Brincidofovir Decreases Adenovirus Viral Burden, Which is Associated with Improved Mortality in Pediatric Allogeneic Hematopoietic Cell Transplant Recipients

**Background:** Adenovirus (AdV) infection is an important cause of morbidity and mortality after hematopoietic cell transplant (HCT). Cidofovir is often used off-label to treat AdV viremia but does not lead to resolution of viremia without T cell immune reconstitution [1]. Brincidofovir (BCV) is an investigational antiviral with high potency in vitro against all AdV subtypes. BCV was evaluated as a treatment for AdV infection or disease in pediatric allogeneic HCT recipients in the AdVise trial (CMX001-304; NCT02087306); primary analyses were previously presented [2]. Herein we further analyze the effect of BCV on AdV viral burden in the subgroup of pediatric HCT patients with clinically significant AdV viremia (≥1000 copies/mL) within 100 days of transplant, and examine the correlation of viral burden with clinical outcome.

**Methods:** In the AdVise trial, patients were treated with oral BCV 2 mg/kg (up to 100 mg) twice weekly for 12 weeks and followed for 36 weeks post-first dose. AdV viremia outcomes were assessed at multiple time points, including clearance of viremia, reductions in viremia, time to clearance, time undetectable, time under 1000 copies/mL, and viral burden measured as area under the viremia-time curve (AUC) and time-averaged area under the viremia-time curve (AAUC).

**Results:** Of the 100 pediatric allo HCT patients enrolled in the AdVise trial, 40 presented with AdV viremia ≥1000 copies/mL within 100 days of transplant. Thirty-four (85%) cleared the virus on BCV, with a median (IQR) time to clearance of 22 (15, 38) days. Twenty-one (53%) of these 40 patients were alive at Week 36. Mean (SD) Week 12 AAUC was 2.4 (0.5) log10 c/mL in patients alive at Week 36 versus 3.3 (1.7) log10 c/mL in patients who died prior to Week 36 (see Figure 1; Satterthwaite t-test *P*=.038). Baseline AdV viremia was positively correlated with AAUC (*R*2 = .30).

**Conclusions:** Rapid declines in AdV viral load, clearance of AdV, and reductions in AdV viral burden were observed in pediatric allogeneic HCT recipients treated with BCV. Viral responses were associated with improved survival. These data support continued development of BCV as the first potential therapeutic for AdV.

**REFERENCES**