



Driven by Patient Need
Inspired by Innovation

Artesunate for Injection® as Combination Therapy for Treatment of CMV in Transplant Recipients

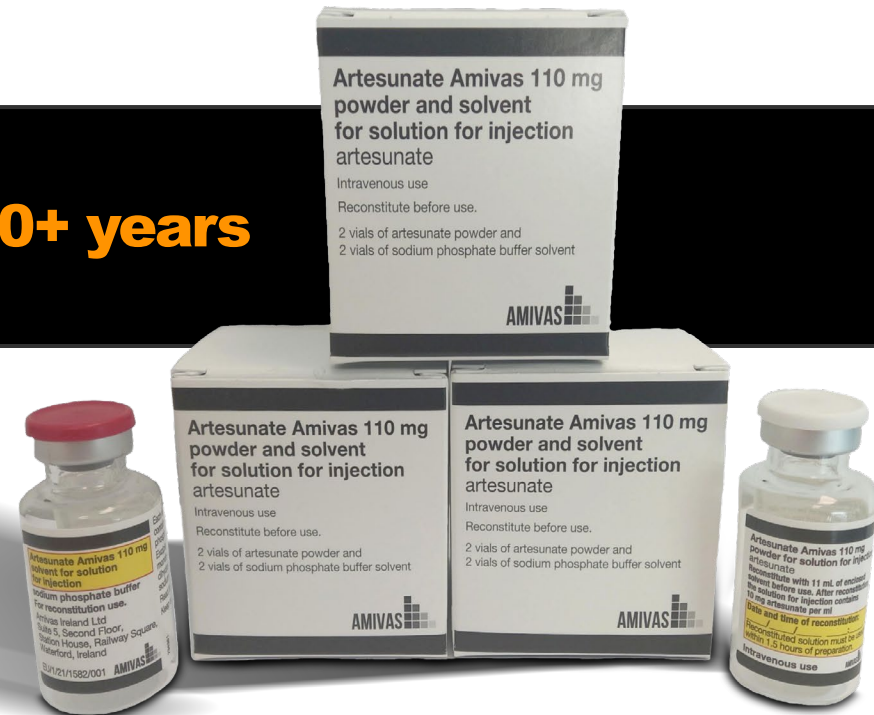
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Sold as

Artesunate for Injection® in U.S. Artesunate AMIVAS® in ROW

Global Standard of Care for 20+ years

Indicated for initial treatment of severe or complicated malaria in adults and children



Study Title:

- Phase 2, Randomized, Open-label, Active Comparator, Dose-ranging Study Evaluating the Efficacy and Safety of Artesunate for Injection[®] in Combination with Ganciclovir or Valganciclovir for the Treatment of Cytomegalovirus infection in Solid Organ Transplant Recipients
- **Methodology:** This study is a randomized, open-label, active comparator-controlled, dose-ranging trial of the efficacy and safety of IV artesunate in combination with GCV or VGCV and SOC treatment compared to GCV or VGCV monotherapy and SOC treatment for clinically significant CMV infection in SOT recipients.
- Eligible patients will be randomized in a 1:1:1 ratio to 1 of 3 treatment groups stratified by type of SOT (kidney vs. non-kidney).
- **Group 1: 2.4 mg/kg** artesunate IV slow bolus over 1-2 minutes once daily for 14 days; **Group 2: 4.8 mg/kg** artesunate IV slow bolus over 4-5 minutes once daily for 14 days. Both groups will receive concomitant GCV or VGCV and SOC according to local institutional practices.

Primary Objective:

- Determine if Artesunate for Injection when administered in combination with IV Ganciclovir (GCV) and/or oral valganciclovir (VGCV) and standard of care (SOC) treatment impacts reduction of cytomegalovirus (CMV) DNAemia compared with those who only received GCV or VGCV and SOC treatment
- **Primary Efficacy Endpoint:** Change from baseline in plasma CMV DNA levels defined as good response (CMV DNA load reduction of more than 0.5 log₁₀ and to a level below 3.0 log₁₀ copies/mL), moderate response (reduction of CMV DNA load of more than 0.5 log₁₀, but not to a level below 3.0 log₁₀ copies/mL) and no response [equal DNA load (i.e. reduction of less than 0.5 log₁₀) or an increase] at Days 14, 21, and 28. CMV viral load will be based on central laboratory test results on plasma samples.

