Administration of Posoleucel

ICD-10 Coordination & Maintenance Committee Meeting
March 2023

Posoleucel is an Investigative T Cell Immunotherapy

T Cell Immunotherapy

- Posoleucel is an investigational polyclonal multi virus-specific T cell (VST) product that recognizes and eradicates actively replicating virus-infected cells
- The cells are derived from peripheral blood mononuclear cells (PBMCs) from seropositive donors
- Rationally designed cell bank, facilitating availability of VSTs covering >95% of patients
- Posoleucel provides an immunologic bridge until patients restore their natural immunity post allogeneic hematopoietic stem cell transplant

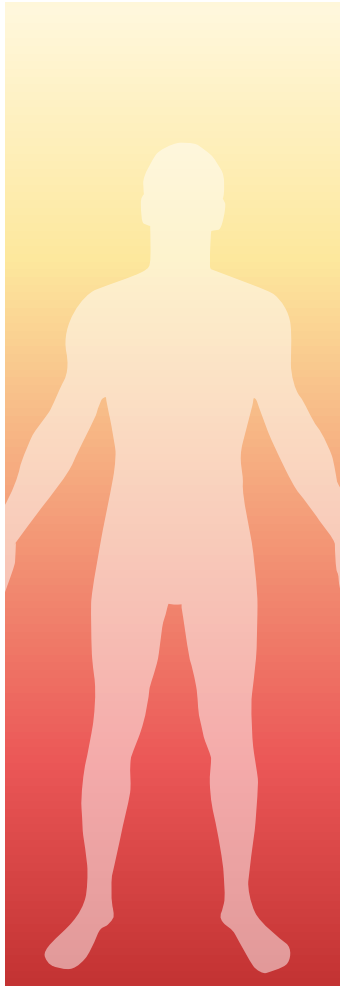
Administration

- Posoleucel will be administered in the inpatient or outpatient place of service depending on the patient's status
- Place of Service Doses administered in the ongoing Phase 3 pivotal trial for virus associated Hemorrhagic Cystitis (vHC):
  - 62% inpatient; 38% outpatient
- Posoleucel is administered for vHC as a course of two infusions separated by approximately 14 days
  - Dose is weight based
  - $2x10^7$ (<40 kg) or $4x10^7$ (≥40 kg) cells
- Intravenous 5-minute push infusion; 1 hour monitoring

FDA and NTAP Status

- FDA:
  - Posoleucel is being investigated in three Phase 3 trials for 3 indications
  - AlloVir plans on submitting a BLA for posoleucel following an analysis of the Phase 3 data.
  - Posoleucel has been granted RMAT designation
- NTAP:
  - There are no current NTAP applications for posoleucel
  - AlloVir plans on applying for an NTAP in conjunction with a potential FDA approval

AlloVir's Therapies Aim to Treat or Prevent Life-Threatening Viral Diseases For Immunocompromised Patients[1-13]



Vulnerable Populations

Single and multiple viral infections are common in the immunocompromised:

- HCT & SOT recipients
- The elderly & the very young
- Patients on chemotherapy or immunomodulators

Limited or No Treatment Options

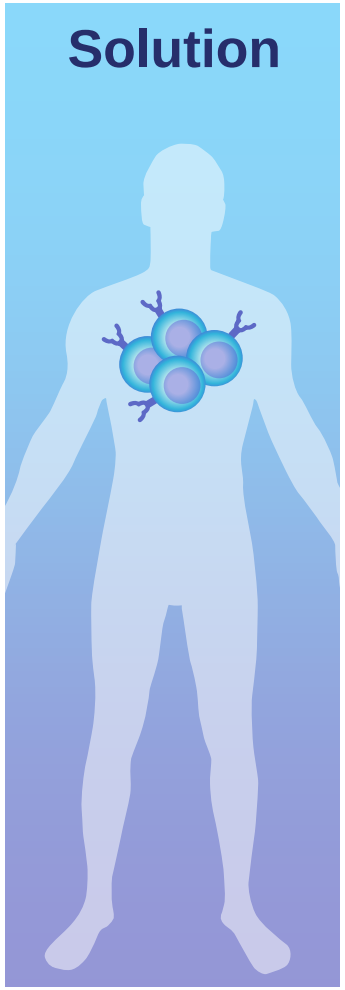
Therapeutic options raise concerns about:

- Lack of efficacy for off-label treatments
- Significant toxicity
- Emergence of resistance

