



Società Italiana di Terapia Antinfettiva  
Antibatterica Antivirale Antifungina

**14° CONGRESSO  
NAZIONALE**

GENOVA | 21-22 novembre 2024

**Novità nella gestione delle  
infezioni batteriche e virali nei  
pazienti trapiantati**

**Maddalena Giannella**

## Conflicts of interest

- ❖ Grants from Pfizer, MSD, Gilead and BioMerieux as a speaker
- ❖ Grants from MSD and Takeda as an advisory board member
- ❖ Research grant from Pfizer



# Outline

## Infections in Solid Organ Transplant patients

### ❖ Virus

- VPI
- CMV, HHV8, EBV

### ❖ Bacteria

- Donor derived infections

# Vaccine-Preventable Infections Among Solid Organ Transplant Recipients in Switzerland

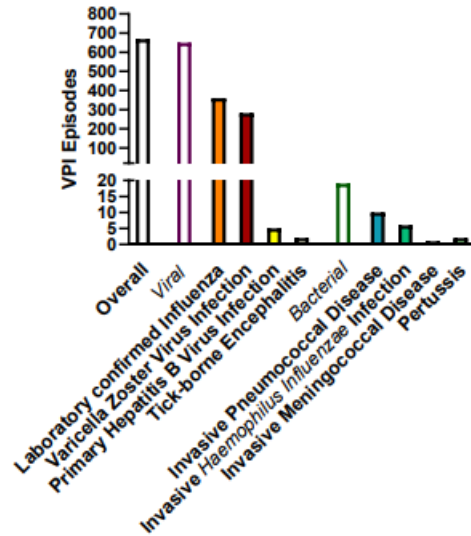
*Walti LN et al. JAMA Network Open. 2023;6(4):e2310687*

What is the incidence rate of vaccine-preventable infections in solid organ transplant (SOT) recipients compared with the general population?

- ❖ Nationwide cohort study used data from the Swiss Transplant Cohort Study on VPIs in individuals who underwent SOT from May 2008 to June 2019 (follow-up until December 2019) and data from the Swiss Federal Office of Public Health on notifiable VPIs in the general population in the same period
- ❖ 4967 SOT recipients (2784 [56.0%] kidney, 1100 [22.1%] liver, 454 [9.1%] lung, 385 [7.8%] heart, and 244 [4.9%] combined) were included
- ❖ 668 VPI episodes in 593 SOT recipients (11.9%), most VPIs occurred late (>1 year)



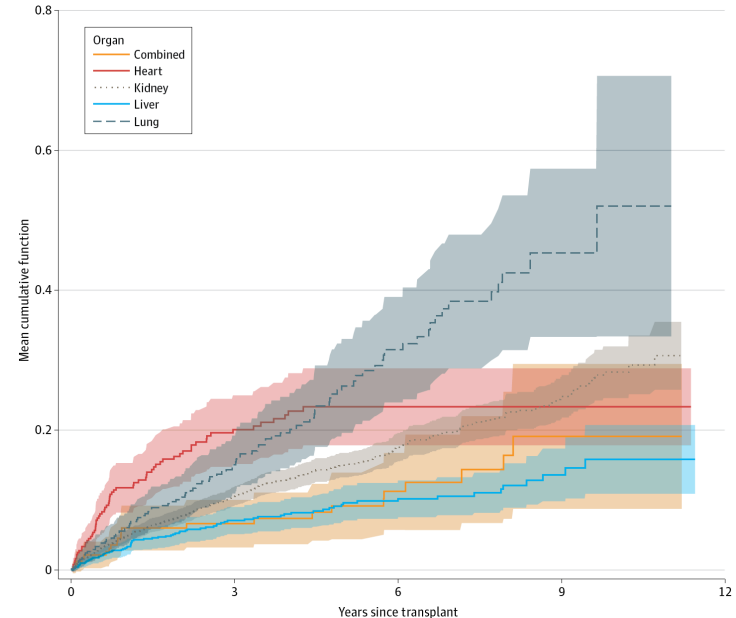
# Vaccine-Preventable Infections Among Solid Organ Transplant Recipients in Switzerland



eTable 3: Time from transplant to VPI occurrence

VPI	Median (IQR), months
Influenza	23.4 (6.9-47.9)
VZV	16.9 (6.2-41.7)
Hepatitis B	13.7 (13.1-32.7)
TBE	16.3 (NA)
IPD	19.0 (15.7-24.5)
IHI	7.76 (0.3-31.2)
Pertussis	44.8 (NA)
IMD	30.6 (NA)

Walti LN et al. JAMA Network Open. 2023;6(4):e2310687



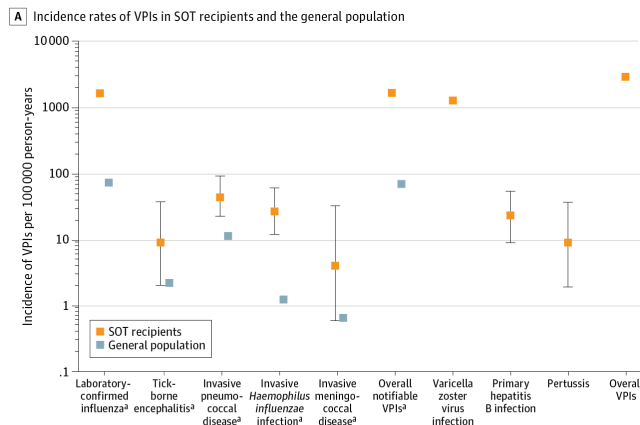
## Associated morbidity and mortality

- Hospitalization, 34.4%
- Graft loss within 90 d, 0.9%
- Death within 30 d, 1.0%

