Final Clinical Outcomes from a Phase 2 Trial of Posoleucel, an Off-the-Shelf, Multivirus-Specific T-Cell Therapy, for the Prevention of Clinically Significant Viral Infections Post-HCT

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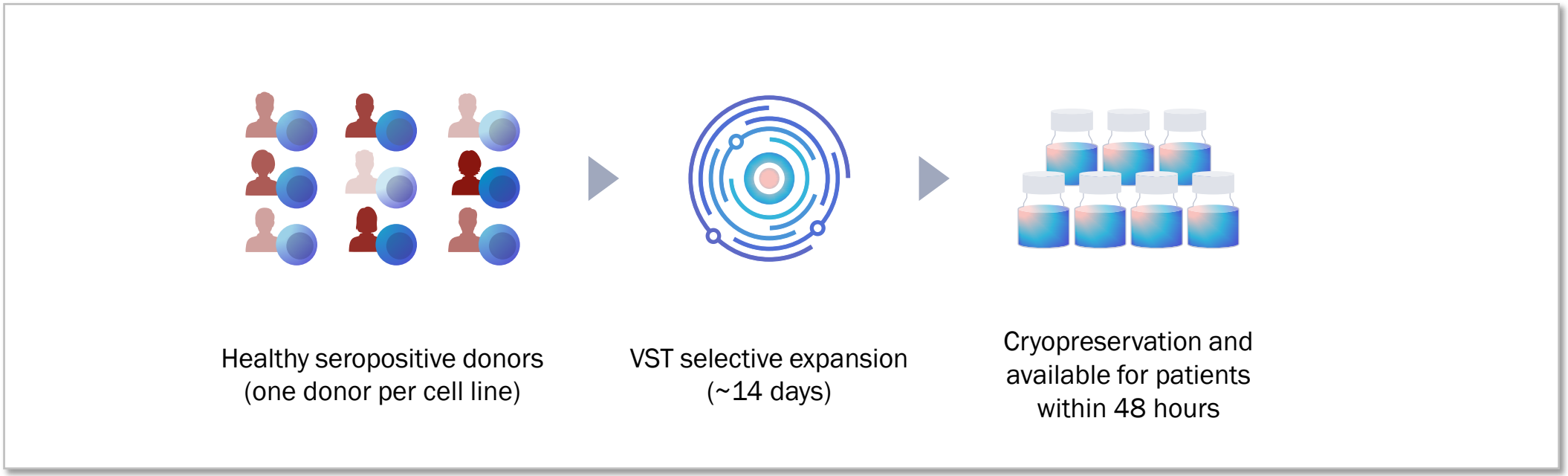
Posoleucel: an Allogeneic, Off-the-shelf, Multivirus-specific T-cell Therapy

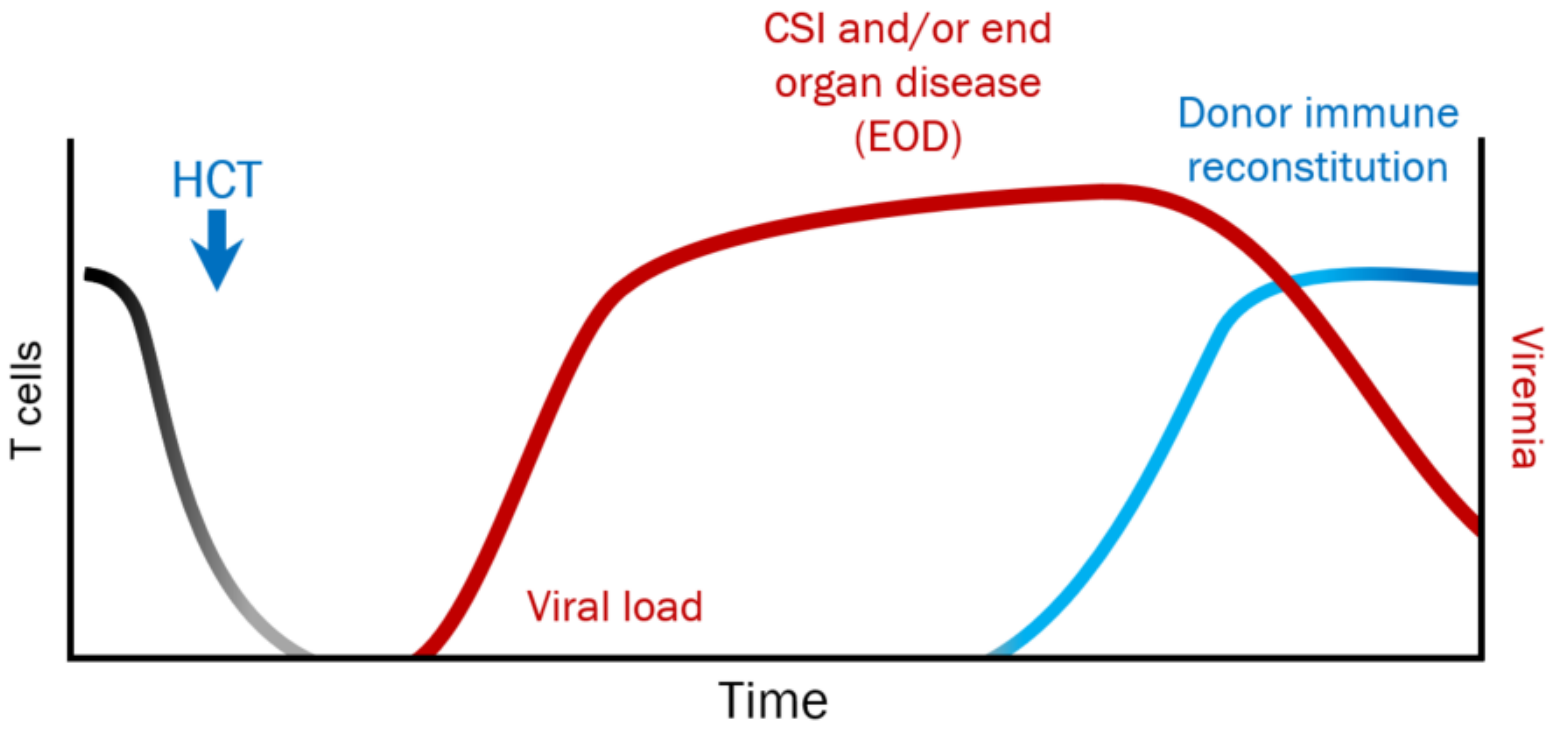
- Targets: adenovirus (AdV), BK virus (BKV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), human herpesvirus-6 (HHV-6), and JC virus (JCV)*
- 95% response rate in Phase 2 CHARMS treatment study[1]



