

Results. There were 120,654 incident cases of HZ seen in hospital or emergency department during the study period. Immunocompromised adults accounted for 13% of these cases despite representing only 3% of the population. The risk of HZ was higher for immunocompromised adults compared with immunocompetent (IRR = 2.8, 95% CI 2.8–2.9) and ranged across type of immunocompromising condition (from 2.4 [95% CI 2.3–2.5] in those with a solid tumor malignancy to 11.0 [95% CI 10.0–12.0] in those who had undergone a hematopoietic stem cell transplant). The risk of any HZ complication was also higher in immunocompromised adults (IRR = 3.5, 95% CI 3.4–3.6) and was highest for disseminated zoster (IRR = 31.5, 95% CI 26.3–37.5).

Conclusion. The risk of HZ and related complications was higher in immunocompromised populations compared with immunocompetent. Our findings underscore the high-risk nature of this population and the potential benefits that may be realized through HZ vaccination of this group.

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1760. Outcomes of Acyclovir-Resistant Herpes Simplex Virus Infections in Hematologic Malignancies and Hematopoietic Cell Transplant

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Background. Acyclovir-resistant (ACVr) herpes simplex virus (HSV) infection management is a challenge in patients with hematologic malignancies (HM) and hematopoietic cell transplant (HCT) recipients.

Methods. Retrospective review of patients aged ≥ 18 years with underlying HM and/or HCT and culture-positive ACVr HSV between 1/1/2009 and December 1/2017 at a tertiary cancer center. Clinical, laboratory, microbiological, and treatment data collected.

Results. 33 patients identified; 25 (76%) acute leukemias, 3 (9%) chronic myeloid leukemia/chronic lymphocytic leukemia (CML/CLL), 3 (9%) lymphoma, 2 (6%) other HM, and 32 (97%) had HCT. Median age of patients was 59 years (25–73) and 64% of them are females. HCT type: 22 (67%) matched unrelated donor, 3 (9%) cord blood, and 7 (21%) matched related donor. All patients were on acyclovir prophylaxis prior to diagnosis. The median time to onset of ACVr HSV infection was 147 days after transplant. Infection site: 16 (49%) oral, 10 (30%), ano-genital, 5 (15%) oral and esophagus/lung, 2 (6%) esophagus/lung. Pertinent laboratory data on day of viral culture (median/range): white blood cell (WBC) 4.6 cells/ μ L (0.1–85.9), absolute neutrophil count (ANC) 2,316 cells/ μ L (0–17,000), absolute lymphocyte count (ALC) 574.5 cells/ μ L (0–84,182). Serum creatinine at start and end of treatment are 0.8 mg/dL (0.32–1.98) and 0.92 mg/dL (0.36–2.7), respectively. The median duration of treatment was 30 days (4–116). Treatment: 20 (61%) foscarnet, 2 (6%) cidofovir, 4 (12%) foscarnet and cidofovir, 1 (3%) valacyclovir, 5 (15%) high-dose acyclovir, 1 (3%) unknown. 8 (24%) received adjunctive topical therapy: 5 imiquimod, 3 cidofovir. 31 included in outcome analysis (data missing in 2). Infection resolved in 15/31 (48%) while 5/31 (16%) had persistent infection. Median ANC and ALC in those with resolved vs. persistent infection (respectively): 3,082 cells/ μ L and 642 cells/ μ L vs. 1,895 cells/ μ L and 380 cells/ μ L with a trend toward lower ANC and ALC in patients with persistent infection. Overall mortality was 35% (9/31) while ACVr HSV attributable mortality was 6.4% (2/31).

Conclusion. ACVr HSV is predominantly encountered in allogeneic HCT, particularly the unrelated donor recipients, and lower ANC/ALC may predispose to persistent infection.

