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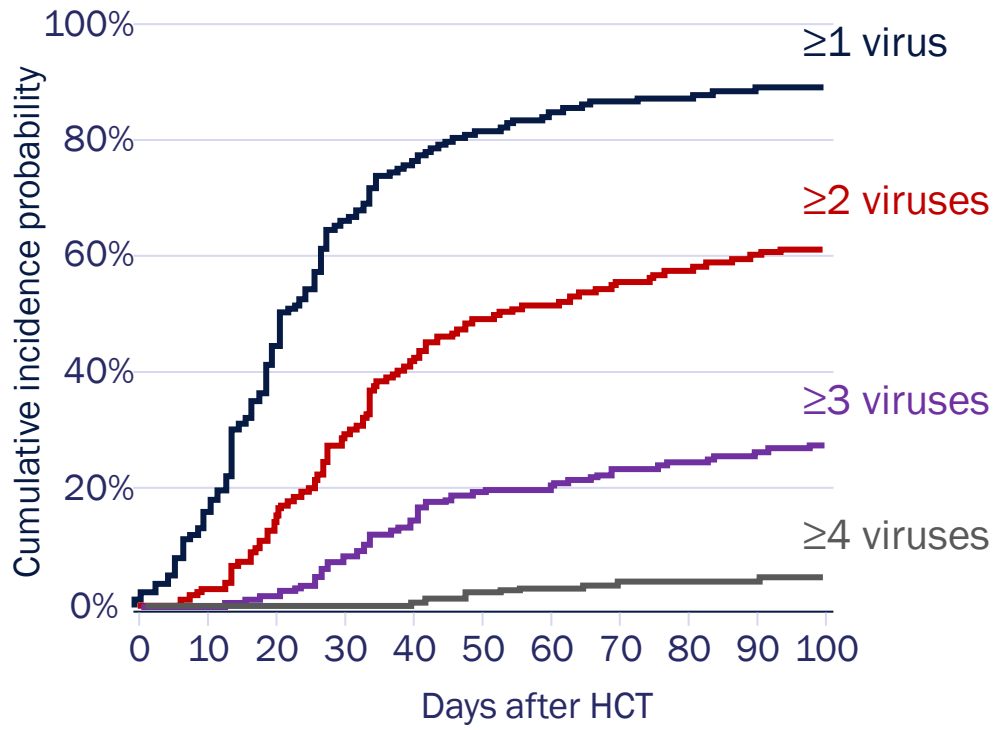
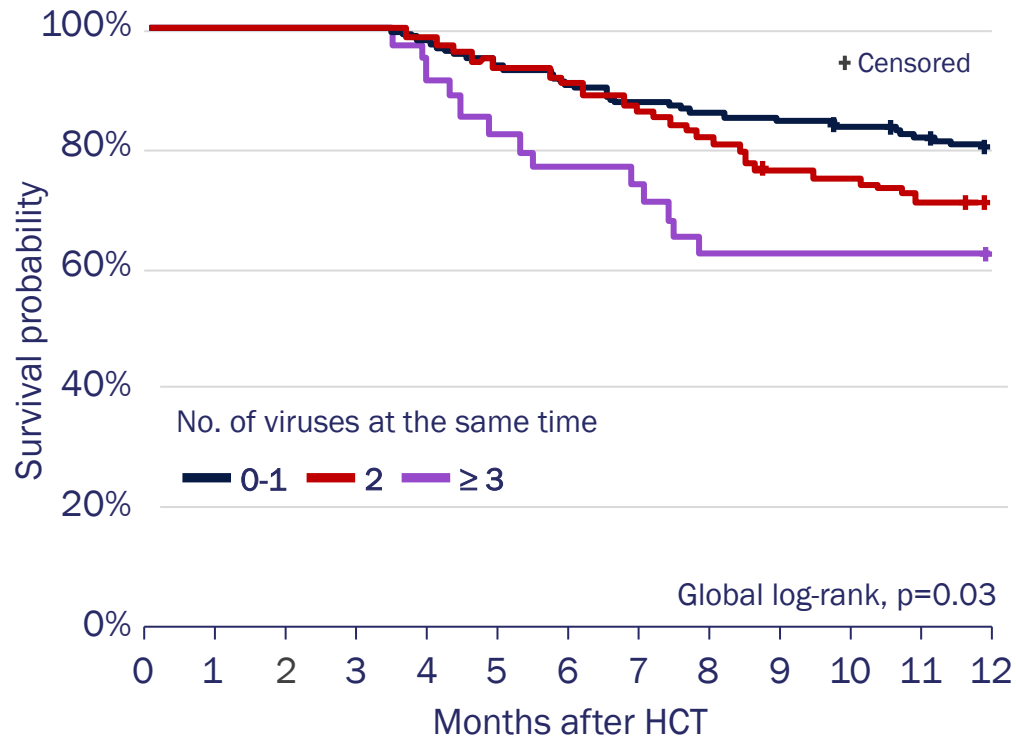
# Multivirus Infections Are Common in Allogeneic HCT Patients and Contribute to Significant Mortality