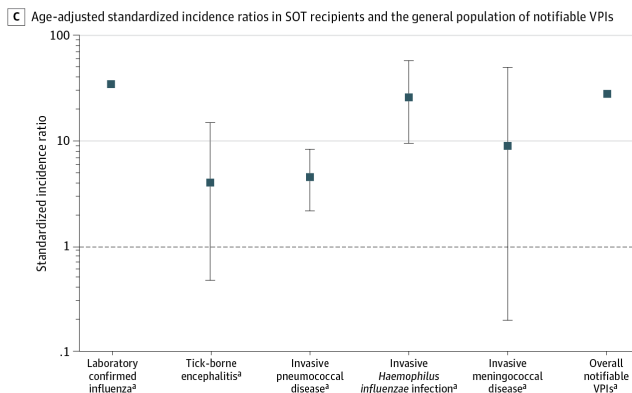
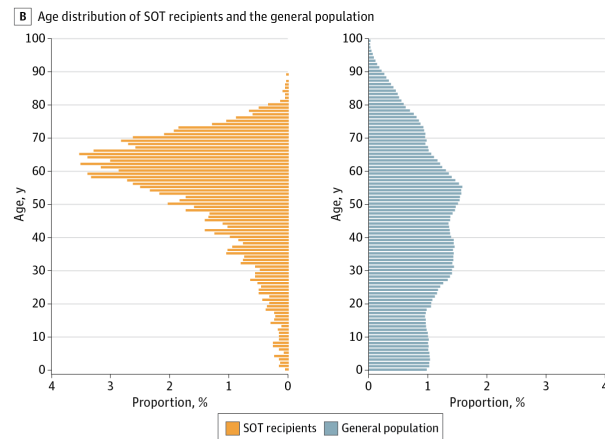


# Vaccine-Preventable Infections Among Solid Organ Transplant Recipients in Switzerland

**Overall incidence rate of notifiable VPI in SOT 30.57 per 1000 PY vs. 0.71 per 1000 PY in general population**



**Walti LN et al. JAMA Network Open. 2023;6(4):e2310687**



**Age-adjusted IRs for influenza and IHI were significantly higher in SOT, IRs for IMD and TBE were not significantly different between the two populations.**

There is an important need for optimization of vaccine strategies in SOT recipients:

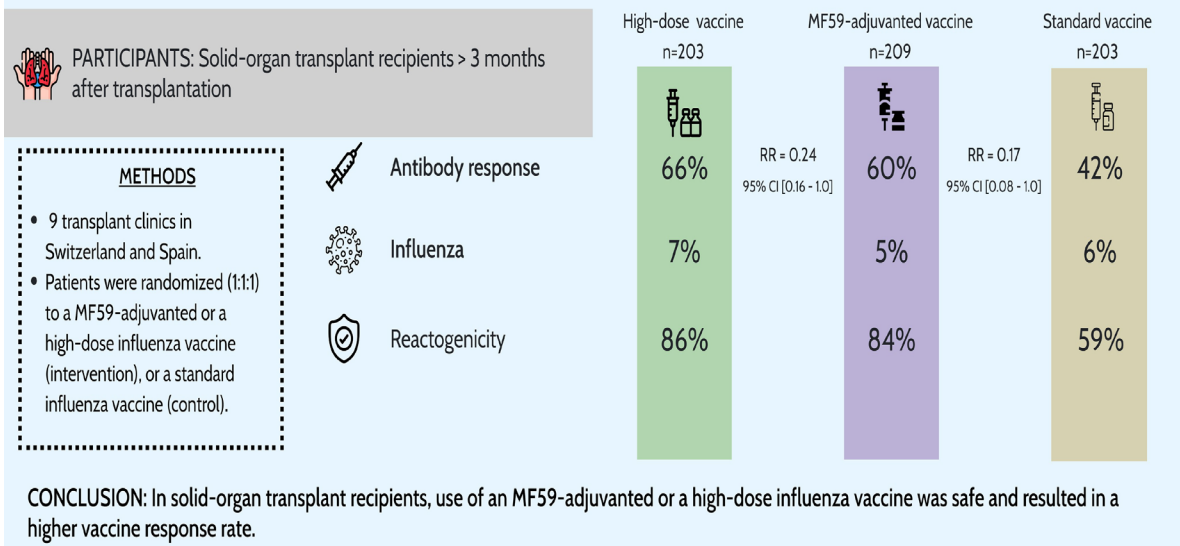
- Immunogenicity
- Logistic difficulties before transplant
- Vaccine hesitancy



# Immunogenicity of High-Dose Versus MF59-Adjuvanted Versus Standard Influenza Vaccine in Solid Organ Transplant Recipients: The Swiss/Spanish Trial in Solid Organ Transplantation on Prevention of Influenza (STOP-FLU Trial)

Mombelli M et al. *Clinical Infectious Diseases* 2024;78(1):48–56

Which is the best strategy for vaccinating solid organ transplant recipients against influenza?



- ❖ 68% KT recipients and median time after transplantation was 42 months
- ❖ 23/35 (66%) influenza episodes were diagnosed only through surveillance testing, 2/9 clinical episodes were complicated with bacterial pneumonia (1 in the MF59-adjuvanted and 1 in the HD vaccine group). None was admitted to ICU or died.
- ❖ Only 1 SAE related to vaccination (panniculitis after HD). Low rates of de novo anti-HLA Ab and biopsy proven rejection in all groups.





## L'ospedale che vaccina

In corsia

27 Aprile 2023



***Screening and vaccination pre-SOT offered in our outpatient facility by the same ID transplant team that will follow the patient during hospitalization and after transplantation***

Da martedì 2 maggio è attivo l'ambulatorio dedicato alle vaccinazioni dei pazienti più fragili: si parte con 1000 pazienti per il primo anno, l'obiettivo è di arrivare a 4000.

Il progetto, messo a punto dagli infettivologi Pierluigi Viale e Luciano Attard, prevede in questa prima fase la somministrazione di vaccini a pazienti candidati al trapianto di cuore, fegato, reni e polmone, a chi ha ricevuto una nuova diagnosi di infezione da HIV, e a pazienti colpiti da malattie infiammatorie croniche intestinali che stanno per iniziare una terapia con immunosoppressori.





