Real-World Outcomes for Pediatric and Young Adult Patients with Relapsed or Refractory (R/R) B-Cell Acute Lymphoblastic Leukemia (ALL) Treated with Tisagenlecleucel: Update from the Center for International Blood and Marrow Transplant Research (CIBMTR) Registry


1Department of Pediatrics, UT Southwestern Medical Center, Dallas, TX, USA; 2Cancer and Blood Disease Institute, Children’s Hospital Los Angeles, Los Angeles, CA, USA; 3CIBMTR® (Center for International Blood and Marrow Transplant Research), Department of Medicine, Medical College of Wisconsin, Milwaukee, WI, USA; 4Department of Pediatric Hematology/Oncology/Bone Marrow Transplantation, Medical College of Wisconsin, Milwaukee, WI, USA; 5Department of Pediatrics, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, USA; 6Department of Pediatrics, Children’s Mercy Hospital, Kansas City, MO, USA; 7Dana-Farber Cancer Institute & Boston Children’s Hospital Cancer and Blood Disorders Center, Boston, MA, USA; 8Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; 9Department of Pediatrics, Duke University Medical Center, Durham, NC, USA; 10Cancer and Blood Disorders Institute, Johns Hopkins All Children’s Hospital, St. Petersburg, FL, USA; 11Department of Pediatrics, University of Colorado School of Medicine and Children’s Hospital of Colorado, Aurora, CO, USA; 12Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA; 13Novartis Healthcare Pvt. Ltd, Hyderabad, India; 14Novartis Farmaceutica, Madrid, Spain; 15Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; 16Division of Oncology, Children’s Hospital of Philadelphia, Philadelphia, PA, USA
Disclosures

**SJ:** None. **MAP:** Medexus, Equilibrium and Mesoblast: Scientific advisory boards; Novartis: Scientific advisory boards, sponsored invited educational talks; Miltenyi: Study support, sponsored invited educational talks; Adaptive: Study support. **AM:** None. **Z-HH:** None. **CLP:** Novartis and Incyte: Membership on an entity’s Board of Directors or advisory committees. **EMH:** Boehringer Ingelheim (spouse COI only): Speakers bureau; VIDA Diagnostics (spouse COI only): Honoraria; Polarean (spouse COI only): Scientific advisory committee. **SPM:** Cue Biopharma, Inc.: Current employment; Novartis: Ad hoc advisory boards. **SN:** Kite/Gilead, Novartis, Iovance and GlaxoSmithKline: Ad hoc advisory boards. **PLM:** Novartis and Bluebird Bio: Local PI for clinical trial. **BO:** None. **AKK:** None. **RHR:** Novartis: Honoraria; Tessa Therapeutics: Research funding; Pfizer: Consultancy. **RT:** Novartis: Current employment. **SR:** Novartis: Current employment. **JW:** Novartis: Current employment. **AA:** Novartis: Current employment and current holder of individual stocks in a privately held company. **MCP:** Bristol Myers Squibb, Novartis, Kite Pharma and GlaxoSmithKline: Research funding; Bristol Myers Squibb: Consultancy. **SAG:** Novartis, Servier, Vertex and Kite: Research and/or clinical trial support; Novartis, Allogene, Adaptimmune, TCR2, Cabaletta, Juno, CBMG, GlaxoSmithKline, Cellectis, J&J/Janssen, CRISPR/Vertex, Roche, Humanigen, Jazz, TCR2, Cellectis, Allogene and Cabaletta: Study steering committees, consulting, or scientific advisory boards.
Background

- ALL is the most common form of childhood cancer; B-cell precursor ALL accounts for >80% of ALL cases¹

- Disease relapse may occur in 15–20% of pediatric patients with ALL; outcomes for these patients are poor, with 5-year survival estimates of ~50%²⁻⁴

- Tisagenlecleucel is an autologous CD19-directed T-cell immunotherapy, in which a patient’s own T cells are modified to fight cancer

- In the registrational ELIANA trial of tisagenlecleucel in pediatric/young adult patients (≤25 years of age) with R/R B-cell ALL (NCT02435849), ORR was 82% with 24 months’ follow-up⁵

  - Pooled data from ELIANA and the earlier ENSIGN trial revealed similar outcomes upon stratification by age (<18 years and ≥18 years)⁶

ALL, acute lymphoblastic leukemia; ORR, overall response rate; R/R relapsed or refractory

Tisagenlecleucel in the real-world setting

Approved for the treatment of pediatric and young adult patients (up to 25 years of age) with R/R B-cell precursor ALL in August 2017 (USA)¹

The CIBMTR collects data on patients who receive commercial tisagenlecleucel from treatment centers

Early real-world data for tisagenlecleucel from the CIBMTR registry reported similar efficacy to ELIANA, with no new safety signals²