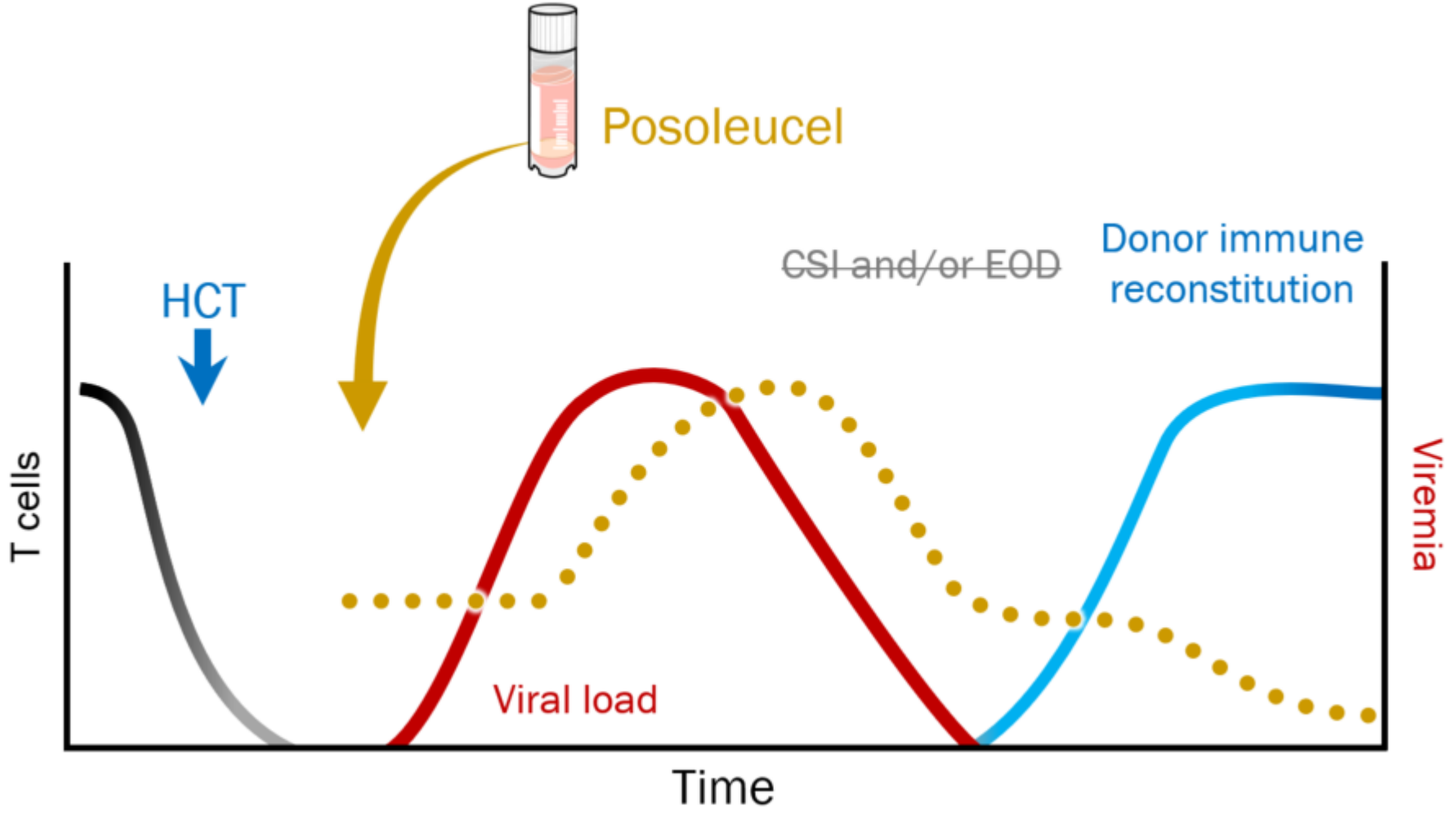
*JCV activity based on homology with BKV

1. Pfeiffer et al. *Clin Cancer Res*. 2022 (in press).

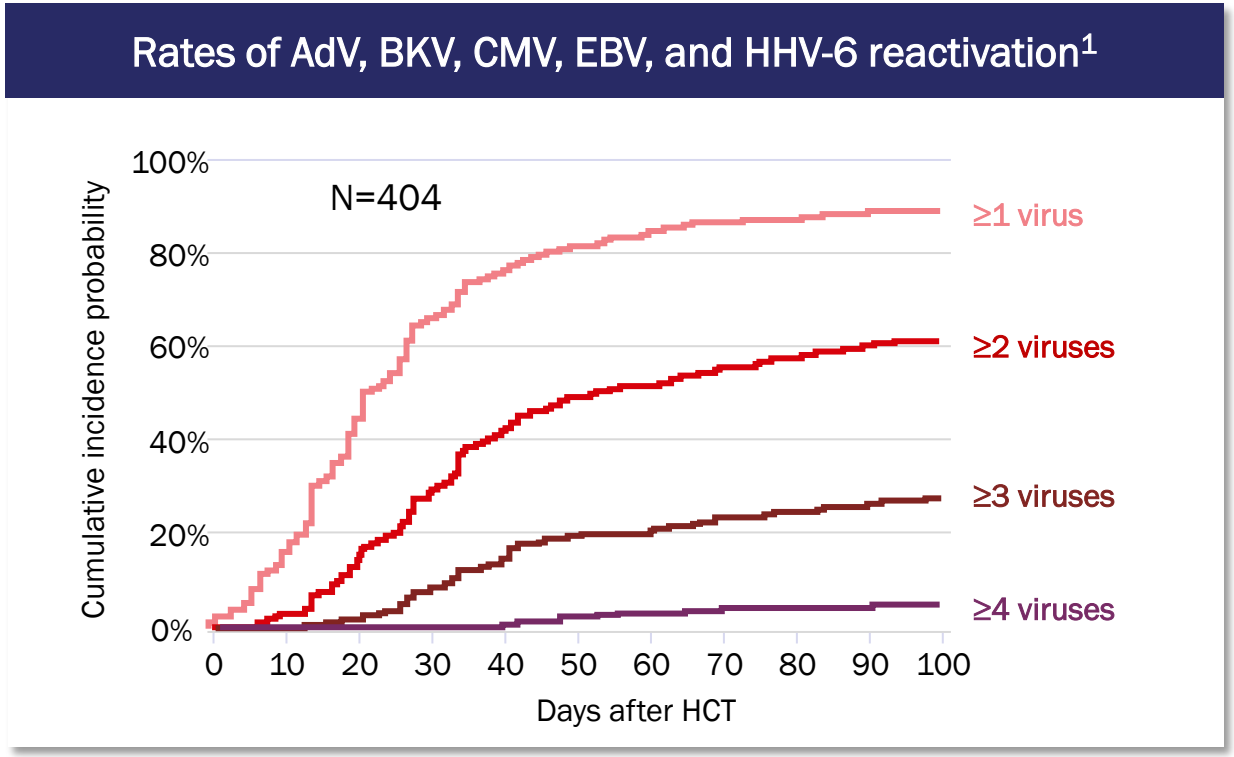
Virologic and Immunologic Landscape Post Allo-Hematopoietic Cell Transplantation (HCT) (without Posoleucel)



