Posoleucel as Preemptive Therapy for BKV Infection in Kidney Transplant Recipients: Safety and Tolerability in a Phase 2 Trial

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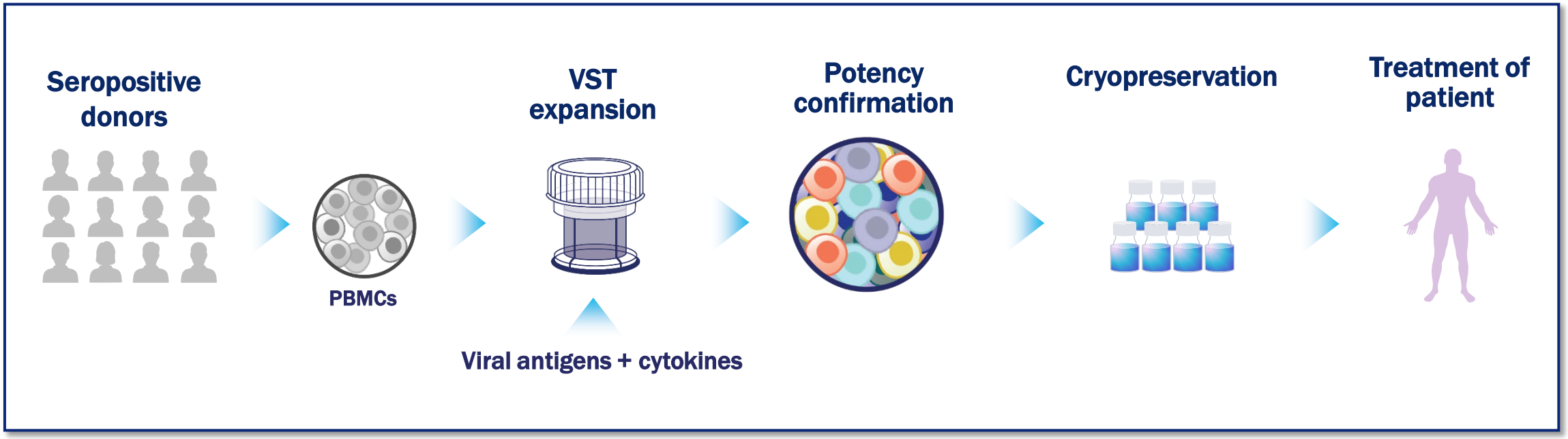
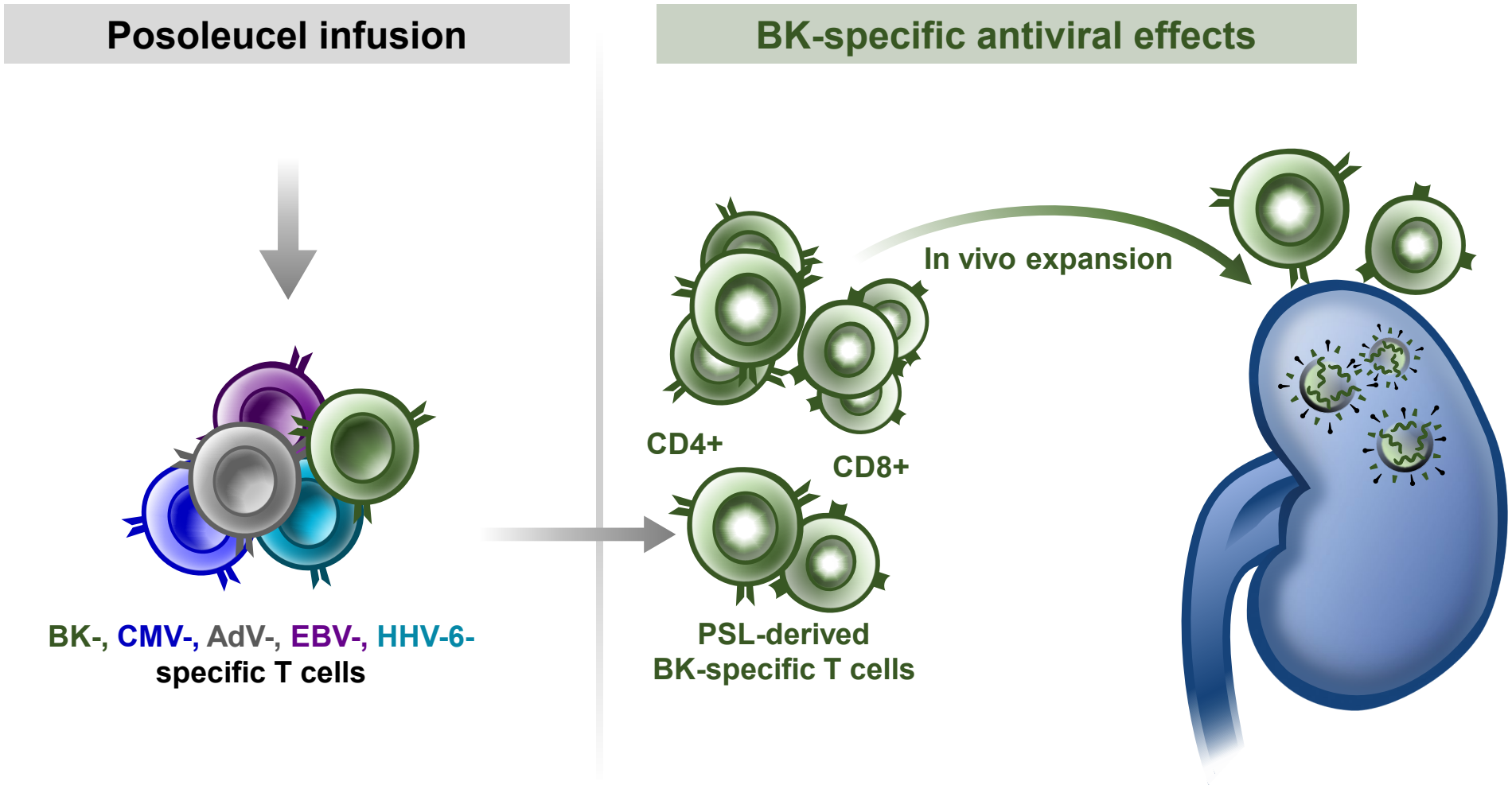
Posoleucel

