27es JNI 2026 PARIS
et la région Île-de-France Palais des Congrès
Journées Nationales d'infectiologie
du jeudi 18 juin au samedi 20 juin 2026
Journée Nationale de Formation
des Paramédicaux en Infectiologie
Vendredi 19 juin 2026

Le CMV

Dr Giovanna Melica
Maladies Infectieuses et Immunologie Clinique
GH Henri Mondor APHP

Déclaration d'intérêt de 2014 à 2025

- Intérêts financiers : non
- Liens durables ou permanents :non
- Interventions ponctuelles : AZ, MSD, Pfizer, Gilead, Moderna, GSK
- Intérêts indirects :non

Plan de la présentation

- **Épidémiologie**
- **Virologie, diagnostic et definitions**
- **Atteintes cliniques: immunocompetent, SOT et allogreffe CSH**
- **Traitement: SOT et allogreffe CSH**
- **Prévention: SOT et allogreffe CSH**

Épidémiologie

60–90 %

séroprévalence adulte mondiale

0,2–2 %

naissances avec CMV congénital

1ère

cause infectieuse de surdité congénitale

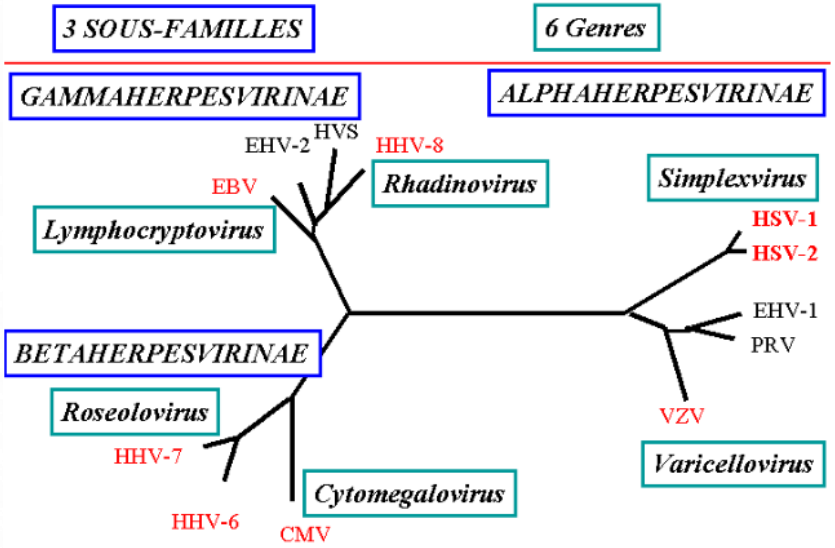
Gradient de seroprevalence Nord Sud

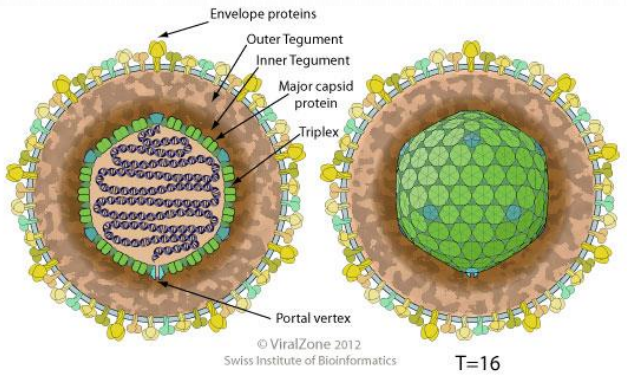
Pays à revenus élevés : 40–70 % (Europe, Amérique du Nord)
Pays en développement : 80–100 % (Afrique subsaharienne, Asie)

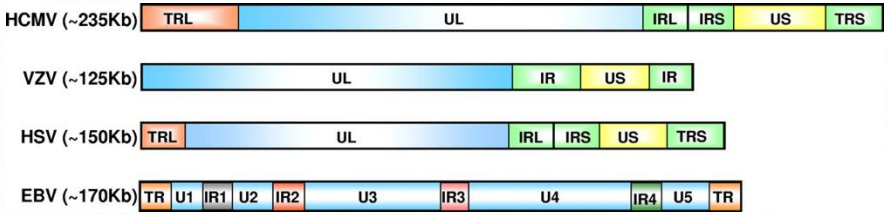
Transmission : contact direct (salive, urine, lait maternel, sang)
Exceptionnel via transfusion produits sanguins