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



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

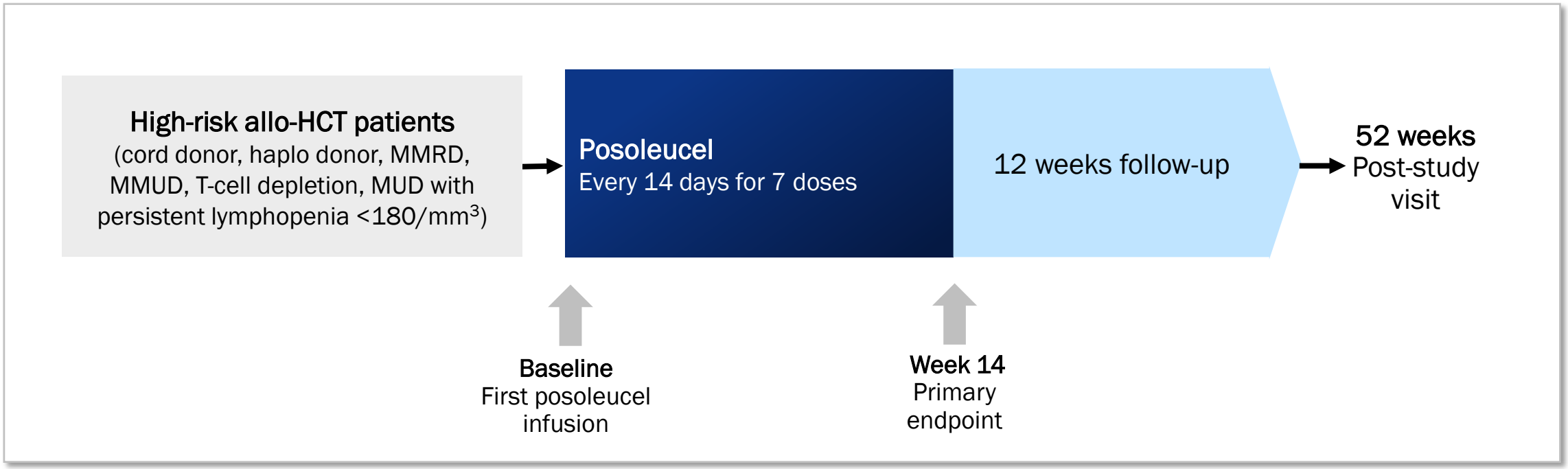


Viral reactivation is common following allo-HCT and is linked to increased morbidity and mortality

- Up to 70% of high-risk allo-HCT patients experience clinically significant infections or end-organ disease[2-8]
- Posoleucel T cells control viremia preventing progression to clinically significant infection or end-organ disease

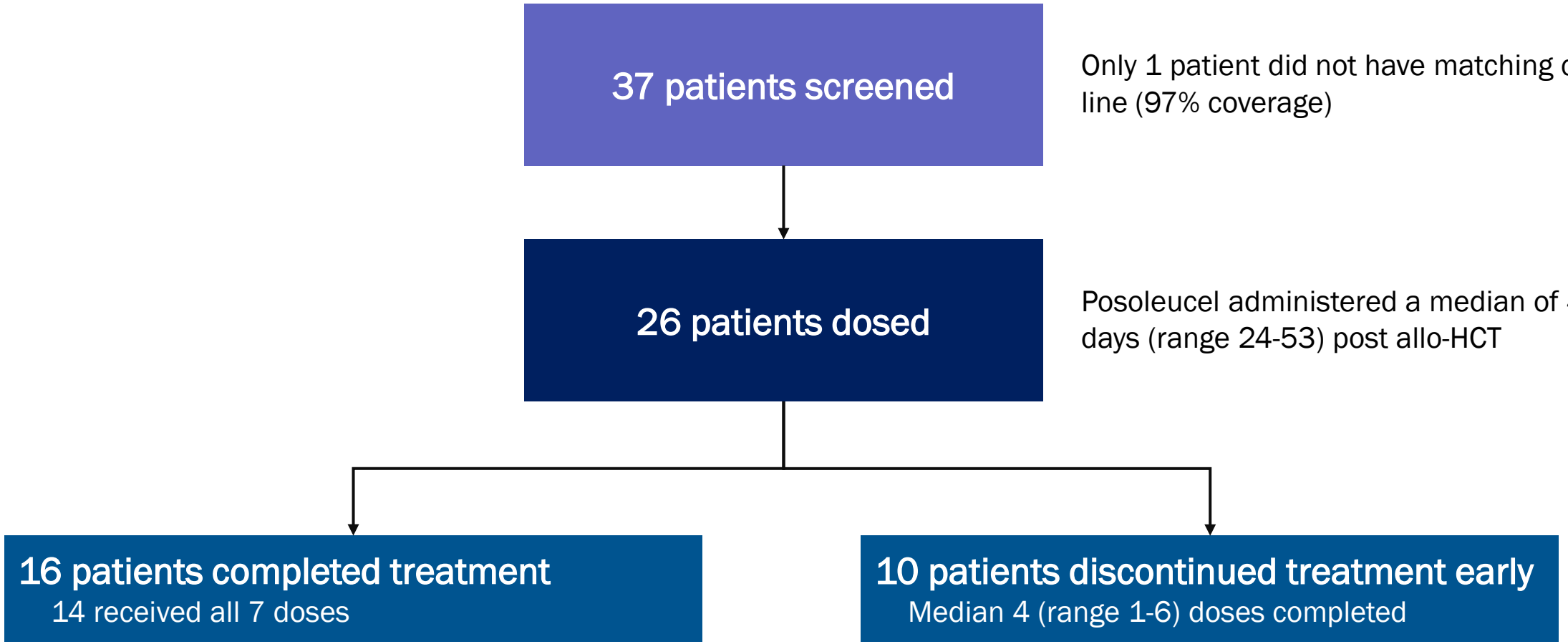
1. Hill et al. *Blood* 2017;129:2316-25; 2. Slade et al. *Transpl Infect Dis* 2017;19:e12629; 3. Mohty et al. *Brit J Haematol* 2019;187e64; 4. Salamonowicz-Bodzioch et al. *Ann Hematol* 2021;100:1283-93; 5. Chang et al. *Biol Blood Marrow Transplant* 2019; 6. El-Zimaity et al. *Blood* 2004; 7. Gargiulo et al. *eCancer* 2014; 8. Gabanti et al. *Transplant Cell Ther* 2022;28:211.e1-211.e9.

Phase 2 Study Design



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

Patient Disposition



Demographic and Baseline Characteristics

Characteristics	N=26
Age, median years (range)	60 (14-76)
Female, 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)
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.

