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Cidofovir in the Treatment of BK Virus–Associated Hemorrhagic Cystitis Following Hematopoietic Stem Cell Transplantation; A Medication Use and Safety Analysis

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WAYNE STATE Cidofovir in the Treatment of BK Virus–Associated Hemorrhagic Cystitis Following Hematopoietic Stem Cell Transplantation; A Medication Use and Safety Analysis

School of Medicine

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INTRODUCTION

Background

BK virus hemorrhagic cystitis (BKV-HC) is a complication after allogeneic hematopoietic stem cell transplant (AlloHCT) for which optimal management is uncertain. Intravenous (IV) and intravesicular (IVES) cidofovir have been used with varying degrees of success in small case series of six to 33 patients. While some series have investigated side effects, none have examined medication errors (Fig 1).

Objective

Determine instances of Cidofovir medication errors and perform root cause analysis to determine contributing factors. Describe efficacy of CDV for BKV-HC

METHODS

- Retrospective single center case series of Allo HCT patients with BKV-HC from 2018-2022 at urban center in Detroit, MI.

Figure 1: Definitions of Terms Related to Drug Safety

Side Effect¹	An effect of a drug that is in addition or beyond its desired effect. Side effects can be harmful or beneficial. Example: acute kidney injury after vancomycin
Medication Error²	Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Example: vancomycin being administered to a patient with a known vancomycin allergy in the chart

1. National Cancer Institute. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/side-effect>. Accessed February 2, 2023.
2. National Coordinating Council for Medication Error Reporting and Prevention. Contemporary view of medication-related harm. A new paradigm. www.nccmerp.org/sites/default/files/nccmerp_fact_sheet_2015-02-v91.pdf. Accessed February 2, 2023.

Figure 2: Root Cause Analysis of Cidofovir Related Medication Error (ME)

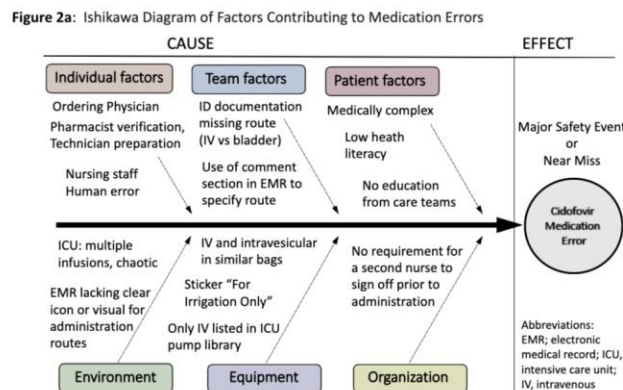
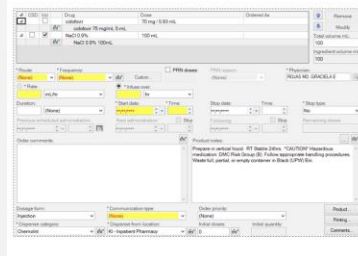


Figure 2b: Intensive Care Unit Pump Library (Only Intravenous Cidofovir Listed)



Figure 2c: Pharmacy CIS lacks specific option for IntraVESicular administration



RESULTS

Table 1. Characteristics of Allogeneic Hematopoietic Stem Cell Transplant Patients Who Received Cidofovir

Age	Sex	Hematological Disease	Conditioning Regimen	Graft Donor Source	CMV D/R	GVHD Prophylaxis	Acute GVHD	CMV Co-infection	HHV8 Co-infection	Adeno Co-infection
P1	48	F	ALL	RIC	MUD	-/+	Tacro/MMF/ATG	Yes	Yes	No
P2	51	M	MDS	MAC	MUD	-/-	Tacro/MMF/ATG	Yes	No	No
P3	49	F	MDS	MAC	MRD	-/+	Tacro/MMF	Yes	No	No
P4	63	M	MDS	RIC	MRD	-/+	Tacro/MMF/ATG	Yes	Yes	No
P5	48	M	NHL	RIC	MUD	+/+	Tacro/MMF/ATG	Yes	Yes	Yes
P6	32	F	MDS	RIC	MMUD	-/+	Tacro/MMF/Cyto	No	Yes	No

Adeno, Adenovirus; ALL, Acute lymphoblastic leukemia; ATG, Anti-T cell thymoglobulin; CMV D/R, Cytomegalovirus donor/recipient serostatus; Cyto, Cyclosporin; GVHD, Graft versus host disease; HHV8, Human herpes virus 8; MAC, Myeloablative chemotherapy; MDS, Myelodysplastic Syndrome; MRD, Matched related donor; MMF, Mycophenolate mofetil; MMUD, Mismatched unrelated donor; MUD, Matched unrelated donor; NHL, Non-Hodgkin Lymphoma; RIC, Reduced intensity conditioning; Tacro, Tacrolimus

Table 2. Clinical Course, Medication Characteristics, and Outcomes for Allogeneic HSCT Patients Treated with Cidofovir

Days HSCT to of HC	Grade	Viremia log/ml ²	Virus ¹ log/ml ²	Number of Cidofovir Doses	Route of Administration	Days between doses	Days from Cidofovir to resolution	AKI after Cidofovir	Three Month Recurrence	12 Month Mortality	Adverse Events	
P1	50	1	2.5x10 ⁶	5.66x10 ⁶	4	IV	2	NR	Yes	D	Dead	None
P2	76	4	1.5x10 ⁶	2.50x10 ⁶	2	IV, IVES	1	NR	Yes	D	Dead	Pain, Spasms, Major Safety Event
P3	179	2	N/A	2.50x10 ⁶	7	IV	7	116	No	Y	Alive	Pain
P4	35	4	1.6x10 ⁶	2.50x10 ⁶	10	IV, IVES	8	76	Yes	D	Dead	Pain, Spasms, Near-Miss Safety Event
P5	27	2	N/A	2.50x10 ⁶	1	IV	0	20	No	N	Alive	Spasms
P6	55	3	N/A	2.10x10 ⁶	6	IV	6	30	Yes	D	Dead	None

AKI, Acute Kidney Injury; HC, Hemorrhagic Cystitis; HSCT, Hematopoietic stem cell transplant; IV, Intravenous; IVES, IntraVESicular; N/A, test was not performed; NR, No resolution
¹highest value during course of disease

DISCUSSION

- Six patients received Cidofovir (Four IV, Two IV and IVES)
- Median BKV-HC grade was 2.5, three patients had BK Viremia
- Five patients had microscopic resolution of hematuria. However, four of the six patients died and one patient had recurrence of BKV-HC within 90 days
- There were two MEs, one near miss of an incorrect IV order for IVES route, and one major safety event where IVES was administered IV.
- RCA analytics revealed multiple contributing factors including similarity in dosing and similar pump library designation

CONCLUSIONS

- In the case series to describe medication errors for CDV treatment of BKV-HC, one in three patients experienced a ME.