December 10, 2024 @ 5pm Central European Time/11am Eastern US/8:30pm Indian Time

Speaker	Title
Webinar Chairs: <b>Hans Hirsch</b> , University of Basel, Switzerland <b>Michael Ison</b> , National Institutes of Health, United States	
<b>Pauline Vetter</b> , University of Geneva, Switzerland	Management Approaches for Influenza in Immunocompromised
<b>Jose Luise Pinana</b> , University of Valencia, Spain	Management of RSV in Immunocompromised
<b>Fareed Khawaja</b> , MD Anderson Cancer Center, United States	Approach to Management of COVID-19 in Oncology and HSCT Patients
Panel Discussion	

Session in Collaboration with ESGREV

Drug	Target	Route	Indications	Major toxicities	Activity against other herpes viruses	Comments
Cidofovir	UL54 DNA polymerase	IV	Treatment	Nephrotoxicity, myelosuppression, ocular, and alopecia	Yes: HSV, VZV, and HHV6	Alternative for treatment due to high risk of toxicity
Foscarnet	UL54 DNA polymerase	IV	Treatment	Nephrotoxicity, electrolyte loss, and myelosuppression	Yes: HSV, VZV, and HHV6	Alternative for treatment due to high risk of toxicity
Ganciclovir	UL54 DNA polymerase	IV	Treatment and prophylaxis	Myelosuppression, especially leukopenia and neutropenia	Yes: HSV, VZV, and HHV6	First-line treatment of CMV disease, especially if severe and life-threatening
Maribavir	UL97 kinase	Orally or by mouth	<b>Treatment resistant and refractory CMV</b>	Dysgeusia and gastrointestinal effects	In vitro: EBV (no data in vivo)	<b>Poor CNS penetration</b> Consider adding HSV-active drug during high-risk periods May increase levels of immunosuppressants
Letermovir	UL56, UL51, UL89 terminase	IV, orally or by mouth	Prophylaxis	Gastrointestinal effects	None	Consider adding HSV-active drug during high-risk periods Low barrier of resistance May increase levels of immunosuppressants
Valganciclovir	UL54 DNA polymerase	Orally or by mouth	Treatment and prophylaxis	Myelosuppression, especially leukopenia and neutropenia	Yes: HSV, VZV, and HHV6	First-line treatment of asymptomatic and mild-to-moderate CMV disease

# **Letermovir Prophylaxis for Cytomegalovirus in Hematopoietic-Cell Transplantation**

**Marty FM N Engl J Med 2017;377(25):2433-2444**

**Efficacy and safety of extended duration letermovir prophylaxis in recipients of haematopoietic stem-cell transplantation at risk of cytomegalovirus infection: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial**

**Russo D et al. Lancet Haematol 2024;11(2):e127-e135**

**Letermovir vs Valganciclovir for Prophylaxis of Cytomegalovirus in High-Risk Kidney Transplant Recipients: A Randomized Clinical Trial**

**Limaye AP JAMA 2023;330(1):33-42**



# CMV-RNAemia as new marker of active viral replication in transplant recipients

Piccirilli G et al. *Journal of Clinical Microbiology* 2024

Is CMV-RNAemia a better marker of active replication than CMV-DNAemia in patients receiving LMV?

- ❖ LMV induces release of free CMV-DNA fragments (abortive infection) leading to misinterpretation of molecular results
- ❖ To prove active replication CMV viremia (shell vial method) and CMV-DNAemia post-DNase (DNase test) should be used

CMV-RNAemia by CMV RNA ELITE InGenius instrument

Cassaniti I et al. *Am J Transplant.* 2021;21:1622–1628

	LMV prophylaxis	LMV off-label treatment	Pre-emptive therapy	Total n=44
HSCT	23	4	6	33
Liver	0	1	3	4
Heart	0	2	2	4
Kidney	0	0	3	3
CMV-DNAemia-pos/total	97/106	35/37	95/111	227/254
CMV-RNAemia-pos/total	14/106	9/37	50/111	73/254
N° pos CMV-DNAemia/CMV-RNAemia episodes	25/6	7/6	15/15	47/27
Sensitivity, specificity	14.4%, 100%	25.7%, 100%	52.6%, 100%	32.2%, 100%



# CMV-RNAemia as new marker of active viral replication in transplant recipients

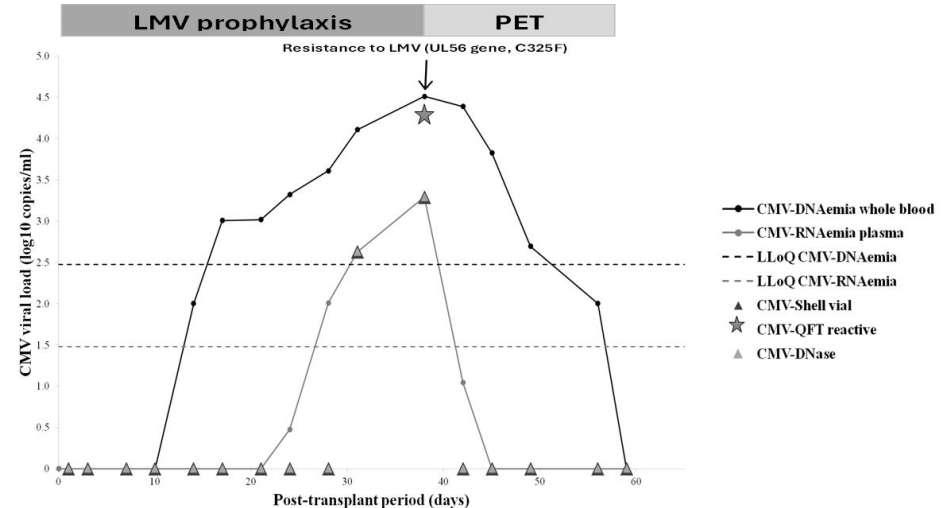
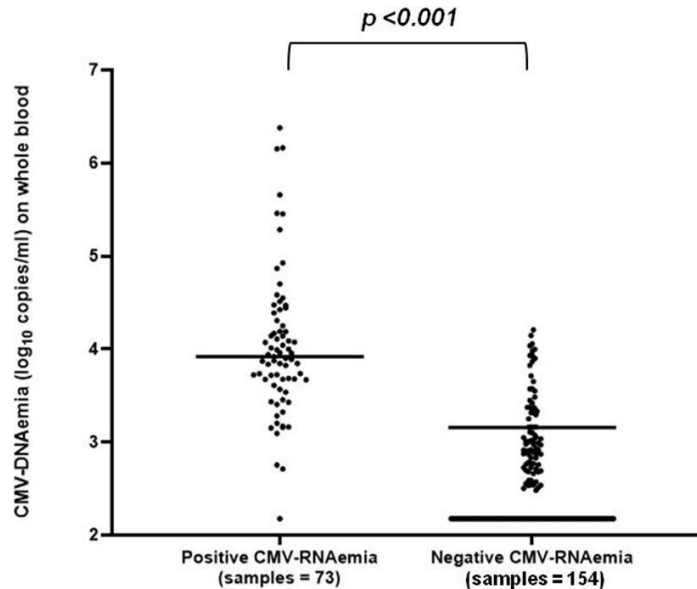
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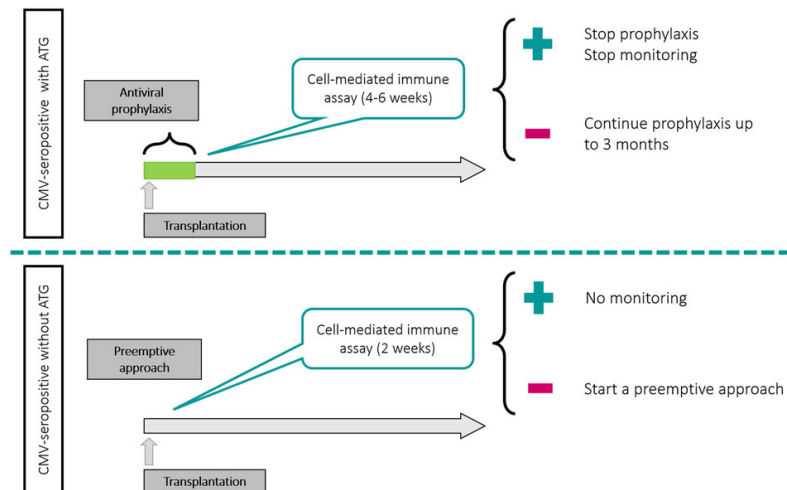
CMV-RNAemia by CMV RNA ELite InGenius instrument