Patient Characteristics (N=33)	
Age (median)	59 years old (25-73)
Female (%)	64%
Diagnosis	
AML/MDS	16 (48%)
ALL	9 (27%)
Lymphoma	3 (9%)
CML/CLL	3 (9%)
Other*	2 (6%)
HM or HCT Type	
Allogeneic	32 (97%)
Matched unrelated	22 (67%)
Matched related	7 (21%)
Cord	3 (9%)
Autologous	0 (0%)
CLL	1 (3%)
Site of Infection	
Oral	16 (49%)
Ano-genital	10 (30%)
Oral and deep organ*	5 (15%)
Deep organ*	2 (6%)
Labs	
WBC (median)	4.6 (0.1-86)
ANC (median)	2316 (0-17,000)
ALC (median)	574.5 (0-84,000)
Baseline Scr	0.8 (0.32-1.98)
End of treatment Scr	0.92 (0.36-2.7)
Onset of infection	147 days
Treatment	
Foscarnet	20 (61%)
Cidofovir	2 (6%)
Foscarnet or cidofovir	4 (12%)
Acyclovir	5 (15%)
Valacyclovir	1 (3%)
Unknown	1 (3%)
Adjunct therapy	
None	24
Topical cidofovir	5
Topical imiquimod	3
Topical acyclovir	1
Treatment duration (days)	30 days (4-116)

AML = acute myeloid leukemia, ALL = acute lymphocytic leukemia, CLL = chronic lymphocytic leukemia, CML = chronic myeloid leukemia, CLL = chronic lymphocytic leukemia, MDS = myelodysplastic syndrome, Myelo = myeloid, HM = hematologic malignancy, HCT = hematopoietic cell transplant, *deep organ = esophagus or lung involvement, WBC = white blood cell count, ANC = absolute neutrophil count, ALC = absolute lymphocyte count, Scr = serum creatinine

Outcomes (n=31)	
Resolution	15 (48%)
Persistent HSV disease	5 (16%)
Mortality due to HSV	2 (6.4%)
Overall mortality	11 (35%)

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1761. 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), a nucleotide analog antiviral, is active against multiple dsDNA viruses relevant in HCT recipients. Despite a broad spectrum of activity, CDV utility is limited due to nephrotoxicity. We describe our experience with CDV in a large contemporary cohort from a single Institution.

Methods. Retrospective review of adult HCT recipients who received CDV for any indication from 2011 to 2017. Initiation and duration of CDV treatment were at physicians' discretion. CDV exposure and indications, Serum Creatinine (sCr) and outcomes were extracted from medical records and hospital databases.

Results. Of 1,235 HCT recipients, 54 (4.4%) received ≥1 dose of CDV. Stem cell source was peripheral blood in 39 (72%) patients, cord blood in 13 (24%) and marrow in 2 (4%); 42 (78%) patients received CD34+ selected HCT. At CDV initiation, 23 (43%) patients had active GvHD and 16 (30%) received systemic steroids. CDV was started a median of 85.5 days (range 14–335) post HCT, given for a median of 3 doses (range 1–13) for a median of 2 weeks (range 1–17). Indications were adenovirus (ADV) infection in 35 patients, CMV in 19, BK virus in 21 and HHV6 in 3 patients. Nineteen (35%) patients had >1 dsDNA virus. Forty-one (76%) patients received CDV (3–5 mg/kg) once weekly, mainly for ADV or CMV, and 13 received CDV (≤1 mg/kg) once to thrice weekly, mostly for BK hemorrhagic cystitis (N = 12).

Baseline sCr was mean 0.88 mg/dL (standard deviation [SD] = 0.37) at CDV initiation, mean 1.07 mg/dL at end of treatment (EOT) (SD = 0.57, N = 48, P = 0.004) and mean 1.23 mg/dL at EOT + 2 weeks (SD = 0.72, n = 28, P = 0.027). At EOT, 13 patients (24%) had acute kidney injury (AKI, ≥1.5-fold increase from baseline sCr). Of those, 12 (92%) received concomitant nephrotoxic drugs. AKI was attributed to other etiologies by treating physician in six patients. Of 51 patients with follow-up at EOT, 29 (57%) had clinical response to CDV treatment. Nineteen (35%) patients died ≤ 4 weeks from last CDV dose.

Conclusion. 24% of highly immunocompromised HCT patients experienced AKI following CDV treatment for dsDNA viruses. The co-administration of nephrotoxic medications and the direct effect of infection limit our ability to assess the relative impact of CDV on renal function. Our data underscores the need for safer treatment options for HCT patients with life-threatening infections with dsDNA viruses.

