

# **Posoleucel (ALVR105), an Off-the-Shelf, Multivirus-Specific T-Cell Therapy, for the Prevention of Viral Infections Post-HCT**

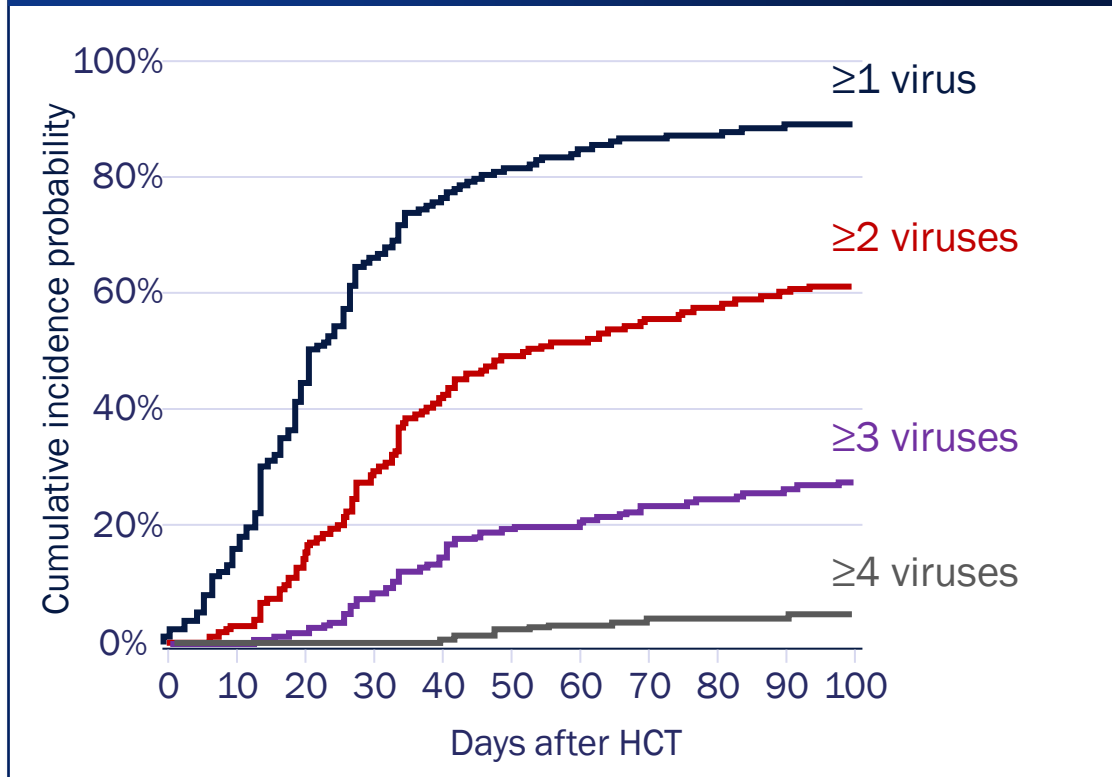
## **Results from an Open-Label Cohort of a Phase 2 Trial**

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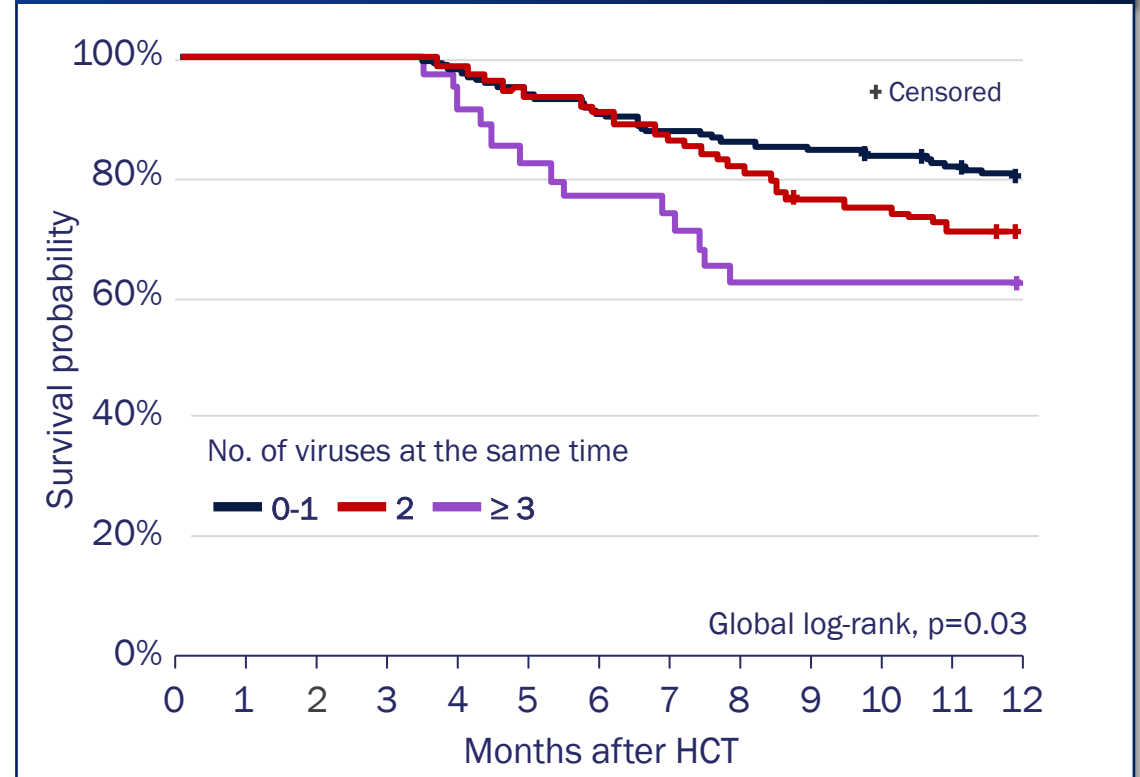
# Multivirus Infections Are Common in Allogeneic HCT Patients and Contribute to Significant Mortality

