Final Clinical and Biomarker Data from a Phase 2 Trial of Posoleucel, an Off-the-shelf, Multivirus-specific T Cell Therapy, for Prevention of Clinically Significant Viral Infections Post-HCT

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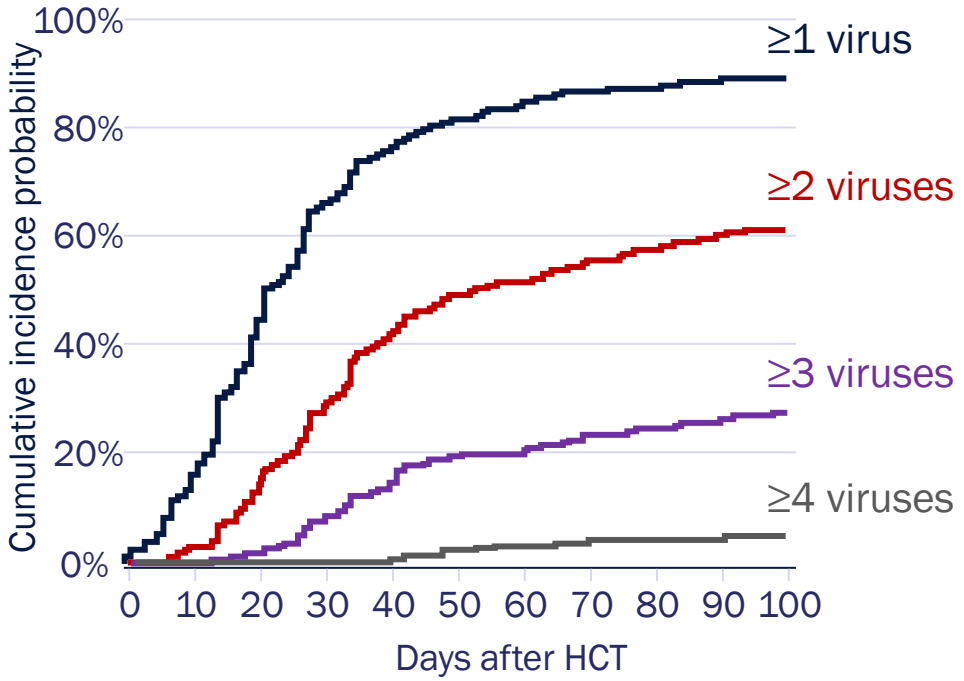
Disclosures

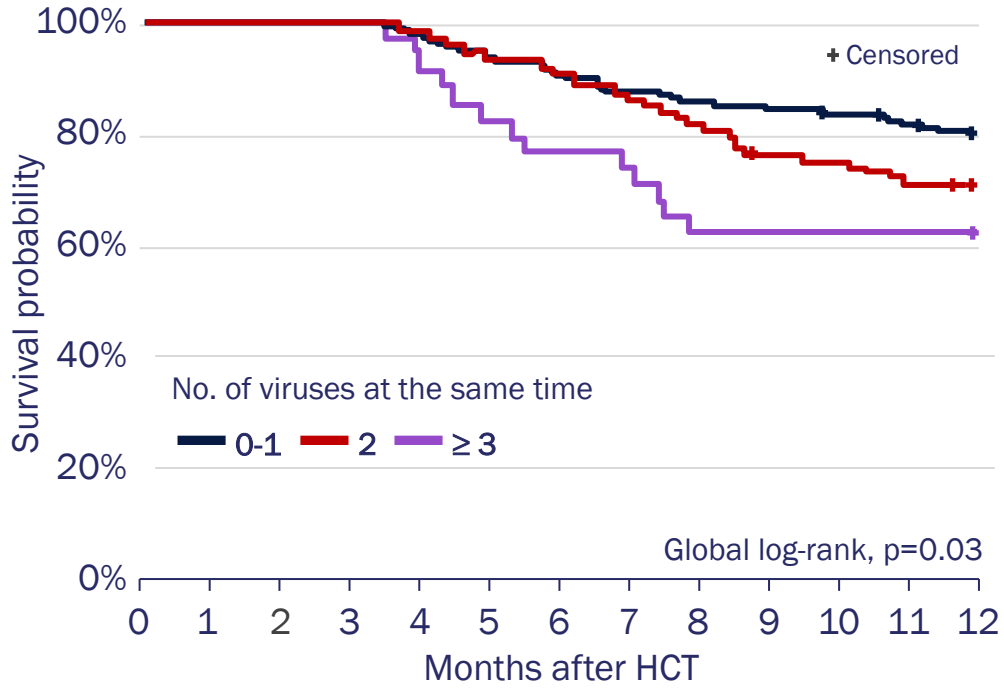
- Advisory Board Meetings participation for Kite, Omeros, Kadmon, Sanofi and Incyte.
- Research grant from Kite.

Allo-HCT Patients Have a High Risk of Viral Reactivation Which Can Lead to Clinically Significant Infections or Disease

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)

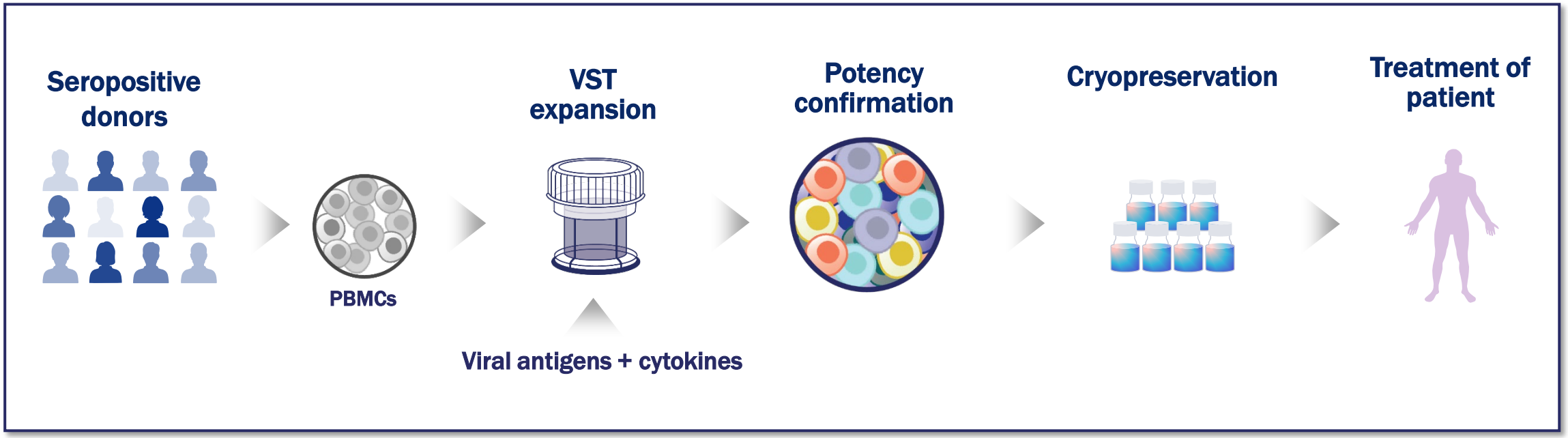


- Mortality directly correlates with viral burden: each 10-fold increase in viral burden translates to a nearly 40% increase in overall mortality[1]