Kirupanantha RP, Lab Med 2026

Virologie





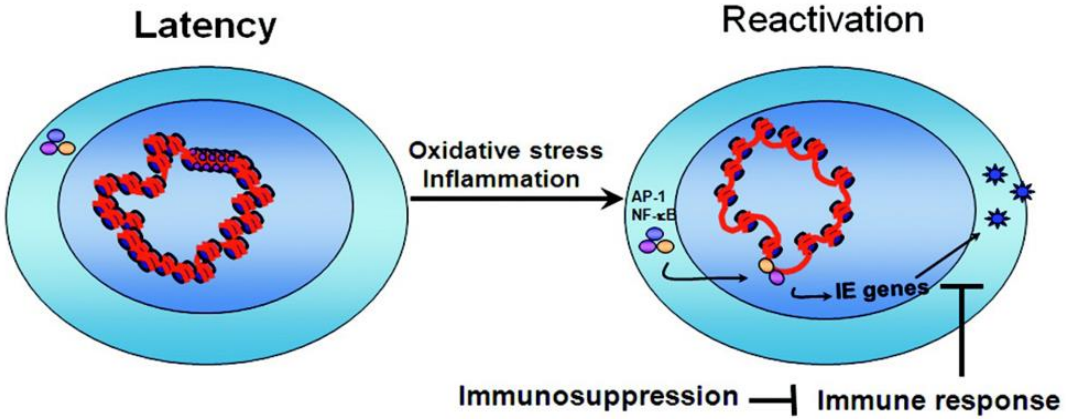


Virus à ADN double brin
Le plus grand genome herpesvirus humain

Virologie: latence -réactivation

CD34+ HSC, monocytes

Macrophages, cellules dendritiques, endotheliales, epitheliales



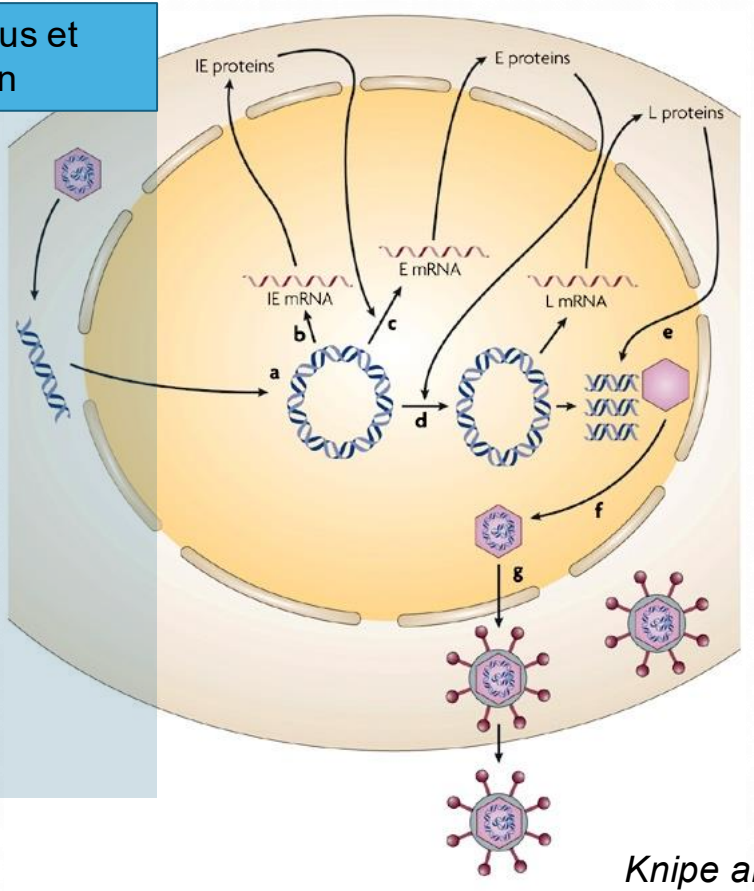
Pas de reconnaissance par le système immunitaire

« Cycle viral lytique »

