CHIMERIX, INC.

BMT Tandem 2015 Abstract

Title: Preliminary Results from the AdVise Study Evaluating Brincidofovir (BCV, CMX001) for the Treatment of Disseminated and High-Risk Adenovirus (AdV) Infection

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Background: AdV is associated with significant morbidity and mortality. No drug is currently approved for AdV. BCV is an orally available lipid-conjugate of cidofovir (CDV) that has demonstrated promise as preemptive therapy in allo HCT patients (pts) with asymptomatic AdV viremia (VL) in a Phase 2 study. The pilot portion of a Phase 3 BCV study for AdV (CMX001-304, AdVise Study; NCT02087306) was initiated in MAR2014. Preliminary results for 26 subjects enrolled through 15JUL2014 are described (data cut-off 12SEP2014). **Methods:** All subjects receive open-label BCV 100 mg (≥ 50 kg) or 2 mg/kg (< 50 kg) twice a week. **Results:** For the 26 subjects, median age = 6.5 y (range: 0-29), 58% < 12 y; 20 allo HCT pts (16 with disseminated disease), 4 solid organ transplant pts and 2 chemotherapy pts; median VL in plasma by quantitative polymerase chain reaction (PCR) at baseline (BL) 4.8 $\log_{10}$ c/mL (range: undetectable [< 2 $\log_{10}$; < LOD] to > 10 $\log_{10}$) (n = 23); 46% were AdV positive in respiratory secretions, 58% in urine, 58% in stool by qualitative PCR; 42% (11/26) had prior IV CDV exposure. Median BCV treatment duration 54 days (range: 1 to 108). Suppression of plasma AdV VL to < LOD by quantitative PCR was 61% (14/23) at any time on-treatment and 52% (12/23) at last on-treatment value. Median change in plasma AdV VL from BL to nadir was -1.4 $\log_{10}$ c/mL (range: -8.0 to 0.6), with 65% (15/23) achieving ≥ 3 $\log_{10}$ decrease to nadir (or to < LOD). Individual plots of plasma AdV VL over time are shown in the figure. In subjects with positive qualitative AdV PCR at BL, 42% (5/12) cleared AdV in respiratory secretions, 33% (5/15) in urine and 27% (4/15) in stool. Six of the 11 subjects with prior IV CDV achieved AdV VL < LOD and one had > 2 $\log_{10}$ decline at last on-treatment value. Treatment-related AEs requiring premature BCV discontinuation were limited to severe diarrhea (in two subjects). Among the 48 subjects enrolled through 19SEP2014, there were 17 deaths, including two of seven subjects with asymptomatic disease (29%), in 11 of 29 allo HCT subjects with disseminated AdV (38%) and four of 12 subjects with non-allo HCT disseminated AdV (33%), representing an overall mortality rate to-date of 35% (17/48), with a median duration of observation of 57 days for living pts. Safety and efficacy data from newly enrolled subjects will be included in the presentation. **Conclusions:** These preliminary results from 26 subjects enrolled in the pilot portion of AdVise show mortality rates of < 40% across subjects with limited and disseminated AdV and across populations with varying identified risk factors (HCT, SOT, other); these are lower mortality rates than those in the literature for disseminated disease. AdV viremia was suppressed to undetectable in over half of enrolled subjects. No new safety concerns were identified in this complex patient population. These data support progression to definitive Phase 3 BCV study for AdV.