1. Hill et al. *Blood* 2017;129:2316-25.

Posoleucel (ALVR105)

- Allogeneic, off-the-shelf, multivirus-specific T-cell (VST) therapy targeting AdV, BKV, CMV, EBV, HHV-6, and JCV*
- The cell bank is rationally designed to ensure availability of partially HLA-matched VSTs to >95% patients (minimum 2 HLA allele-match)
- Posoleucel (PSL) is designed to control viremia preventing progression to CSIs

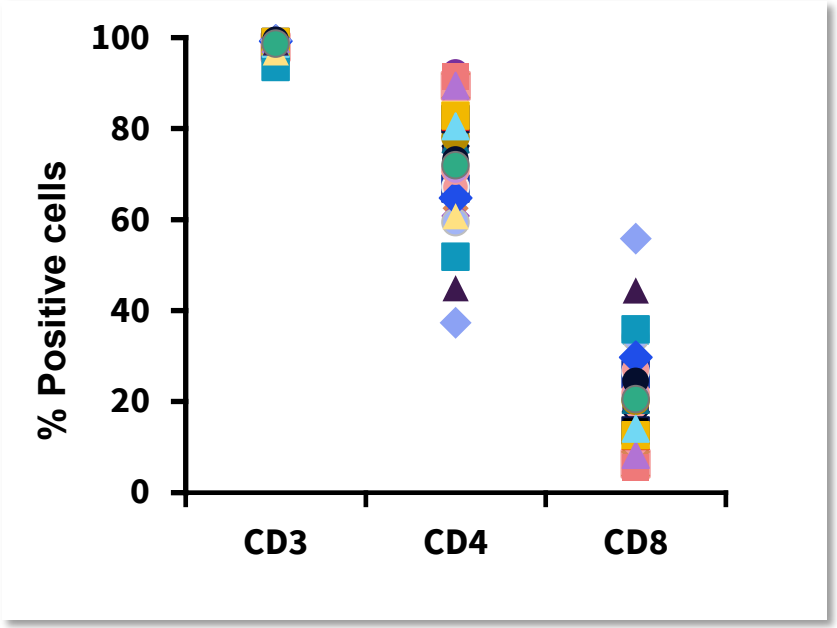


*JCV activity based on homology with BKV

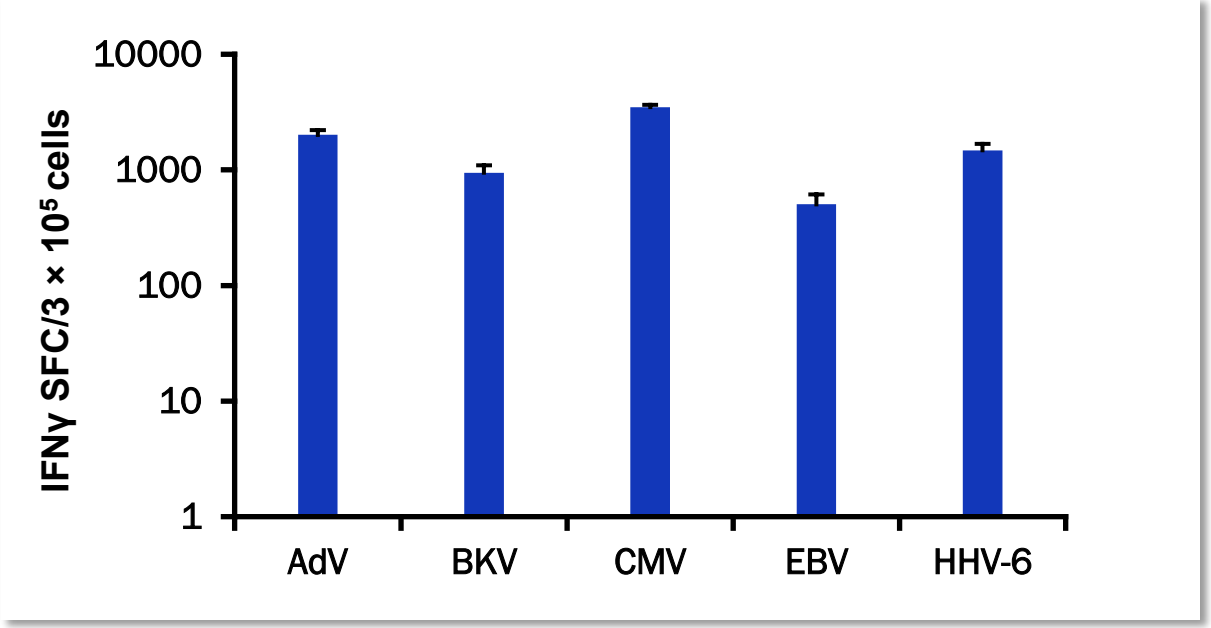
Posoleucel Is Composed of Functional Virus-Specific T Cells with Low Alloreactive Potential

- Posoleucel is composed of polyclonal $CD4^+$ and $CD8^+$ T cells potent against each of the target viruses[1]
- The selective enrichment of virus-specific T cells during manufacturing process yields VSTs with low alloreactive potential

PSL is T cell enriched



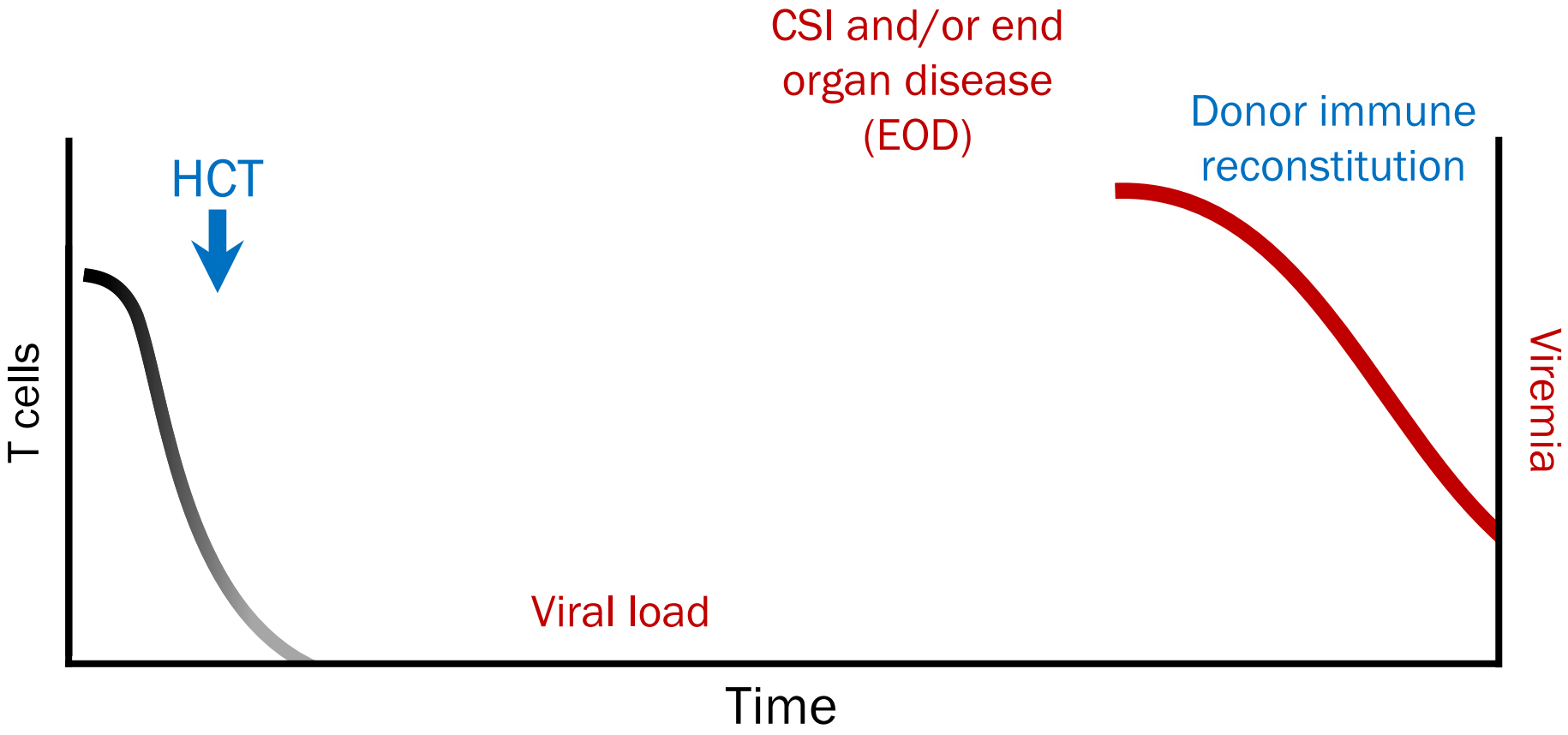
PSL composed of functional virus-specific T cells