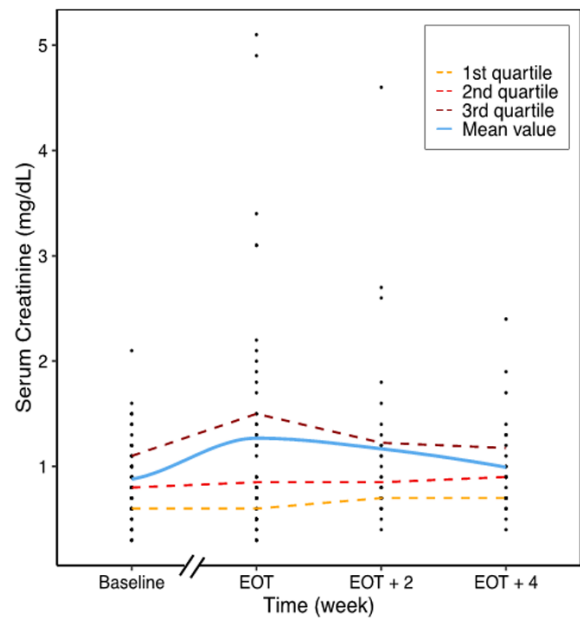


Figure 1: Creatinine at baseline (day of first cidofovir dose ± 1), End of treatment (EOT), EOT + 2 weeks and EOT + 4 weeks.

	N = 54	%
ADV alone	18	33
ADV + BK virus	4	8
ADV + CMV	6	11
ADV + BK virus + CMV	5	9
ADV + HHV6	2	4
BK virus alone	11	20
BK virus + CMV	1	2
CMV alone	6	11
CMV + HHV6	1	2

Table 1: Indications for cidofovir administration. ADV: Adenovirus, CMV: Cytomegalovirus, HHV6: Human Herpes virus 6.

HCT type		AKI ¹ at EOT		No AKI ¹	
		N=13	%	N=41	%
Conventional		3	23	9	22
	T cell depleted	10	77	32	78
Cidofovir timing	≤30 days from HCT	4	31	3	7
	≤100 days from HCT	7	54	26	63
	>100 days from HCT	6	46	15	37
Cidofovir dose	Low (0.25 - 1mg/kg)	0		13	32
	High (3-5mg/kg)	13	100	28	68
Cidofovir number of doses	1-3	9	69	21	51
	>4	4	31	20	49
Active GVHD at cidofovir start		4	31	19	46
Abnormal baseline creatinine		4	31	11	27
EOD involving genitourinary tract		3	23	20	49
Concomitant nephrotoxic drugs ²		12	92	32	78
Death within 4 weeks from last dose		8	62	11	27

Table 2: Characteristics of patients with acute kidney injury. ¹Acute kidney injury defined as a rise of ≥1.5 times the baseline value. ²Including vancomycin, aminoglycosides, cyclosporine, tacrolimus, amphotericin b and intravenous voriconazole/posaconazole. AKI: Acute kidney injury, EOT: End of treatment, HCT: Hematopoietic cell transplantation, GVHD: Graft versus host disease, EOD: End organ disease.

	N	Probable ¹		Proven ¹		Clinical response ²		% death within 4 weeks	
Adenovirus	35				18	51	11	31	
All EOD	30	25	5	12	40	14	47		
EOD involving GIT ³	15	11	4	8	53	8	53		
EOD involving GUT ⁴	3	3	0	2	67	0			
EOD involving more than one site	11	10	1	2	18	8	73		
BK virus	21			12	57	6	29		
EOD (All involving GUT ⁴)	19	19	0	11	58	5	26		
CMV	19			7	37	10	53		
All EOD	5	2	3	3	60	1	20		
EOD involving GIT	3	1	2	2	67	0			
EOD involving lungs	1	0	1	0		1	100		
Retinitis	1	1	0	1	100	0			

Table 3: EOD: End organ disease, GIT: Gastrointestinal tract, GUT: Genitourinary tract, CMV: Cytomegalovirus. ¹Definition of probable and proven end organ disease based on standard criteria. ²Clinical response as implied by treating physician's clinical impression. ³Duodenitis, colitis or both. ⁴Mainly hemorrhagic cystitis.

