

# Adenovirus Viremia is Associated With Substantially Prolonged Hospitalization in Pediatric Allogeneic Hematopoietic Cell Transplant Recipients

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## BACKGROUND

- Allogeneic hematopoietic cell transplant (allo-HCT) is a resource-intensive procedure necessitating a prolonged stay in hospital in the post-transplant period.
- Estimates vary, but the average length of hospital stay after allo-HCT in pediatric patients has been reported as 39 days (range 16-177).<sup>1</sup>
- Post-transplant recovery period can be further prolonged by the occurrence of infection,<sup>1,2</sup> including adenovirus (AdV) infection, substantially increasing healthcare costs.<sup>3</sup>
  - As well as prolonged transplant hospitalization, viral infections such as AdV infections can lead to hospital readmission.<sup>2,3</sup>
- Pediatric allo-HCT patients are at particularly high risk of AdV infections in the post-transplant period, potentially prolonging length of hospital stay or leading to readmission.
- To date, there is little published evidence on the impact of AdV infection during the post-transplant period on prolongation of transplant hospitalization or readmission.
- In order to assess the potential impact of AdV infection on healthcare resource utilization, we analyzed the duration of hospitalizations among pediatric allo-HCT recipients with and without AdV infection from a large multicenter observational study.

## METHODS

- AdVance is a multicenter, multinational study of the incidence, management, and clinical outcomes of AdV infections in adult and pediatric allo-HCT recipients in 7 countries in Europe: the United Kingdom, Spain, France, Italy, Germany, the Netherlands, and Czech Republic.
- This study was conducted retrospectively across 50 centers and included recipients of allo-HCT between January 1, 2013 and September 30, 2015.
- Pediatric allo-HCT recipients (<18 years) who had AdV infection diagnosed in the first 6 months after transplantation were identified.
- Hospitalizations were categorized as transplant hospitalization or readmission (any hospitalization after discharge from the transplant hospitalization). Patients may have been readmitted more than once.
- Hospitalizations were further categorized according to whether AdV was noted in the discharge summary or if any positive AdV test was noted during the hospitalization.
  - For hospitalizations during which a positive AdV test was noted, 2 subgroups were also analyzed: those with any viremia and those with clinically relevant viremia  $\geq 1000$  copies/mL in blood.
  - Hospitalizations during which the patient died were excluded to avoid the introduction of bias.
- Data were also analyzed according to underlying disease conditions stratified by the following categories:
  - Malignant
  - Non-Malignant Immunocompetent
  - Non-Malignant Immunodeficient.

## RESULTS

- Overall, the AdVance study included 1738 pediatric allo-HCT recipients; of whom, 558 were diagnosed with an AdV infection in the first 6 months following allo-HCT transplant. After excluding data from 36 patients who died during the initial transplant hospitalization and 2 patients for whom full hospitalization data were not available, data were available for 520 pediatric allo-HCT recipients.
  - At the transplant hospitalization, 155 had no positive AdV test, and 365 had a positive AdV test, 209 of whom had viremia, with 144 developing clinically relevant viremia  $\geq 1000$  copies/mL (Figure 1).
- The median duration of the transplant hospitalization was 54 days (range 18-499) for patients who had a positive AdV test, 60 days (range 27-499) for patients who had any AdV viremia, and 64 days (range 27-499) for those with clinically relevant viremia  $\geq 1000$  copies/mL (Figure 2).
- In contrast, in patients who did not have AdV infection during the transplant hospitalization, the median length of stay was 42 days ( $p < 0.01$  for comparisons with patients with any positive AdV test or viremia).
- For readmissions, median length of stay was also longer for those during which the patient had AdV viremia (18 days) or viremia  $\geq 1000$  copies/mL (21 days), compared with those in which the patient did not have a positive AdV test (5 days) during that readmission (Figure 3).
  - 12 patients had more than 1 readmission.

