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SOCIEDAD ESPAÑOLA DE FARMACIA HOSPITALARIA
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Sapere Aude
Reflexión ante nuevos retos

SAUPERE AUDE: ACTUALIDAD FARMACOTERAPEUTICA (I)

Profilaxis en pacientes de alto riesgo: entre hongos y virus

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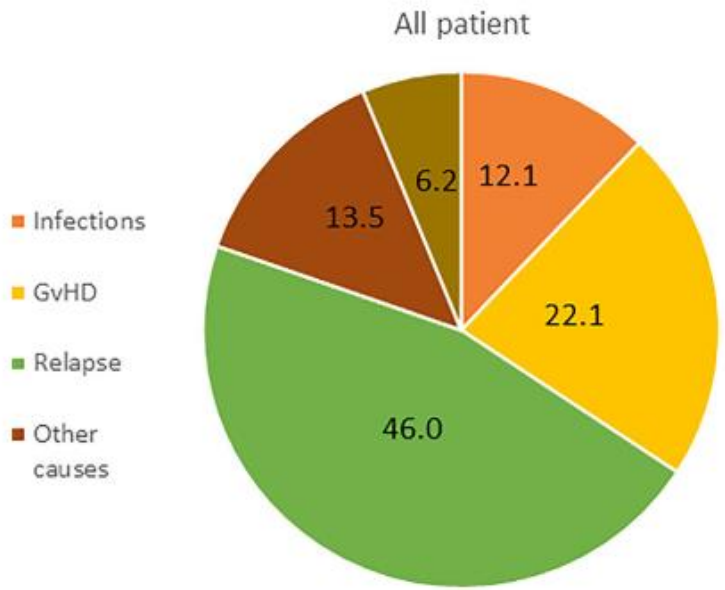
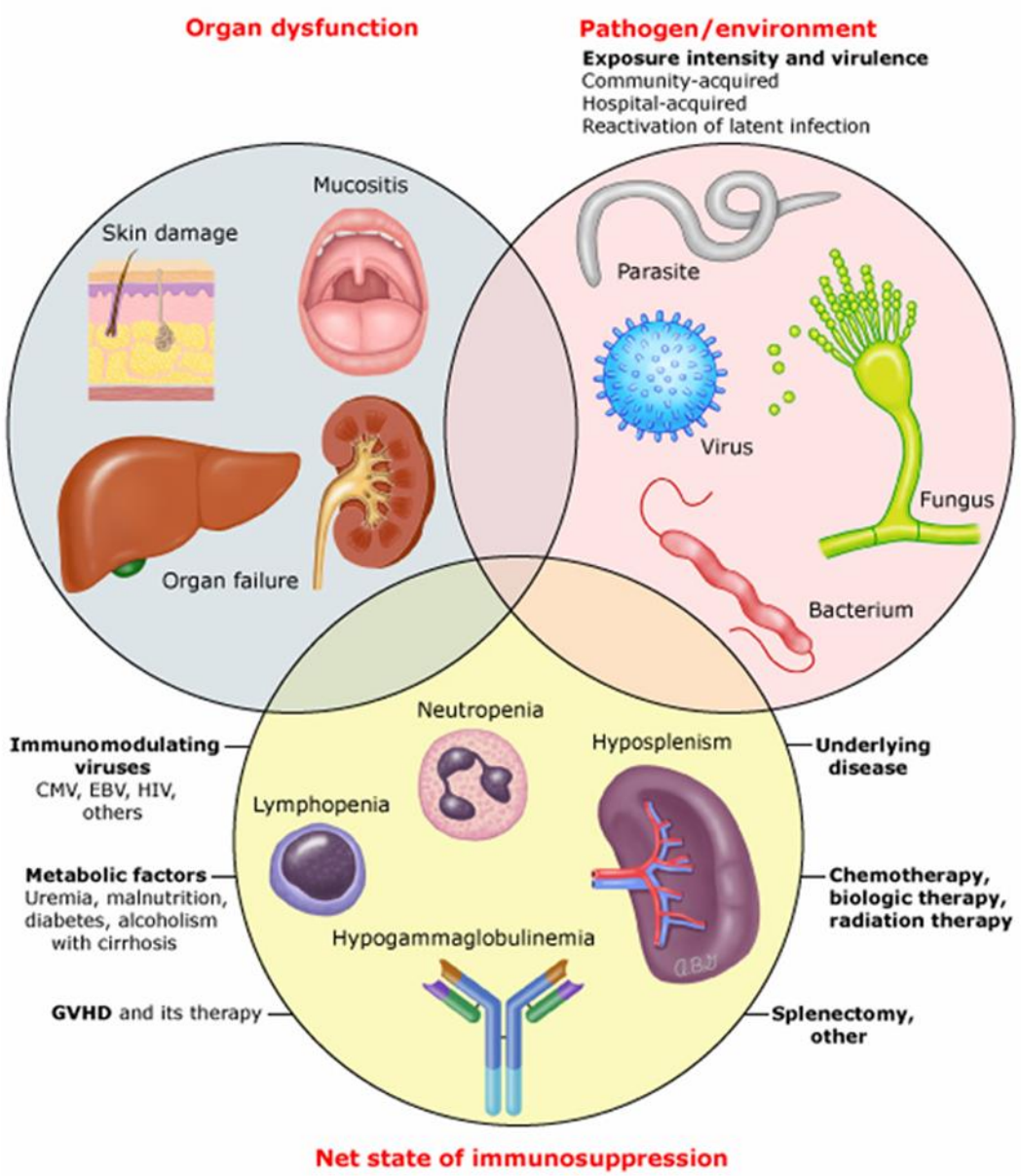
ORIGINAL ARTICLE