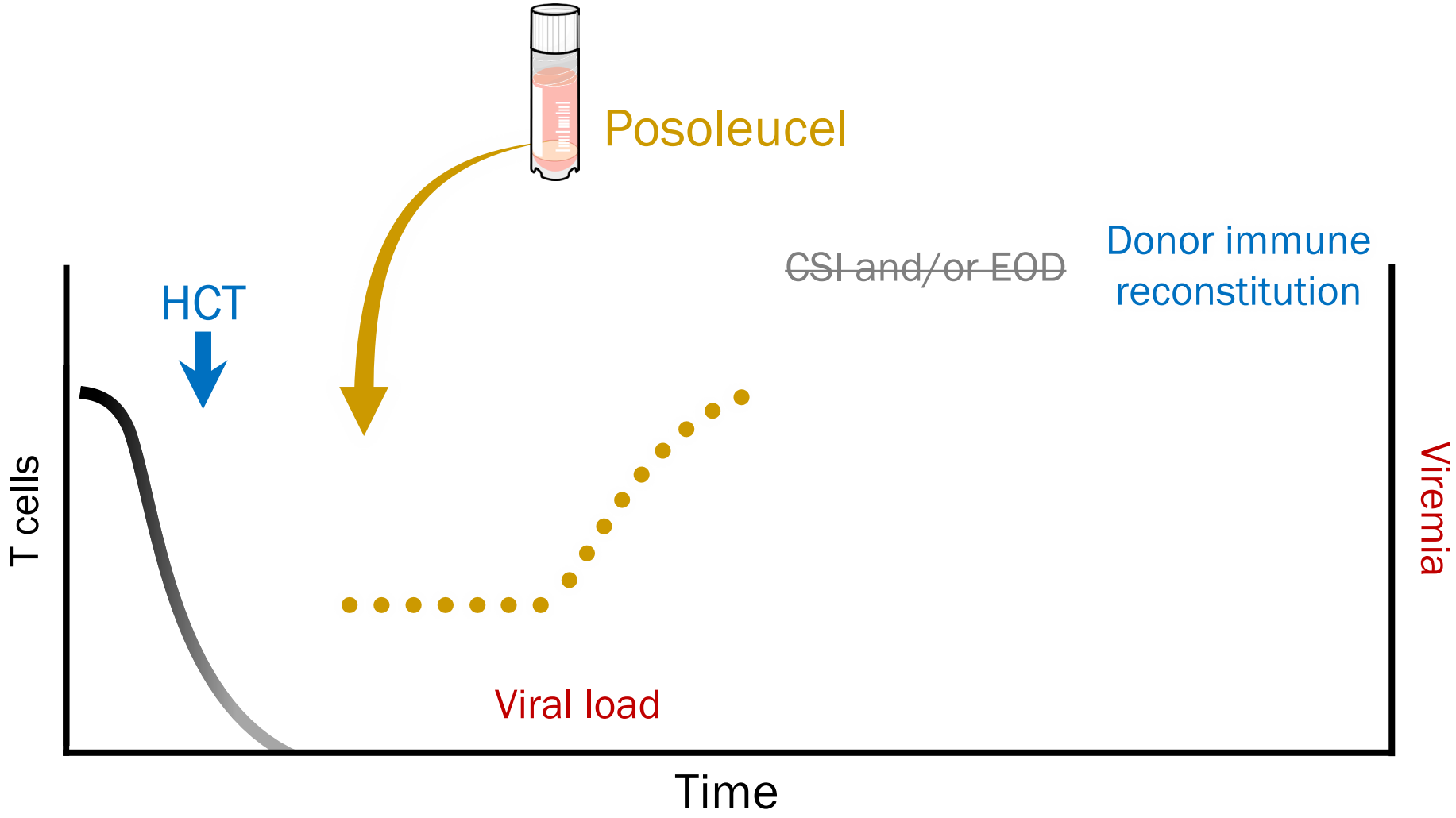
n=33

1. Papadopoulou et al. *Sci Transl Med*. 2014;6:242.

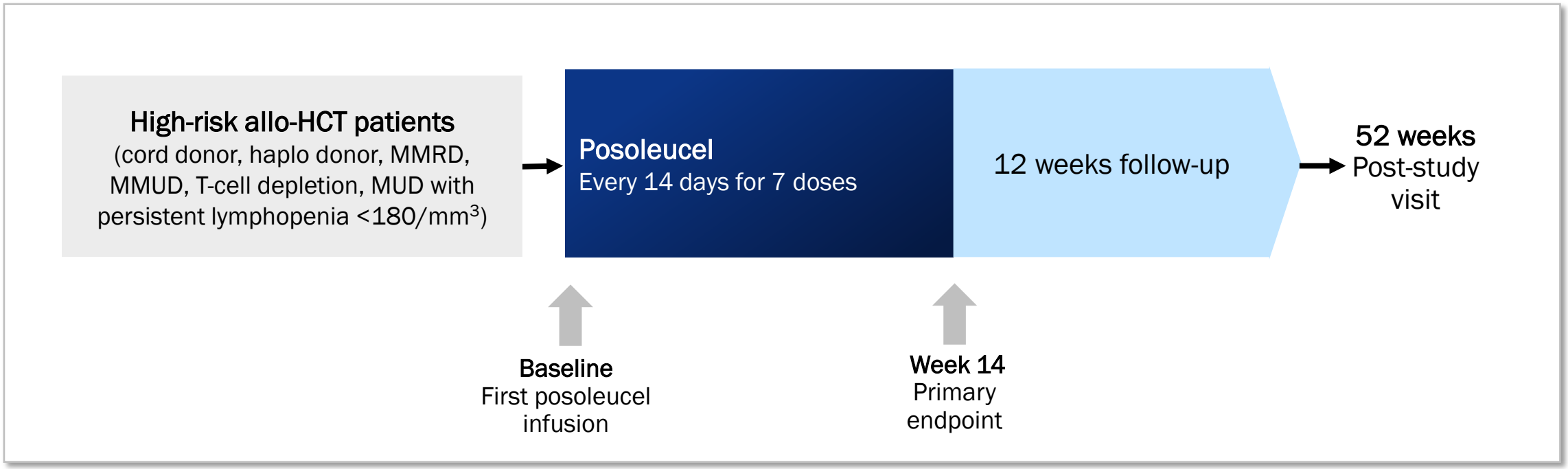
Virologic and Immunologic Landscape Post Allo-Hematopoietic Cell Transplantation (HCT) (without Posoleucel)