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1762. Genotype Prevalence and Molecular Characteristics of Human Adenovirus in Pediatric Hematopoietic Stem Cell Transplant Recipients

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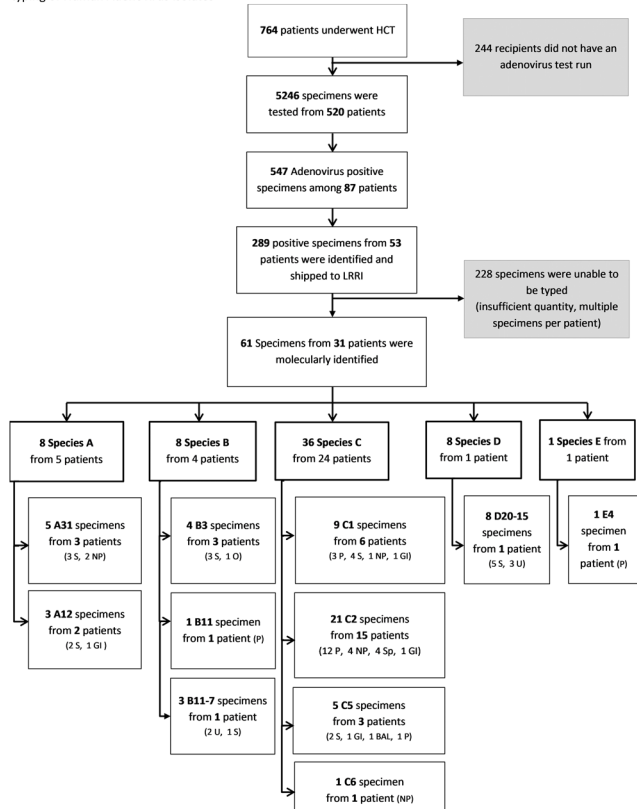
Background. Human adenovirus (HAdV) is a documented source of morbidity and mortality after hematopoietic cell transplant (HCT); however, there are limited data documenting HAdV species and type in this population. Understanding the molecular characteristics of HAdV could inform the development and assessment of interventions. The species and type of HAdV-positive specimens are detailed using an archived convenience sample of specimens obtained in pediatric HCT recipients.

Methods. The cohort included autologous and allogeneic HCT recipients between January 2000 and December 2013. An archived clinical repository of frozen specimens was interrogated to identify residual HAdV-positive specimens, which were sent to Lovelace Respiratory Research Institute (LRRRI) to determine species and type. Medical chart review was performed to determine whether an isolate was related to HAdV disease or HAdV-attributable death.

Results. There were 547 HAdV PCR-positive clinical specimens from 87 HCT recipients. Of the 547 specimens, 289 were identified from an archived repository and sent to LRRRI to determine species and type, and HAdV was successfully isolated and typed from 61 (Figure 1). Species C was the most common species (59.0%) with C2 being the most frequent type (34.4%). Of the 15 recipients with type C2, plasma was the most common specimen source (57.1%). Three recipients with C2 had this species and type detected from multiple sources (Tables 1 and 2). Among those with a typing result, type C2 also was responsible for 33.3% of all HAdV-attributed disease and 38.1% of all HAdV-attributed death.

Conclusion. Species C was the most common species to be isolated in a convenience sample of HAdV-positive clinical specimens from a single-center cohort of pediatric HCT recipients. Type C2 was most commonly associated with HAdV disease and attributable death. These results suggest HAdV species and type influence the impact of HAdV in this patient population. The findings need to be confirmed in prospective cohorts but suggest real-time molecular typing may be relevant and provide possible targets for the development of future interventions. These results must be interpreted with caution; not all clinical specimens were available for molecular typing, and it is possible C2 is easier to isolate from archived specimens.

Figure 1: Flow diagram of specimens collected from Pediatric Hematopoietic Cell Transplant (HCT) Recipients to typing of Human Adenovirus isolates



Abbreviations: HCT = Hematopoietic Cell Transplant P=Plasma/Blood; NP=Nasopharyngeal aspirate; S=Stool; U=Urine; BAL=Bronchoalveolar lavage; GI=Gastrointestinal tissue; Sp=Sputum; L=Liver; O=Other