## Incidence of AdV, BKV, CMV, EBV, or HHV-6 infection[1] (N=404)




## Overall survival, number of viruses at the same time[1] (N=358)




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

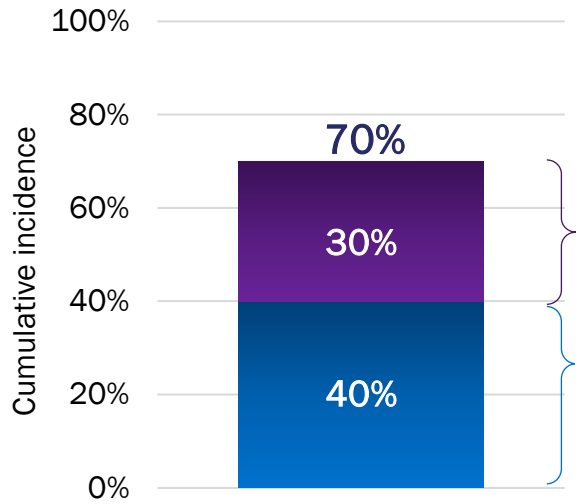
HCT: hematopoietic cell transplant; AdV: adenovirus; CMV: cytomegalovirus; EBV: Epstein-Barr virus; HHV-6: human herpesvirus 6.

1. Hill et al, *Blood* 2017

# 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




Viral complications in high-risk allo-HCT not captured in EMR databases[1-6]

Unrelated donor HCT: EMR database analysis[a]

[a]>1400 patients identified between Jan 2018 and Apr 2021 through use of ganciclovir, valganciclovir, foscarnet, cidofovir, or rituximab or ICD-9/10 code for viral disease where available (does not include virus-associated hemorrhagic cystitis)

### Conservative estimate

- Not all viral infections or diseases captured[7]
- EMR database does not include patients with haploidentical HCTs

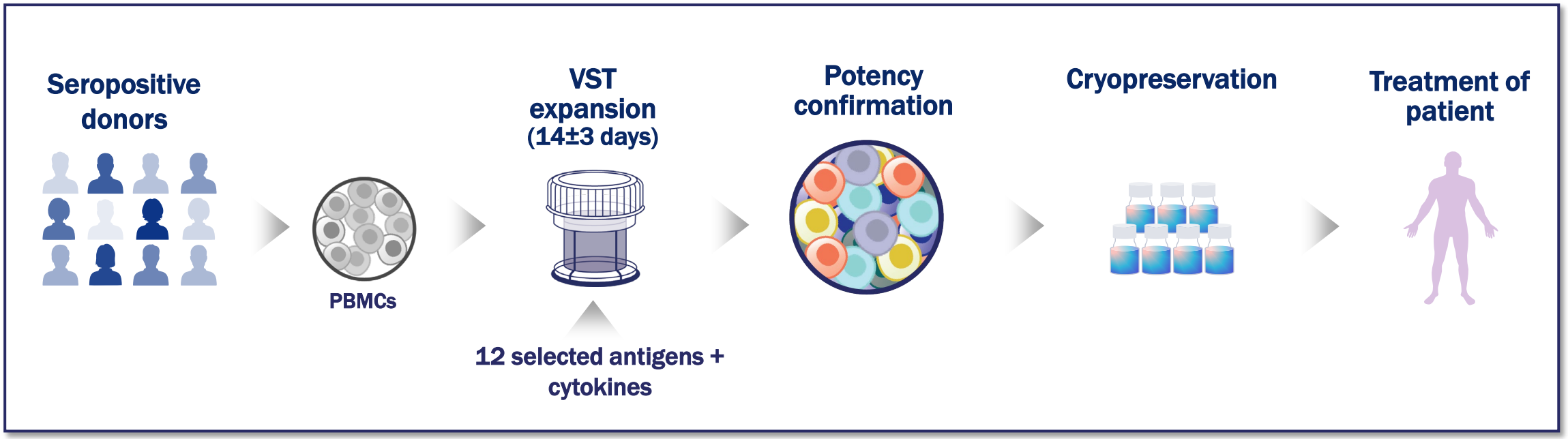
**There is an unmet need for preventive therapies targeting multiple viruses in high-risk allo-HCT patients**



