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Brincidofovir (CMX001) Experience in Renal Transplant Patients for Treatment of Refractory CMV Infection

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Background: Brincidofovir (CMX001, BCV) is an oral nucleotide analog, in Phase 3 development for CMV prevention, with broad-spectrum in vitro antiviral activity against double stranded DNA (dsDNA) viruses, including cytomegalovirus (CMV), adenovirus, BK virus and herpes simplex viruses. BCV was administered in patients with refractory or resistant dsDNA viral infections, including CMV infections, in an expanded access protocol (Study 350).

Methods: Renal transplant patients with refractory CMV infection who received BCV >/= one week were evaluated for safety and efficacy. Five patients (4 renal and 1 renal/pancreas transplant recipients) with resistant or refractory CMV infection were given BCV 100-200 mg twice weekly.

Results: Five adult patients (44-56 years of age) were treated with BCV for CMV viremia (3/5 viremia only) and CMV syndrome (2/5). Three patients received 2 or more renal transplants prior to BCV treatment. All patients received immunosuppressants (IS) and 1 had an increase in IS therapy during BCV treatment. All received previous treatments for CMV (Foscarnet 2/5, GCV 1/5, vGCV 3/5). Initial BCV doses ranged from 100 to 200 mg twice weekly with a median duration of treatment of 91 days (10-171). At the end of treatment, 3 patients had a complete virologic response (<LOD, 100c/mL), one had a -2.4 log response, and one had an increase of +0.4 log. Resistance testing confirmed pre-existing viral resistance to GCV in 4/5 patients with one patient developing CDV resistance on therapy. The most common adverse event was diarrhea (3/5 patients) and one of the patients with unresolved viral infection was withdrawn due to diarrhea on day 10. The other patient with unresolved viral infection was withdrawn due to worsening CMV viremia at day 147 after an increase in IS therapy. CMV viral infection resolved while receiving BCV monotherapy in 3 patients.

Conclusion: Patients with resistant and refractory CMV, who have failed standard therapies, may respond to BCV treatment. Further evaluation of BCV for treatment and prevention of dsDNA viral infections, especially CMV, is warranted.