Trends in underlying causes of death in allogeneic hematopoietic cell transplant recipients over the last decade

Andreas Søborg[1] | Joanne Reekie[1] | Henrik Sengeløv[2] |

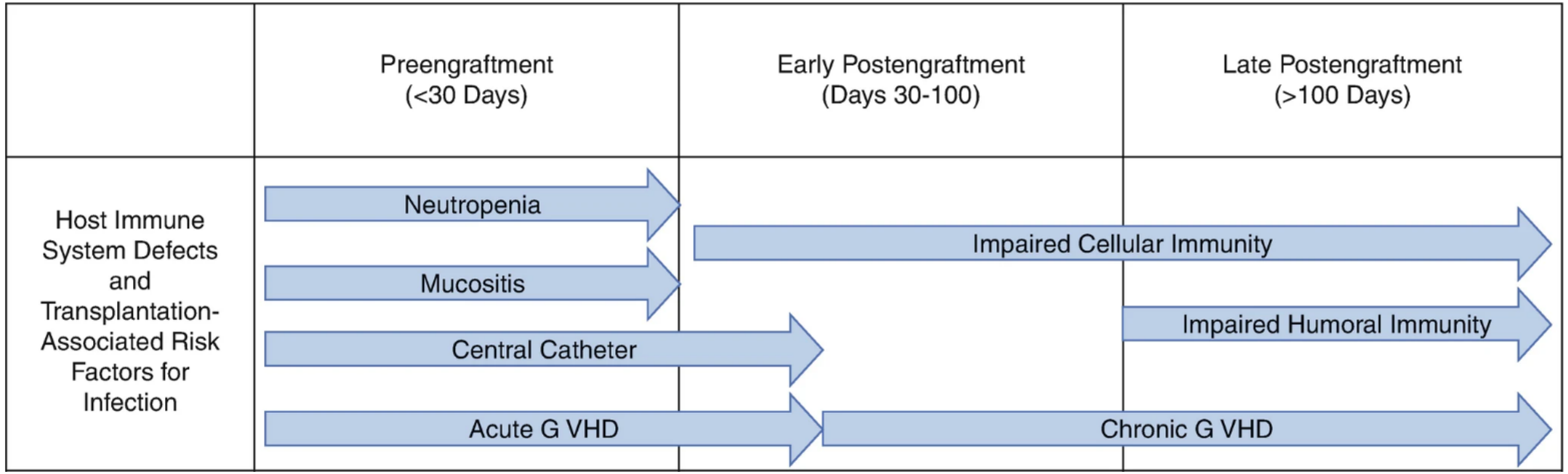




Población de mayor riesgo

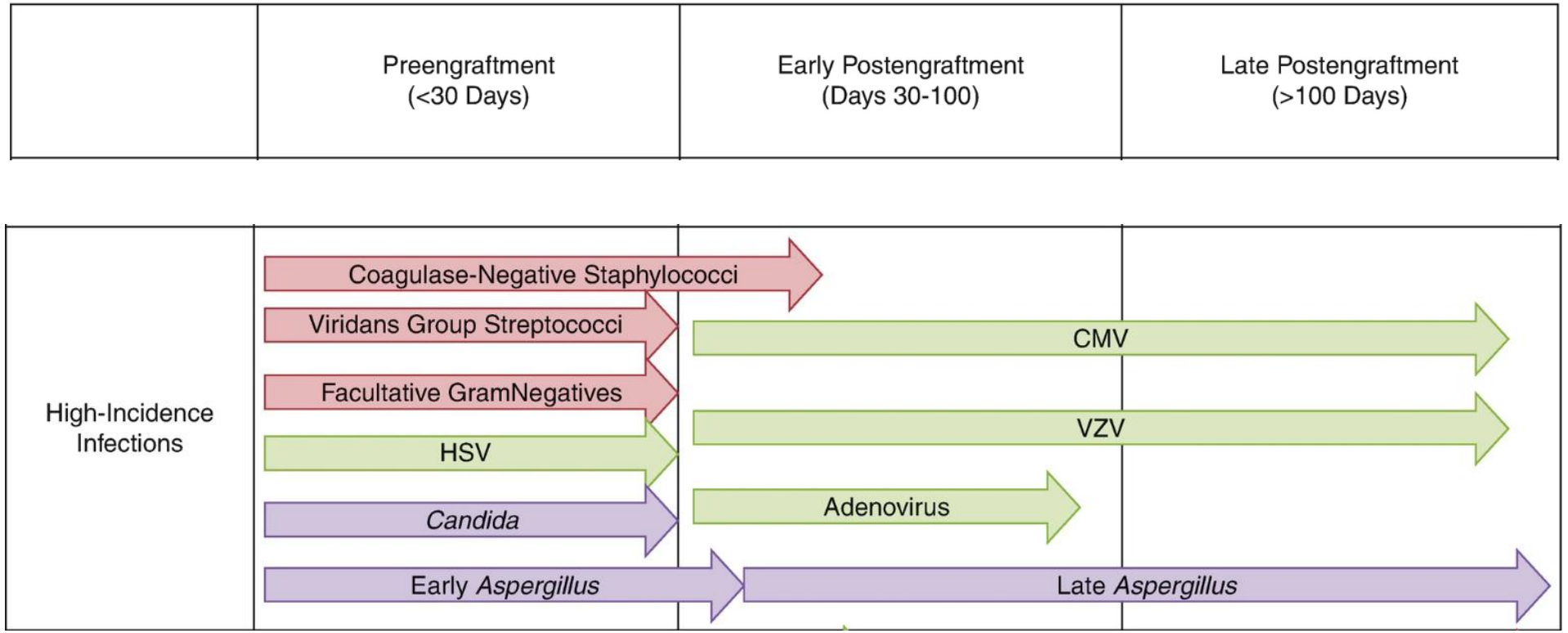
John R Wingard, MD. Prevention of infections in hematopoietic cell transplant recipients. UpToDate 2025.

