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

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

- Mortality directly correlates with viral burden: each 10-fold increase in viral burden translates to a nearly 40% increase in overall mortality\(^1\)

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

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

- T cells
- Viral load
- CSI and/or end organ disease (EOD)
- Donor immune reconstitution
- HCT
- Viremia

Time
Virologic and Immunologic Landscape post Allo-HCT (with Posoleucel)
Phase 2 Prevention Study Design

High-risk allo-HCT patients (cord donor, haplo donor, MMRD, MMUD, T-cell depletion, MUD with persistent lymphopenia <180/mm³) → Posoleucel Every 14 days for 7 doses → 12 weeks follow-up → 52 weeks Post-study visit

Baseline First posoleucel infusion
Week 14 Primary endpoint

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

37 patients screened

26 patients dosed

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

Posoleucel administered a median of 43 days (range 24-53) post allo-HCT

16 patients completed treatment
14 received all 7 doses

10 patients discontinued treatment early
Median 4 (range 1-6) doses completed

- 3 relapse/progression
- 3 GVHD
- 2 return to home state
- 2 pt choice due to unrelated complications (UTI, C. diff.)
## Demographic and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N=26</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, median years (range)</strong></td>
<td>60 (14-76)</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
<td>12 (46)</td>
</tr>
<tr>
<td><strong>Non-Caucasian or Latino, n (%)</strong></td>
<td>12 (46)</td>
</tr>
<tr>
<td><strong>Diagnosis, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>17 (65)</td>
</tr>
<tr>
<td>Myelodysplasia/Myeloproliferative</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Sickle cell anemia</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Other*</td>
<td>2 (8)</td>
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<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N=26</th>
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</thead>
<tbody>
<tr>
<td><strong>Donor type, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Haploidentical</td>
<td>12 (46)</td>
</tr>
<tr>
<td>Mismatched unrelated</td>
<td>9 (35)</td>
</tr>
<tr>
<td>Matched unrelated†</td>
<td>4 (15)</td>
</tr>
<tr>
<td>Umbilical cord blood</td>
<td>1 (4)</td>
</tr>
<tr>
<td><strong>Myeloablative conditioning, n (%)</strong></td>
<td>12 (46)</td>
</tr>
<tr>
<td>PTCy, n (%)</td>
<td>20 (77)</td>
</tr>
<tr>
<td>Letermovir use at baseline, n (%)</td>
<td>16 (62)</td>
</tr>
<tr>
<td>Viremia at baseline, n (%)‡</td>
<td>12 (46)</td>
</tr>
</tbody>
</table>

*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

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

*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\(^1\)-\(^3\)

Frequency of TNF-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

- 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

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

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