# Cytomegalovirus Cell-Mediated Immunity: Ready for Routine Use?

Bestard O et al. Transpl Int 2023;36:11963

Ref	SOT type, N	CMV risk	CMI assay	Intervention	Results
Kumar AJT 2017	All SOT, 27	R+ and D+/R-	QTF-CMV	Test at EOT, secondary AP if neg	Lower incidence of relapse in pos pts
Westall Transplantation 2019	Lung, 118	R+ and D+/R-	QTF-CMV	Test at 5, 8 and 11 months, stop AP if pos	Lower CMV replication in the graft, longer duration AP
Jarques CID 2020	Kidney, 160	R+	T-SPOT.CMV	Stratify pts at transplant, then randomize to PE vs AP	Higher incidence of CMV replication in high-risk group, better performance of AP
Paez-Vega CID 2022	Kidney, 150	R+ on ATG	QTF-CMV	Test at 30, 45, 60 and 90 days, stop AP if pos	Similar incidence of CMV replication/disease, <b>shorter duration of AP, lower incidence of neutropenia</b>
Manuel CID 2023	Kidney, 164 Liver, 21	R+ on ATG and D+/R-	T-Track-CMV	Test at 30, 60, 90, 120, 150, 180 days, stop AP if pos	Similar incidence of CMV replication/disease, <b>shorter duration of AP</b>



# **Maribavir for Refractory or Resistant Cytomegalovirus Infections in Hematopoietic-cell or Solid-organ Transplant Recipients: A Randomized, Dose-ranging, Double-blind, Phase 2 Study**

**Papanicolaou et al. Clin Infect Dis 2019;68:1255-64**

## **Maribavir for Refractory Cytomegalovirus Infections With or Without Resistance Post-Transplant: Results From a Phase 3 Randomized Clinical Trial**

**Avery R et al. Clin Infect Dis 2022;75(4):690-701**

## **Treatment for First Cytomegalovirus Infection Post-Hematopoietic Cell Transplant in the AURORA Trial: A Multicenter, Double-Blind, Randomized, Phase 3 Trial Comparing Maribavir With Valganciclovir**

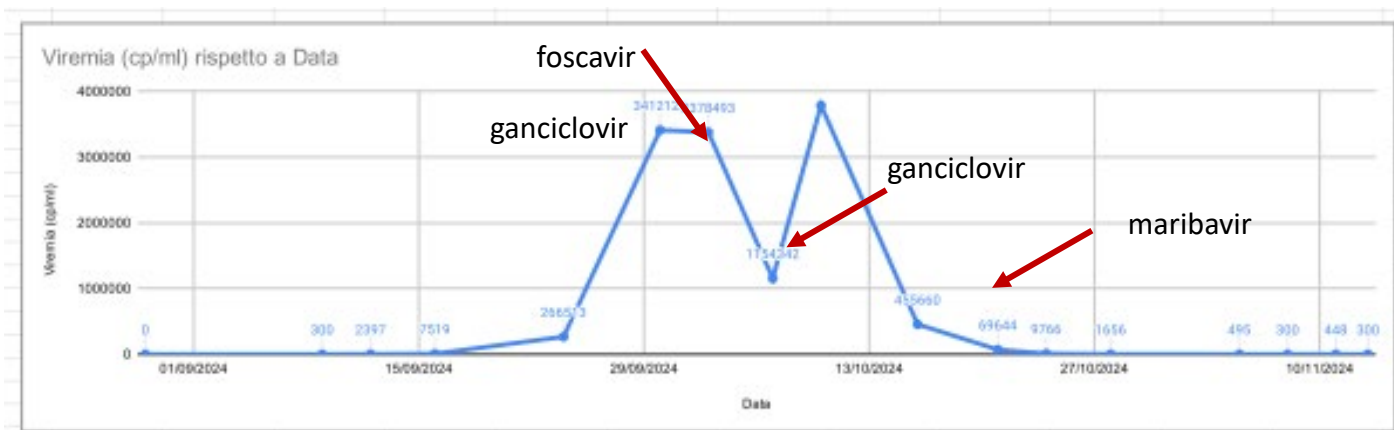
**Papanicolau G et al. Clin Infect Dis 2024 20;78(3):562-572**