Virologic and Immunologic Landscape post Allo-HCT (with Posoleucel)



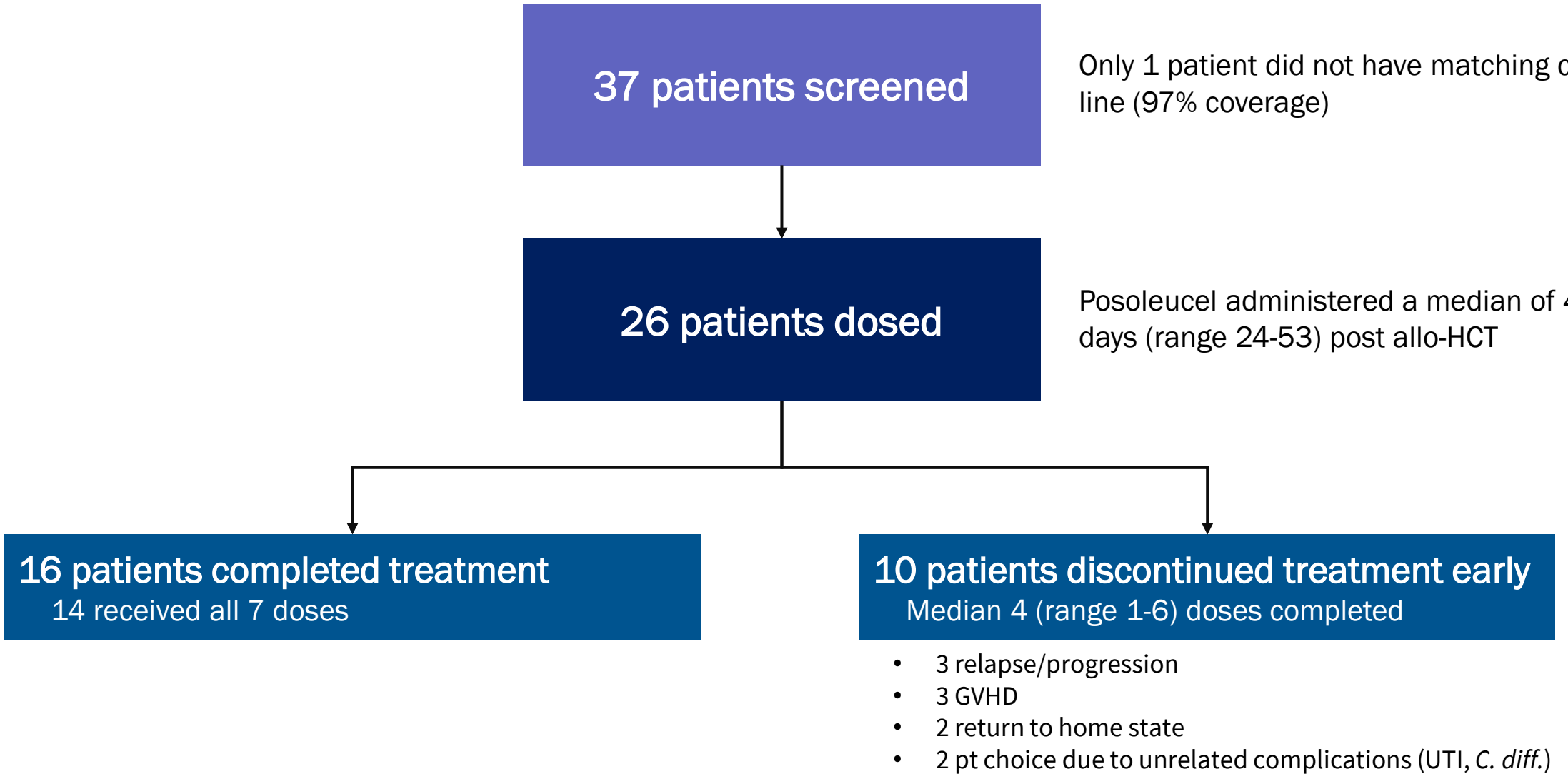
Phase 2 Prevention Study Design



Primary endpoint: The number of new onset clinically significant infections* through Week 14

*Clinically significant infections include both clinically significant viremia and end-organ disease

Patient Disposition



Demographic and Baseline Characteristics

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

Characteristics	N=26
Donor type, n (%)	
Haploidentical	12 (46)
Mismatched unrelated	9 (35)
Matched unrelated†	4 (15)
Umbilical cord blood	1 (4)
Myeloablative conditioning, n (%)	12 (46)
PTCy, n (%)	20 (77)
Letermovir use at baseline, n (%)	16 (62)
Viremia at baseline, n (%)‡	12 (46)

*Multiple myeloma and adrenoleukodystrophy.
†Matched unrelated transplant recipients included if also met another high-risk criterion: T-cell depletion or persistent lymphopenia.
‡Viremia at baseline: 1 AdV, 8 BKV, 2 EBV, and 5 HHV-6 viremia(s) in 12 patients.