Here we report updated data from the CIBMTR registry on pediatric and young adult patients with R/R B-cell ALL who received tisagenlecleucel, stratified by age (<18 and ≥18 years)

ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; R/R, relapsed or refractory


Oral presentation at the 2021 ASH Annual Meeting & Exposition, held December 11–14, 2021
Study design

- Non-interventional prospective study using data from the CIBMTR cellular therapy registry
- Patients treated in the USA and Canada
- Descriptive comparisons of CIBMTR data with ELIANA and between the <18 and ≥18 years age groups

**Efficacy outcomes**
- BOR of CR/CRi, MRD response, DOR, EFS, RFS, OS
  - Evaluated in patients with ≥12 months of follow-up

**Safety outcomes**
- CRS, ICANS, prolonged neutropenia and thrombocytopenia, death
  - Evaluated in patients who completed 100-day assessment

**Efficacy set**
- N=410

**Safety set**
- N=493

**Infused set**
- N=561

- <18 years
  - N=290
- ≥18 years
  - N=120

**Ongoing efficacy and safety follow-up**

*Center-reported; †ASTCT grading criteria; ‡Patients who died or discontinued prior to data cut-off were also included; §At time of infusion

ASTCT, American Society of Transplant and Cellular Therapy; BOR, best overall response; CIBMTR, Center for International Blood and Marrow Transplant Research; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; CRS, cytokine release syndrome; DOR, duration of response; EFS, event-free survival; ICANS, immune effector cell-associated neurotoxicity syndrome; MRD, minimal residual disease; OS, overall survival; RFS, relapse-free survival
Baseline characteristics (1/2)

In general, patient characteristics were similar between patients aged <18 and ≥18 years

<table>
<thead>
<tr>
<th>Baseline characteristics (all infused patients)</th>
<th>All patients (N=561)</th>
<th>&lt;18 years (N=389)</th>
<th>≥18 years (N=172)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at infusion, years (range)</td>
<td>13.80 (0.40–25.90)</td>
<td>10.40 (0.40–17.90)</td>
<td>21.95 (18.00–25.90)</td>
</tr>
<tr>
<td>Age &lt;3 years, n (%)</td>
<td>40 (7.1)</td>
<td>40 (10.3)</td>
<td>NA</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>334 (59.5)</td>
<td>228 (58.6)</td>
<td>106 (61.6)</td>
</tr>
<tr>
<td>Down syndrome, n (%)</td>
<td>30 (5.3)</td>
<td>27 (6.9)</td>
<td>3 (1.7)</td>
</tr>
<tr>
<td>Cytogenetics, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal 11q23/MLL rearrangement</td>
<td>82 (14.6)</td>
<td>63 (16.2)</td>
<td>19 (11.0)</td>
</tr>
<tr>
<td>Ph+ ALL prior to infusion</td>
<td>34 (6.1)</td>
<td>18 (4.6)</td>
<td>16 (9.3)</td>
</tr>
<tr>
<td>Karnofsky/Lansky score &lt;80, n (%)</td>
<td>77 (13.7)</td>
<td>50 (12.9)</td>
<td>27 (15.7)</td>
</tr>
<tr>
<td>Median prior lines of therapy, n</td>
<td>3</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Prior treatment, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allogeneic HCT</td>
<td>144 (25.7)</td>
<td>98 (25.2)</td>
<td>46 (26.7)</td>
</tr>
<tr>
<td>CAR-T cell therapy</td>
<td>11 (2.0)</td>
<td>7 (1.8)</td>
<td>4 (2.3)</td>
</tr>
<tr>
<td>Blinatumomab/inotuzumab</td>
<td>98 (17.5)/51 (9.1)</td>
<td>55 (14.1)/23 (5.9)</td>
<td>43 (25.0)/28 (16.3)</td>
</tr>
</tbody>
</table>

- The median time from receipt of leukapheresis product at the manufacturing site to shipment was 26 days (N=522; IQR: 25–32)
- Patients received a median CAR-positive T-cell dose of 1.9 x 10^6 cells/kg (N=534; range: 0.1–5.3)

ALL, acute lymphoblastic leukemia; CAR, chimeric antigen receptor; HCT, hematopoietic cell transplant; IQR, interquartile range; MLL, mixed-lineage leukemia; NA, not applicable; Ph+, Philadelphia chromosome-positive
Patients aged ≥18 years appeared to have greater disease burden at baseline than those aged <18 years

