Autologous Epstein-Barr Virus (EBV)-Specific T Cells (Baltaleucel-T): Preliminary Results from a Multicenter, Multinational Phase 2 Study for Treatment of EBV-Associated NKT Cell Lymphoma

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Key Messages

- Patients with advanced Epstein-Barr virus (EBV) associated NKT lymphoma (NKT-L) have limited treatment options.
- We conducted a phase 2 study in patients with advanced NKT-L using autologous EBV-specific T cells (Baltaleucel-T, CMD-003).
- Baltaleucel-T was safe and did not cause cytokine release syndrome (CRS) or neurotoxicity.
- Baltaleucel-T has the potential to induce remissions in patients with advanced EBV+ NKT-L.

Methods

The study was conducted at sites in France, South Korea, the UK and the US. Baltaleucel-T was manufactured at the time of relapse or at any time in high risk patients. To prepare the product, 200 mL of whole blood was collected from the patient and the product was manufactured at a central facility from peripheral blood mononuclear cells using EBV peptide stimulation (LMP-1, LMP-2, EBNA1 and BARF1) in the presence of antigen presenting cells and cytokines (IL-4, IL-7 and IL-15) to yield ex-vivo expanded EBV-specific T cells. The manufacturing time was 25 days; "vein-to-vein" time was 40 days to deliver the product.

Key Patient Selection Criteria

- Key Inclusion Criteria for Whole Blood Collection
  - Diagnosis of extranodal NKT-L per WHO (lymphoma required to be EBV+ by EBV assay)
  - Active Disease: Clinically suspected or documented relapse/progression following an EBV peptide-based chemotherapy
  - High-risk disease (regardless of chemotherapy status and disease relapse/progression).
- Key Inclusion Criteria for Baltaleucel-T Infusion
  - All criteria for whole blood collection plus documented active disease (based on imaging, elevated EBV level or clinical signs/symptoms)

Key Exclusion Criteria for Whole Blood Collection

- Known CNS lymphoma
- NKT-Lymphoma
- Any prior allogeneic hematopoietic stem cell transplant
- Asparaginase refractory disease
- Third or greater relapse

Key Exclusion Criteria for Baltaleucel-T Infusion

- Failure to meet selection criteria for Baltaleucel-T infusion (primarily no active disease)
- Previous course of autologous T-cell therapy
- All criteria for whole blood collection plus documented active disease (based on imaging, elevated EBV level or clinical signs/symptoms)

Efficacy Summary

- 15 patients with active disease were infused with Baltaleucel-T
- 5 patients had no measurable disease at baseline
- 3 progressed and 2 had no evidence of disease at last follow up
- 10 patients had measurable disease at baseline
- 2 withdrew early due to progressive disease
- 8 were evaluable for 8 weeks (evaluable disease population)
- In the predefined evaluable disease population, the ORR per lungo criteria was 62.5% (5/8; 3 CR, 2 PR).
- Including all patients with measurable disease (intent to treat analysis) the ORR was 50% (5/10).
- Median duration of response (DoR) = 3.5 months
- Median OS = not reached; OS 63% at 1 year
- Median PFS = 5.0 months
- Median follow up = 11.2 months
- All responding patients were alive at last follow up

Disease Summary All Infused Patients, N=15

| Age (years, median, range) | 38, 22-72 |
| Race | Asian 3 |
| | Black or African-American 1 |
| | American Indian or Alaska native 1 |
| White | 7 |
| Not reported | 3 |

| Gender (Female/Male) | 6/9 |

Patient Disposition, All with Whole Blood Collection, N=45

| Cell Product Infused | 15 |
| Cell Product Not infused | 30 |
| Rationale for Non-infusion | 8 were evaluable at 8 weeks (evaluable disease population) |

Treatment Emergent Serious Adverse Events, N=15

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Event as Reported</th>
<th>Relatedness</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and Infestations</td>
<td>S. Mammillaria infection</td>
<td>Not related</td>
<td>Recovered/resolved</td>
</tr>
<tr>
<td>Neoplasms benign, malignant and unspecified</td>
<td>Lymphoma</td>
<td>Possible</td>
<td>Recovered/resolved</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Pulmonary embolism</td>
<td>Unlikely</td>
<td>Recovered/resolved</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea, emesis</td>
<td>Not related</td>
<td>Recovered/resolved</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>Dacrocystitis</td>
<td>Unlikely</td>
<td>Recovered/resolved</td>
</tr>
<tr>
<td>Investigations</td>
<td>Blood bilirubin increased</td>
<td>Possible</td>
<td>Recovered/resolved with sequelae</td>
</tr>
</tbody>
</table>

No infusion related toxicity, cytokine release syndrome or neurotoxicity.

Safety Summary

- The study was conducted at sites in France, South Korea, the UK and the US.
- Baltaleucel-T was manufactured at the time of relapse or at any time in high risk patients.
- To prepare the product, 200 mL of whole blood was collected from the patient and the product was manufactured at a central facility from peripheral blood mononuclear cells using EBV peptide stimulation (LMP-1, LMP-2, EBNA1 and BARF1).

Conclusion

Our study demonstrates feasibility, clinical activity and safety of administration of single agent autologous EBV-specific T cells (Baltaleucel-T) in patients with advanced, relapsed NKT-L in a multicenter, multinational trial. These results require validation in a larger cohort.