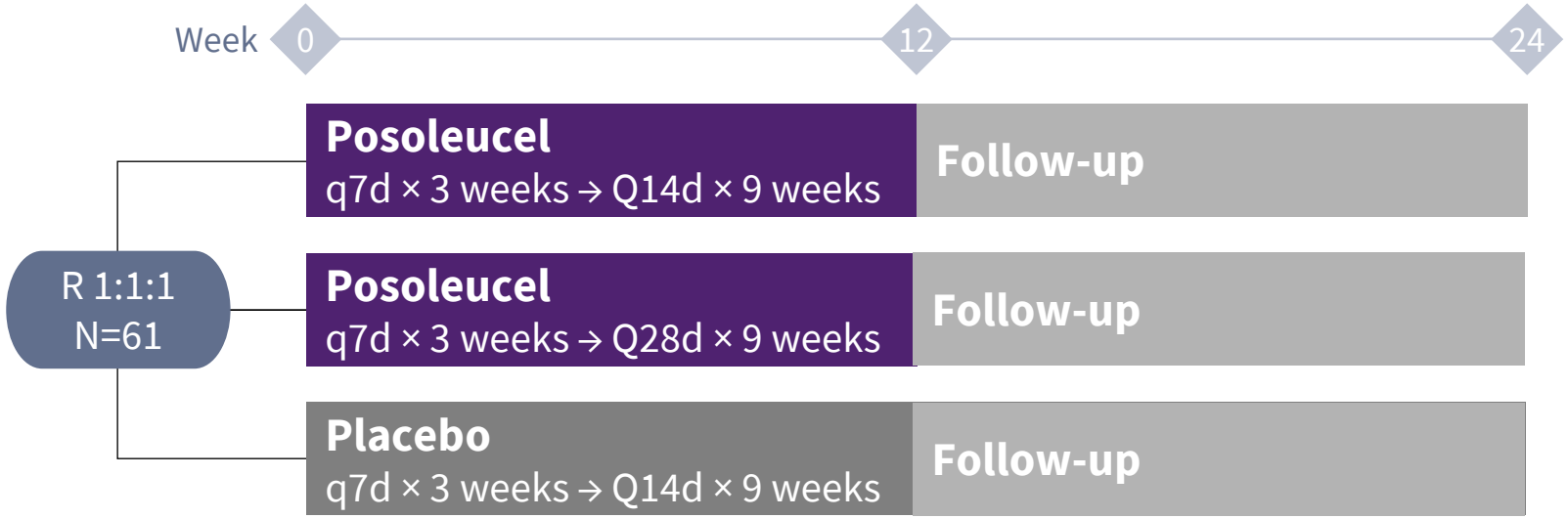
- Allogeneic, off-the-shelf, multivirus-specific T-cell (VST) therapy targeting AdV, BKV, CMV, EBV, HHV-6, and JCV
- The cell bank is rationally designed to ensure availability of partially HLA-matched VSTs to >95% patients



