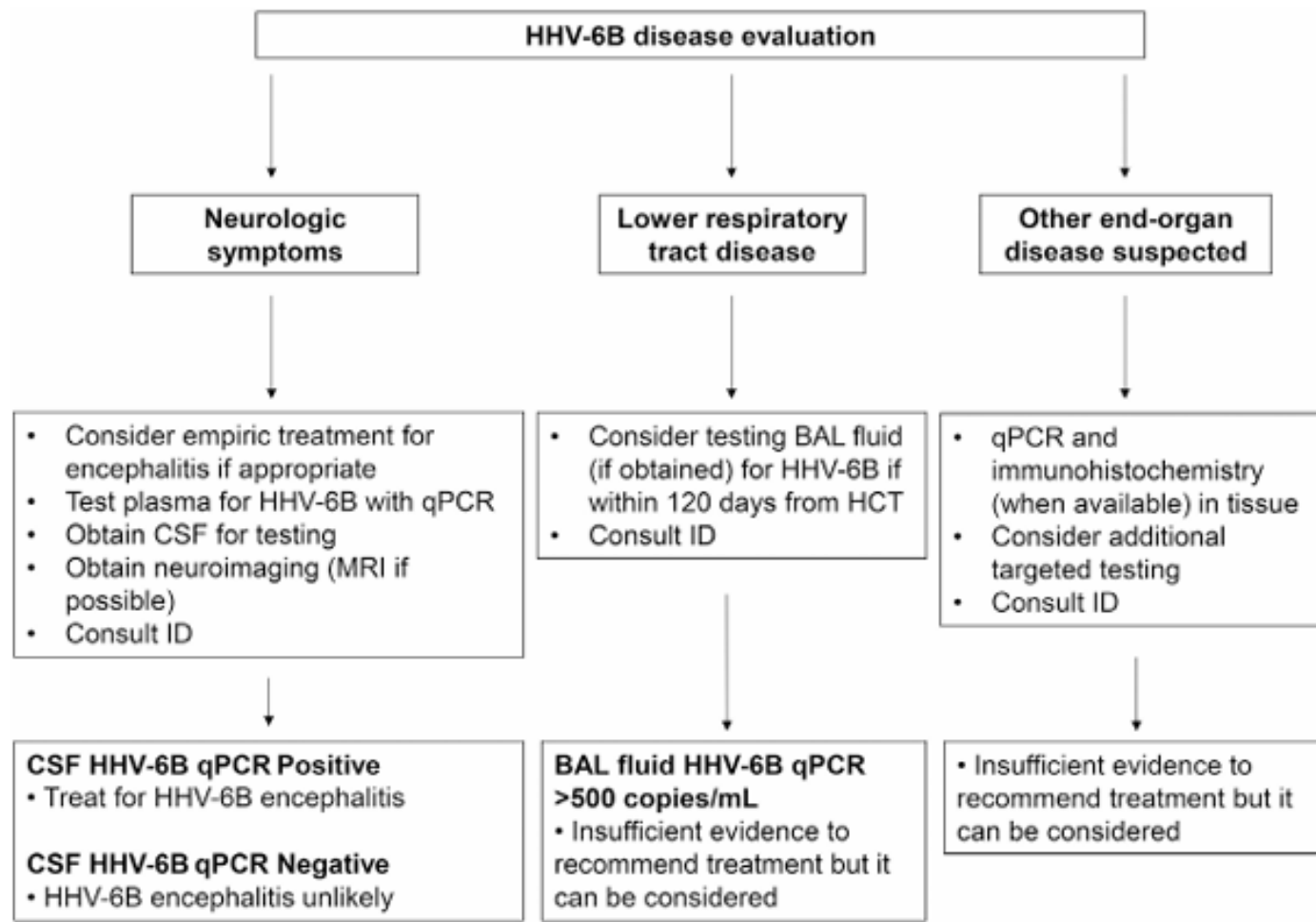


Figure 1. Algorithm for HHV-6B disease evaluation and management. Testing and management by clinical manifestation of HHV-6B reactivation. BAL indicates bronchoalveolar lavage; CSF, cerebrospinal fluid; ID, infectious diseases; MRI, magnetic resonance imaging; qPCR, quantitative polymerase chain reaction. Immunohistochemistry testing is available at Coppe Laboratories (Waukesha, Wisconsin, USA).