# Case vignette

- ❖ 23 anni, allo HCT per HL, D+/R+, pregressa riattivazione CMV, donatore aploidentico, ciclofosfamide
- ❖ Letermovir interrotto a 70 gg per intolleranza GI >>> aGVHD trattata dapprima con alte dosi di steroidi poi ruxolitinib
- ❖ Colite da CMV



*personal clinical case*

	Age, Gender, Underlying disease  Type and year of Transplant	Serostatus and  Prophylaxis strategy	Prior exposure to (V)GCV peak viral load	IS regimen	CMV Retinitis time to	Resistance gene detected	Type and duration (in months) of antiviral treatment	Immunosuppressive modifications and Adjuvant Treatment	Clinical and Virological resolution of retinitis and time from diagnosis (days/months)
<b>Patient 1</b>	40 years, female Bowel insufficiency post total enterectomy  SOT (Multivisceral: Liver, Pancreas, Bowel) - 2016	D+/R+  Prophylaxis with GCV	25 days  53.199 cp/ml	Steroids FK 506	7	Test R 13/12/16: UL97 (M460V)  Test R 23/01/17: UL97 (M460V) and UL54 (Q578H+E756D)  Test R 26/09/17: WT	GCV, FOS, VGC from June 2016 Until April 2017 (10 months)	Leflunomide,  CMV- Immunoglobulines	Clinical: 2 months  Virological: 2 months
<b>Patient 2</b>	50 years, Female T Leukemia/Linfoma  HSCT - 2013	D-/R+  Pre-emptive strategy	72 days  36.651 cp/ml	Steroids	5	//	VCGV, FOS, VCGV from September 2013 until February 2014 (5 months)	//	Clinical: 8 months  Virological: //
<b>Patient 3</b>	62, Male ANCA + vasculitis/ glomerulosclerosis  SOT (Kidney) - 2020	D+/R-  Prophylaxis with GCV	47 months (!)  16.751 cp/ml	Steroids, FK 506 MMF	48	UL97 (L595F)	FOS	Stop MMF	Clinical: None (lost of vision left eye).  Virological: 1 month (CMV-DNA on blood negative, No further vitreous humor sampling was performed)



# Literature overview on CMV retinitis in SOT recipients

- ❖ Prevalence: **2.9% (retrospective chart review)-15% (systematic screening among viremic pts)**, within 4-156 months after SOT
- ❖ Clinical presentation: **in viremic pts the majority were asymptomatic**, in the other studies **viremia was seldom detected or low level**, 1/4 bilateral eye involvement, concomitant other CMV disease localizations
- ❖ Diagnosis: fundoscopic examination, PCR on aqueous
- ❖ Risk factors: allograft rejection, belatacept, D+/R- serostatus, type of SOT?, **association with R/R CMV**
- ❖ Management: no clear the impact of systemic **plus intra-vitreous** antiviral administration; **vitrectomy** is the standard treatment of retinal detachment secondary to CMV retinitis
- ❖ Outcome: reduction visual acuity 40-50%, relapse 20%, visual loss 7%

**Chung et al, Transplantation 2007; Eid et al, Transpl Infect Dis 2008: 10: 13-18;  
Zhang et al, Viruses 2024, 16, 1427; Scherger et al, Transplantation Proceedings, 56, 1696–1701 (2024);  
Janicka-Maszke Z et al, Transplantation Proceedings, 54, 1158–1166 (2022)**

# Use of Letermovir as Salvage Therapy for Drug-Resistant Cytomegalovirus Retinitis

Turner et al, Antimicrobial Agents and Chemotherapy 2019

Feature	Information for patient:			
	A (66-y-old male)	B (50-y-old male)	C (46-y-old male)	D (66-y-old male)
CMV risk factor	Bilateral orthotopic lung transplant (CMV donor+/recipient-)	Bilateral orthotopic lung transplant (CMV donor+/recipient-)	Orthotopic heart transplant (CMV donor+/recipient-)	Orthotopic heart transplant (CMV donor+/recipient-)
Comorbidities	Sarcoidosis, chronic kidney disease	Interstitial lung disease, chronic kidney disease		
Disease burden	CMV syndrome retinitis	CMV syndrome retinitis	CMV syndrome retinitis colitis	Retinitis
Plasma CMV DNA at start of letermovir	342 IU/ml	1,416 IU/ml	745 IU/ml	<137 IU/ml
Prior CMV prophylaxis	Valganciclovir	Valganciclovir	Valganciclovir	Valganciclovir
Prior antiviral treatment	CMV IgG, ganciclovir, valganciclovir, maribavir, foscarnet	Ganciclovir, valganciclovir, maribavir, foscarnet	Ganciclovir, valganciclovir, foscarnet	CMV IgG, ganciclovir, valganciclovir, foscarnet
Known CMV mutations prior to letermovir initiation	M460V (UL97)	Q578H (UL54)	M460I (UL97), likely mixed population at N408K (UL54)	H520Q (UL97), C603W (UL97), T503I (UL54)
Letermovir dose (mg daily)	720	960 <sup>a</sup>	720	720
Concomitant therapies	CMV IgG, foscarnet (V) <sup>b</sup>	CMV IgG, foscarnet (V), ganciclovir (V)	n/a	CMV IgG, foscarnet (V)
Duration of follow-up (weeks)	38	38	33	34
Virologic suppression on letermovir	Unsuppressed	Unsuppressed	Unsuppressed	Suppressed
Mutations conferring letermovir resistance	Negative for UL56 mutations	C325F mutation detected in UL56	C325Y mutation detected in UL56	Letermovir resistance testing not performed
Management of rebound viremia and/or letermovir resistance	Letermovir stopped on day 138, transitioned to valganciclovir and CMV IgG; subsequently achieved virologic suppression	Letermovir stopped on day 110, transitioned to valganciclovir (given reversion of prior UL54 mutation); subsequently achieved virologic suppression	Letermovir stopped on day 102, transitioned to foscarnet; subsequently achieved virologic suppression	n/a <sup>c</sup>
Clinical outcome	Improved on retinal exam	Improved on retinal exam	Improved on retinal exam	Improved on retinal exam