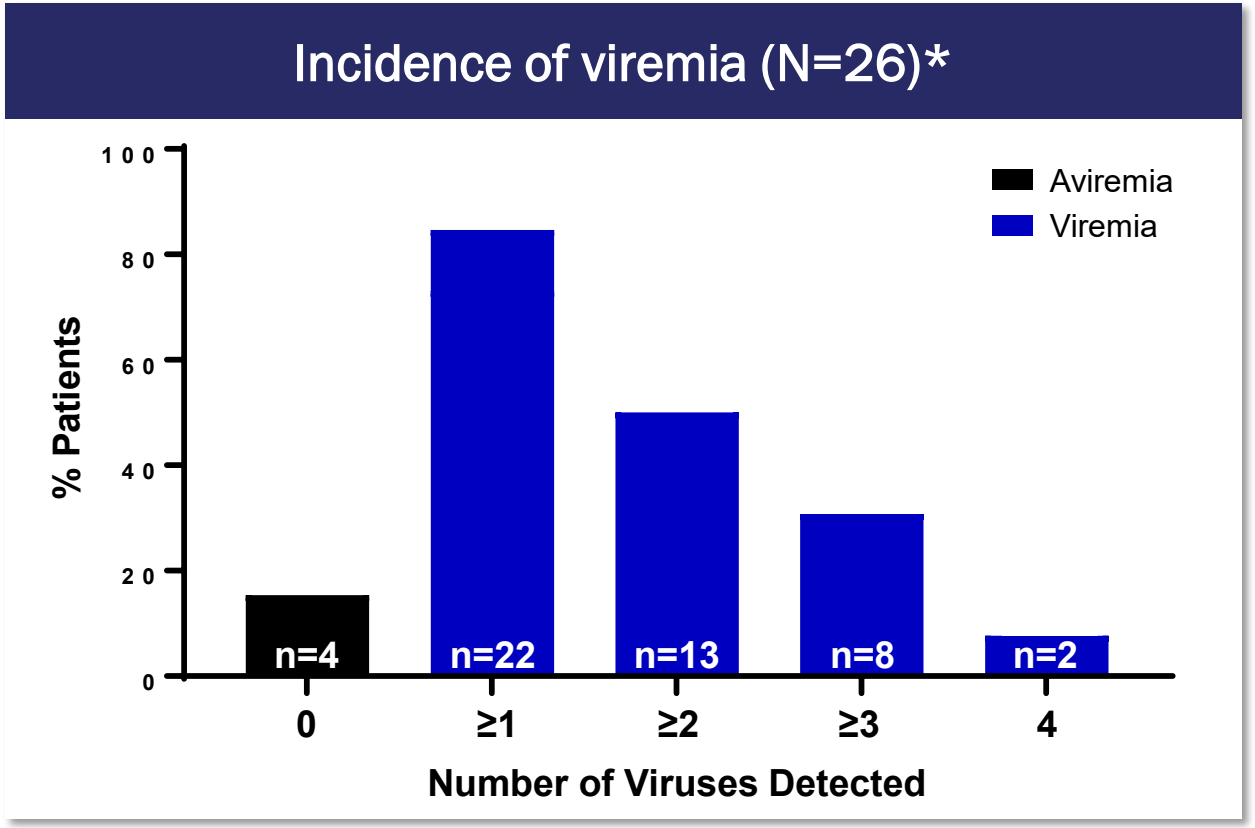
Safety and Tolerability

- 5/26 (19%) patients had grade II-IV acute GVHD
- All deaths related to relapse/progression of underlying disease (none treatment related)
- 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.

Expected Rates of Viral Reactivation through Week 14

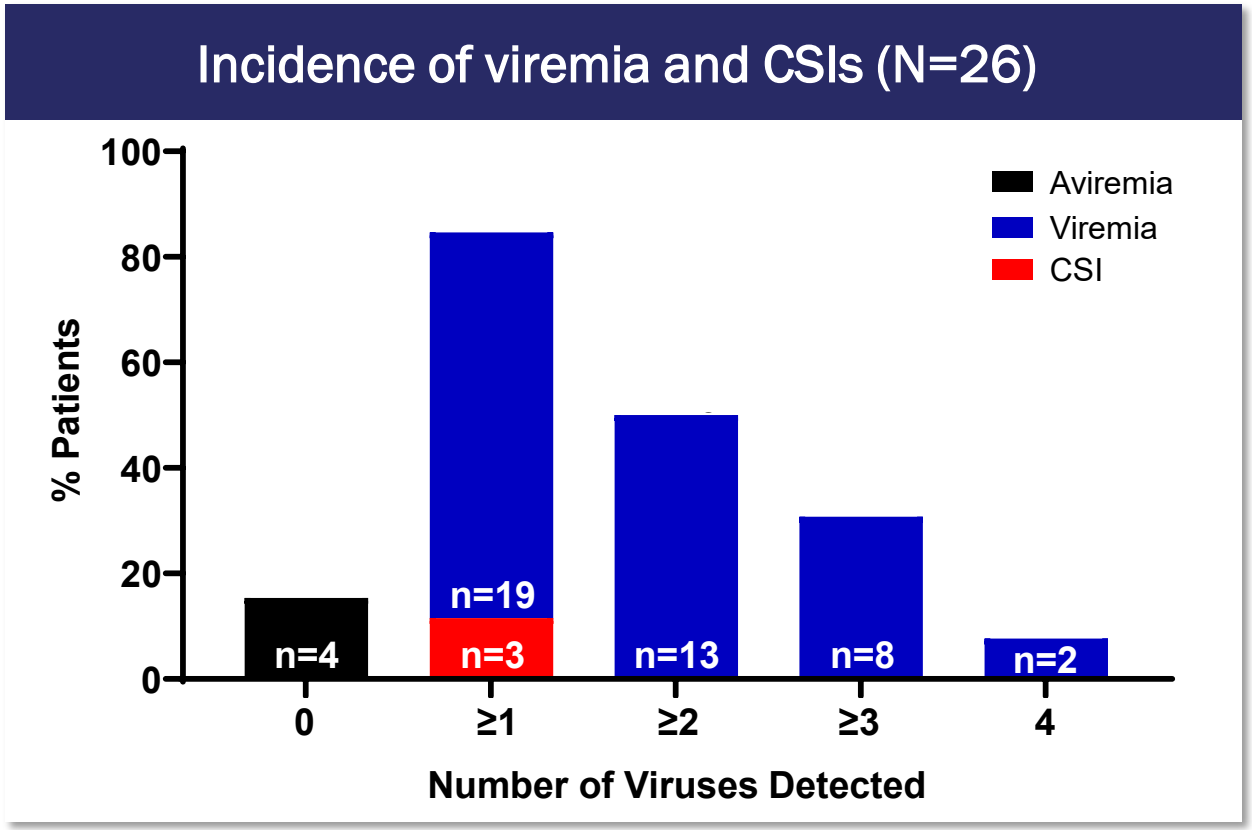


- 85% of patients reactivated ≥1 of posoleucel's target viruses through Week 14
  - Similar to previously published data in high-risk allo-HCT patients[1]
  - 10 of 14 patients (71%) who were aviremic at baseline reactivated during the study

*Viremia defined as viral load >LLOQ at one or more instance during the primary endpoint (Day 0 – Wk 14).