Incidence of AdV, BKV, CMV, EBV, or HHV-6 infection<sup>1</sup>  
(N=404)



- 61% of patients were treated with antiviral therapies, excluding rituximab, within the first 100 days

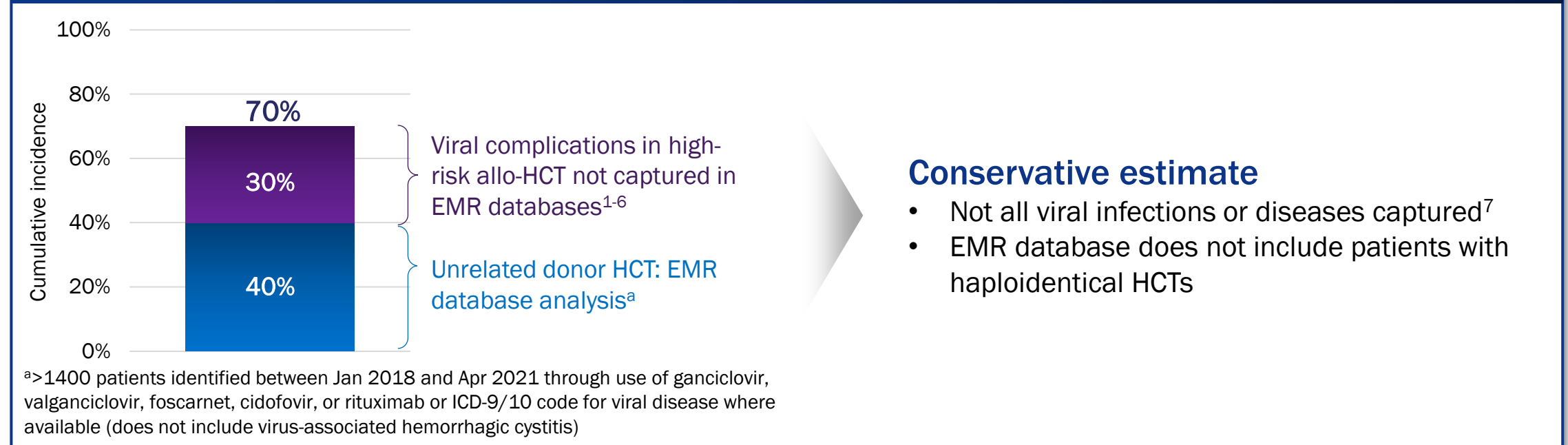
Overall survival, number of viruses at the same time<sup>1</sup>  
(N=358)



# Approximately 70% Incidence of Clinically Significant Infection and Disease in High-Risk Allo-HCT Patients due to AdV, BKV, CMV, EBV, HHV-6, or JCV

- Allogeneic HCT (allo-HCT) patients are at high risk for common double-stranded DNA infections: AdV, BKV, CMV, EBV, HHV-6, and JCV
- Allo-HCT patients at highest risk: haploidentical donor, UCB, MMUD, MUD, MMRD, T cell depletion

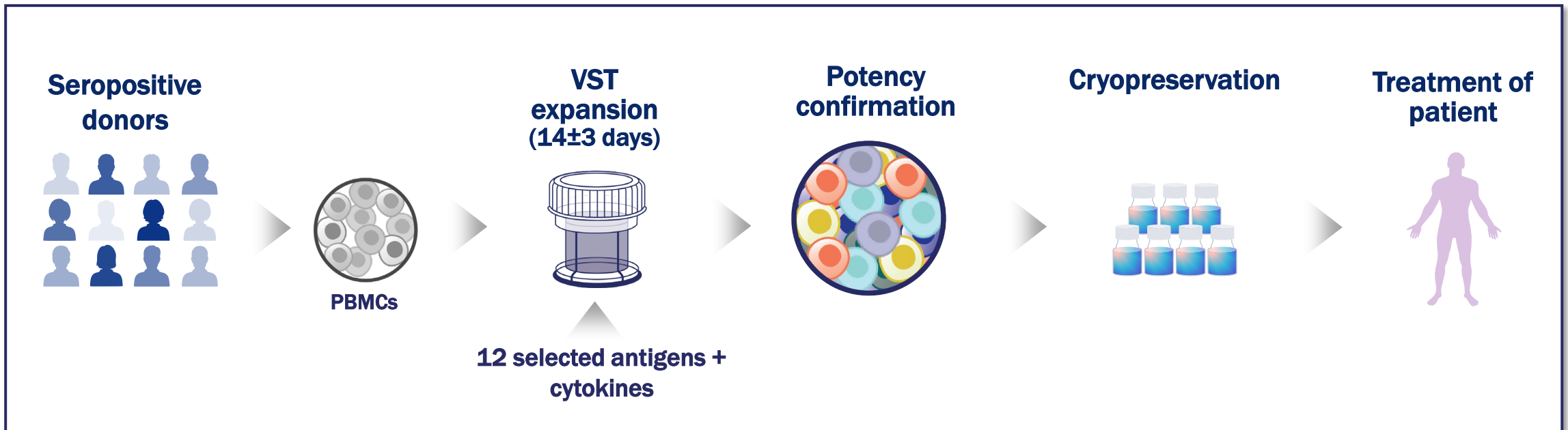
## Estimated incidence of clinically significant viral infection or disease