Secondary Efficacy Objectives:

- Evaluating the dose response on all efficacy endpoints for IV artesunate plus GCV or VGCV and SOC treatment compared to GCV or VGCV and SOC treatment
- **Secondary Efficacy Endpoints:**
 - Proportion of patients with plasma CMV DNAemia below the lower limit of quantitation (LLOQ) at Day 7, 14, 21, 28, 35, 42, 49, and 56
 - CMV DNA viral load at baseline, Day 7, 14, 21, 28, 35, 42, 49 and 56
 - CMV DNA viral load decay half-life ($T_{1/2}$) (to determine antiviral efficacy)
 - Time to clinically relevant drop in CMV DNA viral load (≥ 0.5 log₁₀ reduction)
 - In patients with CMV syndrome at baseline, resolution of clinical signs/symptoms of the syndrome at Day 7, 14, 21, 28, 35, 42, 49, and 56

Exploratory Objectives:

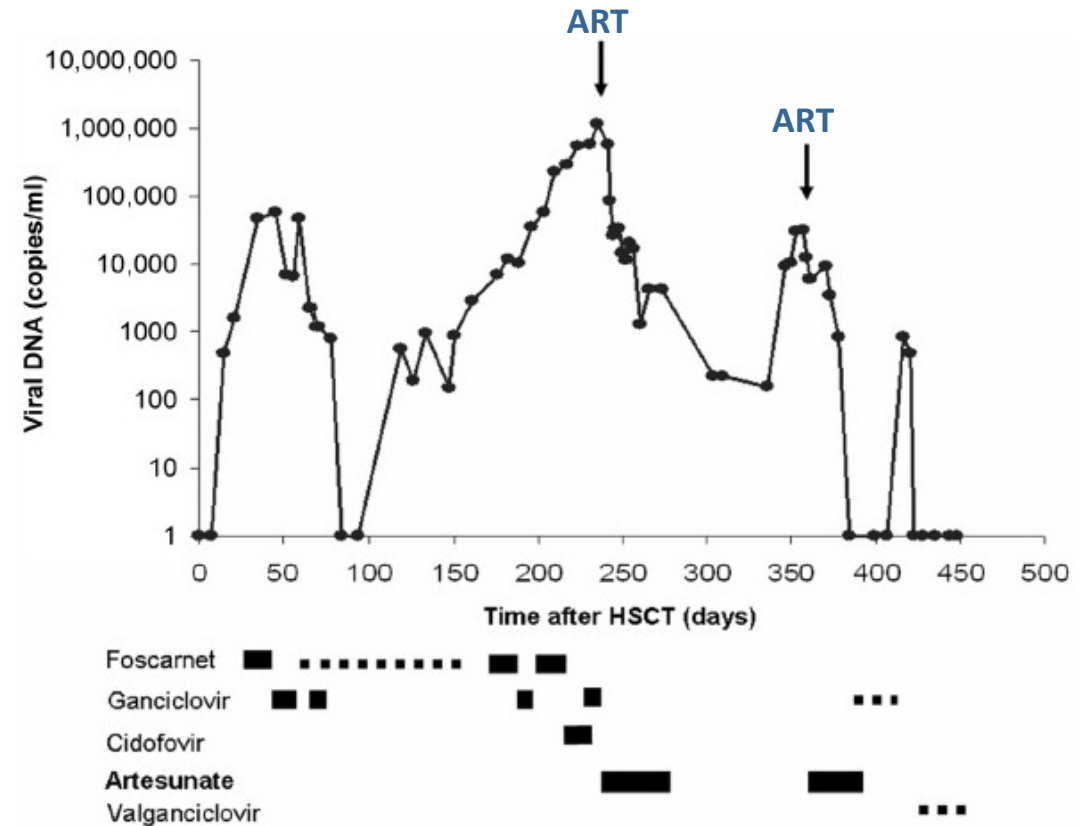
- Determining if CMV resistance to GCV or VGCV at baseline correlates with lack of viral load reduction
- Determining if development of CMV resistance to GCV or VGCV occurs during and after treatment and if this is associated with lack of viral load reduction

Why IVAS in SOT patients with CMV disease?

- Artesunate has demonstrated potent effects against CMV in in vitro and animal models of CMV infection, even against GCV-resistant strains ([Efferth-2008](#), [Ho-2014](#), [Kaptein-2006](#)).
- Artesunate concentrations up to 8.5 μM in the plasma have been reported (equivalent to 3.3 $\mu\text{g/mL}$) ([Byakika-Kibwika-2012](#)) majority of CMV AD169 in vitro studies show viral half maximal inhibitory concentration (IC_{50}) values between 2 and 4 μM .
- Case reports have been published where patients with SOT (2 lung and 1 kidney transplant recipients) received oral artesunate for resistant CMV infections ([Germi-2014](#)). In 22 HSCT patients, Artesunate effectively controlled CMV replication in 74% of patients, with CMV being cleared in 19% of episodes ([Gokarn-2023](#)).

Artesunate is synergistic when combined with antivirals – rapid decline of CMV

Artesunate plus Ganciclovir (IV) or Valganciclovir (oral) in combination therapy for the treatment of cytomegalovirus (CMV) infection in solid organ transplant recipients



Shapira, M.Y., et al., *Artesunate as a potent antiviral agent in a patient with late drug-resistant cytomegalovirus infection after hematopoietic stem cell transplantation*. Clin Infect Dis, 2008. 46(9): p. 1455-7.