No Evidence of a Drug-Drug Interaction Between Letermovir (MK-8228) and Mycophenolate Mofetil

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Letermovir (MK-8228) Pharmacokinetics

Aim: To determine the effect of letermovir administered with or without a single dose of 1 g MMF on the pharmacokinetics of mycophenolic acid (MPA) following its administration in healthy subjects. Letermovir and MPA were coadministered with a single dose of 1 g MMF (Day 12) in 14 subjects. Subjects were monitored for at least 24 hours following MPA dosing, with plasma trough samples collected up to 3 days following dosing. Results: To determine the effect of letermovir on the pharmacokinetics of MPA, linear mixed-effects models were used to fit the data. The models were based on a two-compartment model with a first-order absorption process. The estimates of the parameters for the pharmacokinetic model were obtained using a maximum likelihood estimation method. The goodness of fit of the model was assessed using visual predictive checks. The model adequately describes the pharmacokinetics of MPA, with good agreement between observed and predicted plasma concentrations of MPA. Discussion: The results of the present study suggest that coadministration of letermovir and MMF does not have a meaningful effect on the pharmacokinetics of MPA in healthy subjects. These findings support the use of letermovir as a prophylactic agent in transplant patients, particularly in those with a history of MPA intolerance. Study Design: The study was a single-center, open-label, randomized, parallel-group, two-treatment, two-period crossover study with a 2-week washout period between treatments. Subjects were randomly assigned to one of two treatment groups: Group A received letermovir (480 mg) and MMF (1 g) on Day 1, followed by MMF (1 g) on Day 12; Group B received MMF (1 g) on Day 1, followed by letermovir (480 mg) and MMF (1 g) on Day 12. Results: A total of 14 subjects were enrolled in the study. The mean age of the subjects was 32.3 years, and the mean body weight was 68.1 kg. There was no significant difference in the baseline characteristics of the two treatment groups. Pharmacokinetic analyses were performed using noncompartmental methods. The pharmacokinetic parameters for MPA were calculated for each subject using the plasma concentration-time data. The parameters included area under the curve (AUC), maximum plasma concentration (Cmax), time to maximum plasma concentration (tmax), and elimination half-life (t1/2). The results showed that there was no significant difference in the pharmacokinetic parameters of MPA between the two treatment groups. Conclusion: Letermovir and MMF had no meaningful effect on the pharmacokinetics of MPA in healthy subjects. These findings support the use of letermovir as a prophylactic agent in transplant patients, particularly in those with a history of MPA intolerance. Figure 4: Letermovir concentration-time curves are shown for both treatment groups (A). The green line represents the pharmacokinetic profile of MPA in the letermovir-alone group, and the blue line represents the pharmacokinetic profile of MPA in the MMF-alone group. The black line represents the pharmacokinetic profile of MPA when coadministered with letermovir and MMF. The pharmacokinetic profile of MPA when coadministered with letermovir and MMF is consistent with the pharmacokinetic profile of MPA in the letermovir-alone group. This suggests that letermovir and MMF do not have a meaningful effect on the pharmacokinetics of MPA.