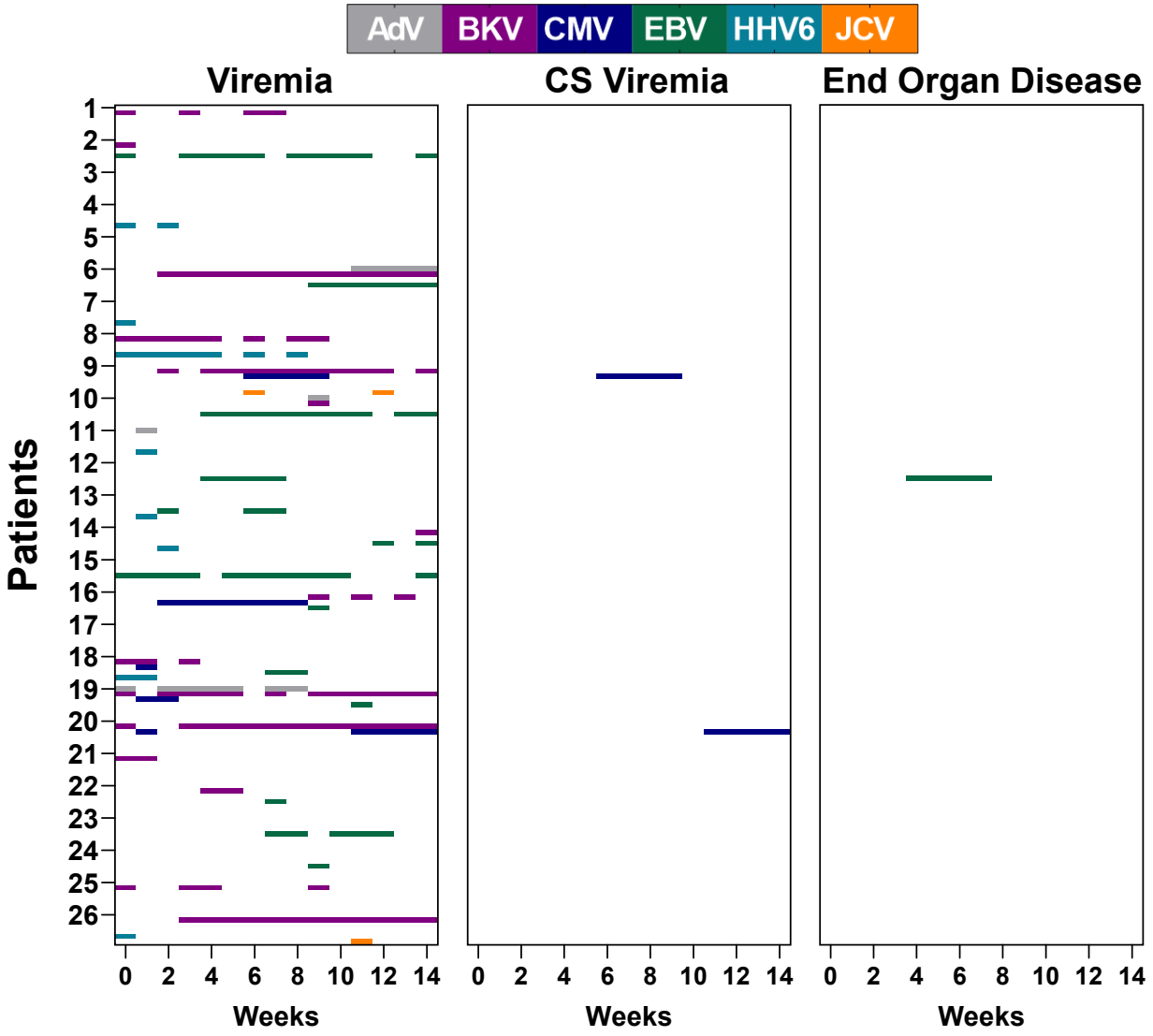
Safety and Tolerability in First 26 Weeks

- 5/26 (19%) patients had grade II-IV acute GVHD
- No episodes of cytokine release syndrome
- One secondary graft failure assessed by investigator as unrelated to posoleucel

Patients with events, n (%)	N=26
Any TEAEs	26 (100)
SAEs	19 (73)
Treatment-related SAEs*	3 (12)
Discontinuation of posoleucel due to TEAEs	4 (15)
Deaths due to TEAEs	4 (15)
TEAEs of special interest	14 (54)
Acute GVHD II-IV	5 (19)
Acute GVHD III-IV	2 (8)
Any chronic GVHD	5 (19)
Cytokine release syndrome	0
Infusion reaction†	1 (4)
Graft failure	1 (4)

*1 skin GVHD, 1 hypersensitivity reaction, 1 chronic pulmonary GVHD.
†This event resolved, and patient received an additional 2 doses of posoleucel.

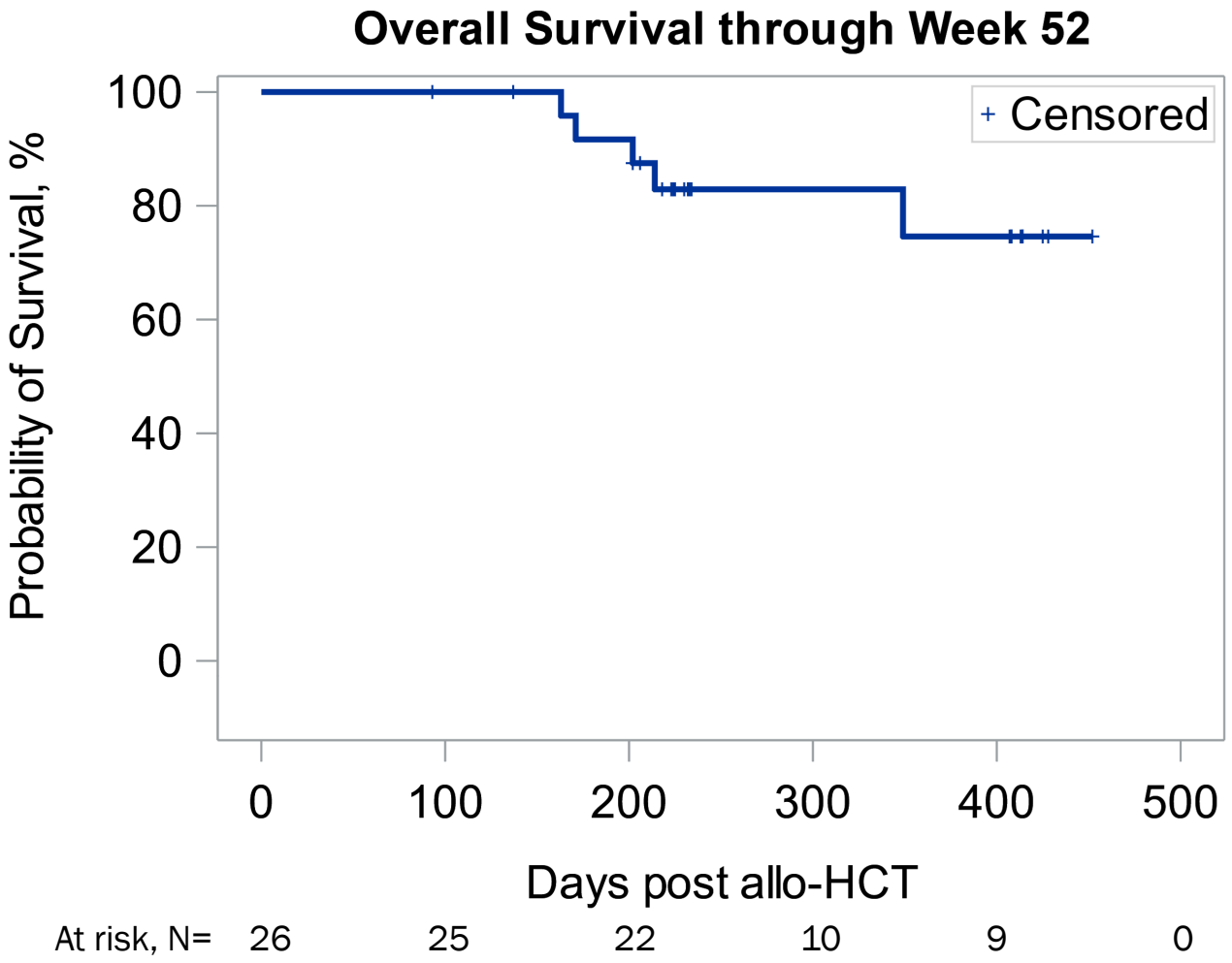
Low Rates of Clinically Significant Infections through Week 14 (Primary Endpoint)



- 22 (85%) of patients developed 1+ virus; 13 (50%) 2+ viral reactivations
- 3 (12%) CSIs* observed despite high rate of viral reactivations
- 4 (15%) additional CSIs occurring in the secondary endpoint
  - 2 (50%) in setting of chemotherapy due to relapse

*2 patients with asymptomatic & pre-emptively treated CMV infection; 1 patient with EBV PTLD in the setting of high-dose steroid.