<table>
<thead>
<tr>
<th>Baseline characteristics (all infused patients)</th>
<th>All patients (N=561)</th>
<th>&lt;18 years (N=389)</th>
<th>≥18 years (N=172)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most recent disease status prior to infusion, n (%)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary refractory</td>
<td>75 (13.4)</td>
<td>53 (13.6)</td>
<td>22 (12.8)</td>
</tr>
<tr>
<td>First relapse</td>
<td>153 (27.3)</td>
<td>103 (26.5)</td>
<td>50 (29.1)</td>
</tr>
<tr>
<td>Second relapse</td>
<td>89 (15.9)</td>
<td>58 (14.9)</td>
<td>31 (18.0)</td>
</tr>
<tr>
<td>≥Third relapse</td>
<td>50 (8.9)</td>
<td>28 (7.2)</td>
<td>22 (12.8)</td>
</tr>
<tr>
<td>Morphologic CR</td>
<td>193 (34.4)</td>
<td>146 (37.5)</td>
<td>47 (27.3)</td>
</tr>
<tr>
<td>MRD negative</td>
<td>102 (18.2)</td>
<td>75 (19.3)</td>
<td>27 (15.7)</td>
</tr>
<tr>
<td>MRD positive</td>
<td>84 (15.0)</td>
<td>67 (17.2)</td>
<td>17 (9.9)</td>
</tr>
<tr>
<td>Bone marrow blast percentage prior to infusion, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>131 (23.4)</td>
<td>93 (23.9)</td>
<td>38 (22.1)</td>
</tr>
<tr>
<td>&gt;0 to &lt;5%</td>
<td>117 (20.9)</td>
<td>86 (22.1)</td>
<td>31 (18.0)</td>
</tr>
<tr>
<td>≥5%</td>
<td>176 (31.4)</td>
<td>119 (30.6)</td>
<td>57 (33.1)</td>
</tr>
<tr>
<td>≥50%</td>
<td>82 (14.6)</td>
<td>49 (12.6)</td>
<td>33 (19.2)</td>
</tr>
<tr>
<td>Extramedullary disease prior to infusion, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>410 (73.1)</td>
<td>295 (75.8)</td>
<td>115 (66.9)</td>
</tr>
<tr>
<td>Yes</td>
<td>89 (15.9)</td>
<td>51 (13.1)</td>
<td>38 (22.1)</td>
</tr>
<tr>
<td>Isolated CNS disease</td>
<td>56 (10.0)</td>
<td>33 (8.5)</td>
<td>23 (13.4)</td>
</tr>
</tbody>
</table>

*Disease status prior to infusion was not reported for one patient in the <18 years age group
CNS, central nervous system; CR, complete remission; MRD, minimal residual disease

Oral presentation at the 2021 ASH Annual Meeting & Exposition, held December 11–14, 2021
Efficacy outcomes: Response rates

- In the CIBMTR registry, median follow-up in the efficacy set was 25.9 months (range: 12.0–43.6; N=410)

- Overall response rates in the CIBMTR registry were comparable with those observed in ELIANA (86.8% vs 82.3%)\(^1\)

- Overall response rates were similar between the <18 and ≥18 years age groups (88.6% vs 82.5%)

---

**Table:**

<table>
<thead>
<tr>
<th></th>
<th>CIBMTR</th>
<th>ELIANA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients</td>
<td>&lt;18 years</td>
</tr>
<tr>
<td>MRD negative response,*</td>
<td>97.9%; n=191/195</td>
<td>97.8%; n=135/138</td>
</tr>
</tbody>
</table>

---

*Reported during the follow-up period. B-ALL, B-cell acute lymphoblastic leukemia; BOR, best overall response; CAR, chimeric antigen receptor; CIBMTR, Center for International Blood and Marrow Transplant Research; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; HCT, hematopoietic cell transplant; MRD, minimal residual disease; R/R, relapsed or refractory.

Efficacy outcomes: Duration of response

- DOR at Month 12 in the CIBMTR registry was comparable with that observed in ELIANA (61.4% vs 67.4%)¹
- DOR at Month 12 was similar between the <18 and ≥18 years age groups (63.2% vs 57.4%)

¹Error bars depict 95% CIs
CI, confidence interval; CIBMTR, Center for International Blood and Marrow Transplant Research; DOR, duration of response; NE, not estimable

Oral presentation at the 2021 ASH Annual Meeting & Exposition, held December 11–14, 2021
Efficacy outcomes: Event-free survival

- EFS at Month 12 in the CIBMTR registry was comparable with that observed in ELIANA (52.6% vs 57.2%)\(^1\)
- EFS at Month 12 was similar between the <18 and ≥18 years age groups (54.4% vs 49.0%)

*Error bars depict 95% CIs
CI, confidence interval; CIBMTR, Center for International Blood and Marrow Transplant Research; EFS, event-free survival; NE, not estimable

Oral presentation at the 2021 ASH Annual Meeting & Exposition, held December 11–14, 2021
Efficacy outcomes: Relapse-free survival

- RFS at Month 12 in the CIBMTR registry was comparable to that observed in ELIANA (62.5% vs 66%)\(^1\)
- RFS at Month 12 was similar between the <18 and ≥18 years age groups (64.3% vs 58.3%)