Substantial Morbidity & Mortality

Uncontrolled viral diseases can:

- Prolong hospitalization
- Increase risk for GVHD or graft rejection
- Cause end-organ damage
- Result in death



Immunity Restored with VSTs

VSTs are a clinically validated approach to restoring protective T-cell immunity

AlloVir's VSTs:

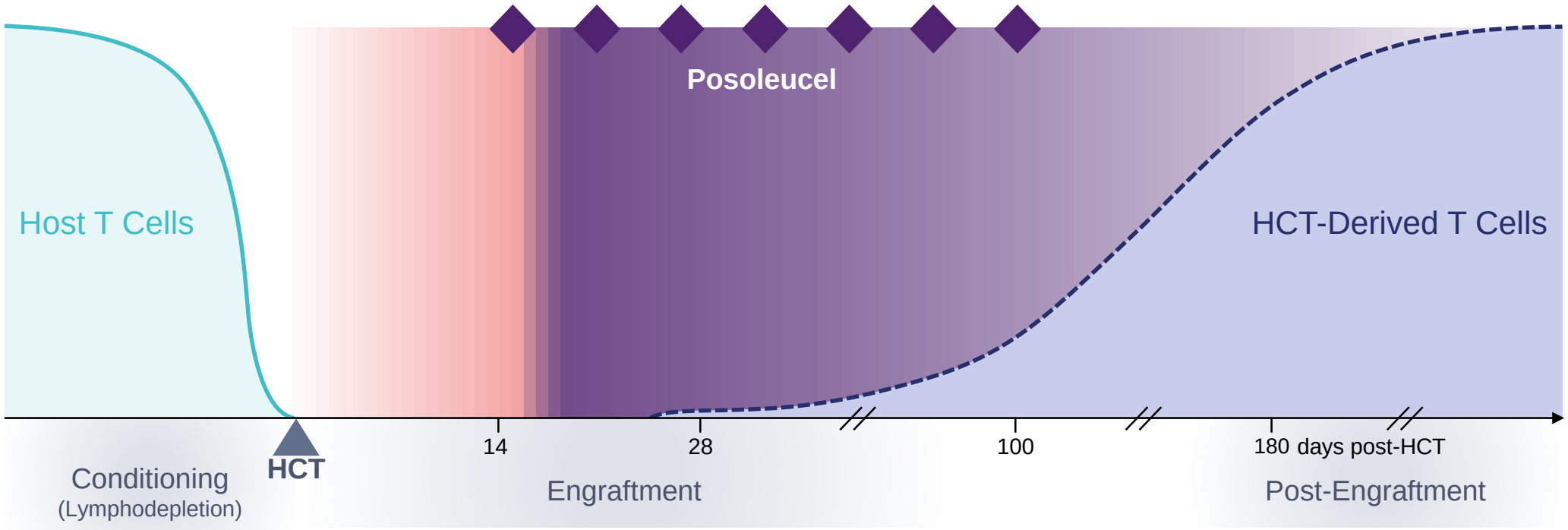
- **Address the underlying immune deficit in high-risk patient populations**
- **Target multiple viruses with limited to no treatment options**
- **Offer off-the-shelf delivery to reach patients quickly**

GVHD = graft vs host disease; SOT = solid organ transplant. 1. Abudayyeh A, et al. *Am J Transplant.* 2016;16:1492-1502; 2. Camargo JF, Komarduri KV. *Hematol Oncol Stem Cell Ther.* 2017;10:233-238; 3. Cesaro S, et al. *Bone Marrow Transplant.* 2018;doi:10.1038/s41409-018-0421-0; 4. Leen AM, et al. *Blood.* 2009;114(19):4283-4292; 5. Perruccio K, et al. *Biol Blood Marrow Transplant.* 2018;24:2549-2557; 6. Saribas AS, et al. Future Virol. 2010;5(3):313-323. doi:10.2217/fvl.10.12; 7. Cho SY, et al. *Kor J Intern Med.* 2018;33:256-276; 8. Law N, Kumar D. *Drugs Aging.* 2017;34:743-754; 9. Gentile G, Antonelli G. *Viruses.* 2019;11:doi:10.3390/v11111049; 10. Kedia S, et al. *J Stem Cell Res Ther.* 2013;doi:10.4172/2157-7633.S3-002; 11. Ison MG, Hirsch HH. *Clin Microbiol Rev.* 2019;32(4):1-33; 12. Jose RJ, et al. *Medicine. 2020.* doi:10.1016/j.mpmed.2020.03.006; 13. Simon AK, Hollander GA, McMichael A. *Proc Biol Sci.* 2015;282(1821):20143085.