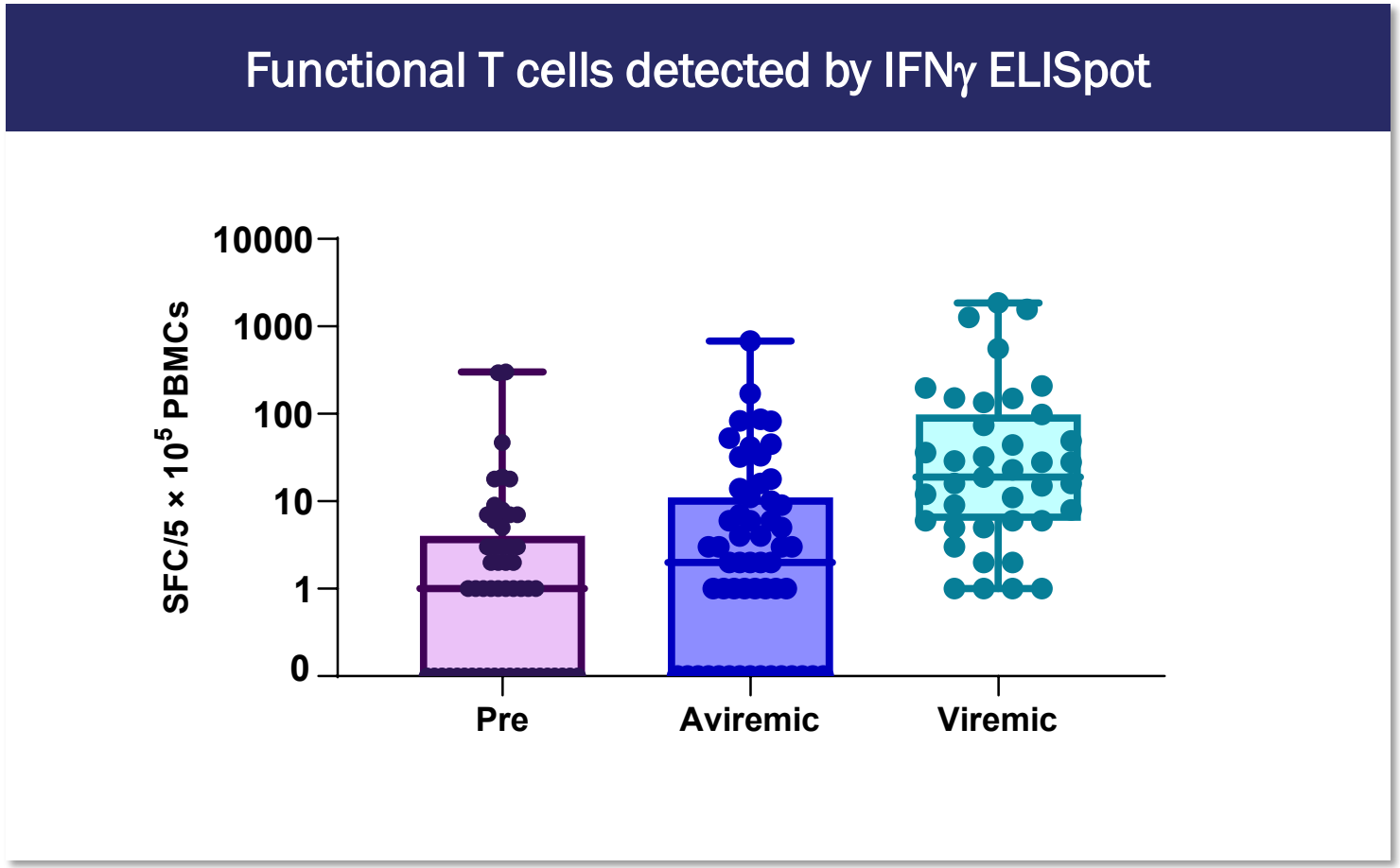
0% Day 400 Non-Relapse Mortality



- All deaths (N=5) due to relapse or disease progression
  - No infection related mortality
- 0% Day 400 NRM compares favorably to historic rates of 9-13% reported for allo-HCT patients[1-3]

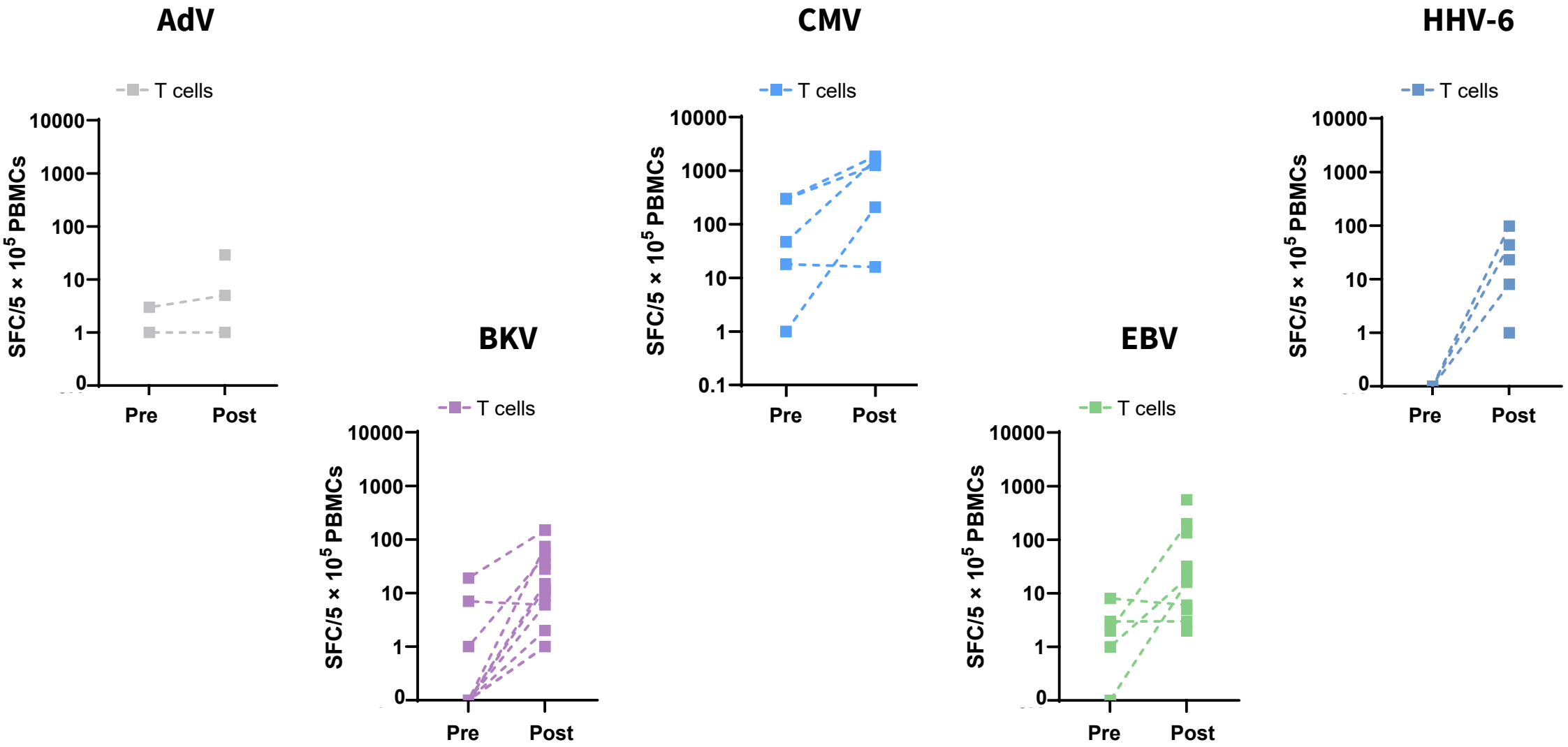
1. Marty F, et al. *N Engl J Med.* 2017;377:2433-44. 2. McDonald GB, et al. *Ann Intern Med.* 2020;172:229-39. 3. Su Y, et al. *Clin Infect Dis*. 2022;75:795-804.