*Measured in patients with BOR of CR/CRi after infusion to relapse or death attributable to any cause; patients were not censored at SCT; †Error bars depict 95% CIs. BOR, best overall response; CI, confidence interval; CIBMTR, Center for International Blood and Marrow Transplant Research; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; NE, not estimable; RFS, relapse-free survival; SCT, stem cell transplant. 1. Grupp SA et al. Oral presentation at ASH Annual Meeting 2018; December 1–4, 2018; abstract 895
Efficacy outcomes: Overall survival

• OS at Month 12 in the CIBMTR registry was comparable with that observed in ELIANA (79.5% vs 77.1%) ¹

• OS at Month 12 was similar between the <18 and ≥18 years age groups (81.9% vs 73.8%)

*Error bars depict 95% CIs
CI, confidence interval; CIBMTR, Center for International Blood and Marrow Transplant Research; NE, not estimable; OS, overall survival
Safety outcomes

- In the CIBMTR registry, median follow-up in the safety set was 23.9 months (range: 2.0–43.6; N=493)
- Safety outcomes in the CIBMTR registry were generally more favorable than those reported for ELIANA
- Safety outcomes were similar between the <18 and ≥18 years age groups
- 113 (22.9%) and 108 (21.9%) of patients experienced prolonged neutropenia and thrombocytopenia, respectively*

---

<table>
<thead>
<tr>
<th>CIBMTR registry (N=493)</th>
<th>ELIANA trial (N=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS</td>
<td></td>
</tr>
<tr>
<td>Median time to onset, days (range)</td>
<td>5 (1–27)</td>
</tr>
<tr>
<td>Median duration, days (95% CI)</td>
<td>7 (6–7)</td>
</tr>
<tr>
<td>ICANS</td>
<td></td>
</tr>
<tr>
<td>Median time to onset, days (range)</td>
<td>7 (1–97)</td>
</tr>
<tr>
<td>Median duration, days (95% CI)</td>
<td>7 (6–9)</td>
</tr>
</tbody>
</table>

*Patients who failed to recover neutrophil/platelet count by Day 30 (including those who never recovered or recovered after Day 30);
†CRS was graded using ASTCT criteria (CIBMTR) or the Penn grading scale (ELIANA); ICANS was graded using ASTCT criteria (CIBMTR); in ELIANA, neurologic events were reported based on CTCAE version 4.03;
§Adverse events of interest <100 days after infusion;
¶Adverse events of interest <8 weeks after infusion


Oral presentation at the 2021 ASH Annual Meeting & Exposition, held December 11–14, 2021

ASTCT, American Society of Transplant and Cellular Therapy; CI, confidence interval; CIBMTR, Center for International Blood and Marrow Transplant Research; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; ICANS, immune effector cell-associated neurotoxicity syndrome; NA, not applicable
Conclusions

• In the CIBMTR registry, patients aged ≥18 years appeared to have a greater disease burden and more prior exposure to blinatumomab and inotuzumab at baseline than patients aged <18 years

• Efficacy outcomes with commercial tisagenlecleucel were similar to those observed in ELIANA\(^1\)–\(^3\)

• Safety outcomes in the CIBMTR registry seemed more favorable than those reported in ELIANA\(^1\)–\(^3\)

• Efficacy and safety outcomes with commercial tisagenlecleucel appeared broadly consistent across age groups (<18 and ≥18 years)

• Ongoing accrual of patient data into the CIBMTR registry will provide further insights into the use of tisagenlecleucel in the real-world setting

Also at ASH 2021: Real-World Efficacy and Safety Outcomes for Patients with Relapsed or Refractory (R/R) Aggressive B-Cell Non-Hodgkin’s Lymphoma (aBNHL) Treated with Commercial Tisagenlecleucel: Update from the Center for International Blood and Marrow Transplant Research (CIBMTR) Registry – presented by Dr Daniel Landsburg (oral presentation 429)
Acknowledgments

• The authors sincerely thank:
  – The patients who participate in the registry and their families
  – Participating centers
  – Treating physicians and support staff

• The CIBMTR® is a research collaboration between the National Marrow Donor Program®/Be The Match® and Medical College of Wisconsin, and operates the Cellular Immunotherapy Data Resource (CIDR); research funding is received from the National Cancer Institute (U24 CA233032)

• The ELIANA trial was sponsored by Novartis Pharmaceuticals Corporation

• All analyses in this presentation were conducted by Novartis Pharmaceuticals Corporation. Medical writing support was provided by Helen Speedy, PhD, of AMICULUM Limited and was funded by Novartis Pharmaceuticals Corporation

Scan to obtain:
• Narrated presentation
• Supplementary material


Copies of this presentation obtained through QR code are for personal use only and may not be reproduced without permission of the authors.