There is an unmet need for preventive therapies targeting multiple viruses in high-risk allo-HCT patients

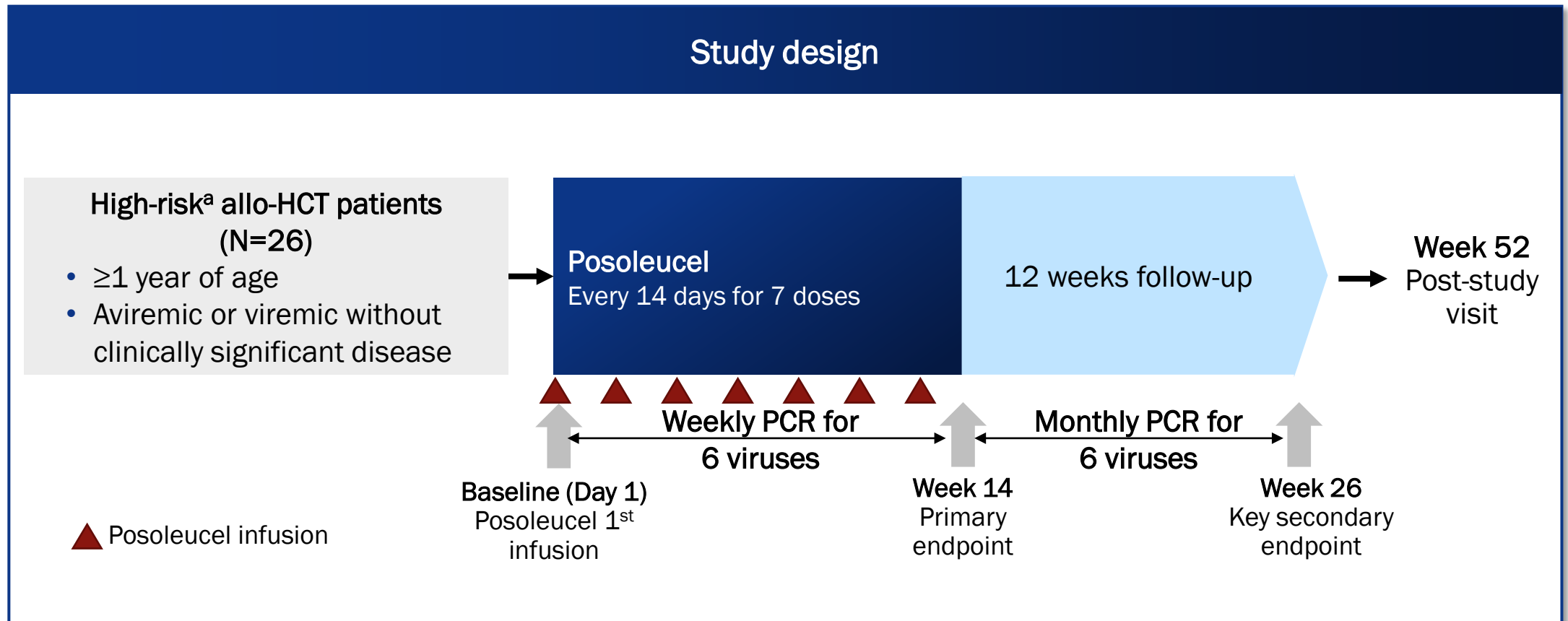
# Posoleucel (ALVR105)

- Allogeneic, off-the-shelf, multivirus-specific T-cell (VST) therapy targeting AdV, BKV, CMV, EBV, HHV-6, and JCV<sup>a</sup>
- 93% response rate in Phase 2 CHARMS study<sup>1</sup>



# Phase 2 Multivirus Prevention Open-Label Study (NCT04693637)

Completed Phase 2 target patient enrollment



<sup>a</sup>High-risk allo-HCT defined as: umbilical cord donor, haploidentical donor, MMRD, MMUD, recipient of T-cell depletion (ex vivo, alemtuzumab, ATG), MUD with persistent lymphopenia <180/mm<sup>3</sup>

# Endpoint

**Primary endpoint: The number of new onset clinically significant infections or episodes of end-organ disease through Week 14**

**Clinically significant viral infection**

Above viral load threshold

- CMV: >910 IU/mL
- EBV/AdV: >10,000 copies/mL OR >1,000 copies/mL and rising<sup>a</sup>