Posoleucel Mechanism of Action: BKV-Specific T Cells Expand in vivo and Eliminate Virus-Producing Cells



Posoleucel Phase 2: BKV Study Design



- Eligibility: adults with kidney transplant ≥28 days prior to enrollment
- Stratified by BK viral load (350 to <10,000 copies/mL and ≥10,000 copies/mL)
- 1° endpoint: safety and tolerability through Week 24
- Key 2° endpoint: reduction in BK viremia

ClinicalTrials.gov NCT04605484

Demographics and Baseline Characteristics

Patients	PSL (q14d + q28d) N=42	PBO N=19
Median age, years (range)	58 (21-75)	59 (47-75)
Female, n (%)	8 (19)	4 (21)
Latino or non-Caucasian, n (%)	24 (57)	10 (53)
Years from KT to day 1, median (range)	1.3 (0.3-7)	1.1 (0.2-14)
Median day 1 eGFR, mL/min/1.73 m^2 (range)	45.5 (19-61)	39 (20-61)
Median day 1 BK VL, cps/mL (range)	8,383 (242-5,421,939)	5,299 (327-7,837,086)
≥50% decrease in IS within 30d randomization, n (%)	2 (5%)	4 (21%)

Treatment groups well balanced except for rates of significant pre-randomization immunosuppression reduction

Safety Results

Patients, n (%)	PSL N=42	PBO N=19
Adverse events (AEs) related to study drug	9 (21)	5 (26)
Grade 3-4 AEs (all unrelated to study drug)[1]	5 (12)	1 (5)
Serious AEs related to study drug	0	0
Treatment D/C due to AEs[2]	1 (2)	0
Infusion reactions	1 (2)	1 (5)
GVHD	0	0
CRS	0	0
De novo donor-specific antibodies	3 (7)	1 (5)
Death	0	0

- 3 PSL patients (7%) had transplant rejection vs 0 in PBO; none related to treatment
  - 1 had rejection during screening
  - 1 had concurrent renal TB
  - 1 occurred 68 days after last dose; IS reduction before rejection
- eGFR remained overall stable

Posoleucel was generally safe and well tolerated

1. Grade 3-4 SAEs: enterococcal bacteremia, urosepsis, proteinuria/rejection. Grade 3 non-serious AEs: uveitis, gout, BKVAN. 2. One patient discontinued study treatment due to TB after 5 doses.

Antiviral Efficacy at Week 24 in Patients with Stable IS

	PSL q14d N=20	PSL q28d N=18	PBO N=14
Pts w/ BK VL decreased by ≥1 $\log_{10}$ BKV DNA copies/mL vs baseline, n (%)	10 (50)	5 (28)	2 (14)
BK VL reduction from baseline, median $\log_{10}$ BKV DNA copies/mL (min, max)	-0.9 (-2.1, 0.1)	-0.45 (-1.8, 0.5)	-0.15 (-2.1, 0.3)
BK VL ≥50% reduction, n (%)	17 (85)*	10 (56)	6 (43)
Change in eGFR^{+}, median mL/min/1.73 m^2 (min, max)	-2.5 (-11, 7)	0 (-16, 20)	0 (-21, 9)

Posoleucel antiviral response greater than placebo

Stable IS: <50% IS reduction w/ 30 (+/- 2) days prior to randomization (N=55); 2 patients lost to follow up, 1 patient withdrew consent
*p<0.05 vs PBO.