Frequency of IFNγ-producing Virus-Specific T Cells



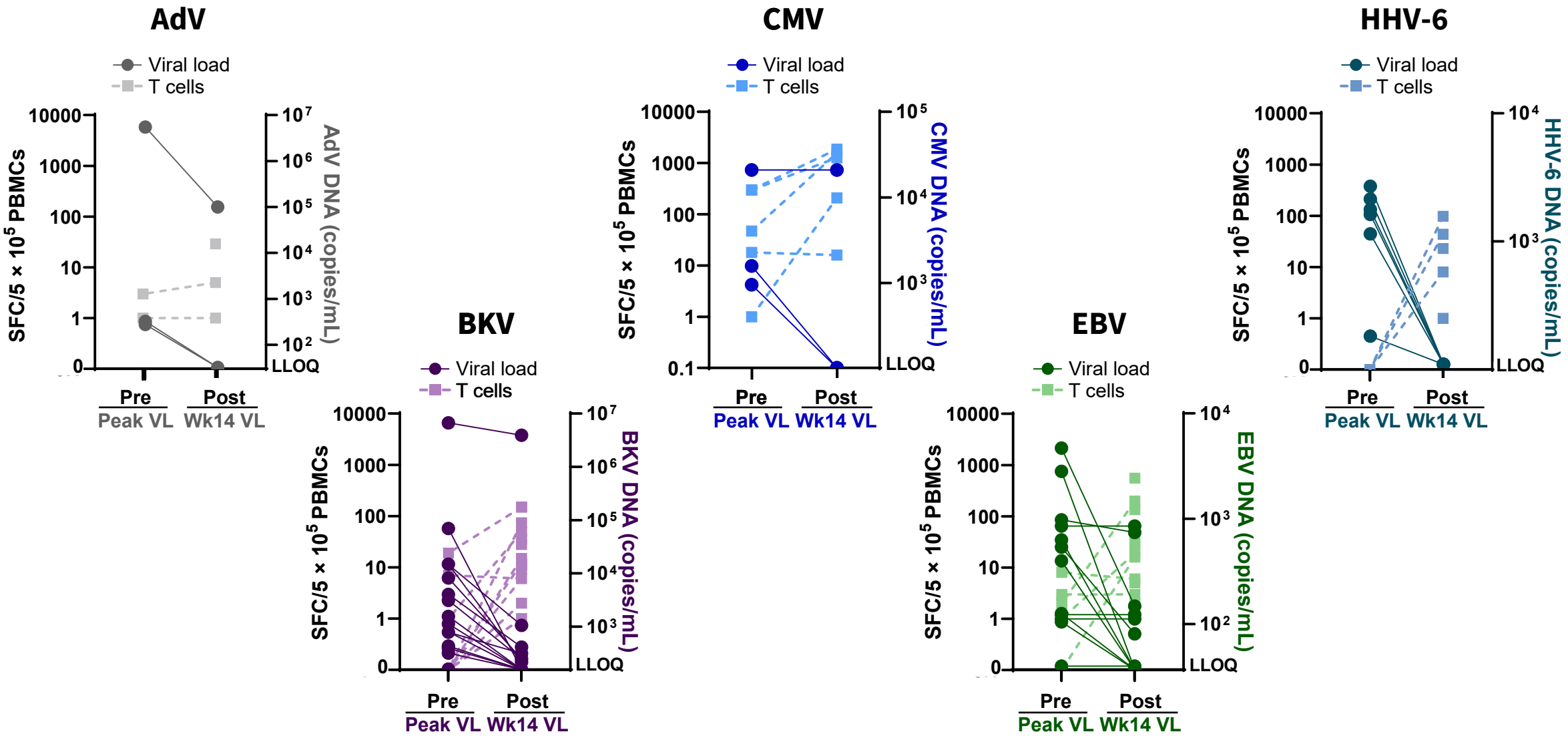
Aggregate ELISpot data shown for N=39/45 viremia (peak response on treatment Wk 1 – Wk 14), N=53 aviremia (peak response on treatment Wk 1 – Wk 14), and N=55 baseline (Pre, Day 0); ELISpot data shown includes three clinically significant infections.

Increased Frequency of IFNγ-producing T Cells Was Associated with Reduction in Viremia



Data shown from patients with available samples at Pre (Day 0) and/or Post (peak response on treatment Wk 1-Wk 14) timepoints.

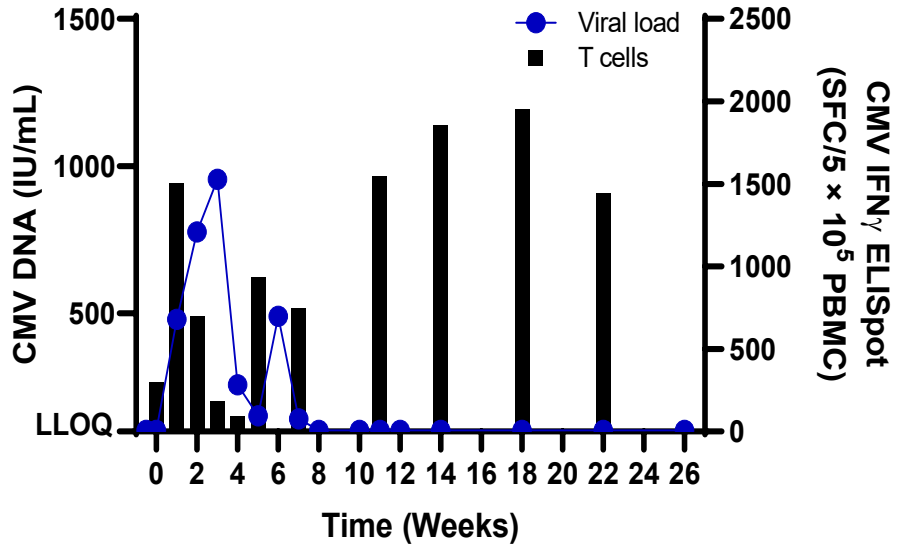
Increased Frequency of IFNγ-producing T Cells Was Associated with Reduction in Viremia