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

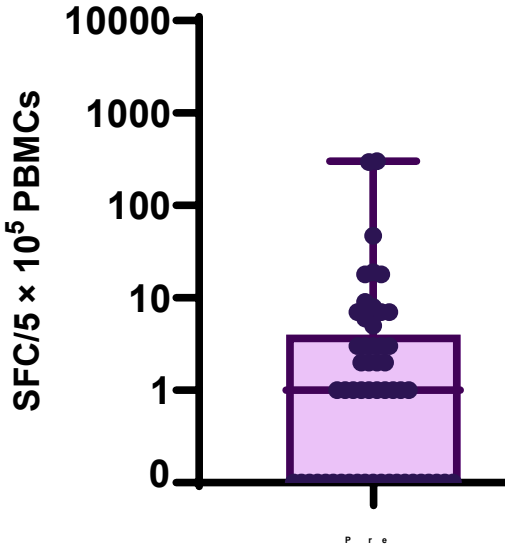
Low Rates of Clinically Significant Infections through Week 14 (Primary Endpoint)



- Despite high rates of viral reactivation, only 3 clinically significant infections were observed through Week 14 (2 CMV, 1 EBV)
- An additional 4 CSIs were observed between Week 14 and 26 (secondary endpoint)

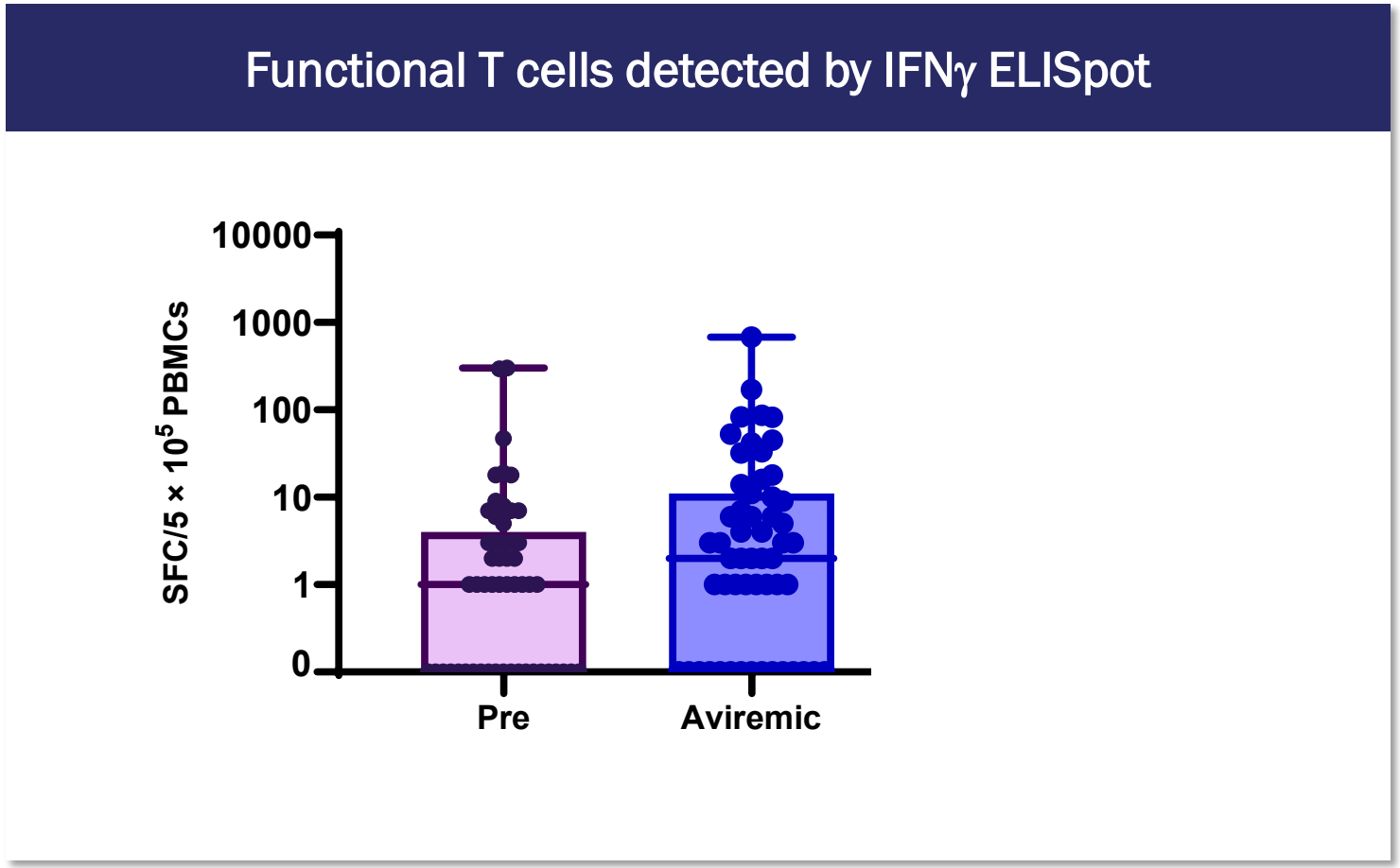
Frequency of IFNγ-producing Virus-Specific T Cells

Functional T cells detected by IFNγ ELISpot



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)

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)

