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

WL Marshall  
*Merck & Co., Inc., Kenilworth, NJ, USA*

C. Badshah  
*Merck & Co., Inc., Kenilworth, NJ, USA*

F. Liu  
*Merck & Co., Inc., Kenilworth, NJ, USA*

Walter K. Kraft, MD  
*Thomas Jefferson University, Philadelphia, USA*, walter.kraft@jefferson.edu

F. Colon-Gonzalez  
*Merck & Co., Inc., Kenilworth, NJ, USA*

See next page for additional authors

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Letermovir (MK-8228) is a new class of inhibitor of the cytomegalovirus (CMV) terminase complex and is approved for the prevention of CMV disease in CMV-seronegative recipients of hematopoietic stem cell transplants (HSCT). Letermovir is a prodrug of the active metabolite, which is the triphosphate form of mycophenolic acid (MPA). Letermovir is coadministered with mycophenolate mofetil (MMF), which is the triphosphate form of MPA. Letermovir and MPA are approved for prophylaxis against CMV disease in allogeneic HSCT recipients who are seronegative for CMV and seropositive for CMV.

Methods: This was an open-label, fixed-sequence, single- and multiple-dose trial to characterize the pharmacokinetic interaction between letermovir and MMF in healthy subjects. 480 mg letermovir daily with a single dose of 1 g MMF was administered on separate days (Day 5) or 7 days on a single occasion (Day 11). PK was assessed at each visit. Plasma samples were tested for both letermovir and MPA. AUC(0-24) and C(max) were calculated for letermovir and MPA. The geometric least-squares mean ratio between treatments (expressed as a percent) was calculated and its 90% CI was reported (90% CI).

Results: Coadministration of 480 mg letermovir at steady state with a single dose of 1 g of MMF had no clinically meaningful effect on the PK of letermovir or MPA. The estimated GMR and 90% confidence interval for the comparison (letermovir with MMF/letermovir alone) were 1.18 (1.04, 1.34) for AUC and 1.08 (0.96, 1.21) for C(max). Letermovir was generally well tolerated by the healthy subjects in this study. AEs occurred in 8 of 14 (57.1%) subjects treated with letermovir alone, 10 of 14 (71.4%) subjects treated with letermovir and MMF, and 8 of 14 (57.1%) subjects treated with MMF alone. The most common AEs reported were nausea (42.9%) and diarrhea (42.9%). The other AEs reported were dizziness, constipation, flatulence, and infection.

Discussion: Coadministration of letermovir and MMF had no clinically meaningful effect on the PK of letermovir or MPA. Coadministration of letermovir and MMF is safe in healthy subjects. Letermovir and MMF may be coadministered without dose adjustment.

Conclusions: Letermovir and MMF may be coadministered without dose adjustment.