1. Slade et al. *Transpl Infect Dis*. 2017; 2. Mohty et al. *Brit J Haematol.* 2019; 3. Salamonowicz-Bodzioch et al. *Ann Hematol*. 2021; 4. Mojtaba et al. *Biol Blood Marrow Transplant.* 2019; 5. El-Zimaity et al. *Blood* 2014; 6. Gargiulo et al. *eCancer* 2014; 7. Gabani et al. *Transplantation and Cellular Therapy,* 2022

# Posoleucel (ALVR105)

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

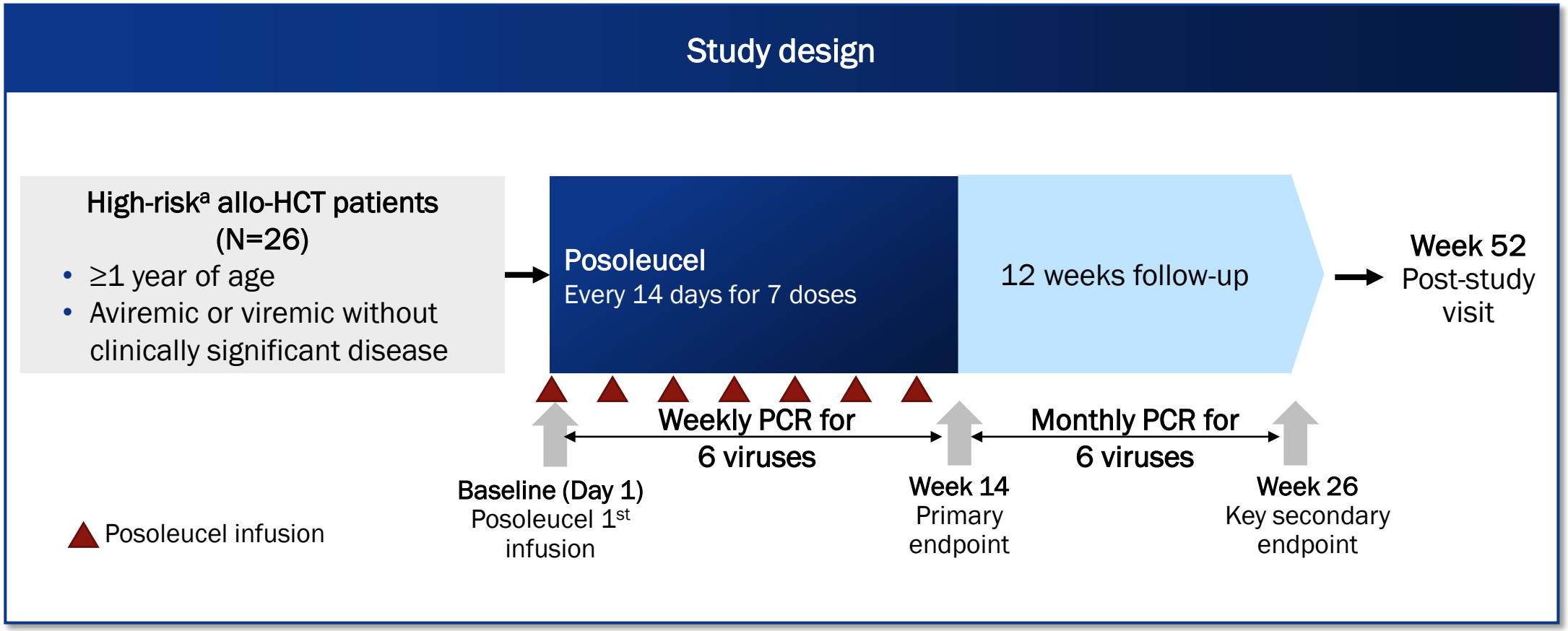



[a]JCV activity based on homology with BKV

1. Tzannou et al. *Blood* 2020

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

## Completed Phase 2 target patient enrollment




[a]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$^3$

# 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<br>• CMV: >910 IU/mL<br>• EBV/AdV: >10,000 copies/mL OR >1,000 copies/mL and rising[a]<br>AND<br>Initiation of preemptive antiviral therapy |
| End-organ disease | Signs or symptoms of organ damage from AdV, BKV, CMV, EBV, HHV-6, or JCV |

[a]Defined as two consecutive results of >1,000 copies/mL with the second result being higher than the first and drawn at least 48 hours after the first