AOO-ISS - 17/10/2024 - 0044227 Class: CNT 01.00



Alla cortese attenzione  
Centri Regionali per i Trapianti  
Loro sedi

Oggetto: indicazioni operative e monitoraggio dei riceventi in caso di riscontro di positività degli anticorpi anti-HHV8 nel donatore di organi e tessuti

	anticorpi anti HHV8 litici	anticorpi anti HHV8 latenti	Monitoraggio ricevente	Livello di rischio post trapianto
Donatore organi	+	-	Ricerca HHV8 DNA mensile per 6 mesi post trapianto. Determinazione Ab anti- litici e anti latenti a 3 e 6 mesi post-trapianto.	Possibile falso positivo. Rischio accettabile post-trapianto. Esclusi i tessuti tranne le cornee.
Donatore organi	Bassa positività	Bassa positività	Ricerca HHV8-DNA mensile per 6 mesi post trapianto. Determinazione Ab anti- litici e anti latenti a 3 e 6 mesi post-trapianto. In assenza di sieroconversione ricerca HHV8-DNA a cadenza semestrale	Possibile falso positivo. Rischio accettabile post-trapianto. Esclusi i tessuti tranne le cornee.
Donatore organi	+	+	Ricerca HHV8 DNA mensile per 6 mesi post trapianto. Determinazione Ab anti- litici e anti latenti a 3 e 6 mesi post-trapianto. In assenza di sieroconversione ricerca HHV8-DNA ogni 3 mesi.	Donatore positivo per HHV8 Rischio accettabile post -trapianto. Esclusi i tessuti tranne le cornee.



Case n°	Age	Sex	SOT type	SOT year	Serostatus	HHV8 dis	Time tpx-disease	Viral load	IL-6	Clinical manifestations/localization	IS management	Antiviral	CHT	Other medications	Outcome
1	61	M	LT	Nov 2016	D+/R-	KICS	4 m	54900	4741	Sierositis, uveitis	FK→mTOR	GCV, CDF	None	TOC	Remission, on FU
2	27	M	KT	Feb 2018	D?/R?	KS	19 m	503	NA	Lymphnodes	MMF→mTOR	None	DOXO	None	Remission
3	57	M	HT	Feb 2018	D?/R-	KICS+KS	14 m	183673	1402	Lymphnodes	FK→mTOR	GCV, CDF	DOXO	None	Remission, on FU
4	60	M	LT	Sept 2019	D?/R?	KICS	13 m	114740	1276	Sierositis, nephropathy	FK→mTOR	CDF	None	TOC	Relapse of KICS + visceral and cutaneous KS
5	66	M	LT	Apr 2021	D?/R?	KICS	10 m	204850	>4794	Sierositis, anemia	None	None	None	None	Death
6	50	M	LT	Sept 2022	D?/R-	KICS + KS	5 m	>10 <sup>7</sup>	772.6	Sierositis, fever	FK→mTOR→stop	GCV, CDF	None	TOC	Remission, on FU
7	66	M	LT	Feb 2023	D?/R-	MCD+KICS	7 m	>10 <sup>7</sup>	332.4	Sierositis, fever	FK→mTOR	GCV, CDF	RTX+DOXO	TOC	Death
8	74	M	KT	Mar 2023	D?/R?	KS	10 m	Neg	<6.4	Cutaneous	MMF→stop	None	None	Laser	Remission, on FU
9	64	F	LT	Jun 2023	D?/R-	KS	11 m	5977	<6.4	Cutaneous, GI, lymph nodes	FK→mTOR	None	DOXO→GCT	None	On FU
10	75	M	KT	Jun 2023	D?/R?	KS	8 m	Neg	<6.4	GI, cutaneous	MMF→mTOR	None	DOXO	None	On FU
11	54	F	LT	Oct 2023	D?/R-	KS	8 m	Neg	<6.4	GI, lymphnodes	FK→mTOR	None	DOXO	None	On FU
12	57	F	LT/KT	Nov 2023	D+/R-	KICS	6 m	>10 <sup>7</sup>	NA	Sierositis, lymphnodes	None	None	None	None	Death



# Serologic screening and molecular surveillance of Kaposi sarcoma herpesvirus (KSHV)/human herpesvirus-8 (HHV-8) infections for early recognition and effective treatment of KSHV-associated inflammatory cytokine syndrome (KICS) in solid organ transplant recipients

Mularoni A et al. Am Journal Transpl 2024

- ❖ ISMETT HHV-8 serology screening routinely performed on D and R since 2011
- ❖ In 2017, specific protocol for the follow-up according with sero-mismatch

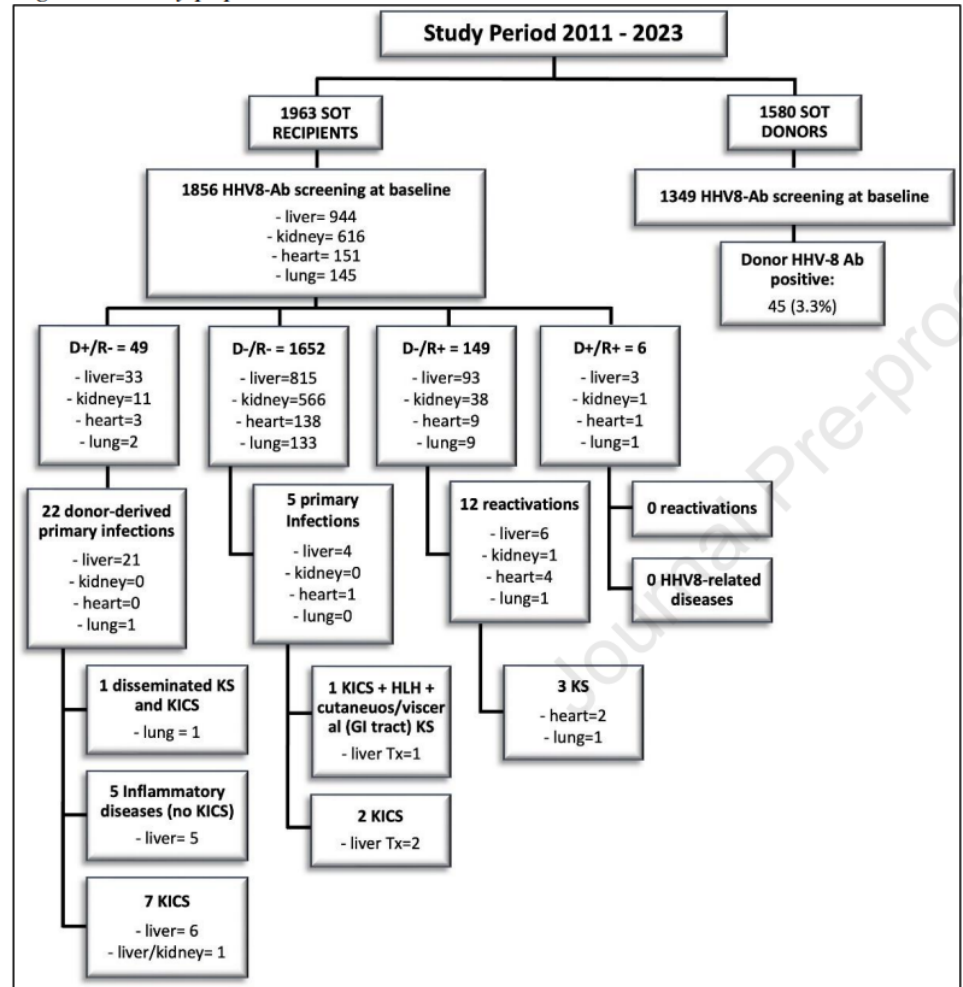
Study aims:

1. the seroprevalence of HHV-8 infection among donors and recipients
2. the incidence of HHV-8 reactivation and primary infection
3. the incidence, clinical characteristics, management, and outcomes of HHV-8-related diseases
4. the inflammatory response and cytokine expression patterns in recipients with KICS





- ❖ HHV-8 seroprevalence: 3.3% (68/1349) in donors and 8.4% in (155/1856) recipients ( $p < 0.0001$ )



4 treated with rituximab survived,  
3 patients not treated with  
rituximab died

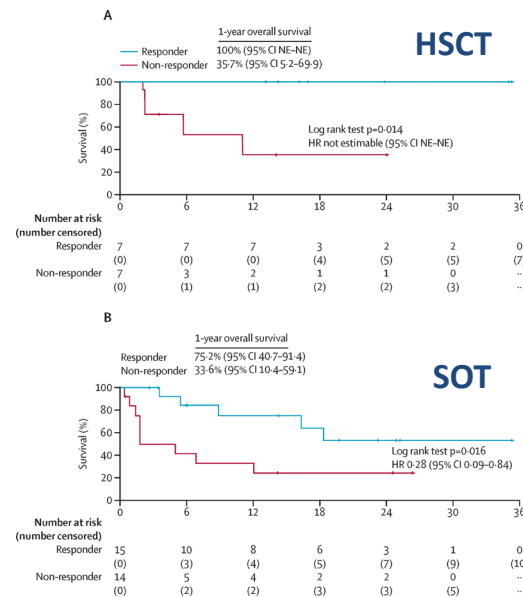
# Tabelecleucel for allogeneic haematopoietic stem-cell or solid organ transplant recipients with Epstein-Barr virus-positive post-transplant lymphoproliferative disease after failure of rituximab or rituximab and chemotherapy (ALLELE): a phase 3, multicentre, open-label trial

Mahadeo KM et al. *Lancet Oncol* 2024;25:376-387

- ❖ Patients with EBV-PTLD relapsed and/or refractory to rituximab after HSCT (n = 14) or to rituximab ± chemotherapy after SOT (n = 29) received three tabelecleucel infusions ( $2 \times 10^6$  cells per Kg) based on a partially matched HLA profile (restriction switch allowed)
- ❖ Median number of cycles 3 (IQR 2-4) in HSCT, and 2 (IQR 1-3) in SOT

	HSCT (n=14)	SOT (n=29)	All (n=43)
Objective response	7 (50%, 23–77)	15 (52%, 33–71)	22 (51%, 36–67)
Complete response	6 (43%)	6 (21%)	12 (28%)
Partial response	1 (7%)	9 (31%)	10 (23%)
Stable disease	3 (21%)	2 (7%)	5 (12%)
Progressive disease	2 (14%)	7 (24%)	9 (21%)
Not evaluable	2 (14%)	5 (17%)	7 (16%)
Median response duration	23 months	15.2 months	23 months

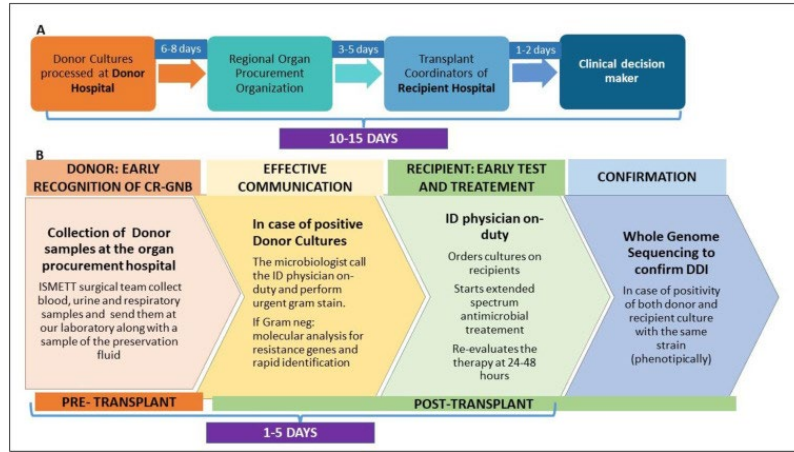
- ❖ Treatment-related AE of any grade in 29%, grade 3–4 in 4% of patients (erythematous rash, hypotension and hypoxia in 1 patient each)



# Donor-derived carbapenem-resistant gram-negative bacterial infections in solid organ transplant recipients: Active surveillance enhances recipient safety

Mularoni A et al. Am J Transplant 2024;S1600-6135(24)00131-X

## Local active surveillance system (LASS): 2015-2021



Transmission risk	Positive specimens
High	<ul style="list-style-type: none"> <li>✓ BSI</li> <li>✓ colonization/infection at the transplanted organ level</li> <li>✓ Preservation fluid</li> </ul>
Low	<ul style="list-style-type: none"> <li>✓ Colonization/infection at non-tx organ level</li> </ul>