Timeline-factores de riesgo



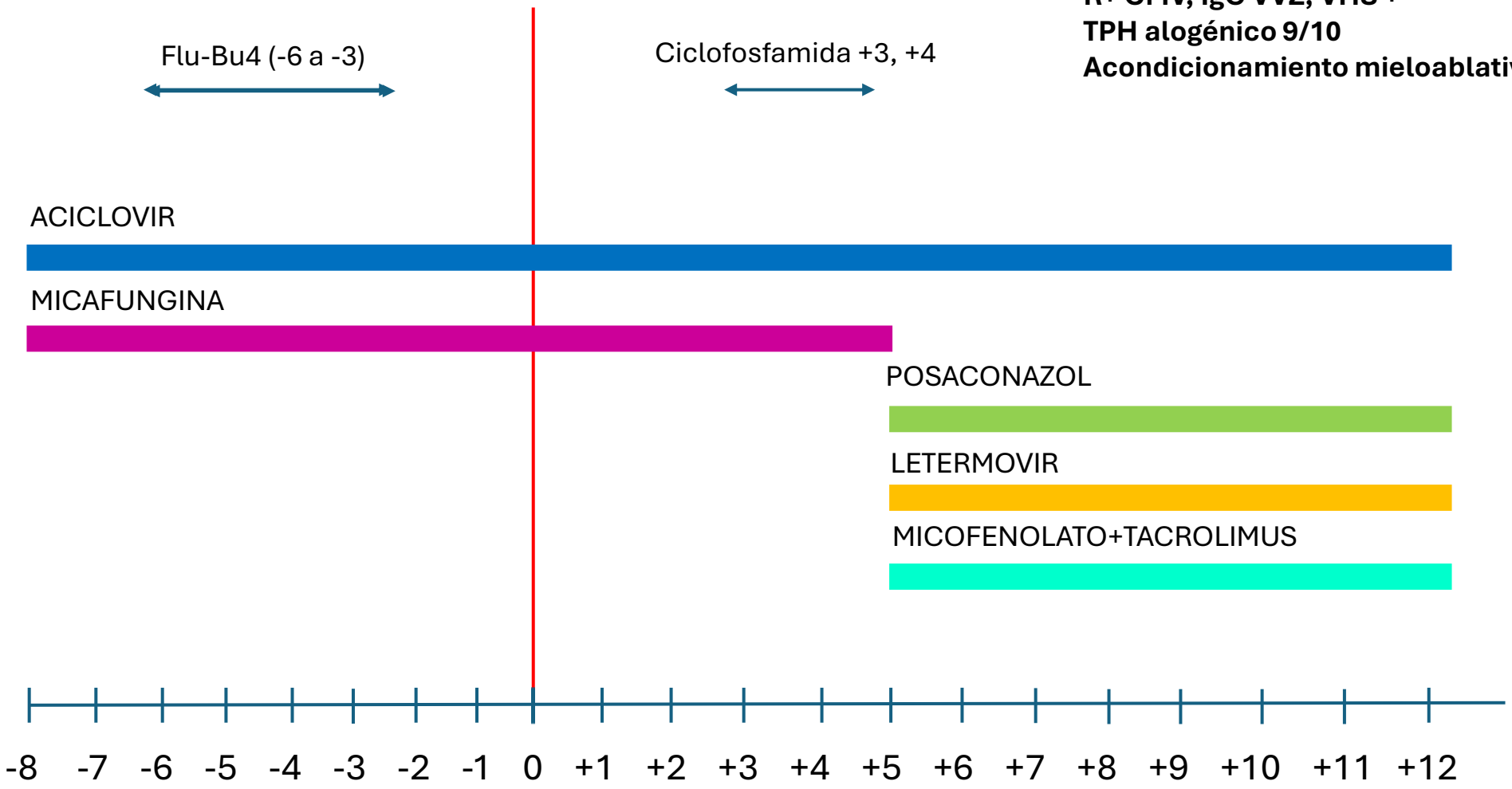
Pereira, M.R et al. (2019). Infections in Allogeneic Stem Cell Transplantation. In: Safdar, A. (eds) Principles and Practice of Transplant Infectious Diseases. Springer, New York, NY.

Timeline-patógenos más frecuentes



**Pereira, M.R et al. (2019). Infections in Allogeneic Stem Cell Transplantation.
In: Safdar, A. (eds) Principles and Practice of Transplant Infectious Diseases. Springer, New York, NY.**

LMA en RC con EMR+
R+ CMV, IgG VVZ, VHS +
TPH alogénico 9/10
Acondicionamiento mieloablativo