Posoleucel Aims to Treat and Prevent Viral Infections and Diseases Until the Patient's Immune System Recovers[1-6]

In the Highest-Risk Window of Susceptibility to Viral Infections Post-Allo-HCT,

VSTs expand in the presence of viral antigens, migrate to the site of infection, kill virus-infected cells and contract after the virus is controlled



a Post 100-day data for proportion of patients with viral detection is from Huang YT, et al, as Hill J, et al only measured out to 100 days.

1. Kedia S, et al. J Stem Cell Res Ther 2013;S3; 2. Ison M, Hirsch H. Clin Microbiol Rev 2019;32:e00042-19; 3. Hill J, et al. Blood 2017;129:2316-25; 4. Huang YT, et al. Biol Blood Marrow Trans 2017;23:1759-66; 5. Stern L, et al. Front Immunol 2018;9:1672; 6. Hill J, et al. Clin Infect Dis 2018;66:368-75.

Our Patented and Highly Efficient Platform Delivers Rapid, Scalable, Off-the-Shelf VST Therapy[1]

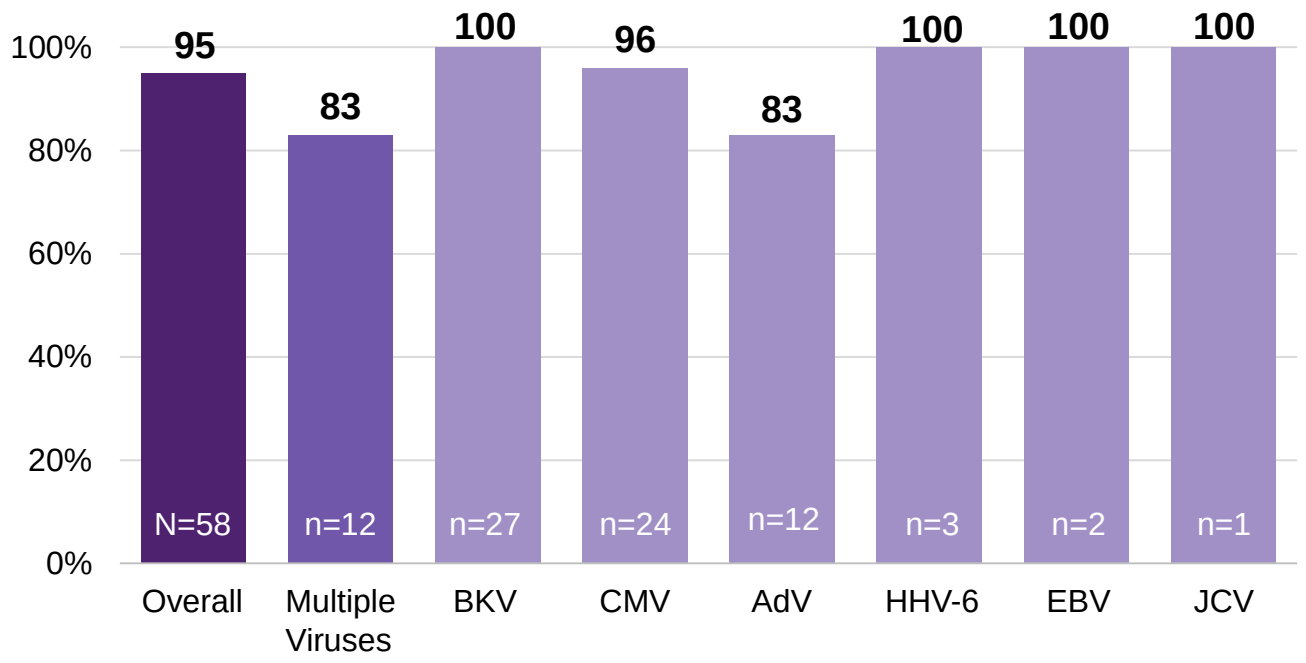
Key Advantages

- Rationally designed cell bank, facilitating availability of VSTs covering >95% of patients
- Our VST platform minimizes antigen competition, enabling retention of VST diversity and polyclonality
- VST potency confirmed against individual target viruses using functional assay
- Simple and robust manufacturing yields hundreds of VST doses from a single donor/production run
- Our VSTs have long-term stability, supporting on-demand, broad availability for patients