**AND**

Initiation of preemptive antiviral therapy

**End-organ disease**

Signs or symptoms of organ damage from AdV, BKV, CMV, EBV, HHV-6, or JCV

# Baseline Demographics

Patients at high risk for viral infections or end-organ disease were enrolled

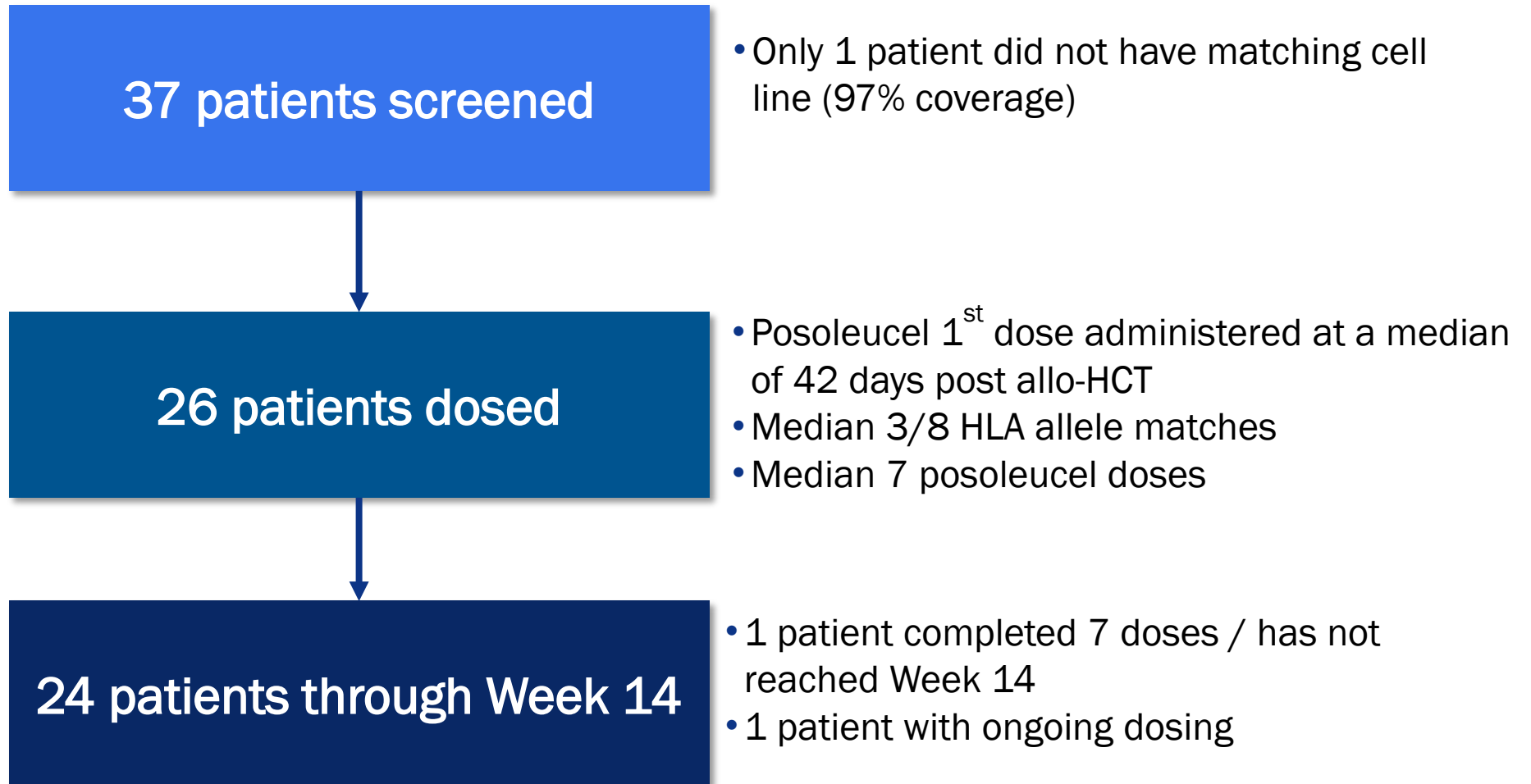
Characteristic	N=26
Age, median years (range)	60 (14-76)
Female	12 (46%)
Non-Caucasian or Latino	12 (46%)
<b>Diagnosis</b>	
Leukemia	17 (65%)
Myelodysplasia/Myeloproliferative	3 (12%)
Lymphoma	2 (8%)
Sickle cell anemia	2 (8%)
Other <sup>a</sup>	2 (8%)

Characteristic	N=26
<b>Donor type</b>	
Haploidentical	12 (46%)
Mismatched unrelated	9 (35%)
Matched unrelated	4 (15%)
Umbilical cord blood	1 (4%)
<b>Myeloablative conditioning</b>	12 (46%)
<b>Baseline viremia<sup>b</sup></b>	11 (42%)
<b>Letemovir prophylaxis</b>	16 (62%)

<sup>a</sup>Multiple myeloma and adrenoleukodystrophy

<sup>b</sup>1 AdV, 7 BKV, 2 EBV and/or 5 HHV-6 viremia(s) detected in 11 patients

# Patient Disposition<sup>a</sup>





# Safety and Tolerability

- No unanticipated treatment-emergent adverse events (TEAEs) or serious adverse events (SAEs) were reported
- 6/26 (23%) grade II-IV acute GVHD
  - Lower than 35-50% of grade II-IV GVHD reported in high risk allo-HCTs<sup>1-3</sup>
  - No association between reported GVHD and number of HLA matches for posoleucel
  - No association between reported GVHD and number of posoleucel doses
- An independent DSMB reviewed safety data and endorsed the initiation of phase 3 study without modification

Events	N=26
Common TEAEs	
Diarrhea	14 (54%)
Weight decrease	6 (23%)
SAEs	16 (62%)
Treatment-related SAE	3 (12%) <sup>a</sup>
Deaths	1 (4%) <sup>b</sup>
Posoleucel discontinuations due to TEAEs	3 (12%) <sup>c</sup>
Adverse events of interest	
Acute GVHD II-IV	6 (23%)
Grade II	2 (8%)
Grade III	4 (15%)
Grade IV	0
Cytokine release syndrome	0
Infusion reaction	1 (4%) <sup>d</sup>

<sup>a</sup>1 patient with infusion reaction; 1 patient with acute GVHD; 1 patient with chronic GVHD.