# Baseline Demographics

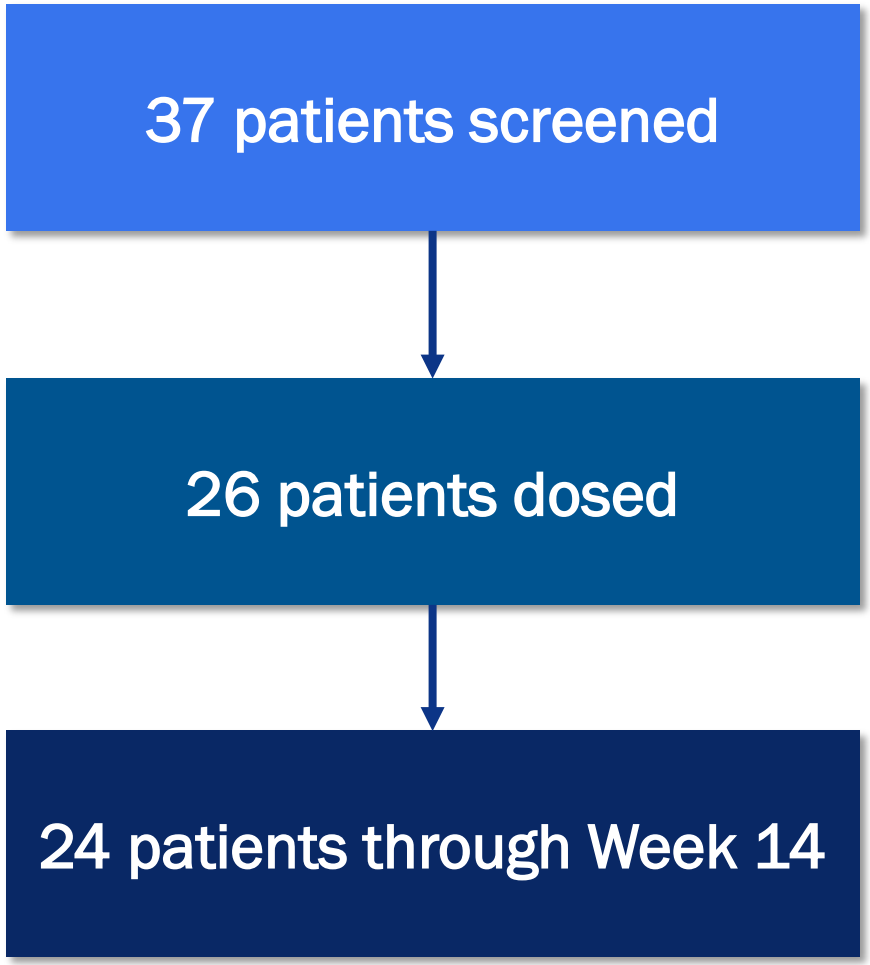
## Patients at high risk for viral infections or end-organ disease were enrolled

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

| Characteristic | N=26 |
|---|---|
| **Donor type** | |
| Haploidentical | 12 (46%) |
| Mismatched unrelated | 9 (35%) |
| Matched unrelated | 4 (15%) |
| Umbilical cord blood | 1 (4%) |
| **Myeloablative conditioning** | 12 (46%) |
| **Baseline viremia[b]** | 11 (42%) |
| **Letermovir prophylaxis** | 16 (62%) |

[a]Multiple myeloma and adrenoleukodystrophy
[b]1 AdV, 7 BKV, 2 EBV and/or 5 HHV-6 viremia(s) detected in 11 patients

# Patient Disposition[a]




- Only 1 patient did not have matching cell line (97% coverage)

- Posoleucel 1st dose administered at a median of 42 days post allo-HCT
- Median 3/8 HLA allele matches
- Median 7 posoleucel doses

- 1 patient completed 7 doses / has not reached Week 14
- 1 patient with ongoing dosing

[a]As of March 9, 2022

# 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[1-3]
  - 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%)[a] |
| Deaths | 1 (4%)[b] |
| Posoleucel discontinuations due to TEAEs | 3 (12%)[c] |
| 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%)[d] |

