

Refractory & Resistant Cytomegalovirus (CMV) in Solid Organ Transplant: Definitions, Risk Factors, Monitoring, and Treatments

Refractory & Resistant CMV



TERM	PROBABLE	DEFINITE
Refractory CMV infection	DNAemia at the same level or higher (but $<1 \log_{10}$) after ≥ 2 weeks of appropriately dosed AVT	DNAemia that increases $>1 \log_{10}$ after ≥ 2 weeks of appropriately dosed AVT
Refractory CMV end-organ disease	Lack of improvement in signs and symptoms after ≥ 2 weeks of appropriately dosed AVT	Worsening in signs and symptoms or progression into end-organ disease after ≥ 2 weeks of appropriately dosed AVT
Antiviral drug resistance	Viral genetic alteration that decreases susceptibility to one or more antiviral drugs	

Risk Factors for CMV Resistance



- Prolonged antiviral drug exposure (median, 5 months for ganciclovir)
- Ongoing active viral replication due to factors, such as:
 - Lack of prior CMV immunity (D+/R-)
 - Strongly immunosuppressive therapy
 - Inadequate antiviral drug dose or delivery

Monitoring for CMV Resistance



WHEN?

- Antiviral drug resistance should be suspected and tested for when there is persistent or recurrent CMV DNAemia or disease during prolonged antiviral therapy

HOW?

- Genotypic assays for viral drug resistance mutations in UL97 and UL54 genes
 - 7 most common (“canonical”) UL97 mutations – 80% cases
 - Several UL54 mutations

Tx of Drug Resistant CMV



- Reduce immunosuppressive therapy to the lowest feasible amount
- Alternate therapies
 - Maribavir ▪ High-dose GCV
 - Foscarnet ▪ Cidofovir

AVT: antiviral therapy; GCV; ganciclovir