1 **https://www.allovir.com/**

Phase 2 CHARMS Treatment Study Demonstrated 95% Efficacy of Posoleucel in Treatment-Refractory Patients[1]

Efficacy: Posoleucel Response Rate*



CR = Viral load return to normal range and resolution of clinical signs/symptoms
PR = ≥50% decrease in viral load and/or 50% improvement of clinical signs/symptoms

Safety: Posoleucel Well Tolerated

- Infusions were well tolerated
  - n=7 developed isolated fever within 24 hours of infusion; no immediate toxicities observed
- 13 cases of acute GVHD
  - n=9 had pre-existing GVHD
  - n=4 *de novo* GVHD; all had transient Grade I skin GVHD resolved with treatment
- No cytokine release syndrome

*Response rate / patient includes partial response (PR) or complete response (CR) by 6 weeks post-posoleucel infusion.

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

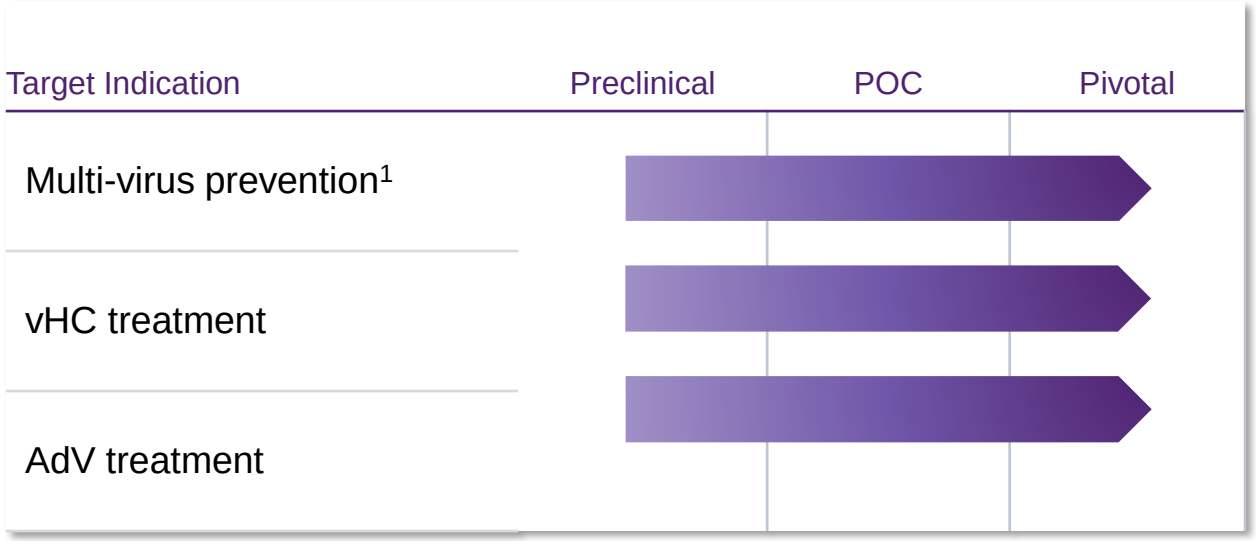
Safety and Tolerability – Phase 2 CHARMS Study[1]

Patients with events in safety reporting period, n (%)	N=58
Patients with any treatment-emergent adverse event (AE)	58 (100)
Patients with treatment-related AEs	25 (43)
Common treatment-related AEs	
Pyrexia	7 (12)
AST increased	5 (9)
Maculopapular rash	5 (9)
Treatment-related SAEs	4 (7)
Any treatment-related grade ≥3 TEAE, n (%)	8 (14)
AE leading to dose reduction, interruption, or discontinuation	0
Cytokine release syndrome	0
Deaths (none related to study treatment)	5 (9)

*Four patients experienced 7 treatment-related SAEs: pyrexia, pneumonia, atelectasis, pulmonary edema, acute GVHD (GI), adenovirus infection, neurological decompensation.