### Proven DDI

- (1) absence of pretransplant infection in the recipient
- (2) evidence of the same microorganism in donor and recipient cultures
- (3) confirmed identity of donor and recipient strains by WGS

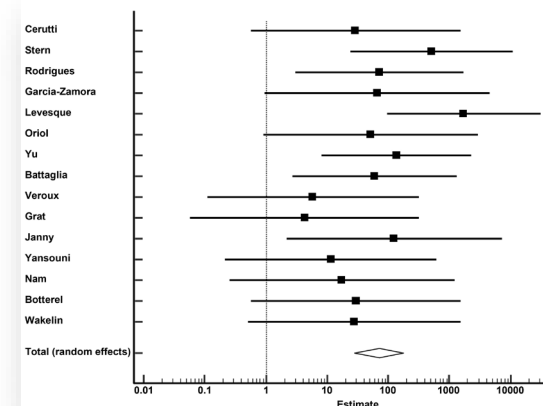
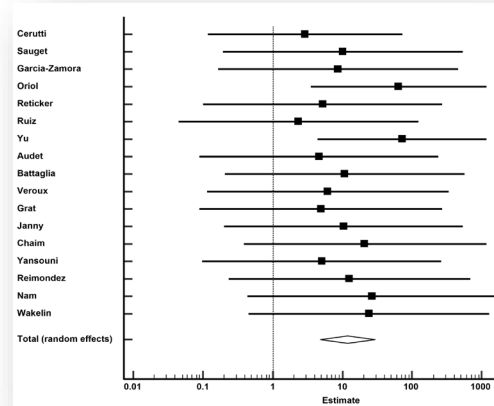
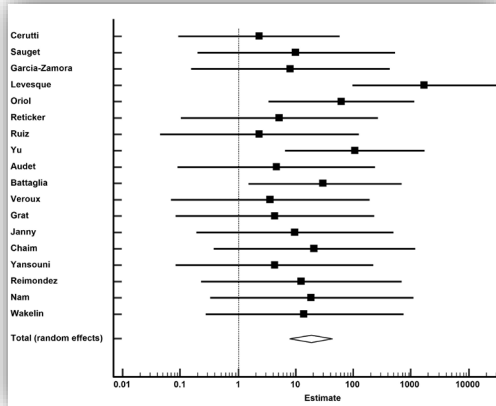
- ❖ 38/791 (4.8%) recipients were at HR of CR-GNB DDI: 24 CR-Kp (23 KPC), 13 CRAb, and 1 MBL *K. aerogenes*
- ❖ All patients received targeted prophylaxis within 72 hours from transplant
- ❖ 11 CR-GNB DDIs were diagnosed and confirmed by WGS
  - Incidence of CR-GNB DDI was 1.4% in all SOT recipients and 29% in HR recipients
  - Median time to transmission was 1.5 days (IQR 1-15)
  - Growth of CR-GNB in PF led to DDI in (7/8) 87% of cases



# The impact of preservation fluid culture on graft site arteritis: A systematic review and meta-analysis

Rinaldi et Al. Transpl Infect Dis. 2022 Dec; 24(6): e13979.

- ❖ What is the role of culturing the graft preservation fluid?
- ❖ Is there a link between positive fluid and graft arteritis development?



SOT recipients with a PF yielding a **high-risk pathogen** showed a significant increased risk of arteritis development compared to low risk/negative PF (OR 18.43; 95%CI 7.83-43.40).

SOT recipients with a PF yielding a **high-risk bacteria** showed a significant increased risk of arteritis development compared to low risk/negative PF (OR 12.02; 95%CI 4.88-29.60).

SOT recipients with a PF yielding a **fungal organism** showed a significant increased risk of arteritis development compared to low risk/negative PF (OR 71.00; 95%CI 28.07-179.56).



# Real-time, random-access organ screening for carbapenem-resistant organisms (CRO) reduces CRO-associated, donor-derived infection mortality in lung transplant recipients

Wen-Yong Zhou et al. *Infection* 2024; 52:403–412

- ❖ Shanghai Chest Hospital, D/LTRs in 2016-2020 (control group) vs. D/LTRs in 2021-2022 (screening group)
- ❖ Screening by Xpert Carba-R test (KPC, NDM, VIM, IMP and OXA-48) on BALF
- ❖ 9/35 (25.7%) donors were declined because of positive screening testing result

	Screening group n=26 (%)	Control group n=19 (%)	p
Pre-operative recipient pos cultures	3 (11.5)	2 (10.5)	1.00
Post-operative recipient pos cultures	23 (88.5)	19 (100)	0.25
<b>CRO isolation positive</b>	<b>9 (34.6)</b>	<b>15 (78.9)</b>	<b>0.01</b>
DDI	5 (19.2)	7 (36.8)	0.31
CRO-DDI	2 (7.7)	6 (31.6)	0.06
<b>Infection-related death within 60 days</b>	<b>2 (7.7)</b>	<b>7 (36.8)</b>	<b>0.02</b>
<b>CRO-DDI related death</b>	<b>1 (3.8)</b>	<b>6 (31.6)</b>	<b>0.03</b>



# Take-home messages

1. Vaccine-preventable infections are common after SOT requiring efforts for optimization of vaccine strategies
2. In patients on letermovir prophylaxis, CMV-RNAemia together with CMV-DNAemia could provide more accurate information on viral kinetics
3. CMV-CMI has proven to be useful in personalizing the duration of prophylaxis in SOT recipients, it could be considered also a supportive tool in patients managed with PET strategy
4. Maribavir: be careful with refractory dis, high dose, aGVHD, T-cell depletion
5. Serologic screening and molecular surveillance of HHV8 facilitate early recognition and effective therapy of KICS
6. Local active surveillance systems aimed at early detecting grafts at high risk for MDRO DDI should be implemented in areas where MDROs are endemic
7. Well done studies assessing correlation between positive PF and DDI are needed
8. Data on clinical impact and cost-effectiveness of the rapid diagnostic assays in SOT recipients are needed