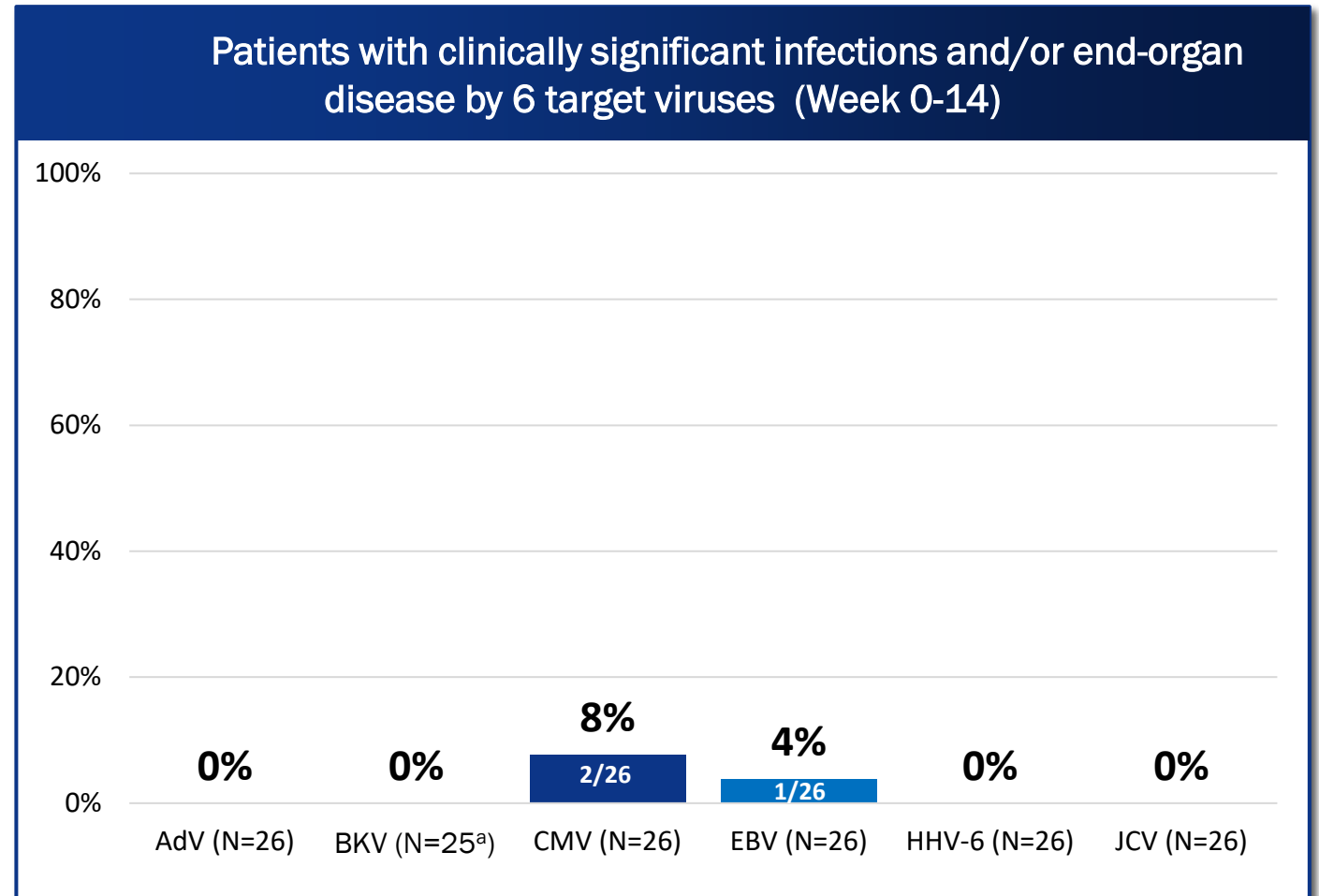
<sup>b</sup>Due to relapse of primary malignancy ~2 months after the 7<sup>th</sup> dose of posoleucel.

<sup>c</sup>1 discontinuation assessed as not related to posoleucel; 2 discontinuations assessed as possibly related to posoleucel.

<sup>d</sup>Tolerated subsequent posoleucel doses with pre-medication (diphenhydramine).