HERPESVIRUS VHS-1y VHS-2, VVZ, CMV, VEB

VIRUS RESPIRATORIOS Gripe, VRS, Adenovirus

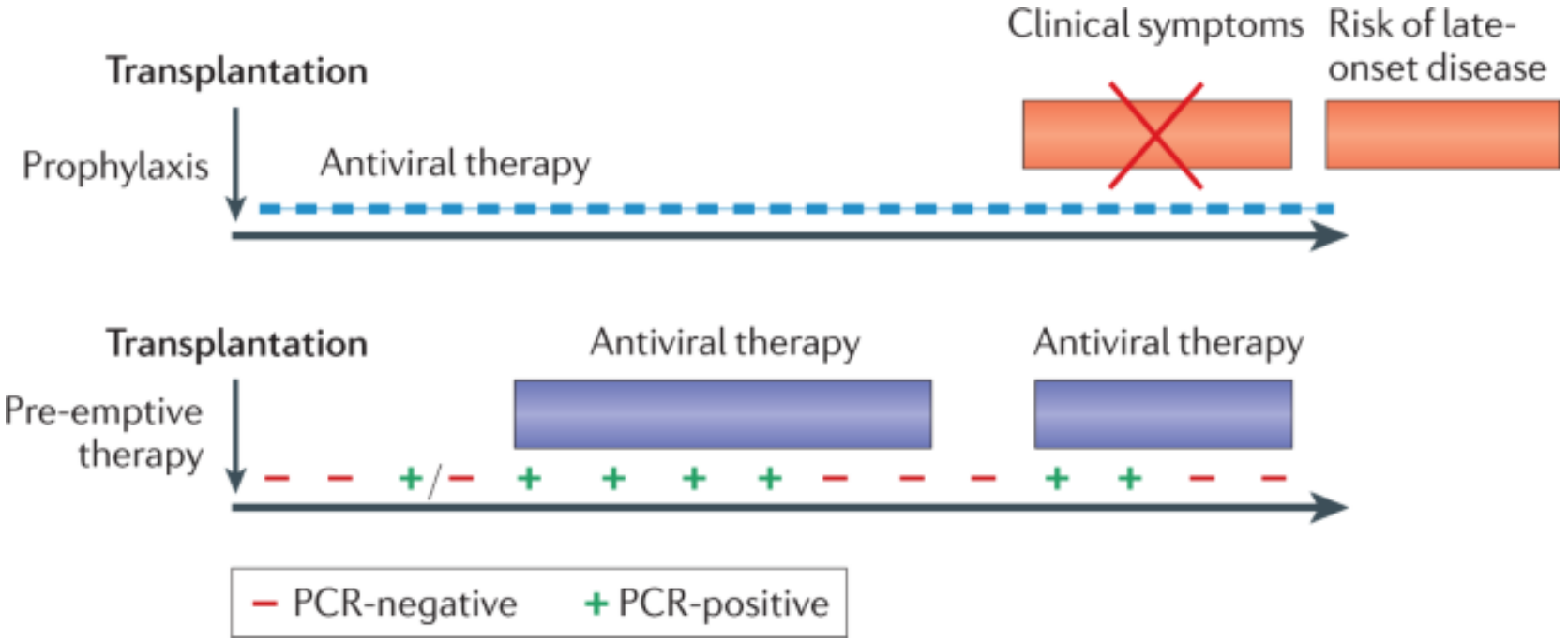
HEPATITIS VIRICAS VHB, VHC

Profilaxis herpesvirus, excluyendo CMV, VEB

	FARMACO	DOSIS	INICIO/DURACION
VHS-1 y VHS-2 Virus del herpes simple	ACV o VCV Todos los ALO, considerar en AUTO si mucositis	ACV: 5 mg/kg/12h; 250mg/m2 IV 400/800 mg/12h ORAL VCV: 500mg/12h ORAL	Durante el acondicionamiento y hasta injerto o resolución de mucositis lo que ocurra primero, puede ser necesario >tiempo si inmunosupresión.
VVZ Virus del herpes zoster	ACV o VCV ALO y AUTO	ACV: 5 mg/kg/12h; 250mg/m2 IV 800 mg/12h ORAL VCV: 500mg/12h ORAL	Durante el acondicionamiento y al menos durante 1 año, para pacientes con tratamiento inmunosupresor hasta 6 meses después de la suspensión.

