Q: Is there any rational to give valganciclovir 450 mg bid instead of 900 mg once daily in normal kidney patients?

A: This is an interesting question. The pharmacokinetics of 450 mg twice daily compared to 900 mg once daily for CMV prophylaxis have not been evaluated in clinical trials to date. Yet, we do administer 450 mg orally twice daily as a renally adjusted dose for 900 mg twice daily to treat mild CMV disease in transplant recipients based on results of the VICTOR trial (Asberg A, et al. Am J Transplant 2009; 9: 1205–13). However, for twice daily prophylaxis you would have to consider the patient’s overall medication regimen, duration of twice daily prophylaxis therapy, and risk factors for medication non-adherence.

Q: What do the presenters feel is the correct way to dose for renal impairment - dosages based on Cockcroft-Gault or an eGFR formula. In obese patients, would you use actual or ideal body weight for CG, or correct eGFR for actual body surface area?

A: The product information for valganciclovir is based on dosage by CG but does not specify which weight to use for the calculation (ideal body weight, adjusted body weight (if patient obese) or actual body weight). In our practice, for obese patients (defined as weight > 20% over calculated ideal body weight) we use adjusted body weight instead. There is also literature to show that using CG with ideal body weight in obese patients may underestimate renal function and underestimate valganciclovir dosing. (Posadas MA et al. Transpl Infect Dis. 2013; 15:551-8). Additionally, it is critical to review the overall trend in renal function and not just base the dosing decision on the value available at one specific time-point. With eGFR, you may compare the values to CG, but eGFR should not be used alone to make valganciclovir dosing decisions. This concept was well-illustrated in a 2014 letter to the editor (Penne E, et al. Antimicrob Agents Chemother. 2014;58:1271-2).

Q: We (in the UK) don’t generally use filgrastim to treat valganciclovir-induced leukopaenia - we just stop the valganciclovir wait for the leucocytes to come back. Is filgrastim often used in the US for this specific indication?

A: Yes-filgrastim is sometimes used off-label for this indication (after other leukopenia-inducing medications have been decreased or discontinued) to allow for continuation of valganciclovir therapy (vs discontinuation for leukopenia). As Dr Gabardi noted in his multi-center study of valganciclovir in CMV D+/R- kidney transplant recipients (Gabardi et al, Transplantation 2015; 99: 7: 1499-1505) the premature discontinuation of prophylaxis, regardless of dose, was associated with CMV disease rates more than double that seen with patients receiving full course of prophylaxis. Filgrastim has proven quite effective at raising leukocyte counts and allowing continuation of valganciclovir and current dose of MPA. We have found very little in the way of adverse events, with only a few patients complaining of bone pain within 24 hours of administration. Due to the outpatient costs and general lack of coverage by outpatient
prescription insurance in the US, we generally administer our doses in our clinic and receive reimbursement for its use as part of the patients’ clinic visit.

Q: Could speakers comment on use of Letermovir for prophylaxis in SOT recipients?

A: As of February 2018, on the clinicaltrials.gov website, there is a multicenter trial (sponsored by Merck) about to begin which will evaluate Letermovir vs valganciclovir 900 mg/day for CMV prophylaxis in adult kidney transplant recipients, so more information to come. It is known to be hepatically eliminated and as a result, based on current product information certainly requires less dose adjustments (particularly with the oral formulation) for patients with renal insufficiency compared to oral valganciclovir. Of note, it is important to remember that Letermovir does NOT offer prophylaxis against HSV 1 and 2. Drug-drug interactions with post-transplant medications will also need to be carefully reviewed.

Q: Any thoughts on dosing in obese patients?