# Preliminary Efficacy Results: Primary Endpoint (Week 14)

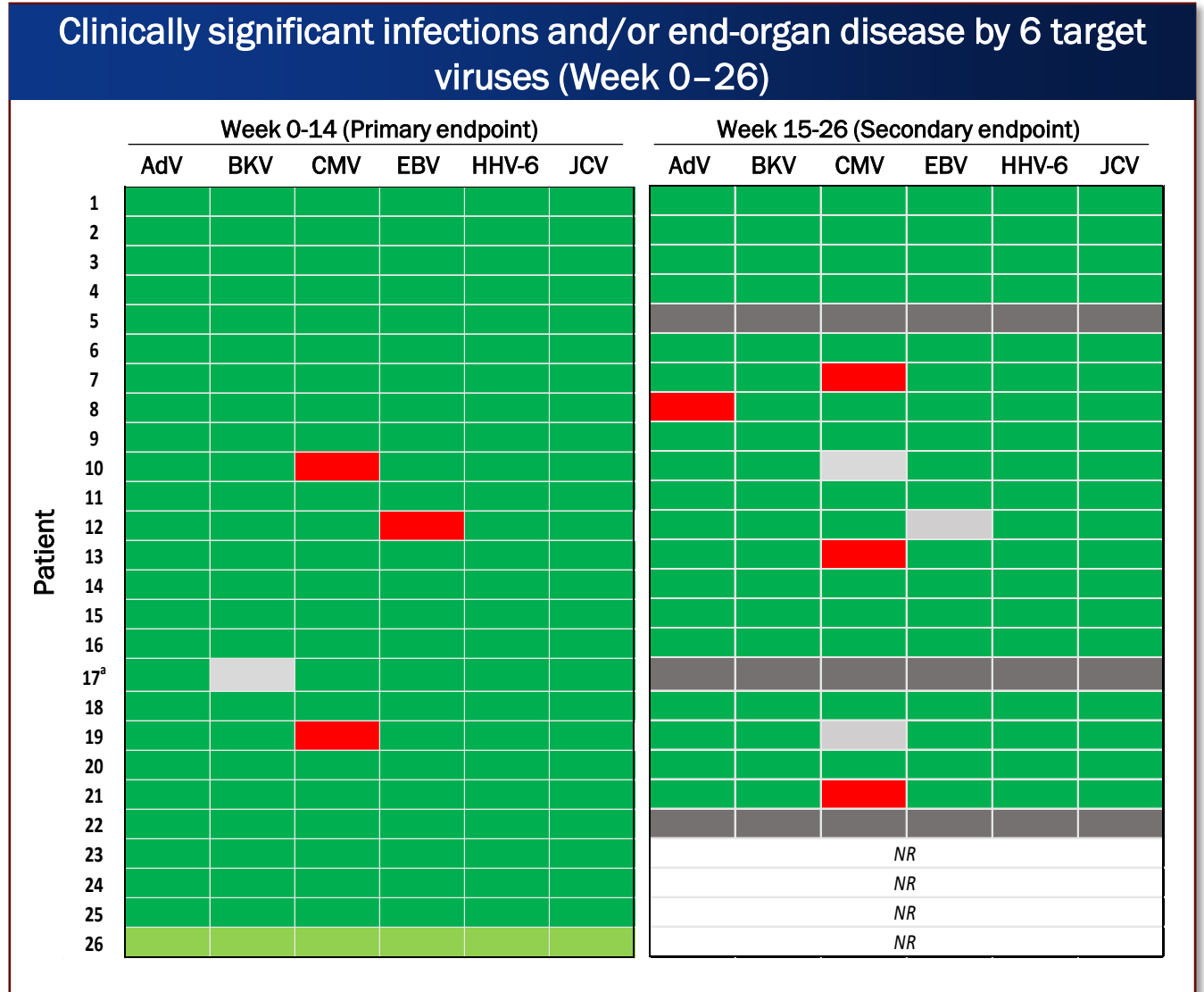
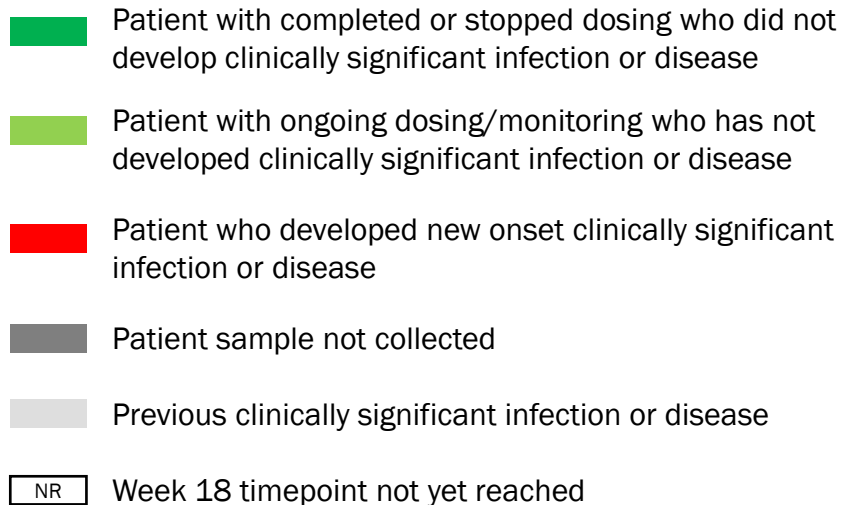
- **2 clinically significant infections**
  - 2 patients started on pre-emptive valganciclovir for CMV
- **1 end-organ disease**
  - 1 patient started on rituximab for EBV-PTLD in the setting of high-dose steroids



<sup>a</sup>One patient excluded due to BKV-associated hemorrhagic cystitis at baseline.