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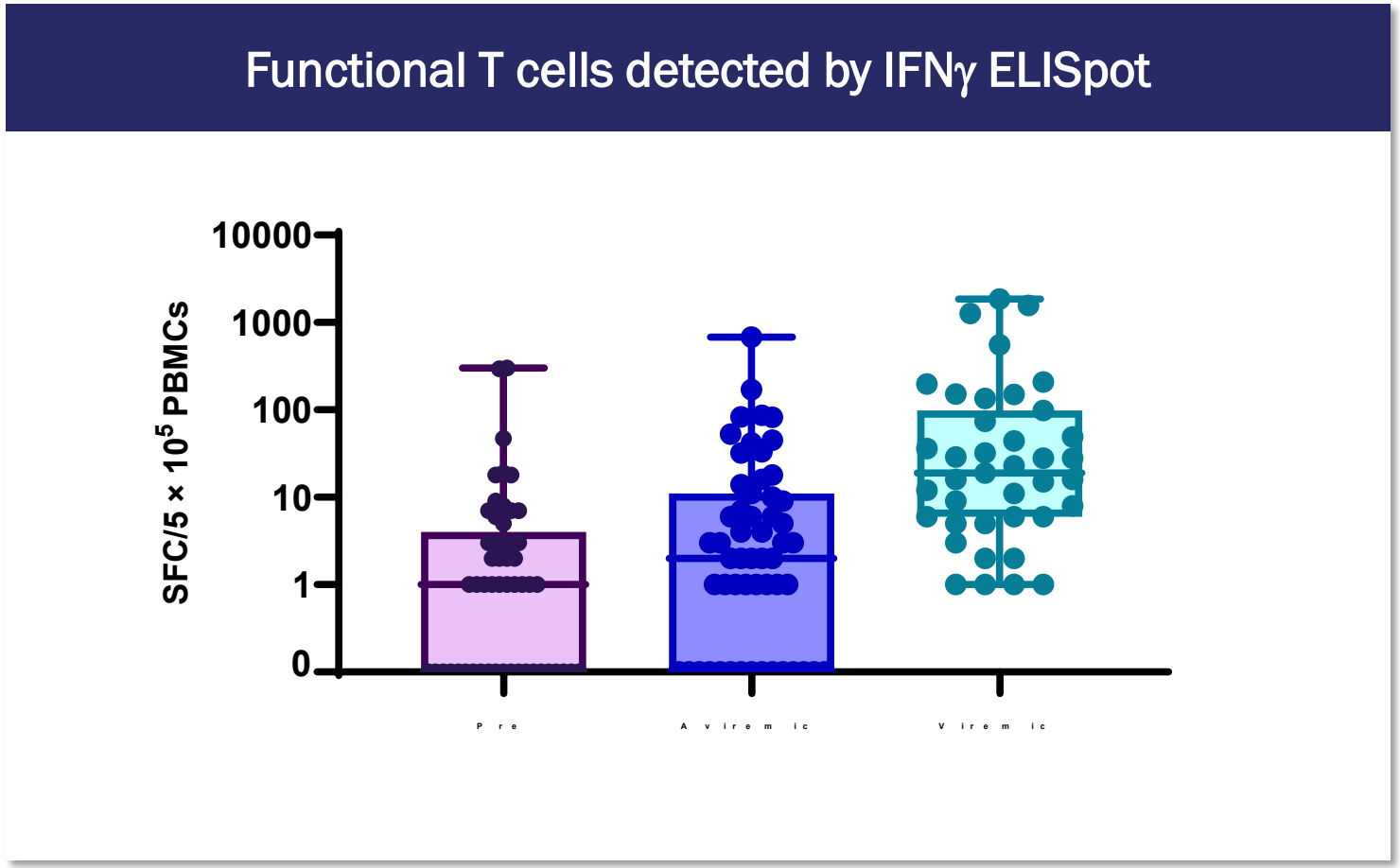
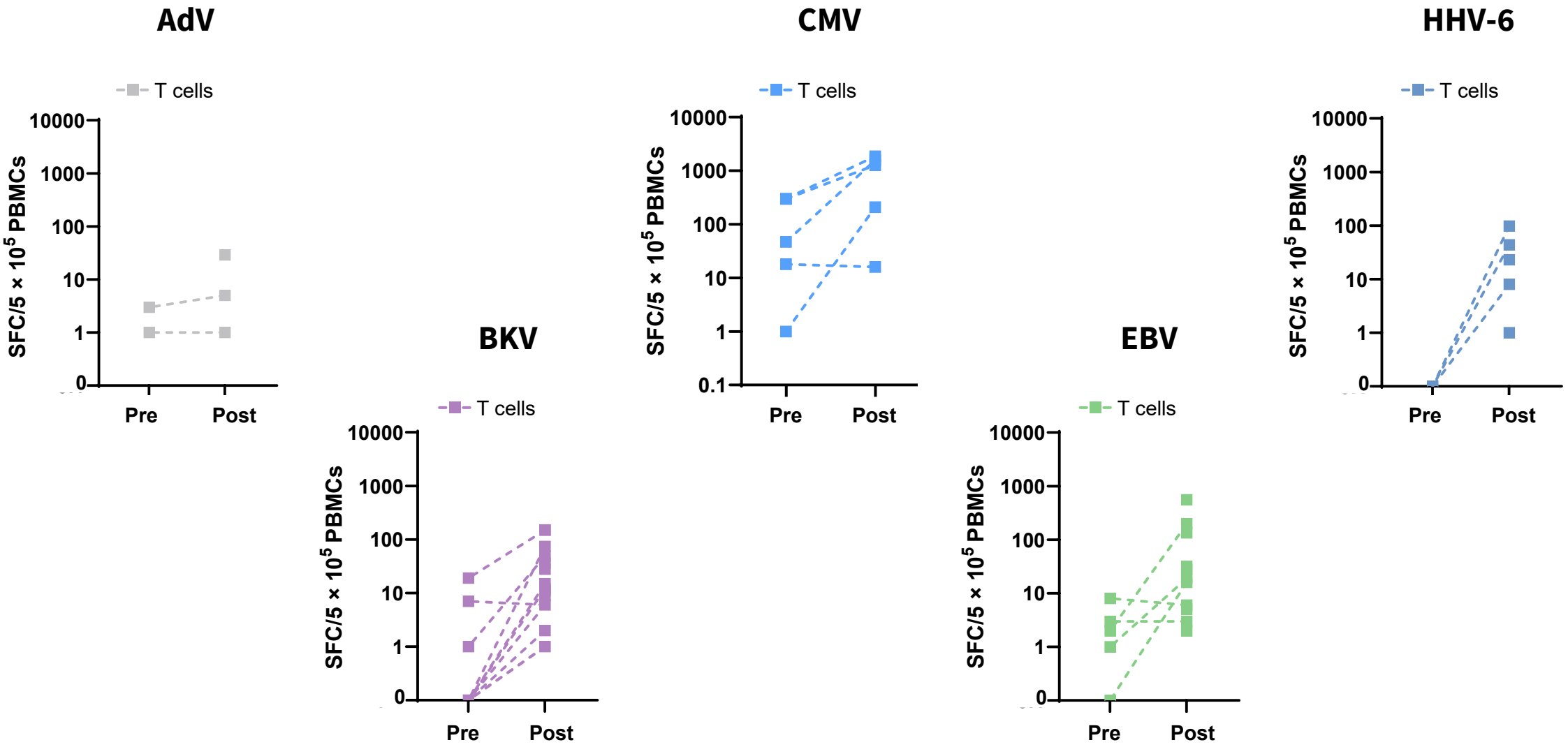