Liu, Viruses 2013

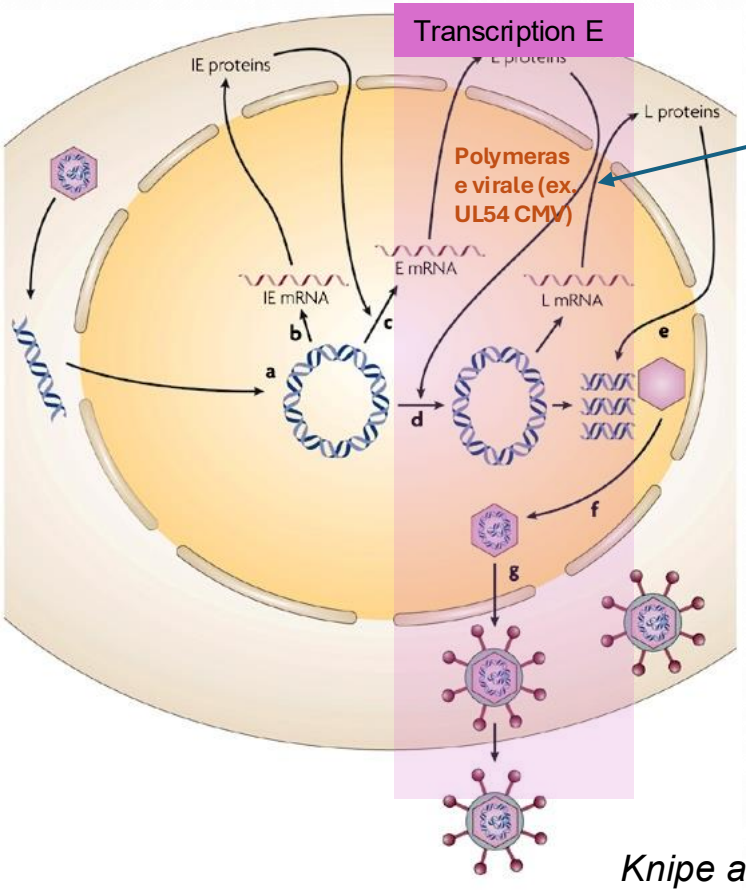
Cycle Viral Lytique

Entrée du virus et décapsidation



Knipe and Cliffe., Nat Rev Microbiol. 2008

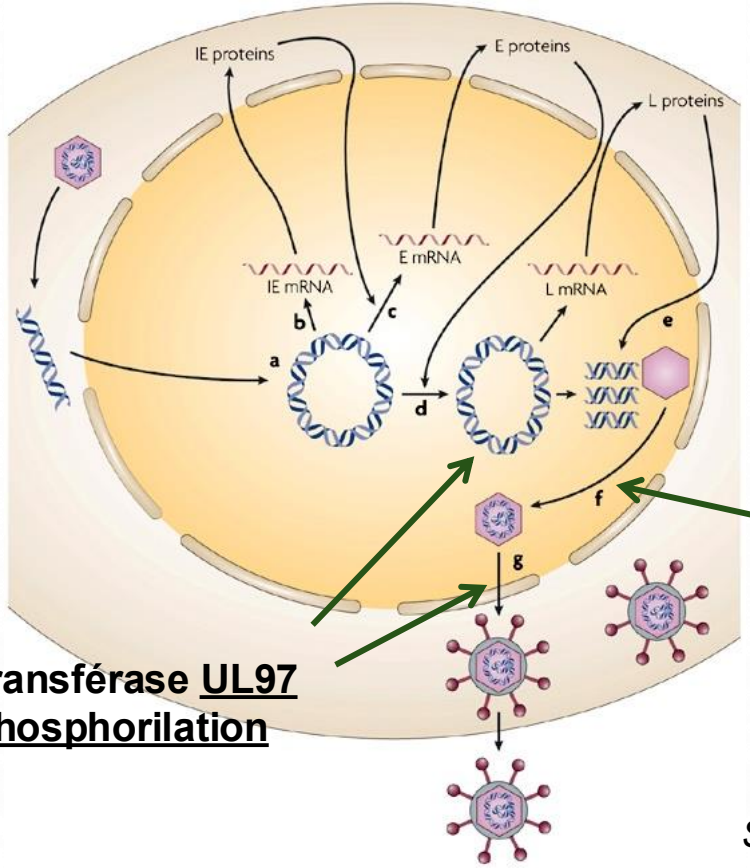
Cycle Viral Lytique

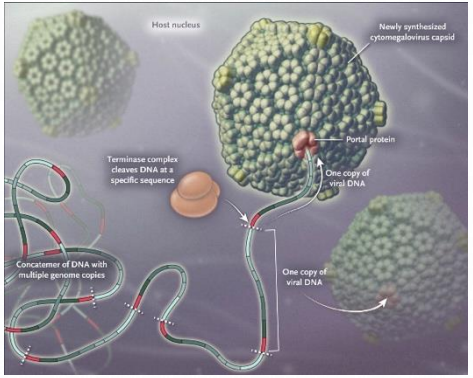


(Val)Ganciclovir
Foscarnet
Cidofovir

Knipe and Cliffe., Nat Rev Microbiol. 2008

Cycle Viral Lytique





(Val)ganciclovir
Maribavir

P-transférase UL97
= phosphorilation

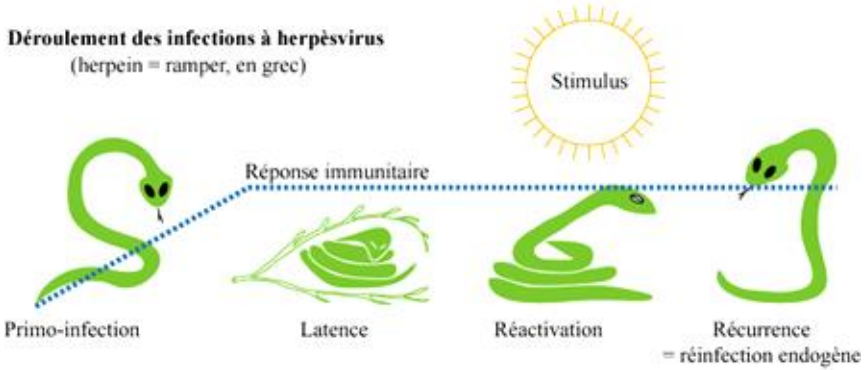
Terminase virale UL56

Letermovir

Sharma et al., J Virol 2015

Histoire naturelle de la maladie

Primo-infection → **Phase viremique** → **Latence (réservoirs)** → **Réactivation**



Transplantation
Hémopathies
VIH

Antiviraux inhibiteurs d'une étape du cycle virale lytique= inactifs sur l'infection latente

Diagnostic et définitions

Diagnostic virologique de l'infection CMV

Direct
Immunodéprimé
Suivi

Indirect
Immunocompétent
(Primo CMV, TMF)

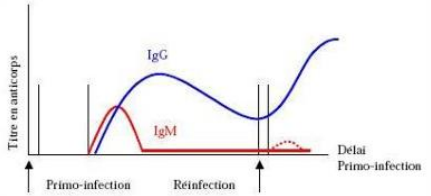
- **Infection CMV** présence ADN CMV par qPCR (IU/ml) sur sang total ou plasma
- Highly sensitive QNAT : < 200 IU/ml

- **Maladie CMV**

Syndrome virale

Atteinte d' organe

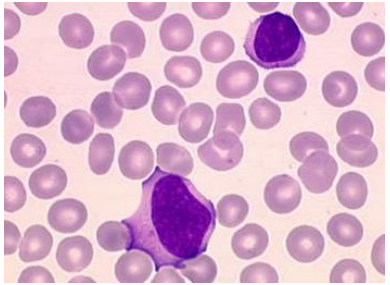
Serologie
IgM: primo, persistent 6-12 mois
IgG: avidité ↑ temps



