EBMT 2015 - Physicians Abstract (including Data and Quality Management)

Topic area: Transplant-specific topics Topic: 13. Infectious complications EBMT15-ABS-1523 Improved Outcomes in Allogeneic Hematopoietic Cell Transplant (allo HCT) Patients Treated with Brincidofovir (CMX001, BCV) for Disseminated Adenovirus (AdV) Disease Compared to Literature: Updated Preliminary Results from the AdVise (CMX001-304) Study

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Preferred Method of Presentation: Oral or Poster Presentation

Introduction: In allo HCT patients (pts) with disseminated AdV disease, mortality is reported to be up to 80%. Antiviral treatment (tx) usually consists of IV cidofovir (CDV), which has a significant risk of nephrotoxicity. BCV is an orally-available, lipid-conjugate of CDV with no evidence of nephrotoxicity in clinical trials. The pilot portion of the Phase 3 AdVise (CMX001-304) study was initiated in March 2014 to enroll ~100 allo HCT and other immunocompromised AdV pts with, or at risk of progression to, disseminated AdV disease, to guide the final study design. As of 10NOV2014, 73 subjects have been enrolled and entered into the database, including 60 allo HCT pts (48 with disseminated AdV disease), 7 solid organ transplant pts and 6 "other" pts. Preliminary safety and virologic results for the 48 allo HCT pts with disseminated disease are described.

Materials (or patients) and methods: All subjects receive open-label BCV 100 mg (≥50 kg) or 2 mg/kg (<50 kg) twice-weekly for 12 wks, extendable up to 24 wks for pts at high-risk of relapse, and are followed for 24 wks post-tx. AdV DNA viral load (VL) in plasma is measured using a quantitative PCR test (limit of detection [LOD] 2 $\log_{10}$ c/mL).

Results: Baseline (BL) characteristics for the 48 subjects are: median (range) age 12 (0.7, 69) y, 65% <18 y; 69% male; median (range) plasma AdV VL 4.6 (< LOD to 7.6) $\log_{10}$ c/mL (n=45); 42% AdV positive by qualitative PCR in respiratory secretions, 60% in urine, 65% in stool; 29% with CMV in plasma, 6% EBV in plasma and 42% BKV in urine; 42% received prior IV CDV. As of 25NOV2014, 5 subjects had completed tx and 21 had discontinued tx prematurely. The most common reasons for tx discontinuation were death (n=11) and adverse event ([AE] n=4). Median (range) tx duration was 38 (1, 141) days (n=45). Virologic response in CDV-naïve and exposed subjects with detectable plasma AdV VL at BL are summarized in the table. In subjects with positive AdV PCR at BL, 65% (13/20) cleared AdV in respiratory secretions, 55% (16/29) in urine and 48% (15/31) in stool. Through 08DEC2014, 40% (19/48) of allo HCT subjects with disseminated AdV disease had died, with a median 71-day observation period for living subjects. No death was attributed to BCV. AEs leading to permanent tx discontinuation attributed to BCV were vomiting and abdominal pain in 1 subject, and acute GVHD in 1 subject.

	Median (range) Change in AdV VL from BL (log_{10} c/mL)		Median (range) Time to Minimum On-tx (days)	Proportion ≥3 log_{10} Reduction in AdV VL or to Undetectable at Nadir
	Minimum On-tx	Last On-tx		
CDV-naive (n=23)	-2.0 (-5.1, 0.5)	-1.8 (-5.1, +2.1)	15 (3, 106)	57% (13/23)
CDV-exposed (n=18)	-1.5 (-5.4, +0.6)	-1.2 (-5.4, +0.6)	15 (4, 77)	72% (13/18)

Conclusion: The observed mortality rate was 40% for allo HCT pts with disseminated AdV disease in AdVise, which is lower than literature rates reported for this pt population (50-80%; Ison 2006, Sandkovsky 2014). BCV showed potent virologic activity in CDV-naïve and exposed pts with no new safety concerns. These preliminary data support expansion of the pilot portion to a definitive Phase 3 study.

References: Ison M. CID 2006:433;31-9; Sandkovsky U, et al. Curr Infect Dis Rep 2014:16:416-24.

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