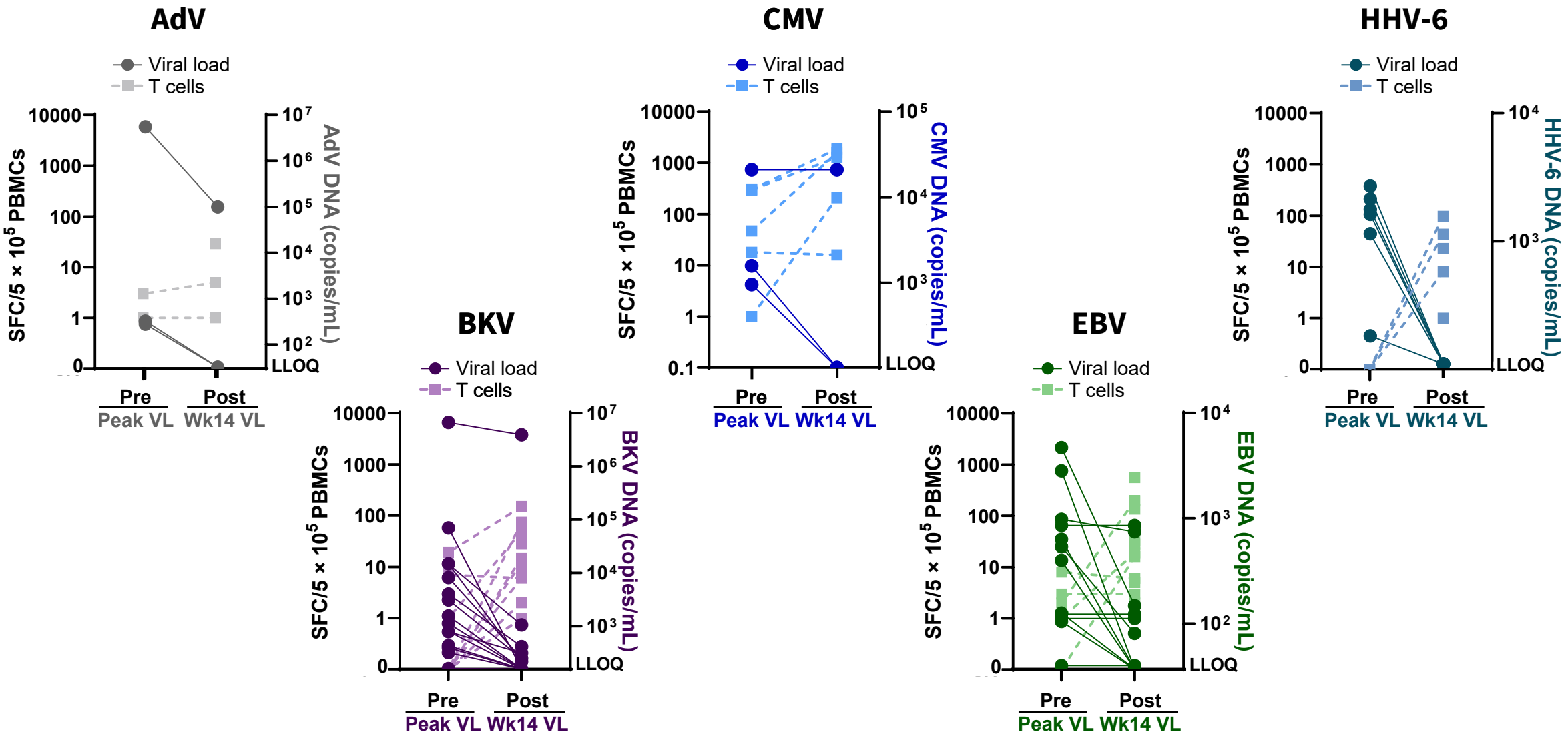
Aggregate ELISpot data shown for N=39/45 viremia (peak response on treatment Wk 1 – Wk 14), N=53 aviremia (peak response on treatment Wk 1 – Wk 14), and N=55 baseline (Pre, Day 0); ELISpot data shown includes three clinically significant infections.

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.

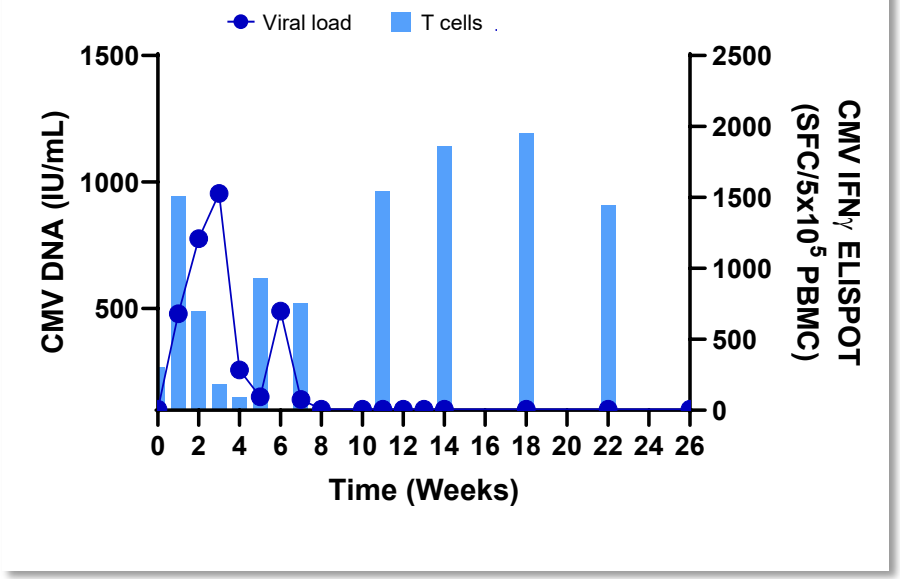
Increased Frequency of IFNγ-producing T Cells Was Associated with Reduction in Viremia



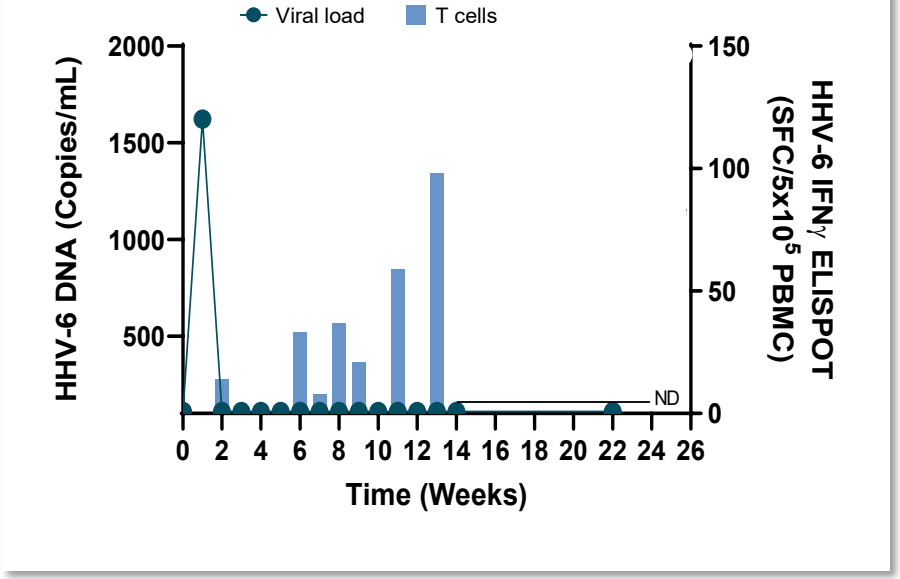
ELISpot data shown from patients with available samples at Pre (Day 0) and/or Post (peak response on treatment Wk 1 – Wk 14) timepoints. Viral load (VL) data shown as peak viral load during primary endpoint period (Pre, Day 0 – Wk 14) and viral load at primary endpoint (Post, Wk 14 or last available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