ACV= aciclovir, VCV= valaciclovir

Tratamiento anticipado vs profilaxis en CMV



Griffiths P, Reeves, M. Pathogenesis of human cytomegalovirus in the immunocompromised host. *Nat Rev Microbiol* 2021; 19: 759–773.

Características de los fármacos utilizados en la prevención de CMV

FARMACO	VIA	DOSIS			EFECTOS SECUNDARIOS	METABOLISMO	INTERACCIONES	ACTIVIDAD FRENTE A OTROS VIRUS
		Profilaxis	Inducción	Mantenimiento				
Ganciclovir	IV		5mg/kg/12h	5mg/kg/24h	Citopenias	Sustrato:OAT1,OAT3	Maribavir	VHS-1,VHS-2,VHZ,VHH6
Valganciclovir	ORAL		900mg/12h	900 mg/24h	Citopenias	Sustrato:OAT1,OAT3	Tenofovir Maribavir	VHS-1,VHS-2,VHZ,VHH6
Foscarnet	IV		90mg/kg/12h 60mg/kg/8h	90mg/kg/24h	Nefrotoxicidad Alteraciones hidroelectrolíticas			VHS-1,VHS-2,VHZ,VHH6
Letermovir	ORAL	480 mg/12h 240 mg/24h si ciclosporina			Náuseas	Inhibidor/sustrato: CYP3A4 Inductor: CYP2C9,CYP2C19 Inductor/sustrato: OAT1,OAT3	Ciclosporina, voriconazol, tacrólimus, sirólimus, estatinas	NO

PRECAUCIONES:

Ajuste de dosis a función renal: Ganciclovir, valganciclovir: ClCr (ml/min), foscarnet: ClCr (ml/min/kg)

Vía de administración (central/periférica): Foscarnet

Profilaxis CMV con letermovir

Pacientes de alto riesgo de reactivación de CMV (BIFIMED)

Profilaxis primaria

Marty FM et al. N Engl J Med 2017; 377:2433-2444.

Profilaxis primaria extendida

Russo, D et al. The Lancet Haematology, 2024; 11(2):e127 - e135.

Profilaxis secundaria

Robin C et al. Biol Blood Marrow Transplant 2020; 26(5):978-984.
Han G et al. Transplant Cell Ther 2025; 31(2): 105.e1-105.e9

Candida spp

PRE-injerto
POST-injerto si EICR severo
CVC

Aspergillus spp

PATRON BINODAL:
-inicio 0 a +100
-inicio >180 días

Profilaxis primaria antifúngica

TRASPLANTE ALOGENICO CON ALTO RIESGO DE IFI POR ASPERGILLUS

TRATAMIENTO DE ELECCION: Voriconazol 200 mg/día
INICIO DEL TRATAMIENTO: Finalización del acondicionamiento
DURACION DEL TRATAMIENTO: ALO sin EICR: +75
ALO con EICR: hasta prednisona <20mg
ALTERNATIVAS: Posaconazol, itraconazol, micafungina

ALTO RIESGO
Leucemia mieloide aguda
Retraso del injerto
IFI previa
Fallo de injerto

Table 5
Drug-Drug Interactions with Antifungal Therapy and Commonly Use Medications in Stem Cell Transplant [276–322]