Table 1
Antiviral Treatment for HHV-6B

Disease Manifestation	Agent	Grade	When to chose	Disadvantage	Duration	
Recommended as first line (All)						
Encephalitis	Foscarnet 90 mg/kg bid IV	All	Pre-engraftment/ cytopenias	Nephrotoxicity	≥3 weeks and clearance of HHV-6B DNA from blood and CSF	
	Ganciclovir 5 mg/kg bid IV	All	Post-engraftment/ risk of kidney injury	Myelotoxicity		
	May be considered as salvage therapy (CIII)					
	Cidofovir 5 mg/kg/week for 2 doses then biweekly	CIII	Salvage therapy	Nephrotoxicity/ poor CNS penetration		
	Combination: Ganciclovir + Foscarnet	CIII	Salvage therapy severe or refractory encephalitis	Toxicities		
May be considered (limited evidence to support) (CII)						
Other end-organ disease (e.g., pneumonia, hepatitis)	Ganciclovir 5 mg/kg bid IV ¹ Foscarnet 90 mg/kg bid IV ¹	CII		Benefit not established	2-3 weeks and clearance from blood and/or tissue site	
Not recommended (DII)						
Asymptomatic viremia ²	Prophylaxis	DII		Efficacy not established/toxicities	Unknown	
	Preemptive therapy	DII				

Kampouri E, Handley G, Phan TL, et al. American Society for Transplantation and Cellular Therapy Series #9: Management of Human Herpesvirus 6B After Hematopoietic Cell Transplantation and Chimeric Antigen Receptor-T-Cell Therapy. *Transplant Cell Ther.* 2025;31(8):480-493.

Specific recommendations for HCT recipients		
53 ChW	HCT recipients should receive COVID-19 vaccine with a three-dose primary schedule of mRNA vaccine.	Allut
54	Vaccination should preferably be initiated at least 6 months after HCT if transmission of SARS-CoV-2 in the community is low.	BIlu
55 New	<i>Earlier vaccination should be considered if there is high prevalence of SARS-CoV-2 in the community. However, early vaccination is associated with a lower likelihood for an immune response.</i>	BIlu
56	There is a risk for worsening/eliciting GVHD in allogeneic HCT recipients. This risk needs to be considered when deciding about time for vaccination.	Allu
57 New	<i>It is possible that the risk for GVHD using the protein-subunit vaccine might be lower and could be considered in individual patients after careful risk assessment.</i>	Not graded
58 New	<i>Additional doses are able to improve the immune response both by allowing an increased proportion of patients to seroconvert and to increase the antibody levels. It is therefore recommended that patients should: a) receive booster doses, b) preferably with the new updated bivalent vaccines (according to authorizations for age).</i>	Allt BIIt
59	Based on data from other vaccines, it is likely that immunity obtained from either pre-transplant SARS-CoV-2 infection or vaccination will be wiped out by the transplant procedure. However, no data currently exists regarding this issue. However, it seems logical from a risk/benefit assessment that such patients should have a full dose new vaccine schedule after transplantation.	BIll
60 New	<i>Such repetition of a complete vaccine schedule will over time result in a large number of vaccine doses and the safety profile of such an approach is currently unknown.</i>	Not graded
61 ChW	HCT patients with previous COVID-19 should be vaccinated with a full program.	Alltu
Specific recommendations for HCT donors		
62	There is no specific recommendation for vaccinating stem cell donors for any other purpose than protecting the donor. However, previous vaccination of the donor might reduce the risk to jeopardize the donation.	Not graded
63 New	<i>There have been reports of transfer of donor immunity to allogeneic HCT recipients. However, whether this can result in protection against SARS-CoV-2 infection or disease in the recipient is unknown.</i>	Not graded