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

Posoleucel is in Phase 3 Development for Three Distinct Indications for the Allogeneic Hematopoietic Cell Transplant Population



1. Prevention of clinically significant infections and end-organ disease caused by AdV, BKV, CMV, EBV, HHV-6 and JCV.

Virus-Associated Hemorrhagic Cystitis (vHC) in allo-HCT: A Devastating Disease With No Approved or Effective Treatment Options

vHC results in severe morbidity & mortality[1-7]		There are no approved or effective therapies[1-7]
Severe bleeding due to hematuria		Red blood cell or platelet transfusions Bladder arterial embolization and/or cystectomy
Severe, prolonged and intractable pain		Narcotics
Life-disturbing urinary symptoms		Continuous bladder irrigation
Kidney dysfunction / failure		Dialysis
Increased mortality		

1. Cesaro S, et al. *J Antimicrob Chemother* 2018;73:12-21; 2. Garguilo G, et al, *ecancer* 2014;8:420; 3. Silva Lde P, et al. *Haematologica* 2010;95:1183-90; 4. Kloos RQ, et al. *Biol Blood Marrow Transplant* 2013;19:1263-6; 5. Type B Briefing Package; 6. Laskin BL, et al. *Clin Infect Dis* 2020;71:3044-54; 7. Gilis L, et al. *Bone Marrow Transplant* 2014;49:664-70.

There is an unmet medical need for patients who develop vHC post allo-HCT

- In 2019, CIBMTR reported 9391 allo-HCTs in the US[1]
  - Healthcare Cost and Utilization Project (HCUP) 2018 data reports 19% of allo-HCT recipients were Medicare beneficiaries[2]
- BK virus is by far the most common cause of vHC.[3] Additional viruses, such as adenovirus, JC virus, cytomegalovirus, and human herpesvirus 6 can also cause v-HC, but less commonly.[3-5]
- A wide range of incidence of BK-HC has been reported:
  - BK-HC has been estimated to occur in 8-25% and 7-54% of pediatric and adult patients, respectively.[3]
  - In a systematic literature review conducted to support AlloVir's US orphan drug application, based on the 14 highest quality studies reflecting a US population, the incidence of BK-HC ranged from 5 to 30.8%.[6]
- The incidence of AdV-HC has been estimated as 0.1% and 2.2%[5,7] and of CMV-HC and HHV-6-HC as 0.9% and 0.3%, respectively.[5]
- Approximately half of patients who develop vHC have Grade ≥3 hematuria (macroscopic hematuria with visible clots).[5,8-11]
- Estimated number of treatable cases of v-HC in the US (2019): 295-1605[12] Potential Medicare patients = 56 - 305[13]

1. 2020 CIBMTR
2. HCUP.net 2018
3. Cesaro S, et al. ECIL guidelines for the prevention, diagnosis and treatment of BK polyomavirus-associated haemorrhagic cystitis in haematopoietic stem cell transplant recipients. J Antimicrob Chemother. 2018;73(1):12-21.
4. Kim YJ, et al. Human herpesvirus-6 as a possible cause of encephalitis and hemorrhagic cystitis after allogeneic hematopoietic stem cell transplantation. Leukemia. 2002;16(5):958-9. .
5. Lunde LE, et al. Hemorrhagic cystitis after allogeneic hematopoietic cell transplantation: risk factors, graft source and survival. Bone Marrow Transplant. 2015;50(11):1432-7.
6. Incidence of Virus-Associated Hemorrhagic cystitis (v-HC) in the US: a Systematic Literature 5. Review. Prepared by ICON Clinical Research Ltd. 29 Sep 2021.
7. Hayden RT, et al. Risk factors for hemorrhagic cystitis in pediatric allogeneic hematopoietic stem cell transplant recipients. Transpl Infect Dis. 2015;17(2):234-41.
8. Imlay H, et al. Presentation of BK polyomavirus-associated hemorrhagic cystitis after allogeneic hematopoietic cell transplantation. Blood Adv. 2020;4(4):617-628
9. Gilis L, et al. High burden of BK virus-associated hemorrhagic cystitis in patients undergoing allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant. 2014;49(5):664-70.
10. Ruderfer D, et al. BK virus epidemiology, risk factors, and clinical outcomes: an analysis of hematopoietic stem cell transplant patients at Texas Children's Hospital. J Pediatric Infect Dis Soc. 2021;10(4):492-501.
11. Nelson AS, et al. Virus-specific T-cell therapy to treat BK polyomavirus infection in bone marrow and solid organ transplant recipients. Blood Adv. 2020;4(22):5745-5754.
12. 295 = 9391 x 50% x (5%+0,1%+0,9%+0,3%) ; 1605 = 9391 x 50% x (30,8%+2,2%+0,9%+0,3%)
13. HCUP 2018; Medicare payer mix for allogeneic hematopoietic stem cell transplant – 19%