Clinique — Sujet immunocompétent

Primo-infection : syndrome mononucléosique (20–30 % symptomatique)

- Fièvre prolongée (> 2 semaines), asthénie, pharyngite, adenopathies
- Syndrome mononucléosique : hyperlymphocytose, lymphocytes atypiques
- Cytolyse hépatique (80 %), hépatosplénomégalie

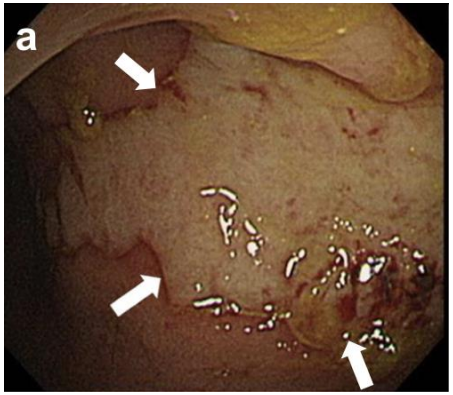


Complications rares

SNC :	méningite, encéphalite, syndrome de Guillain-Barré	**Cœur :**	myocardite, péricardite
Poumon :	pneumopathie interstitielle	**Digestif :**	colite, hépatite sévère

Clinique — Sujet immunocompétent

Faut il traiter?



Situation rare (case reports): âge, comorbidités (diabète)

Oui si

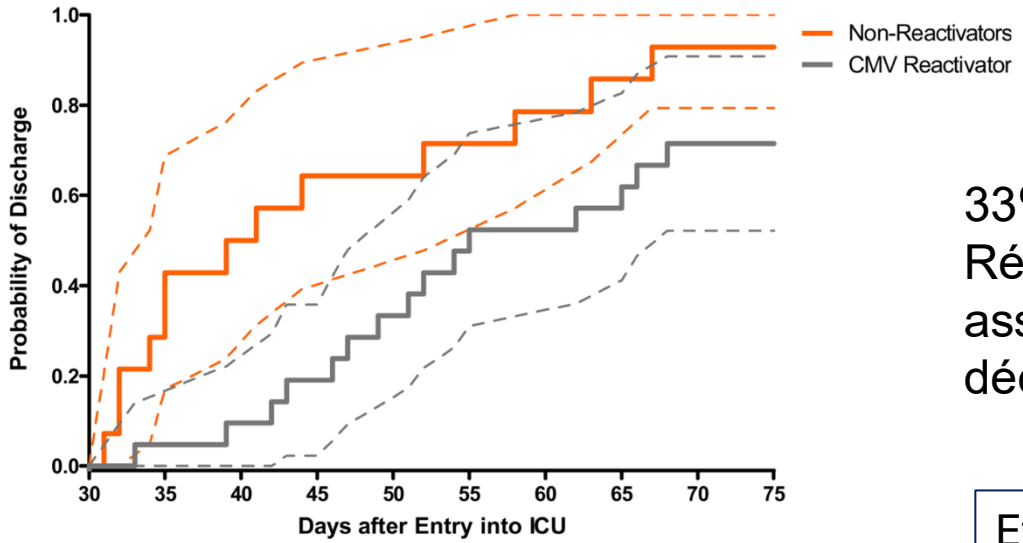
-forme sévère
-lésions tissulaires
-inclusions virales ou PCR CMV +/PCR CMV élevée sang
-colite du sujet âgé (immunosenescence)

ganciclovir/valganciclovir

Lee, BMC Infect Dis 2017; Seo TH, Hepatogastroenterology 2012

Clinique — Sujet immunocompétent

Faut il traiter? ⟶ Quid des réactivations CMV en soins intensifs chez l'immunocompétent?



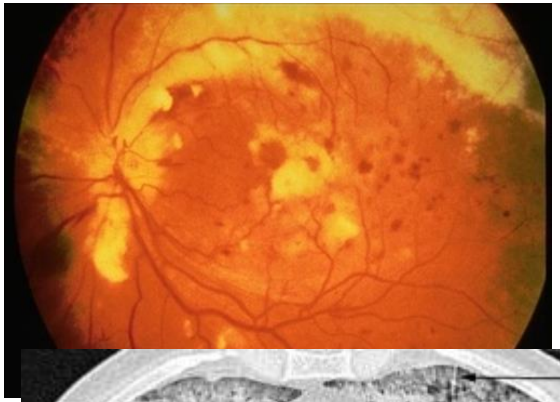
33% PCR CMV+
Réactivation CMV en réanimation associée avec durée de séjour et décès

