Brincidofovir (BCV) Prophylaxis for Herpes Simplex Virus (HSV) and Varicella Zoster Virus (VZV) after Hematopoietic Cell Transplantation (HCT): Clinical Experience at Memorial Sloan Kettering Cancer Center

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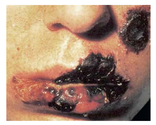
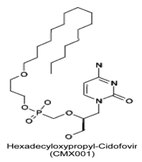
Background



•Herpes simplex (HSV) and Varicella zoster (VZV) viruses may cause serious infections in HCT recipients.

•Universal prophylaxis with ACV has been effective in preventing HSV/VZV infections.



Brincidofovir (BCV; CMX001)

•Broad spectrum oral antiviral

•In vitro activity against HSV/VZV

•In clinical development for CMV prevention

•No clinical experience for HSV/VZV prophylaxis

Objective

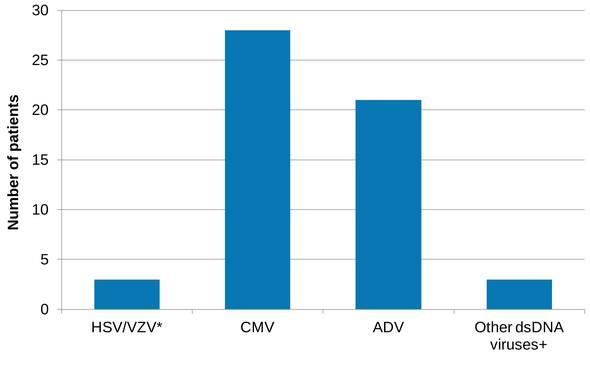
•Report the MSK experience with BCV for HSV/VZV prophylaxis in HCT treated with open label BCV.

Methods

•Allo-HCT patients treated with open label BCV for ≥14 days for any indication from April/2010 and July/2015 were included in the study.

•HSV or VZV reactivation was defined as positive viral culture or PCR and compatible clinical presentation.

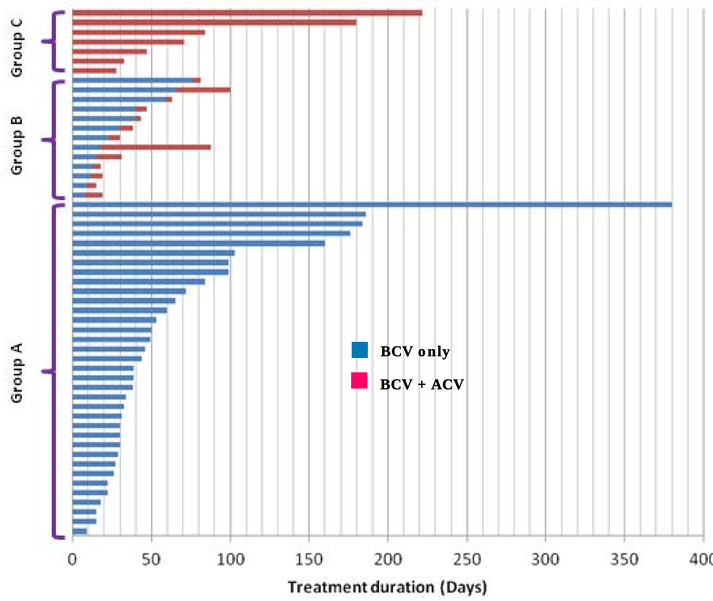
Primary virus treated with BCV



*HSV, ACV resistant (2); disseminated VZV (1)

+BK polyoma virus (1) Human herpes virus 6 (1), John Cunningham virus (1)

Duration of BCV



		Group A	Group B
		N=35	N=13
Days from transplant to start of BCV, median (IQR)		77 (60-163)	112 (78-377)
Duration of brincidofovir only (days)	median IQR, (min, max)	39 (30-78) (7, 186)	38 (19-63) (15, 100)
Total patient-days on BCV only		2,397	409
Dose	≤200mg weekly or 4mg/kg weekly	21	10
	>200mg weekly or 4mg/kg weekly	14	3
Age	<12 years	2	3
	≥12 years	33	10

Abbreviations: BCV, Brincidofovir; IQR, interquartile range; ACV, acyclovir; HSV, Herpes simplex virus; VZV, Varicella zoster virus; pts, patients; min, minimum; max, maximum

Note: Group C had concomitant BCV+ACV for the entire study period; therefore they were excluded from the analysis.

HSV breakthrough infections

Sex/ Age	Transplant type	Indication for BCV	BCV dose	HSV diagnosis from BCV	GVHD	Immunosuppressants at the time of breakthrough infection	Outcome
M/ 58	Peripheral blood T-cell depleted	Oral HSV Resistant to ACV	200mg weekly	30 days	Grade III skin	Methylprednisolone 1mg/kg/day Mycophenolate 1mg q12h Sirolimus 1mg PO daily	Clinical resolution of initial lesions. Intermittent positive HSV PCR during treatment- responding to transient increase in BCV dose.
F/ 59	Umbilical Cord	CMV viremia, HSV	100mg BIW -> 200mg weekly	71 days	Grade II gut	Methylprednisolone 2mg/kg/day Mycophenolate 1mg q 12h Etanercept 25mg	Genital HSV infection during interruption of BCV prophylaxis for severe diarrhea related to GVHD.

Conclusions

•The rate of HSV breakthrough infections was 0.7 cases/1,000 patient-days of BCV prophylaxis. There was no breakthrough VZV among 48 highly immunosuppressed HCT patients .

•Thirty one (56%) patients received BCV 100mg twice weekly. This dose is currently evaluated in clinical trials for CMV prevention in HCT.

• Interruption of BCV prophylaxis and/or impaired GI absorption likely explain the breakthrough HSV infections in 2 patients.

•Our clinical experience supports BCV as a suitable alternative to acyclovir prophylaxis against HSV/VZV in HCT patients.

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