	Isav	Itra	Posa	Vori	L-AMB*	Echid	Metabolism/Transport Effects Clinical Considerations
Conditioning Regimen Chemotherapy(278, 279)							
Busulfan	▲	▲	▲	▲	♦	♦	-Extensive hepatic metabolism; glutathione via GST catalysis • Triazoles may decrease Busulfan clearance, increasing serum concentration. • PK analysis with Busulfan strongly recommended if need to continue concomitant triazole
Carboplatin	♦	♦	♦	♦	♦	♦	-Minimal hepatic metabolism
Cyclophosphamide (280-284)	▲▼	▲▼	▲▼	▲▼	♦	♦	-Substrate: CYP3A4, CYP2C9, CYP2C19, **CYP2B6**, CYP2A6 -Prodrug: Hepatic metabolism to active metabolites • Bi-directional interaction concerns given hepatic metabolism via CYP450 enzymes to active metabolites. • Triazole may inhibit metabolism to active metabolites. • Triazole may increase serum concentration of active metabolites, such as hydroxycyclophosphamide, which is further metabolized to the toxic acrolein degradation product
Etoposide	▲	▲	▲	▲	♦	♦	-Substrate: **CYP3A4, P-gp**, CYP1A2, CYP2E1 • Given high doses of VP16 used during SCT, recommend avoiding concomitant triazole use if able
Fludarabine	♦	♦	♦	♦	♦	♦	-Rapid dephosphorylation
Melphalan	♦	♦	♦	♦	♦	♦	-Hepatic metabolism via chemical hydrolysis
Thiotepa	▼	▼	▼	▼	♦	♦	-Substrate: **CYP3A4, CYP2B6** -Inhibits: CYP2B6 -Prodrug: Hepatic metabolism to active metabolites • Triazole may decrease thiotepa metabolism to active metabolites (TEPA), decreasing efficacy.
Graft-Versus-Host Disease (GVHD)(278, 279, 285, 286)							
Cyclosporine (287)	●	●	●	●	♦	●	-Substrate: **CYP3A4, P-gp** -Inhibits: BCRP/ABCG2, BSEP/ABCB11, CYP2C9, CYP3A4, OATP1B1/1B3, P-gp • See table 4C for empiric dose adjustment considerations. • CSA may increase serum concentration of caspofungin, possibly through competitive inhibition of P-gp. Monitor for adverse events (e.g. hepatotoxicity)
Tacrolimus	●	●	●	●	♦	▼	-Substrate: **CYP3A4, P-gp** • See table 4C for empiric dose adjustment considerations. • Not typically clinically significant, however caspofungin may dec. tacro conc, continue tacro TDM-no empiric dose adjustment recommended
Sirolimus (288)	●	●	●	●	♦	▼	-Substrate: **CYP3A4, P-gp** • See table 4C for empiric dose adjustment considerations. • Not typically clinically significant, however caspofungin may dec. siro conc, continue siro TDM- no empiric dose adjustment recommended
Mycophenolate Mofetil	▲	♦	♦	♦	♦	♦	-Substrate: OAT1/3, OATP1B1/1B3 (SLCO1B1/1B3), UGT1A10, UGT1A8, UGT1A9, UGT2B7 • Isav inhibits UGT-mediated mycophenolic acid conjugation, increased serum conc. of MMF

Douglas AP et al. American Society of Transplantation and Cellular Therapy Series: #8-Management and Prevention of Non-Aspergillus Molds in Hematopoietic Cell Transplantation Recipients. Transplantation and Cellular Therapy 2025; 31 (4): 194-223.

LECTURA RECOMENDADA

1.Pereira MR et al. Chapter 11: Infections in Allogeneic Stem Cell Transplantation. En: Sureda A, editor. The EBMT Handbook. Springer; 2024. p. 209-226.
2.Dadwal SS et al. How I prevent viral reactivation in high-risk patients. Blood 2023; 141 (17): 2062–2074.
3.Ljungman P 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: e451–62.
4.Khawaja F et al. American Society for Transplantation and Cellular Therapy Series #11: Updated Cytomegalovirus Guidelines in Hematopoietic Cell Transplant and Cellular Therapy Recipients. Transplantation and Cellular Therapy 2025 Transplant Cell Ther 2025; 26: S2666-6367.
5.Pagano L et al. Primary antifungal prophylaxis in hematological malignancies. Updated clinical practice guidelines by the European Conference on Infections in Leukemia (ECIL). Leukemia 2025; 39: 1547–1557.
6.Neofytos D et al. American Society for Transplantation and Cellular Therapy Series, #6: Management of Invasive Candidiasis in Hematopoietic Cell Transplantation Recipients. Transplantation and Cellular Therapy 2023; 29 (4): 222-227.
7.Douglas AP et al. American Society of Transplantation and Cellular Therapy Series: #8-Management and Prevention of Non-Aspergillus Molds in Hematopoietic Cell Transplantation Recipients. Transplantation and Cellular Therapy 2025; 31(4):194-223.
8.Brüggemann RJ et al. Management of drug–drug interactions of targeted therapies for haematological malignancies and triazole antifungal drugs. Lancet Haematol 2021; 9: 58–72.

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Gracias

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