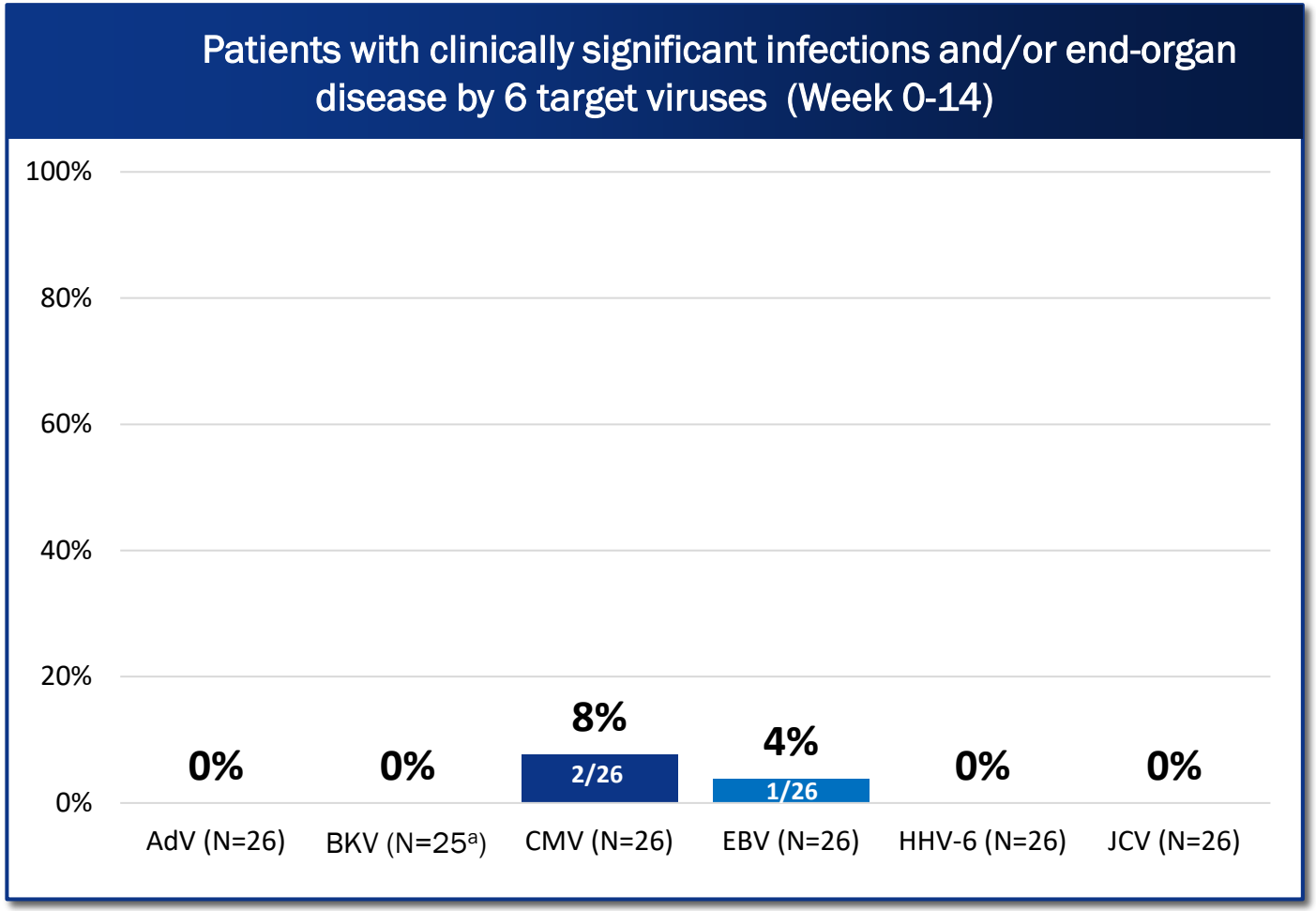
[a]1 patient with infusion reaction; 1 patient with acute GVHD; 1 patient with chronic GVHD.
[b]Due to relapse of primary malignancy ~2 months after the 7th dose of posoleucel.
[c]1 discontinuation assessed as not related to posoleucel; 2 discontinuations assessed as possibly related to posoleucel.
[d]Tolerated subsequent posoleucel doses with pre-medication (diphenhydramine).



1. Malki et al. *Blood Adv*. 2021. 2. Saliba RM, et al. Abstract 31. Presented at: TCT 2020. 3. Chen et al. *Bone Marrow Transplant*. 2017.