Cesaro S, Mikulska M, Hirsch HH, et al. Update of recommendations for the management of COVID-19 in patients with haematological malignancies, haematopoietic cell transplantation and CAR T therapy, from the 2022 European Conference on Infections in Leukaemia (ECIL 9). *Leukemia*. 2023;37(9):1933-1938.

Therapy		
67 ChW	In moderately or severely immunocompromised HM patients, pre-exposure prophylaxis is recommended with long-acting anti-SARS-CoV-2 monoclonal antibodies if active against circulating variants, irrespective of previous vaccination.	BlIt
68 ChW	In HM patients at high risk for COVID-19 progression (not vaccinated, vaccine non-responders or not expected to respond to vaccine) post-exposure prophylaxis is recommended with anti-SARS-CoV-2 monoclonal antibodies if active against the circulating variants.	Allt
69 ChW	In hematological patients with mild-moderate COVID-19, early treatment is recommended, with the followings:	AI
	a) anti-SARS-CoV-2 monoclonal antibodies, if active against the circulating variants	Allt
	b) nirmatrelvir/ritonavir	Allt
	c) remdesivir (<i>main drawback: intravenous administration</i>)	BlIt
	d) molnupiravir (<i>main drawback: lower efficacy</i>)	BlIt
	Dexamethasone should not be used in early treatment of mild-moderate COVID-19	DlIt
70 ChW	In HM patients with moderate COVID-19 requiring oxygen support, or severe COVID-19 (saturation <90–94%%, respiratory rate >30/min) the following treatments are recommended:	
	a) Dexamethasone	Allt
	b) Remdesivir	BlIt
	c) If the patient is seronegative:	
	- monoclonal antibodies, if active against the circulating variants or	BlIt
	- high titer convalescent plasma ^b , if MoAbs are not available	CIII
	d) If severe COVID-19 inflammation ^c , including worsening despite dexamethasone, add the second immunosuppressant:	Allt
	- anti-IL-6 (tocilizumab, sarilumab) or	BlIt
- JAK –inhibitor (baracitinib/tofacinib ^d)	CIIIt	
	- anti-IL1 (anakinra) ^e	CIIIt
71 ChW	In patients with critical COVID-19 (ARDS, sepsis, septic shock, MIV, NIV or vasopressor therapy, the following treatments are recommended:	
	a) dexamethasone	Allt
	b) remdesivir	CIIIt
	c) monoclonal antibodies if active against the circulating variants in NIV patients (no data in MIV patients).	CIIIt
	Add 2 nd immunosuppressant, if COVID-19-related inflammation is present ^c , as:	Allt
	- Anti-IL-6 (tocilizumab, sarilumab)	BlIt

Cesaro S, Mikulska M, Hirsch HH, et al. Update of recommendations for the management of COVID-19 in patients with haematological malignancies, haematopoietic cell transplantation and CAR T therapy, from the 2022 European Conference on Infections in Leukaemia (ECIL 9). *Leukemia*. 2023;37(9):1933-1938.