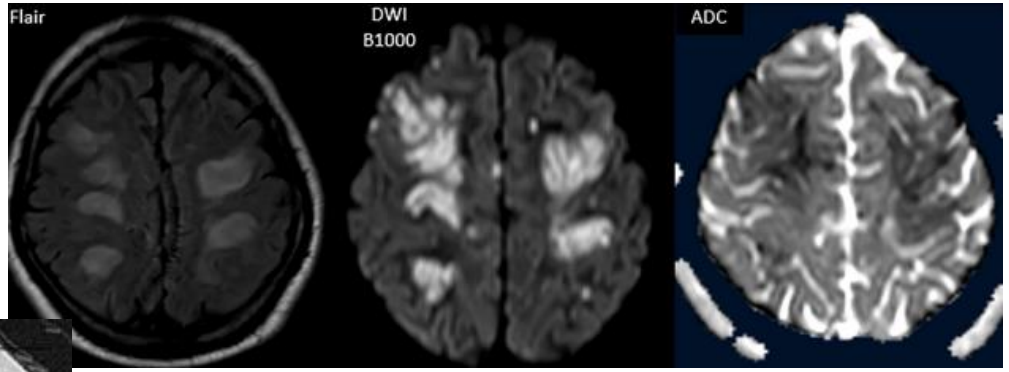
↓

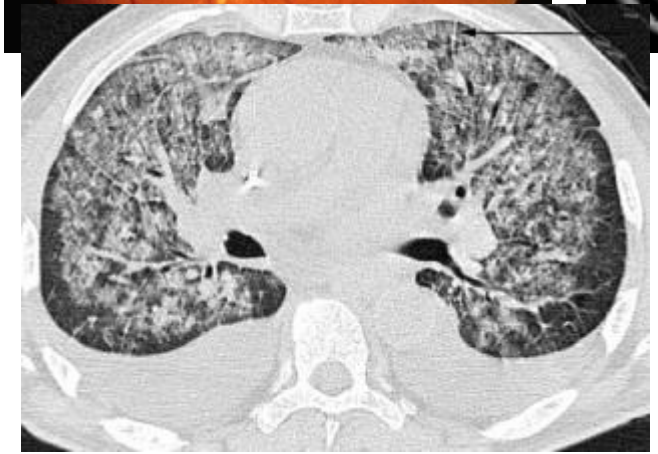
Effet immunomodulateur indirect

Lymaye, JAMA 2008

Clinique — Sujet immunodeprimé







The Troll Is Weakened but Not yet Defeated: An Update on Cytomegalovirus Management in Transplantation From the International CMV Symposium 2025

Camille N. Kotton[1] | Martina Sester[2,3] | Julian Torre-Cisneros[4,5] | The International CMV Symposium Faculty

Chait F, BJR Case Reports 2025; kunihiro Y, Acta Radiol 2015; Kotton C, Transplant Infect Dis 2025

CMV et TOS

Incidence

Arrêt de la prophylaxie:
6%-50 selon l'organe
50% haut risque D+/R−
17% R+
Poumon/Coeur++

Limaye, Clin Microbiol Rev, 2020

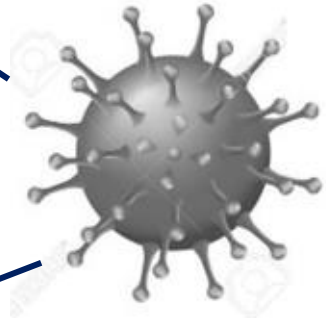
Facteurs de risque

Serostatut D+/R- > D+/R+
Age élevé receveur
SAL
Lymphopénie et MMF
Diabète

Tang, Transplant Immunol, 2022

Infection

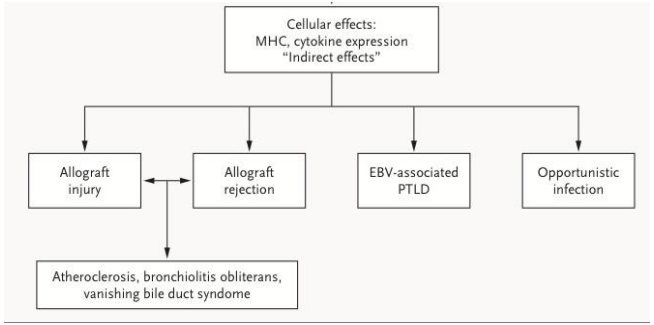
Asymptomatique
DNAemie 2-3log UI/ml



Maladie

Syndrome CMV
fièvre, AEG , leucopénie, cytolyse hépatique
Atteinte invasive: colite (80%), pneumonie, péricardite, néphrite....

Effets indirects

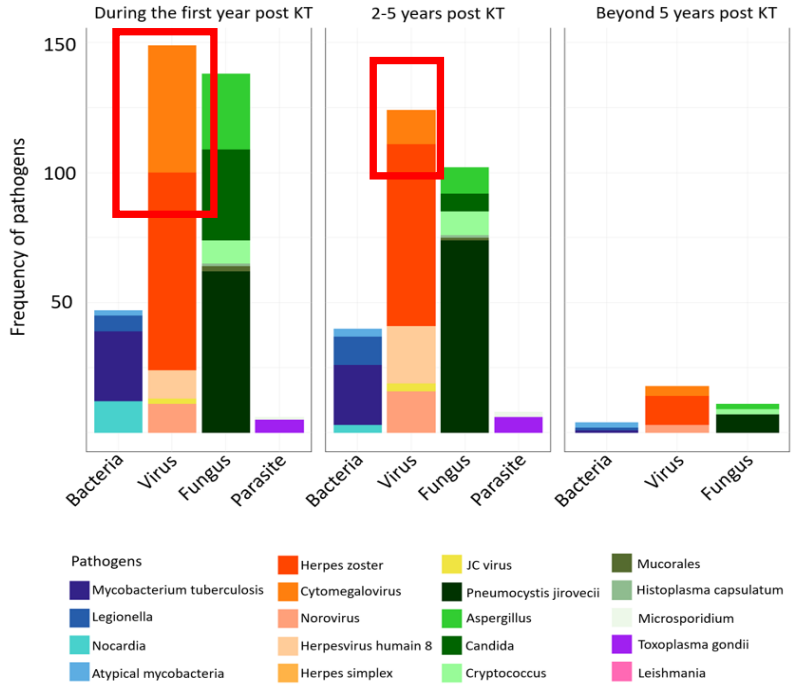


NEJM

Diagnostic

DNAemie
Biopsie tissulaire

CMV et TOS



Hoisnard L. Clin Infect Dis 2026

RESULTS	Late OI *37.5 (21.5-65.5) months post-KT*	Early OI *4.4 (1.5-8.4) months post-KT*	
Herpesvirus (HSV/VZV/CMV)	49/83 (59%)	15/38 (39.5%)	p=0.07
Zoster	36/83 (43.4%)	10/38 (26.3%)	-
Pneumocystosis	12/25 (48%)	0/18	p=0.002
Invasive aspergillosis	3/25 (12%)	10/18 (55.6%)	p=0.01