# Preliminary Efficacy Results: Secondary Endpoint

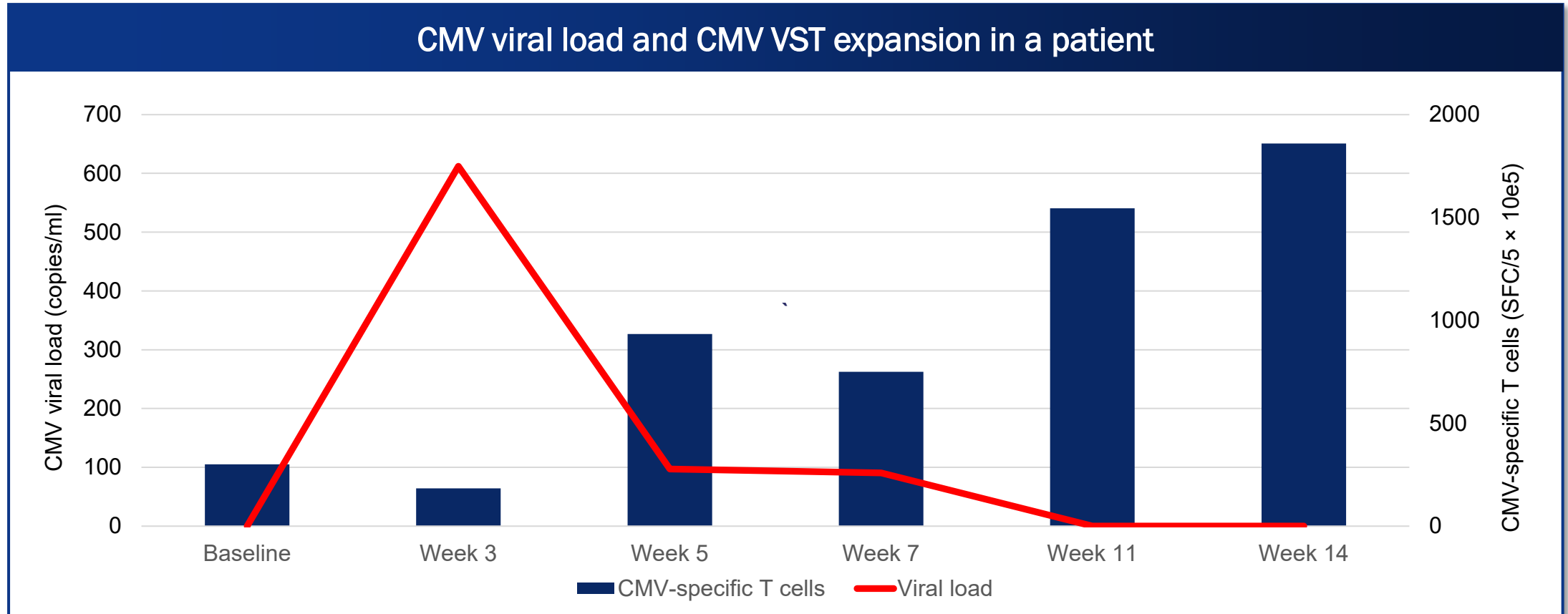
- 4 additional clinically significant infections
  - 3 patient started on pre-emptive valganciclovir for CMV
  - 1 patient started cidofovir for AdV in the setting of high-dose steroids
- No end-organ disease



<sup>a</sup>BKV hemorrhagic cystitis at baseline

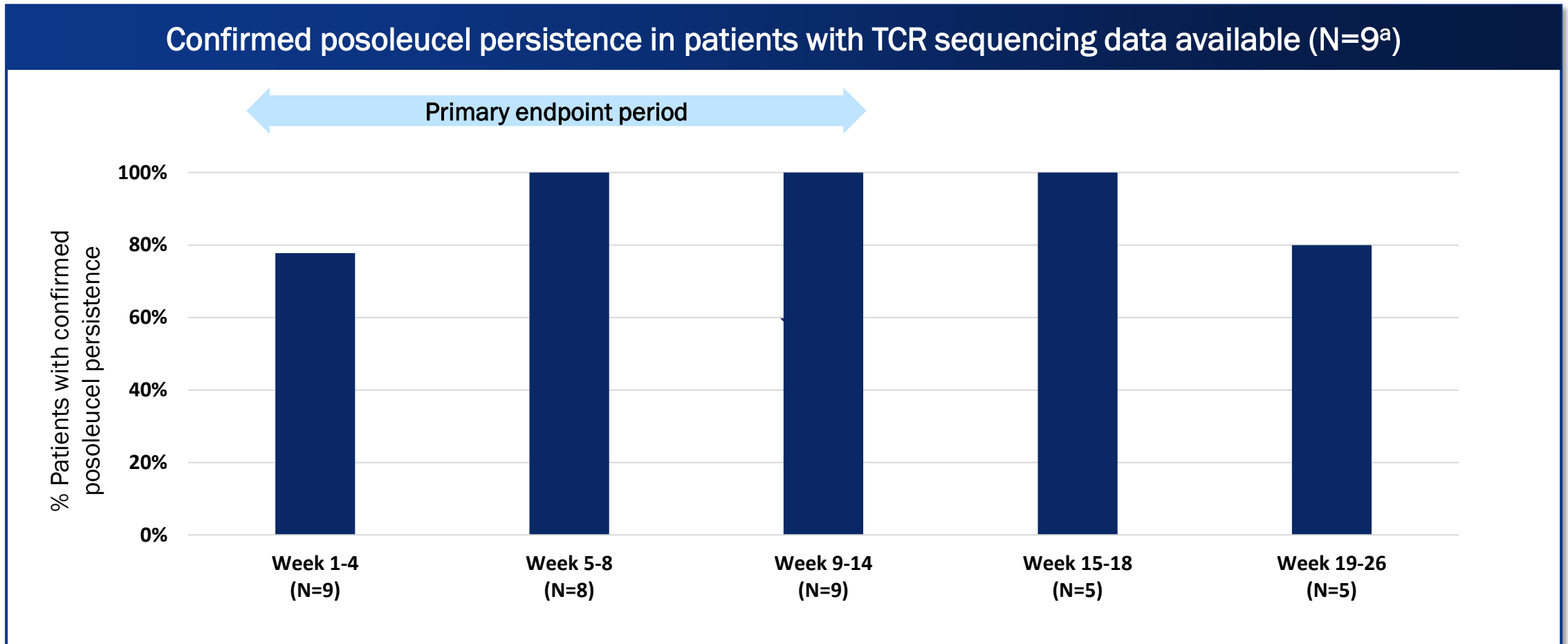
# CMV Infection Controlled without Letemovir or Pre-Emptive Therapy while on Posoleucel