# Preliminary Efficacy Results: Primary Endpoint (Week 14)

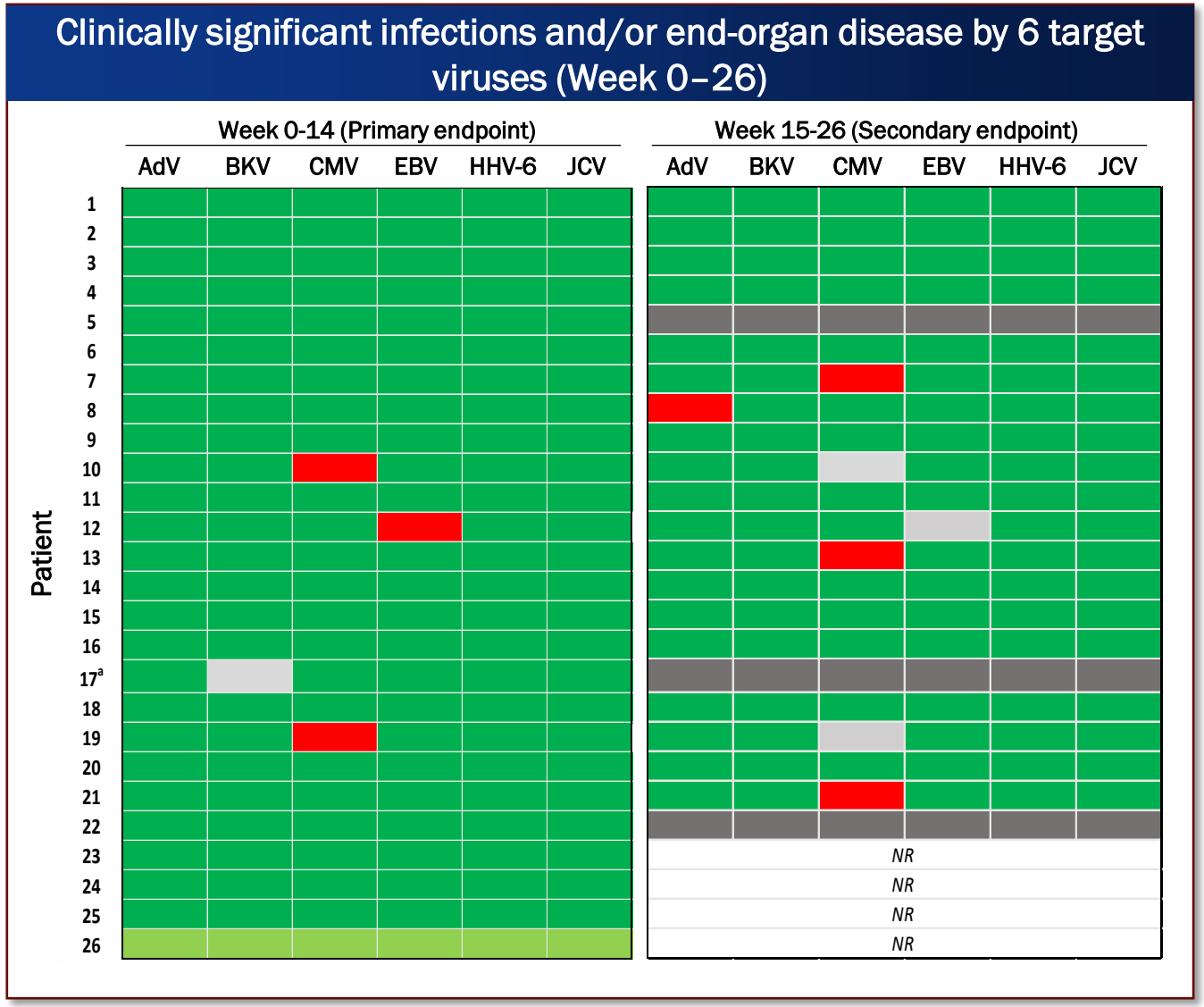
- 2 clinically significant infections
  - 2 patients started on pre-emptive valganciclovir for CMV
- 1 end-organ disease
  - 1 patient started on rituximab for EBV-PTLD in the setting of high-dose steroids




[a]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




Patient with completed or stopped dosing who did not develop clinically significant infection or disease

Patient with ongoing dosing/monitoring who has not developed clinically significant infection or disease