Expansion of Virus-Specific T Cells and Control of Viremia

T cell control of CMV



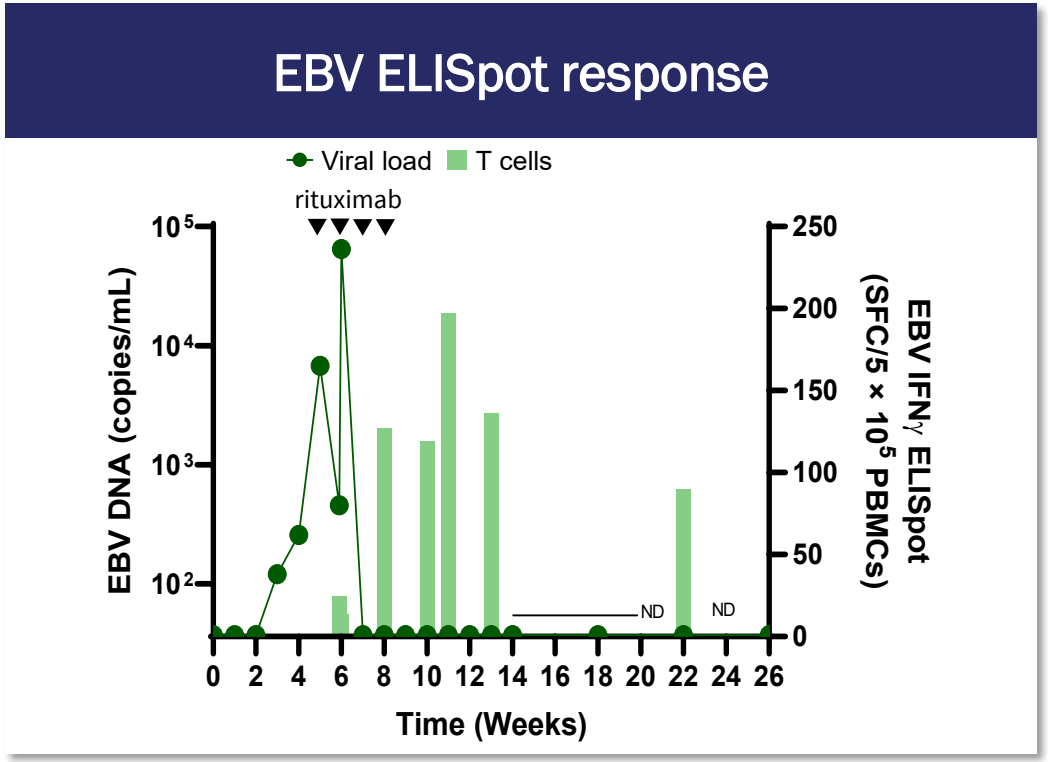
T cell control of HHV-6



ND, not determined (samples not available for ELISpot).

- Confirmed detection of posoleucel T cell receptor clones during viremia

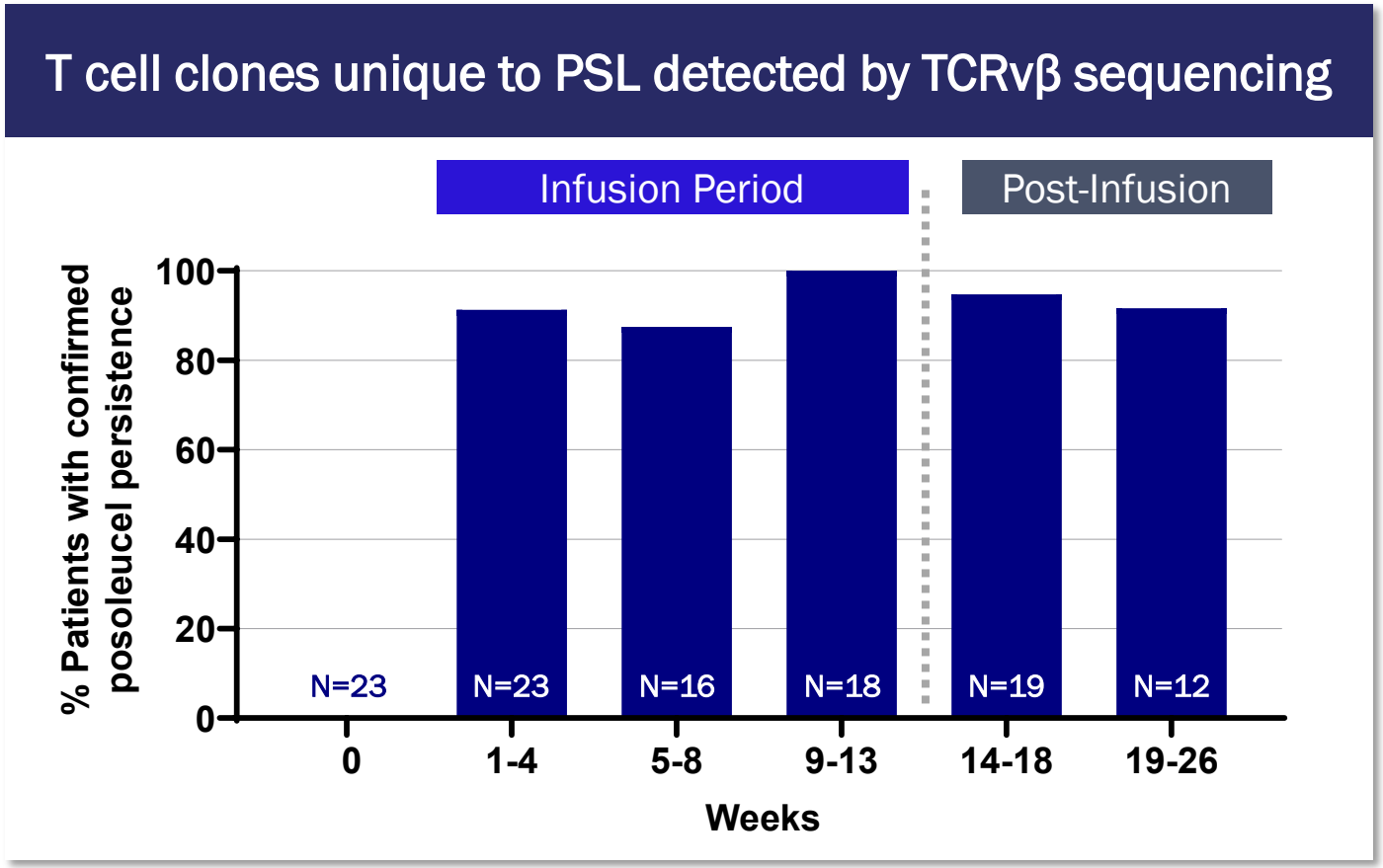
Expansion of Virus-Specific T Cells Observed in Patient with EBV CSI



ND, not determined (samples not available for ELISpot).

- 14-year-old female s/p haploidentical transplant; Treated with high-dose steroids (>2 mg/kg) for infusion reaction and acute GVHD at Weeks 4-8. Posoleucel administered at Weeks 0, 2, 4, 10, 12
- Reactivated EBV and developed post-transplant lymphoproliferative disorder (PTLD) at Week 5 in the setting of high-dose steroids; Received 4 doses of rituximab; PTLD resolved

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 PSL-derived clones (based on tracking TCRvβ sequences) shared by the PSL 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
- 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, Yovana Velazquez, Spyridoula Vasileiou, Ann Leen, Sarah Gilmore for their work on the biomarker analyses

- We extend our thanks to investigators, patients, and families

- This study was funded by AlloVir