- OI Délai médian : 12,5 mois
- Age+++

Esnault, Tranpl Int, 2024

- CMV et belatacept: formes atypiques (rétinites)

Switch < 6 mois
Age +++
Bolus de stéroïdes
Immunosuppression prégreffe
DFG < 25 ml/min

Chavarot, AJT, 2021
Karadkele, AJT, 2021

CMV et allogreffe CSH

Incidence

Incidence à 1 an: 55%
- > J100: 12-45%
- Maladie CMV: 13%
- Sous letermovir 10-30%

Limaye, Clin Microbiol Rev, 2020

Facteurs de risque

Serostatut D-/R+
GVH aigue
HLA Mismatch
Conditionnement myeloablatif
Steroides
Donneur haplo identique

Studer U, Anticancer R 2020

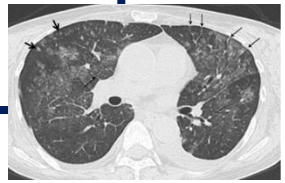
Infection

Asymptomatique
DNAemie 2-3log UI/ml

Maladie

Syndrome
fièvre, AEG , leucopénie, cytolyse hépatique

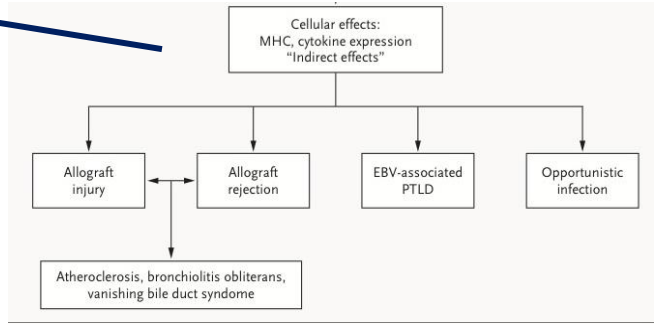
Atteinte invasive
dysfonction d'organe : **pneumonie**, colite, oesophagite,..



Diagnostic

DNAemie
Biopsie tissulaire

Effets indirects



NEJM

Traitement CMV maladie

Transplantation, 2024

Traitement curatif 21 jours

Valganciclovir

IV si malabsorption (forme digestive)

⚠ hemato/fonction rénale (toxicité / résistance)

Surveillance PCR CMV hebdo

Durée 14-21 jours et PCR <seuil

Si + à J21 poursuite du ttt curatif

Foscarnet (transplantation rénale)

↘ **immunosuppression - MMF**


Clinical Infectious Diseases

INVITED ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association

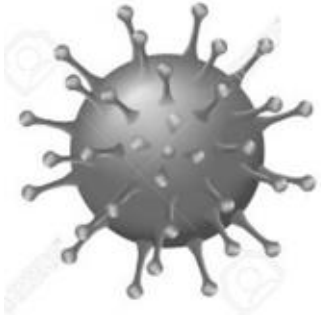
REVIEWS OF ANTI-INFECTIVE AGENTS: Louis D. Saravolatz, Section Editor

Letermovir and Maribavir for the Treatment and Prevention of Cytomegalovirus Infection in Solid Organ and Stem Cell Transplant Recipients

Hannah N. Imlay,[1] and Daniel R. Kaul[2,3]

[1]University of Utah, Department of Internal Medicine, Division of Infectious Diseases, Salt Lake City, Utah, USA, and [2]University of Michigan, Department of Internal Medicine, Division of Infectious Diseases, Ann Arbor, Michigan, USA

Resistance 6-10% SOT, 2-14% allo CSH



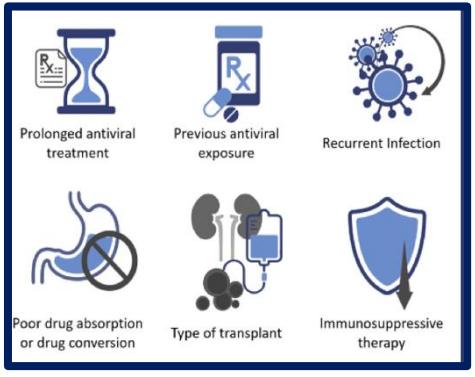
Kasriel N, Am J Transpl 2026

Probable : exposition cumulée > 4 semaines

Réfractaire : ↗ virémie ou < 1 log ↓ après 2 semaines ttt approprié

Ljungman P, Clin Infect Dis 2024

Facteurs de risque



Asberg , AJT 2007 et 2009

Faible barrière génétique

Si CV élevée: Foscarnet

Maribavir: dosage++, dose de charge ou ↑ posologie (R 21% CMV refractaires)