Patient who developed new onset clinically significant infection or disease

Patient sample not collected

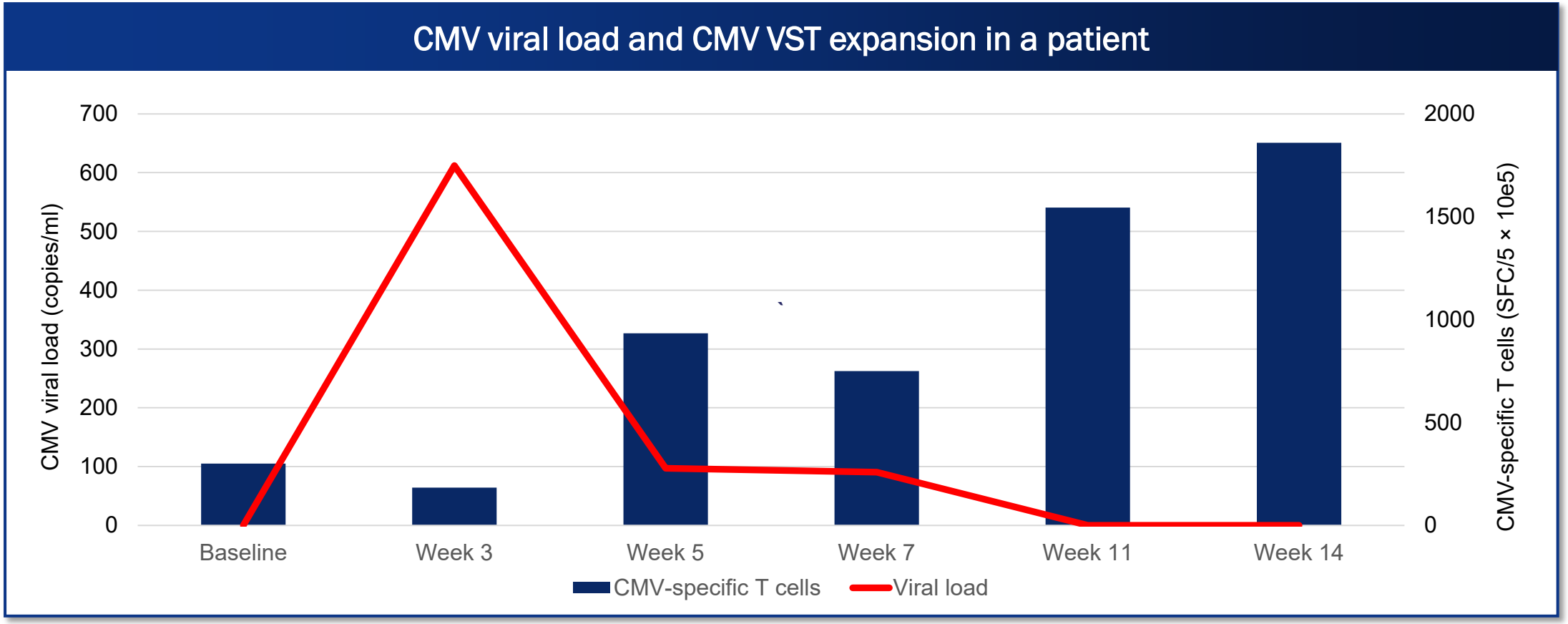
Previous clinically significant infection or disease

NR Week 18 timepoint not yet reached

[a]BKV hemorrhagic cystitis at baseline

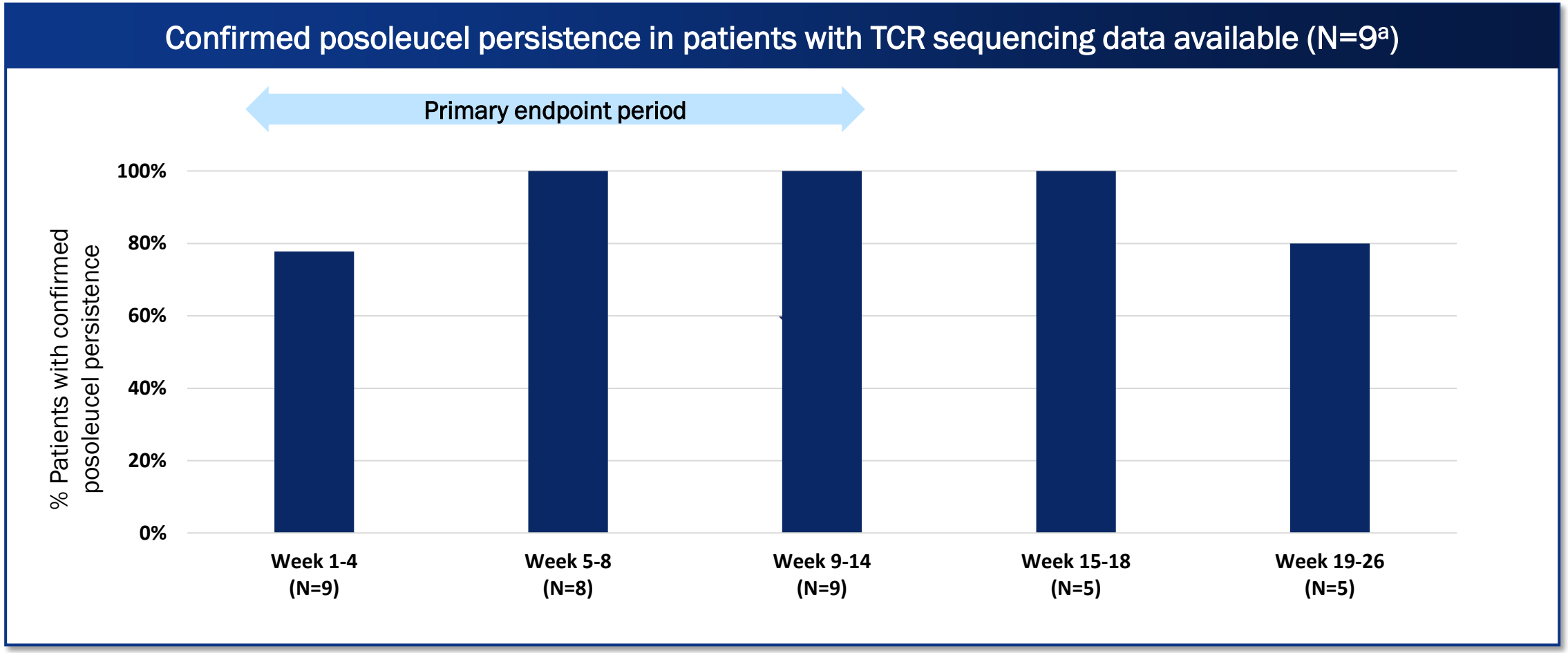
# CMV Infection Controlled without Letermovir or Pre-Emptive Therapy while on Posoleucel

