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WTC 2014 Abstract

Title: Brincidofovir (CMX001) for the Treatment of Serious or Life-threatening Double-stranded DNA Virus Infections in Patients Receiving Liver Transplant as Part of Multiorgan Transplantation

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Body:

Background: Infectious complications remain an important cause of morbidity/mortality following SOT. Brincidofovir (BCV), a nucleotide analog active in vitro against all major human pathogenic dsDNA viruses, is in Phase 3 development for CMV prevention in HCT. Over 400 patients (pts) have received BCV for serious or life-threatening infections with dsDNA viruses under compassionate use (Study CMX001-350, clinicaltrials.gov ID: NCT01143181 or under emergency INDs).

Methods: Ten multiorgan transplant pts (liver ± kidney/pancreas/small bowel) were treated with BCV for serious/life-threatening AdV, BKV, CMV, EBV or VZV infections after failing existing antiviral therapies. BCV was given orally at 2-4 mg/kg or 100-200 mg twice-weekly.

Results: Pt demography and virologic responses [viral load (VL) at baseline (BL) and maximal (Max) and through end-of-treatment (EOT) decreases]/infection outcomes are summarized in the table:

Case	Age	Transplants	Primary dsDNA Virus	BCV Tx Duration (wks)	BL VL (log_{10} c/mL)	Max/EOT VL Decrease (log_{10} c/mL)	Infection Outcome
1	4yrs	L/K/P/SB	EBV	3	>7.7	>-3.6/>-3.6	R
2	3yrs	L/P/SB	AdV	12	3.3	-1.3*/-1.3*	R
3	15yrs	L/P/SB	AdV	26	3.6	-1.6*/-1.6*	R
4	17mos	L/P/SB	AdV	13	2.9	-0.9*/-0.9*	R
5	6mos	L/P/SB	AdV	12	2.7	-0.7*/-0.7*	R
6	2yrs	L/P/SB	CMV	12	7.0	-3.4/-3.3	VR (pt moved)
7	22mos	L/P/SB	EBV	4	7.7	-2.7/-2.7	VR (care withdrawn)
8	4yrs	L/K	BKV	10	4.3	-1.6/-1.6	VR (consent withdrawn)
9	13yrs	L/K	VZV	1	NV	NV	R
10	2yrs	L/SB	AdV	1	7.4	ND	Pt death

ND=no data; NV=no viremia; R=resolved; VR=virologic response; *=undetectable (<100copies/mL)

Two pts died on treatment (#7 intracranial haemorrhage, #10 hepatic failure secondary to aortic thrombus, both unrelated to BCV); 2 pts died >30 days posttreatment (#1 PTLD/Pseudomonas pneumonia, #3 septic shock). No adverse events (AEs) required BCV treatment discontinuation and there were no serious drug-related hepatic AEs.

Conclusions: These data support the continued study of BCV in the treatment of dsDNA virus infections in SOT and other immunocompromised pts. There were no treatment-limiting AEs and some evidence of improved outcomes, though conclusions are limited by small sample size and uncontrolled data collection.