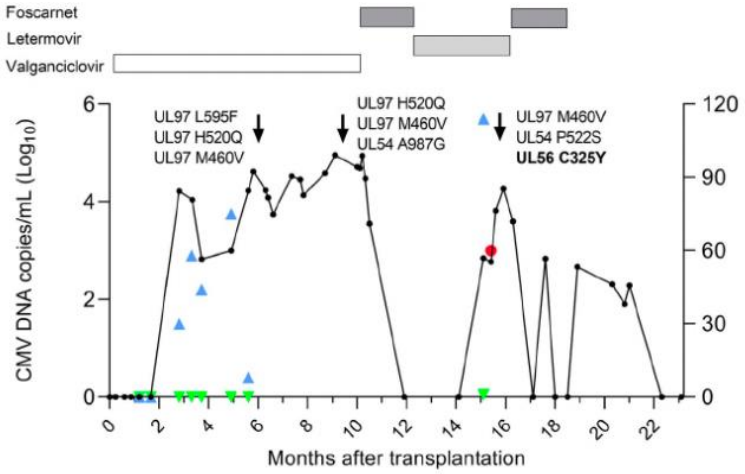
Letermovir: pas d'indication pour le traitement curatif

Received: 11 August 2020 | Revised: 27 October 2020 | Accepted: 8 November 2020
DOI: 10.1111/tid.13515

CASE REPORT AND REVIEW OF THE LITERATURE

WILEY

Emergence of letermovir resistance in solid organ transplant recipients with ganciclovir resistant cytomegalovirus infection: A case series and review of the literature



En association?

Etude LUCY (letermovir+valganciclovir en transplantation renale)

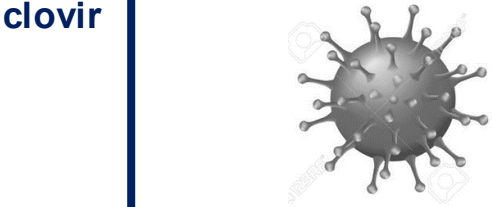
Hoffman E, Transplant Inf Dis 2020

Prevention SOT

1. Prophylaxie - **Valganciclovir**
   - -3 mois R+ SAL
   - -6 mois D+/R-
   - -12 mois poumon

2. Prophylaxie-**Letermovir**

- D+/R- (rein) (autres SOT?)
- Si myelotoxicité
- Pas actif sur autres herpesvirus

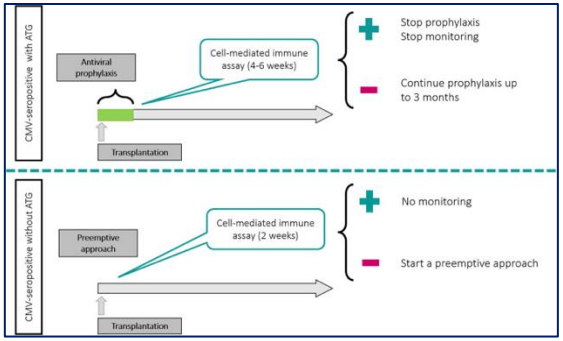


3. Everolimus *Transform*

	EVR	MMF	
12 mois			
Infections and infestations	698 (68.8)	768 (75.9)	0.91 (0.86, 0.96)
BKV infection	59 (5.8)	104 (10.3)	0.57 (0.42, 0.77)
CMV infection	28 (2.8)	137 (13.5)	0.20 (0.14, 0.30)
24 mois			
Infections and infestations	264 (26.0)	317 (31.3)	0.83 (0.72, 0.95)
BKV infection	8 (0.8)	14 (1.4)	0.57 (0.24, 1.35)
CMV infection	2 (0.2)	13 (1.3)	0.15 (0.03, 0.68)

Berger, AJT, 2019

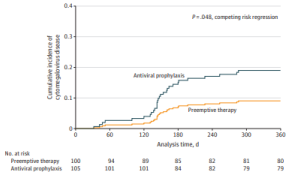
4. Ciblée avec tests immunité cellulaire R+



Bestard, Tranplant Int, 2023; Manuel O, Clin Infect Dis 2024

D+/R-: 77% négatifs à M5 post greffe

2. Préemptive - PCR



Seuil?
Logistique
↓ **Exposition valganciclovir**
↓ **Infections tardives**

Manuel O, AJT 2013; Reiss Gindi N, Infection 2024

Prevention allogreffe CSH

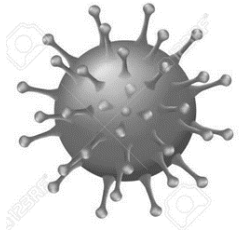
1. Prophylaxie - Letermovir
- ↓ mortalité globale 27%
- ↓ GVH 35%

Attention: blips charge virale, interactions (cyclosporine), prévention autres herpesvirus

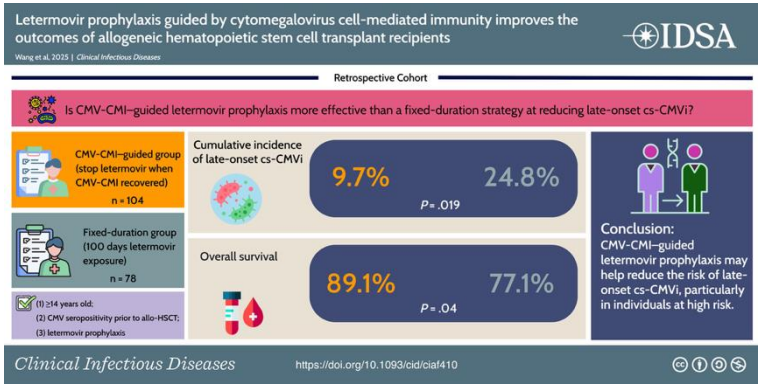
Suivi PCR CMV hebdo J100 ou J200 si haut risque