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



# Posoleucel Persists *in vivo*

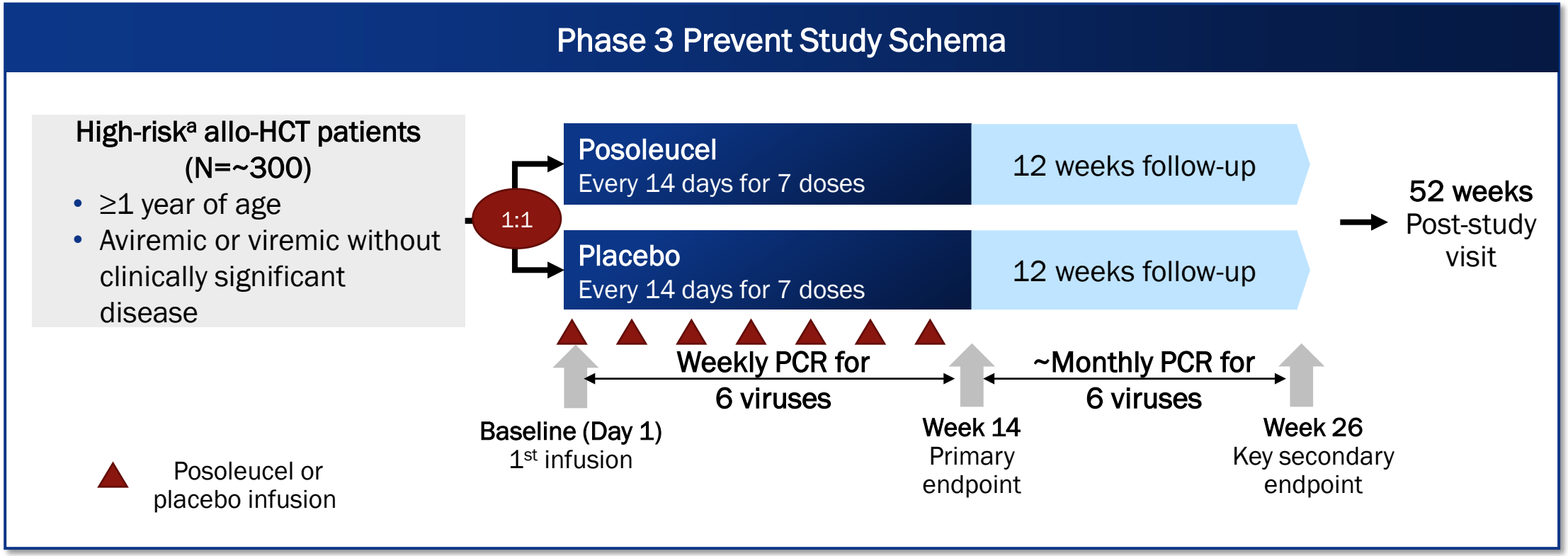
- Posoleucel VSTs detected throughout the infusion period and persisted up to the last time point measured




[a]9 patients received ≥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




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

# Conclusions

- 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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