Table 1. Selected viral reactivation prevention strategies at Fred Hutchinson Cancer Center, City of Hope National Medical Center and Memorial Sloan Kettering Cancer Center

	Fred Hutchinson Cancer Center	City of Hope National Medical Center	Memorial Sloan Kettering Cancer Center	Published guidelines and references
HSV 1, 2	Acyclovir (initially IV, then 800 mg) or valacyclovir (500 mg) twice daily for 1 y or 6 mo after discontinuation of systemic immunosuppression; at least 3 y after UBC transplantation†	Acyclovir (initially IV, then 400 mg twice daily) or valacyclovir (500 mg) twice daily for 1 y or 6 mo after discontinuation of systemic immunosuppression†	Acyclovir (initially IV, then 400 mg twice daily for 1 y or 6 mo after discontinuation of systemic immunosuppression; at least 3 y after UBC transplantation	Tomblyn et al 2009 ³⁴
VZV				
Antivirals	Acyclovir (initially IV, then 800 mg) or valacyclovir (500 mg) twice daily for 1 y or 6 mo after discontinuation of systemic immunosuppression; at least 3 y after UBC transplantation	Acyclovir (initially IV, then 400 mg twice daily) or valacyclovir (500 mg) twice daily for 1 y or 6 mo after discontinuation of systemic immunosuppression	Acyclovir (initially IV, then 400 mg twice daily for 1 y or 6 mo after discontinuation of systemic immunosuppression; at least 3 y after UBC transplantation	Tomblyn et al 2009 ³⁴
Vaccine	No zoster recombinant vaccine (Shingrix) until 24 mo after HCT and ≥8 mo off immunosuppressive therapy and no flare of GVHD No live varicella vaccine	Zoster recombinant vaccine (Shingrix) can be offered at >12 mo after HCT and >6 mo off immunosuppressive therapy and no flare of GVHD No live varicella vaccine	Zoster recombinant vaccine (Shingrix) at ≥12 mo after HCT and no flare of GVHD and immunologic milestones‡ No live varicella vaccine	Hibberd et al 2022 ⁴²
EBV	No routine prophylaxis T-cell depletion: PCR surveillance and preemptive rituximab at ≥1000 copies/mL	No routine prophylaxis T-cell depletion: PCR surveillance and preemptive rituximab at >2000 copies/mL	No routine prophylaxis T-cell depletion, UCB, ATG: PCR surveillance and preemptive rituximab or donor-derived EBV CTL infusion (or third party EBV CTL for UCB)§	Tomblyn et al 2009 ³⁴

Table 1 (continued)

	Fred Hutchinson Cancer Center	City of Hope National Medical Center	Memorial Sloan Kettering Cancer Center	Published guidelines and references
HHV-6	Symptom-based surveillance with PCR work-up in suspected cases	Symptom-based surveillance with PCR work-up in suspected cases	Symptom-based surveillance with PCR work-up in suspected cases	Ward et al 2019 ⁴³
			UCB: PCR surveillance until day 60, treatment based on clinical suspicion for disease	
Adenovirus	Targeted PCR surveillance and preemptive treatment (threshold ≥ 1000 copies/mL) in high-risk settings (TCD, ATG)	Targeted PCR surveillance and preemptive treatment (no fixed viral load threshold) in high-risk settings (TCD, ATG)	Targeted PCR surveillance and preemptive treatment in high-risk settings (TCD, ATG, UCB, Haploidentical, mismatched) Thresholds dependent on time from transplant, donor and graft type	Tomblyn et al 2009 ³⁴
	Low risk setting: symptom-based testing and treatment of disease	Low risk setting: symptom-based testing and treatment of disease	Low risk setting: symptom-based testing and treatment of disease	
BK virus	No specific antiviral prophylaxis	No specific antiviral prophylaxis	No specific antiviral prophylaxis	Cesaro et al 2018 ⁴⁴

Dadwal SS, Papanicolaou GA, Boeckh M. How I prevent viral reactivation in high-risk patients. *Blood*. 2023;141(17):2062-2074.

Question 1

- Letemovir prophylaxis reduces the risk of the following infections:
 - CMV
 - HSV
 - VZV
 - All of the above

Question 2

Which is false above EBV reactivation:

- T cell depletion is a risk factor
- Usually presents many years after transplant
- Rituximab is the treatment
- CD19 depletion in the graft reduces the risk

CMC Vellore
— celebrates —
125 years

1900-2025