2. Si receveur R-
-monitorage PCR CMV
-valaciclovir
≠valganciclovir en prophylaxie

100-200 jours
> 200 jours: patients haut risque



3.Ciblée avec tests immunité cellulaire R+



2. Preemptif
Ganciclovir/Foscarnet
Maribavir si neutropenique

-Modulation durée letermovir
-Indication à prophylaxie secondaire
-Arrêt thérapeutique si charges virales faibles

Vyas A, OFID 2023; Russo D, Lancet Haematol 2024

Messages clefs

The Troll Is Weakened but Not yet Defeated: An Update on Cytomegalovirus Management in Transplantation From the International CMV Symposium 2025

Camille N. Kotton[1] | Martina Sester[2,3] | Julian Torre-Cisneros[4,5] | The International CMV Symposium Faculty

Topic	SOT guideline [1]	ECIL [2] and ASTCT [3] guidelines
Diagnostics	Greater emphasis on CMV-QNAT calibrated to the WHO standard	CMV serology recommended pre-HSCT; pretransplant CMV PCR recommended
Prevention: prophylaxis	Letermovir recommended in D+/R− kidney, investigational in non-kidney transplants; PET option for D+/R− liver	Letermovir standard prophylaxis for R+ recipients through Day 200 for high-risk recipients
Prevention: CMV-CMI testing	Strong recommendation for R+ kidney recipients to personalize prophylaxis duration	Case-by-case determination; potential role in letermovir recipients
Treatment	Valganciclovir/ganciclovir remains first-line; thresholds for treatment duration are challenging in the era of sensitive testing	Ganciclovir/valganciclovir is first-line for treatment; preemptive therapy with weekly monitoring
Resistant/ refractory CMV	Maribavir is the principal alternative for resistance, unless high VLs (prefer foscarnet)	Maribavir is effective with lower toxicity than ganciclovir/foscarnet; second-line approved for ≥ 12 years
Resistance testing	Strong recommendation for genotypic testing after ≥ 4 weeks' exposure and suboptimal response to correctly dosed treatment	Genotypic testing is recommended when resistant or refractory CMV is clinically suspected
CMVIG	Conditional recommendation for severe/refractory disease, hypogammaglobulinemia, and thoracic transplants	Adjunctive therapy in select scenarios; limited evidence
Pediatrics	Prevention strategies include prophylaxis, PET, or surveillance after short-term prophylaxis; more data are needed on new drugs	Letermovir approved for pediatric patients; drug- and weight-based dosing criteria apply

ADN CMV par qPCR (IU/ml)
Seuils?

Standard in HCST; alternative vs valganciclovir in SOT (reinD+/R-)

Place CMI en SOT mais aussi HCST sous letermovir

Maribavir: attention à la resistance

Chercher vite un échec virologique et si possible doser++

Perspectives, limites

Domain	Unmet need
Disease burden	Posttransplant CMV infection persists despite decades of advances.
Guideline implementation	Translation of new (2025) guideline updates into diverse clinical settings is challenged by variable infrastructure, economics, and institutional capacity.
Prevention strategies	Optimal duration of extended prophylaxis is not definitively established; late CMV remains a concern in high-risk patients. Head-to-head comparisons of prophylaxis vs. preemptive therapy approaches are needed. Evidence on letermovir for non-kidney SOT organs and R+ recipients remains limited.
Antiviral management	Despite improved toxicity, new agents introduce new challenges such as resistance and access/cost (e.g., maribavir resistance emerges more frequently than with ganciclovir). Resistant/refractory CMV infection remains a significant issue for some patients. Standardized viral load thresholds are needed to define when preemptive therapy initiation is needed.
Immune monitoring	Immune monitoring capabilities are limited by a lack of widespread availability and broad expertise, and a lack of a standardized CMI assay.
Vaccination	Lack of effective CMV vaccines remains a major deficit despite recent development efforts.
Translation of clinical evidence	Large, pragmatic studies ("mega-trials") are needed to definitively answer key clinical questions with robust sample sizes.

- Logistique-Cout
- Infections tardives
- Prophylaxie-Preemptif? CMI
- Résistances++

Merci

Résumé antiviraux anti-CMV

- **Inhibiteurs de l'ADN polymérase virale (UL54)** première ligne dans la prise en charge thérapeutique de l'infection/maladie CMV
  - Ganciclovir, foscarnet et cidofovir
    - Agit en bloquant la synthèse de l'ADN viral
    - Toxicités importante et problème de résistance

- **Inhibiteur de la terminase (letermovir)**
  - Agit en inhibant l'encapsidation et le clivage du génome virale par la terminase virale
  - Première ligne en traitement prophylactique des patients greffes de CSH et greffes rein

❖ **Inhibiteur de la phosphotransferase virale (maribavir)**
  - Agit en bloquant l'activité kinase de la phosphotransférase UL 97
  - Approval pour le traitement d'infections CMV réfractaires à une première ligne chez les patients greffes CSH et OS
  - Données de vie réelle attendus : QUID de la bithérapie Maribavir + letermovir ou Maribavir + GCV etc… en cas d'échec ?