vHC is Evaluated On a Graded Scale

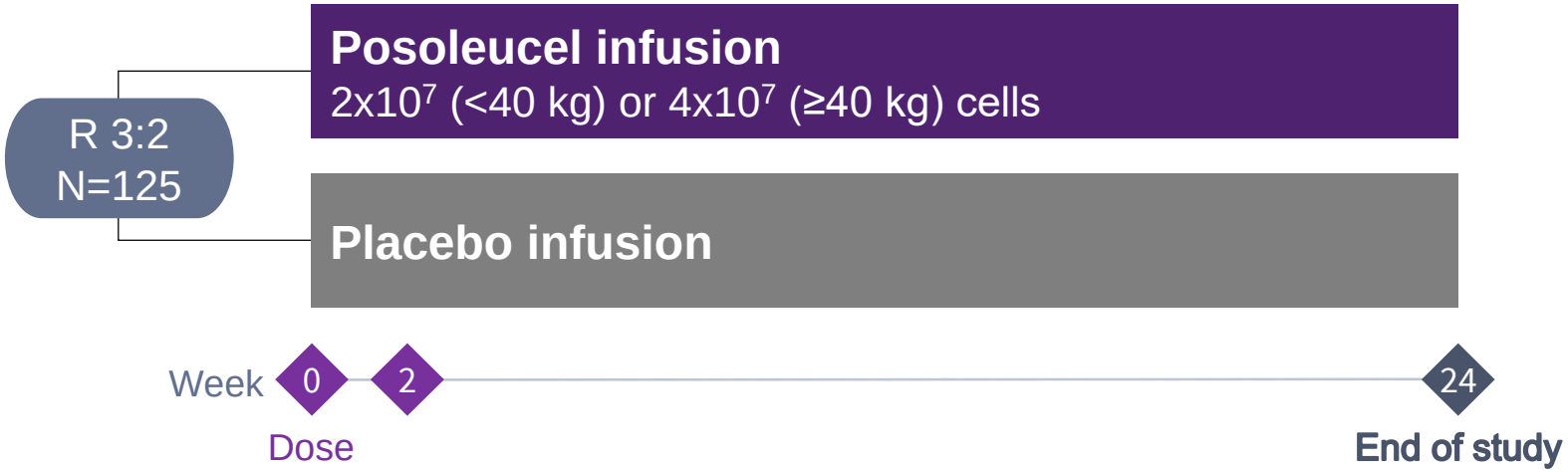
vHC Grade Description (adapted from Bedi, et al[1]):

- **Grade 0:** No hematuria; urine appears clear or yellow (ie, non-bloody) on visual assessment; urinalysis is negative for blood.
- **Grade 1:** Microscopic hematuria; urine appears clear on visual assessment, but urinalysis is positive for blood and urine microscopy shows ≤100 RBCs/HPF.
- **Grade 2:**
  - Macroscopic hematuria but no clots on visual assessment

    OR
  - Microscopic hematuria: urine appears clear on visual assessment, but urinalysis is positive for blood and urine microscopy shows >100 RBCs/HPF.
- **Grade 3:** Macroscopic hematuria with evidence of visible clots
- **Grade 4:** Same as Grade 3 with HC-associated renal impairment (new onset elevation of creatinine to ≥1.5 × ULN and considered by the Investigator to be HC-related) or transfusion requirements secondary to hematuria (packed RBCs and/or platelets).

1. Bedi A, et al. Association of BK virus with failure of prophylaxis against hemorrhagic cystitis following bone marrow transplantation. J Clin Oncol. 1995 May;13(5):1103-9.

Phase 3 Registrational Trial for Treatment of Virus-Associated Hemorrhagic Cystitis Is Enrolling Patients in the U.S., Europe and Asia



- Phase 3, multicenter, double-blind, placebo-controlled
- Key eligibility criteria: patients with vHC following allo-HCT
  - Clinical signs and/or symptoms of cystitis
  - Macroscopic hematuria with visible clots (Grade ≥3)
  - Viruria with BK virus or another posoleucel target virus
- Primary endpoint: time to resolution of macroscopic hematuria

ClinicalTrials.gov NCT04390113.

Documentation of the Administration of Posoleucel

- **How will posoleucel utilization be tracked?**
  - Posoleucel would be captured in common documentation methods for providers (medical records, physician notes, revenue codes, pharmacy and chargemaster files, etc.)