A Single Center Experience with Cidofovir for the treatment of double stranded (ds) DNA viruses in Hematopoietic Cell Transplant (HCT) recipients.

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Background

- Cidofovir (CDV) is a nucleotide analogue antiviral active against all dsDNA viruses relevant in hematopoietic cell transplant (HCT) recipients.
- Despite a broad spectrum of activity, CDV utility is limited due to nephrotoxicity.
- In this single center study we aimed to evaluate:
  1. CDV administration practice and indications
  2. Serum creatinine (sCr) dynamics following CDV treatment
  3. Factors associated with acute kidney injury (AKI) following CDV treatment

Methods

- Retrospective review of adult HCT recipients in MSKCC who received CDV for any indication from 2011 to 2017.
- Initiation and duration of CDV treatment were at physicians' discretion.
- CDV exposure and indications, laboratory data and outcomes were extracted from medical records and hospital databases.

Results

- Of 1,235 HCT recipients, 54 (4.4%) received ≥1 dose of CDV.
- Baseline sCr at CDV initiation was 0.88 mg/dL (mean, SD=0.37) while at end of treatment (EOT) it was 1.07 mg/dL (mean, SD=0.57, N=48, P=0.004) and at EOT + 2 weeks it was 1.23 mg/dL (mean, SD=0.72, n=28, P=0.027) .
- At EOT, 13 pts (24%) had acute kidney injury (AKI) defined as ≥ 1.5-fold increase of baseline sCr. Of those, 12 (92%) received concomitant nephrotoxic drugs, and in six, AKI was attributed to other etiologies by treating physician.
- Of 51 patients with follow-up at EOT, 29 (57%) had clinical response to CDV according to treating physician.
- Nineteen patients (35%) died within four weeks from last CDV dose.

Conclusions

- In this highly immunocompromised cohort, 24% of patients experienced AKI following CDV treatment.
- Concomitant nephrotoxic medications and potential impact of dsDNA viruses on renal function preclude determination of the relative contribution of CDV to AKI.
- Safer treatment options are needed for HCT patients with life threatening infections with dsDNA viruses.

Table 1. Baseline patient characteristics

		N=54 (%)
Demographics	Age, Median years (IQR)	54.5 (44-62)
	Gender: Female	28 (52)
HCT characteristics		
Donor type	Matched related donor	12 (22)
	Matched/Mismatched unrelated donor	42 (78)
HCT source	Cord blood	13 (24)
	Peripheral stem cells	39 (72)
	Bone marrow	2 (4)
HCT manipulation	CD34+ selection	42 (78)
Immune-suppression	Active GvHD at CDV initiation	23 (43)
	Systemic steroid treatment at CDV initiation	16 (30)

Figure 1. Indications for CDV administration
19 patients had concomitant infection with more >1 dsDNA virus (two dsDNA viruses in 14 patients and three in five patients).

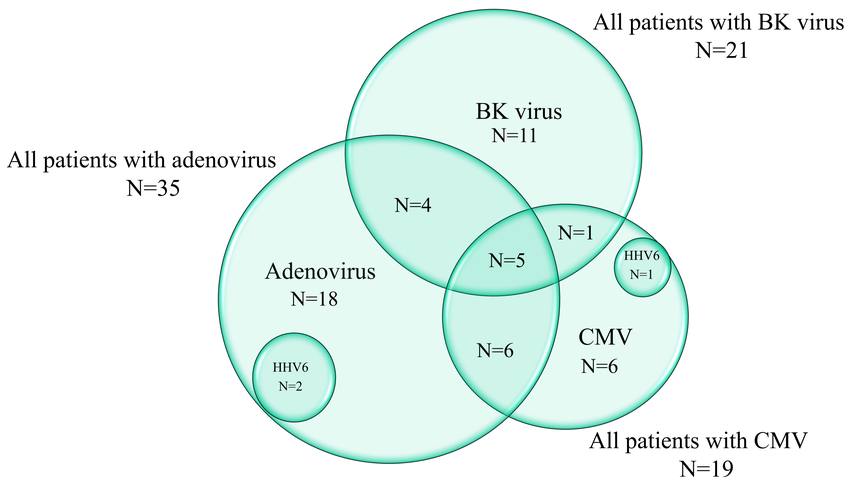

Table 2. CDV dosing and administration

	N=54 (%)
Days from HCT to first CDV dose – median (range)	88.5 (14-335)
Number of CDV doses - median (range)	3 (1-13)
Duration of CDV treatment – median (range)	2 weeks (1-17 weeks)
CDV dose – High dose (3-5 mg/kg, 1/w)	41 (76%)
Low dose (≤1 mg/kg, 1-3/w)	13 (24%)

Figure 2. Serum creatinine
Mean serum creatinine is higher in the end of CDV treatment compared to baseline and later tends to improve. Creatinine rise is mainly observed in patients in highest quartile of baseline creatinine

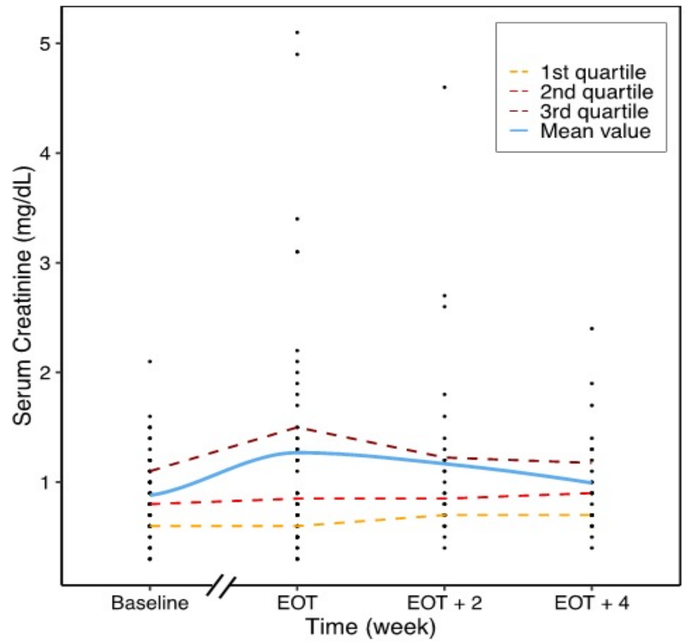

Figure 3. Percentage of patients with AKI at end of CDV treatment by patients subgroups: (A) by time from HCT to first CDV dose; (B) by CDV dose; (C) by baseline creatinine

AKI defined as sCr at end of treatment ≥1.5 times baseline sCr.