- 61-year-old with MMUD HCT for cutaneous T cell lymphoma; CMV serostatus: D-/R+
- Discontinued letemovir 1 day prior to 1<sup>st</sup> posoleucel dose; completed 7 posoleucel doses
- Expansion of functional (IFN $\gamma$ -producing) VSTs coincident with control of viremia
- Confirmed detection of posoleucel VST-derived TCRs during dosing period



# Posoleucel Persists *in vivo*

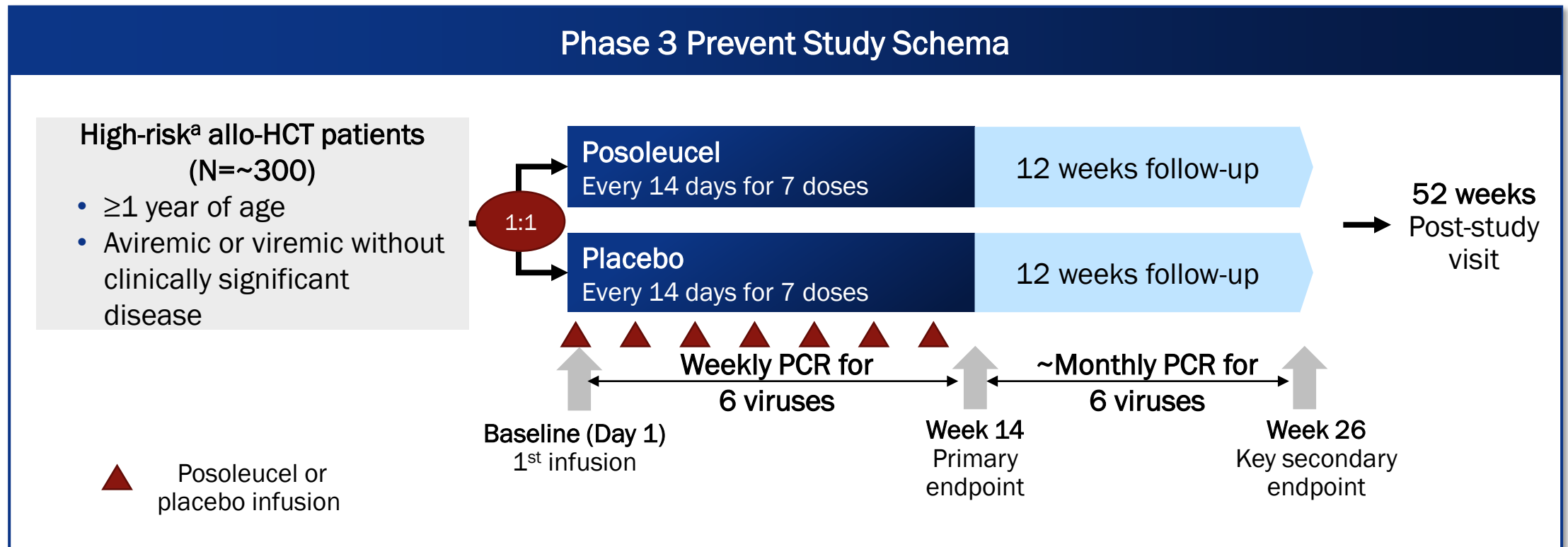
- Posoleucel VSTs detected throughout the infusion period and persisted up to the last time point measured



<sup>a</sup>9 patients received  $\geq 6$  posoleucel doses were analyzed.

# Phase 3 Multivirus Prevention Study (EBMT Poster P309)

- First placebo-controlled registrational study to evaluate an off-the-shelf, multivirus-specific T-cell therapy for the prevention of clinically significant infections or episodes of end-organ disease due to 6 target viruses in high-risk allo-HCT patients
- Global Phase 3 Multivirus Prevention Study has been initiated



<sup>a</sup>High-risk allo-HCT defined as: umbilical cord donor, haploidentical donor, MMRD, MUD, MMUD, recipient of T-cell depletion (ex vivo, alemtuzumab, ATG),

# Conclusions

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- Approximately 70% of high-risk allo-HCT patients develop clinically significant viral infections or disease due to AdV, BKV, CMV, EBV, HHV-6, or JCV
- Phase 2 Multivirus Prevention study:
  - Demonstrated **>95% coverage of posoleucel** in target population
  - High-risk allo-HCT patients receiving posoleucel had low rates of clinically significant viral infections
  - Repeat dosing of posoleucel was generally safe and well tolerated
  - Expansion of functional VSTs detected
  - Posoleucel detected during the infusion period and persisted
- Phase 3 Multivirus Prevention Study has been initiated

# Acknowledgments

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