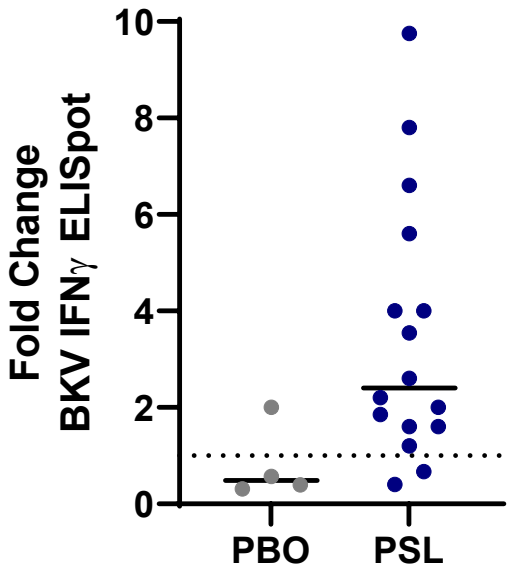
Antiviral Efficacy at Week 24 in Patients with Stable IS and BK VL ≥10,000 cps/mL

	PSL q14d N=8	PSL q28d N=8	PBO N=4
Pts w/ BK VL decreased by ≥1 log_{10} BKV DNA copies/mL vs baseline, n (%)	6 (75)	5 (63)	1 (25)
BKV VL reduction, median log_{10} BKV DNA copies/mL (min, max)	-1.4 (-2.1, 0.1)	-1.5 (-1.8, -0.2)	-0.4 (-2.1, -0.01)
BK VL ≥50% reduction, n (%)	7 (88)	7 (88)	2 (50)
Change in eGFR^{+}, median mL/min/1.73 m^2 (min, max)	-5 (-11, 6)	0 (-16, 9)	-7 (-21, 9)

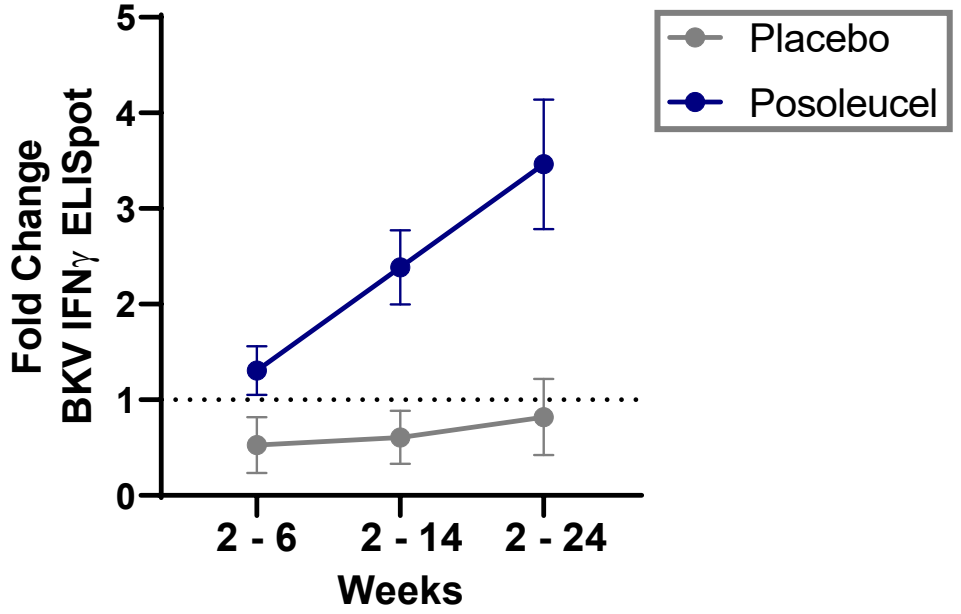
Posoleucel antiviral activity greatest in patients with high BK viral load

BK-specific T Cell Responses in Patients with Stable IS and BK VL ≥10,000 cps/mL

BKV IFNγ+ T cells



Change BKV IFNγ+ T cells over time



- PSL treated participants had greater increases of BKV IFNγ+ T cells versus PBO
- PSL treatment has a cumulative effect on BKV IFNγ+ T cells
- Presence and persistence of PSL confirmed by TCRvβ deep sequencing, with higher levels detected in the high VL group

Peak ELISpot response plotted through Wk 24 (left) or Wk 2-6, 2-14, or 2-24 (right). Data plotted as fold change from pre-dose with minimum of 5 SFC.

Conclusions

- Posoleucel was generally safe and well-tolerated
  - Safety profile consistent with that observed in stem cell transplant recipients
- Posoleucel demonstrated clinically meaningful antiviral efficacy in kidney transplant patients with BK viremia, for whom there are no currently approved therapies
  - BK VL reduction was greatest in patients with higher VLs and with more frequent posoleucel dosing
  - BK VL reduction was associated with an increase in the circulating frequency of BKV IFNγ+ T cells
- These data support advancing posoleucel for the treatment of BK viremia in kidney transplant patients