FIGURE 1. OVERVIEW OF THE HOSPITALIZATION ANALYSIS POPULATION

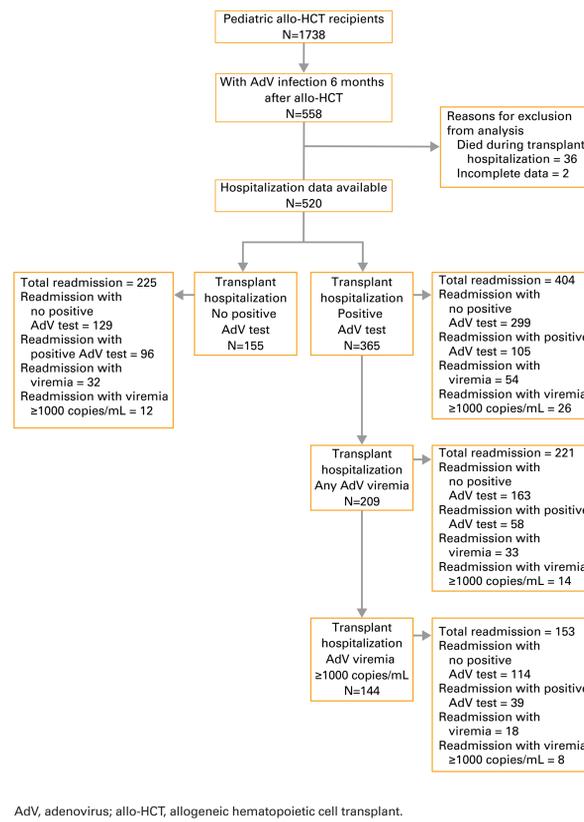


FIGURE 2. ADV INFECTION AND ADV VIREMIA LEAD TO LONGER DURATION OF TRANSPLANT HOSPITALIZATION IN PEDIATRIC PATIENTS

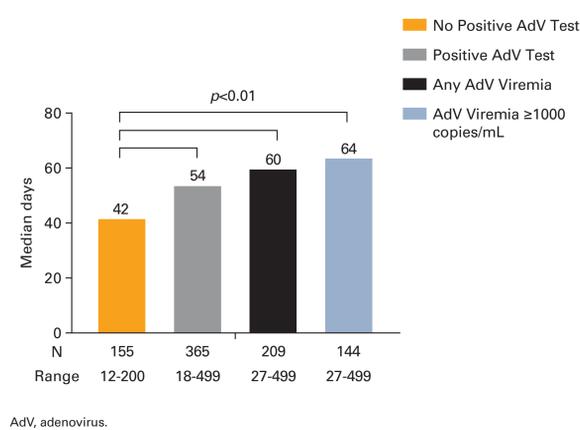
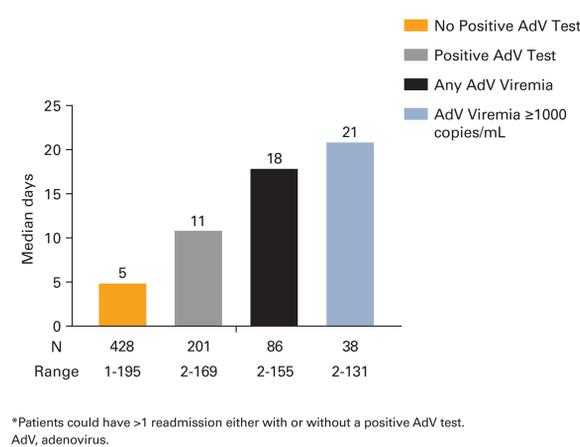


FIGURE 3. ADV INFECTION AND ADV VIREMIA LEAD TO LONGER DURATION OF HOSPITAL STAY FOR READMISSIONS\* IN PEDIATRIC PATIENTS



- In the subgroup of pediatric allo-HCT recipients who developed clinically relevant viremia  $\geq 1000$  copies/mL, the differences in length of hospital stay relative to those with no positive AdV test were significant for patients with malignancy or non-malignant immunodeficiency (Table 1).
  - For patients with malignancy and AdV viremia  $\geq 1000$  copies/mL, median duration of transplant hospitalization was 56 days compared with 42 days for patients with malignancy who had no positive AdV test (Table 1).
  - Patients with non-malignant immunodeficiency who had AdV viremia  $\geq 1000$  copies/mL had the longest hospital stay for the transplant hospitalization, with a median length of stay of 92 days compared with 43 days for patients with similar underlying condition who had no positive AdV test (Table 1).

Table 1. Across all underlying disease conditions, pediatric allo-HCT recipients with AdV viremia  $\geq 1000$  copies/mL had longer hospital stay

Underlying Disease	Transplant Hospitalization		Readmissions	
	No Positive AdV Test*	AdV Viremia $\geq 1000$ *	No Positive AdV Test*	AdV Viremia $\geq 1000$ *
<b>Malignant</b>	N=104	N=88	N=309 <sup>†</sup>	N=26 <sup>‡</sup>
Mean days (SD)	49 (25)	73 (47)	10 (15)	29 (30)
Median (range)	42 (19-200)	56 (27-305)	6 (1-174)	18 (2-102)
<b>Non-Malignant Immunocompetent</b>	N=26	N=9	N=25	N=2
Mean days (SD)	45 (17)	103 (149)	12 (16)	55 (65)
Median (range)	42 (12-84)	52 (35-499)	6 (2-81)	55 (9-101)
<b>Non-Malignant Immunodeficient</b>	N=25	N=47	N=94	N=10
Mean days (SD)	51 (29)	105 (59)	11 (23)	50 (43)
Median (range)	43 (14-127)	92 (29-282)	5 (1-195)	34 (2-131)

\*Excludes hospitalizations ending with death. <sup>†</sup>Length of stay is significantly longer than transplant hospitalization with no positive AdV test (Mann-Whitney-Wilcoxon test). <sup>‡</sup>Number of readmissions, patients may have undergone >1 readmission. AdV, adenovirus; SD, standard deviation.

## CONCLUSIONS

- AdV infection in pediatric allo-HCT recipients is associated with significant medical resource utilization, as measured by duration of hospital stay.
- Pediatric allo-HCT recipients with AdV viremia  $\geq 1000$  copies/mL were hospitalized 22 days longer than those without AdV infection.
- In pediatric patients with AdV viremia  $\geq 1000$  copies/mL, longer hospitalizations were observed for those patients with non-malignant immunodeficiency.
  - Subsequent readmissions were also longer for these patients.
- Additional analysis from the AdVance study (see poster B043) has shown that screening and monitoring for AdV in pediatric allo-HCT recipients is almost universal and frequent and patients are treated according to current best practices.<sup>4</sup>
- In this analysis, patients who reached clinically relevant viremia  $\geq 1000$  copies/mL during their hospitalization had the longest duration of stay during both the transplant hospitalization and subsequent readmissions.

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## DISCLOSURES:

APM, CP, MZ, KR, and SV are investigators in the AdVance study sponsored by Chimerix. EV, TB, EM, and GN are employees of the study sponsor, Chimerix. JM is an employee of Analytica-Laser, a research consultancy who conducted the study on behalf of the sponsor, Chimerix.

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