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Switch from Existing Antivirals to Brincidofovir Leads to Improving Renal Function

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Introduction: Cidofovir (CDV) and foscarnet (FOS) have been associated with nephrotoxicity, precluding use in renally impaired patients and shortening treatment in others. Brincidofovir (BCV; CMX001), in Phase 3 development (SUPPRESS Trial) for prevention of CMV post-hematopoietic cell transplant (HCT), is a nucleotide analogue with broad-spectrum double-stranded DNA (dsDNA) antiviral activity and a favorable safety profile.

Methods: Study 350 provided expanded access to BCV for life-threatening dsDNA infections. Most subjects were HCT (72%) or solid organ transplant (16%) recipients, and 25% were enrolled due to concerns of nephrotoxicity. Baseline (BL) and on-treatment Glomerular filtration rates (GFR), estimated using the MDRD4 (adults) and Schwartz (children) formulas, were evaluated in subjects with prior CDV +/- FOS and no concomitant CDV or FOS use, regardless of indication and other nephrotoxic agent use.

Results: Median BL GFR for 37 subjects with prior but no concomitant CDV use was 87 mL/min. Thirty-two (86%) subjects had a maximum GFR≥BL during treatment, and had a median of 6 weeks of BCV, compared to 2 weeks for those subjects without GFR improvement. For subjects with BL GFR<60mL/min, 13/14 had max GFR≥BL (8/13 had >20mL/min increase); 10/14 subjects had last on-treatment GFR≥BL (7/10 had >20mL/min increase). For subjects with BL GFR<30mL/min, 6/6 had max GFR≥BL (4/6 had >20mL/min increase); 5/6 had last GFR≥BL (4/5 had increase >20mL/min).

Similar analyses were performed on 66 subjects with prior but no concomitant CDV and/or FOS use. Fifty-five (83%) subjects had a max GFR≥BL. Of these, increases from BL >20mL/min were seen in 53% subjects with BL GFR<60mL/min and 71% with BL GFR<30mL/min.

Conclusions: These data suggest BCV has no negative impact on renal function and may allow recovery of renal function when sufficient time elapses after discontinuation of the contributing antiviral. This supports continued investigation of brincidofovir as a potential treatment option for subjects with or at risk for dsDNA virus infections and at high risk for renal impairment, including kidney transplant recipients.