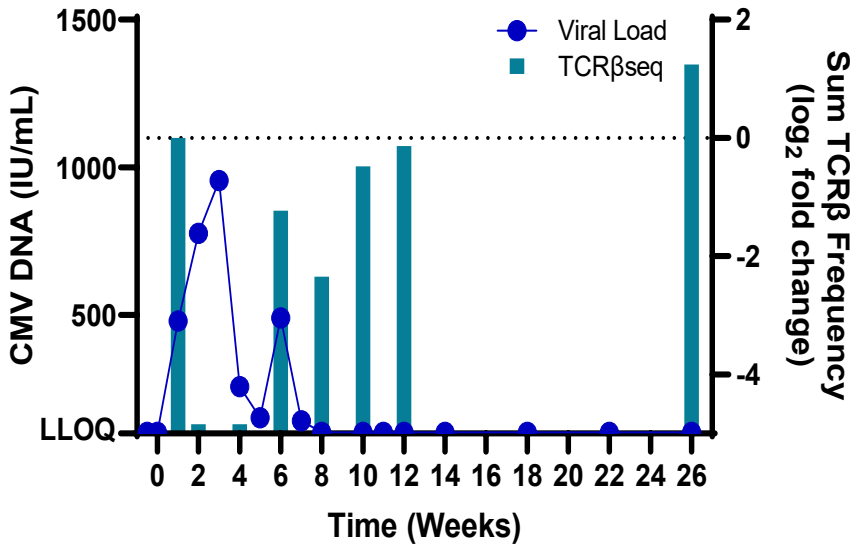
ELISpot data shown from patients with available samples at Pre (Day 0) and/or Post (peak response on treatment Wk 1 – Wk 14) timepoints. Viral load (VL) data shown as peak viral load during primary endpoint period (Pre, Day 0 – Wk 14) and viral load at primary endpoint (Post, Wk 14 or last available time point); viral load data from CSIs excluded.

Expansion of Virus-Specific T Cells and Control of Viremia

CMV ELISpot Response

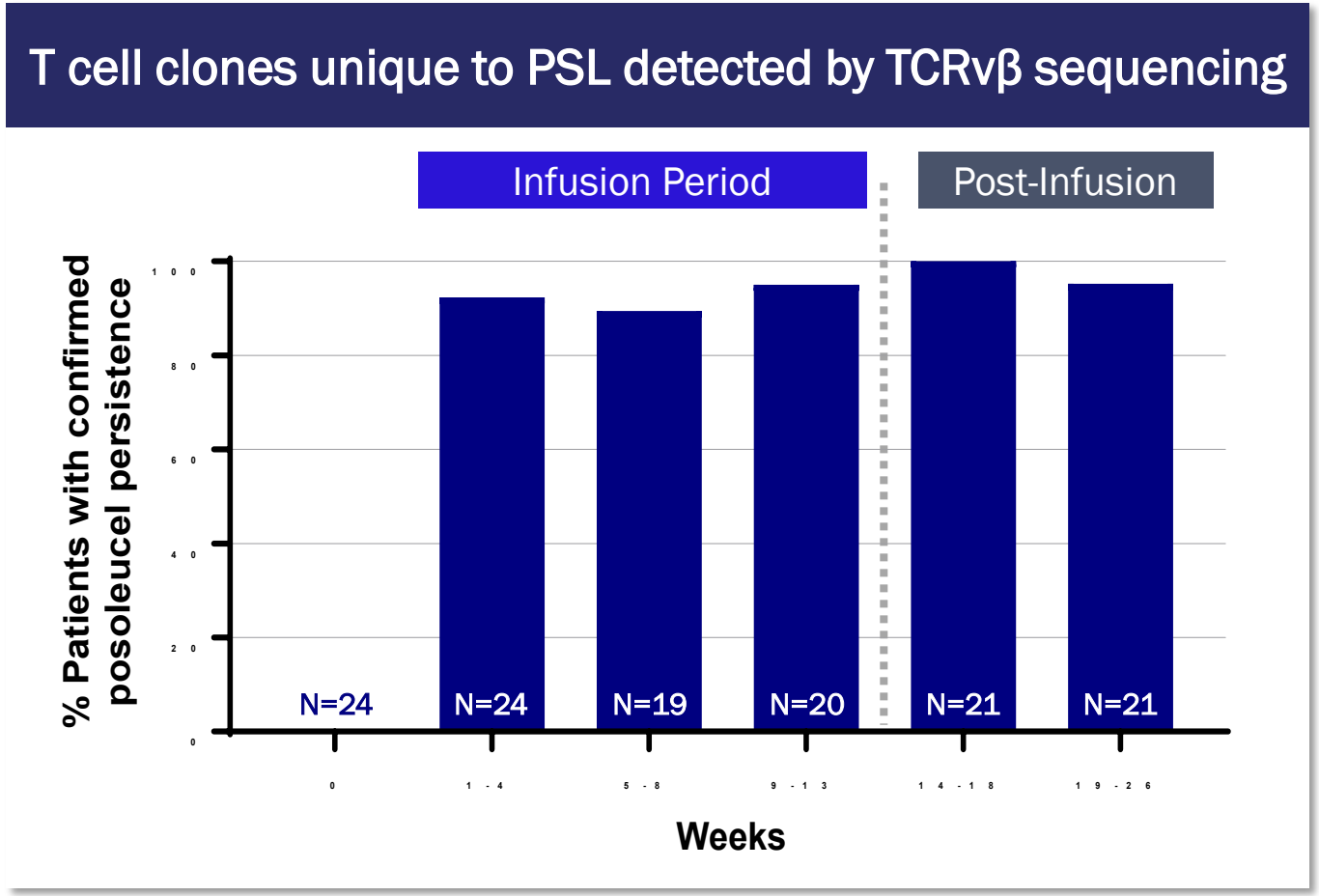


Change in Frequency of PSL VSTs



- 61-year-old male MMUD; CMV serostatus D-/R+; discontinued letermovir prior to 1st posoleucel dose; received all 7 posoleucel doses
- Expansion of functional CMV VSTs coincident with control of CMV viremia, not requiring antiviral treatment
- Confirmed detection of posoleucel TCRs during viremia with changes in frequencies coincident with viremia

TCRβ Clones Unique to PSL Are Detected During Infusion and After



- Posoleucel clones detected in patients with available TCR sequencing data
  - During infusion period
  - Up to 14 weeks after last infusion

Presence of posoleucel-derived clones (based on tracking TCRvβ sequences) shared by the posoleucel product and post-infusion peripheral blood samples

Conclusions

- Low rates of clinically significant infections or end-organ disease were observed in this high-risk allo-HCT population
- 0% Day 400 Non-relapse mortality and no infection related mortality
- Treatment with up to 7 doses of posoleucel over 12 weeks was well tolerated
  - Rates of GVHD were similar in frequency and severity to those expected in high-risk allo-HCT population
- Viral control was associated with expansion of reactive T cells
  - The presence of posoleucel was confirmed during and after infusion period
- These data support the ongoing global, randomized, placebo-controlled Phase III clinical trial of posoleucel for the prevention of clinically significant infections and end-organ disease (NCT05305040)

Acknowledgments

- Thanks to Manik Kuvalekar, Ayumi Watanabe, and Yovana Velazquez for their work on the biomarker analyses
- We extend our thanks to investigators, patients, and families
- This study was funded by AlloVir