Tisagenlecleucel in Pediatric and Young Adult Patients With Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia: Final Analyses From the ELIANA Study


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Abstract S112

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Disclosures

- Novartis (consulting fees, advisory boards, presentations, educational events, Data Safety Monitoring Board, support for attending meetings and travel)
- Amgen (advisory boards, educational events, support for attending meetings and travel)
- Celgene, Servier, and Jazz Pharmaceuticals (advisory boards, support for attending meetings and travel)
- BMS, Cellectis, and Kite (advisory boards)
- Spanish Pediatric Hematology and Oncology Society and in the I-BFM Study Group of Childhood Leukemia (leadership or fiduciary role)
- CAR-T cell clinical trials (principal investigator)
Introduction

• Pediatric and young adult patients with r/r B-ALL experience a treatment journey characterized by diminishing likelihood of a cure and increasing morbidity with each additional line of salvage therapy

• Tisagenlecleucel is an autologous CD19-directed chimeric antigen receptor (CAR) T-cell therapy approved for use in pediatric and young adults with B-ALL and adults with B-cell lymphomas
  – In the primary analysis of the global Phase II ELIANA trial (NCT02435849), tisagenlecleucel provided high rates of remission (>80%) in children and young adults with r/r B-ALL, with 62% of responders remaining relapse-free at 24 months\textsuperscript{1,2}

• Here, we report the efficacy and safety analyses in patients followed up for a maximum of 5.9 years post-tisagenlecleucel infusion
**ELIANA Study Design**

### Key Eligibility Criteria

- **Inclusion**
  - r/r B-cell ALL, aged 3-21 years\(^a\)
  - Bone marrow with ≥5% lymphoblasts

- **Exclusion**
  - Isolated extramedullary disease relapse
  - Prior CD19-directed or gene therapy

### Study Treatment

- **Lymphodepleting chemotherapy prior to infusion**
  - Fludarabine 30 mg/m\(^2\) IV daily for 4 doses
  - Cyclophosphamide 500 mg/m\(^2\) IV daily for 2 doses

- **Tisagenlecleucel dose range (single infusion)**
  - 0.2 to 5.0 \(× 10^6\) cells/kg for patients ≤50 kg
  - 0.1 to 2.5 \(× 10^8\) cells for patients >50 kg

### Endpoints

- **Primary endpoint:** Overall remission rate (CR + CRi) within 3 months
  - 4-week maintenance of remission
  - IRC assessment

- **Secondary endpoints**
  - MRD status, DOR, RFS, OS, EFS, cellular kinetics, safety

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\(^a\)Age of 3 years at the time of screening to age of 21 years at the time of initial diagnosis.

ALL, acute lymphoblastic leukemia; CD, cluster of differentiation; CR, complete remission; CRi, CR with incomplete blood count recovery; DOR, duration of response; EFS, event-free survival; IRC, independent review committee; IV, intravenous; MRD, minimal residual disease; OS, overall survival; r/r B-ALL, relapsed or refractory B-cell acute lymphoblastic leukemia; RFS, relapse-free survival.
Patient with Down syndrome died due to cerebral hemorrhage.

CD19 status at relapse was characterized based on MFC-MRD assay and NGS analysis. (Pulsipher et al., 2022, Blood Cancer Discovery).

Among the 69 responders within 3 months post-infusion, 10 patients (14%) had alloSCT in remission and 7 patients (10%) had alloSCT after relapse.

Death due to lower respiratory tract infection (n=1)

*Patient with Down syndrome died due to cerebral hemorrhage. CD19 status at relapse was characterized based on MFC-MRD assay and NGS analysis. (Pulsipher et al., 2022, Blood Cancer Discovery).

alloSCT, allogeneic stem cell transplantation; CD, cluster of differentiation; CR, complete remission; CRi, CR with incomplete blood count recovery; D, day; MFC, multiparametric flow cytometry; MRD, minimal residual disease; mo, month; NGS, next-generation sequencing; NRM, non-relapse related mortality; RFS, relapse-free survival.
### Key Baseline Demographics and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (N=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range), years</td>
<td>11 (3-24)</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>45 (57)</td>
</tr>
<tr>
<td>Prior alloSCT, n (%)</td>
<td>48 (61)</td>
</tr>
<tr>
<td>Lines of prior therapies, median (range), n</td>
<td>3 (1-8)</td>
</tr>
<tr>
<td>Disease status, n (%)</td>
<td></td>
</tr>
<tr>
<td>Primary refractory</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Relapsed</td>
<td>73 (92)</td>
</tr>
<tr>
<td>Morphologic blast count in bone marrow, median (range), a (%)</td>
<td>74 (5-99)</td>
</tr>
<tr>
<td>CNS status classification, n (%)</td>
<td></td>
</tr>
<tr>
<td>CNS-1</td>
<td>67 (85)</td>
</tr>
<tr>
<td>CNS-2</td>
<td>10 (13)</td>
</tr>
<tr>
<td>CNS-3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

*Morphologic blast count in bone marrow is the maximum from biopsy or aspirate prior to enrollment. *<sup>a</sup>Patient was CNS-3 at screening and was <CNS-3 prior to infusion.

*alloSCT, allogeneic stem cell transplantation; CNS, central nervous system.*
High Response Rate Post Tisagenlecleucel

<table>
<thead>
<tr>
<th>BOR Within 3 Months by IRC assessment</th>
<th>All Patients N=79 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>49 (62)</td>
</tr>
<tr>
<td>CRi</td>
<td>16 (20)</td>
</tr>
<tr>
<td>No response</td>
<td>7 (9)</td>
</tr>
<tr>
<td>Not evaluable</td>
<td>7 (9)</td>
</tr>
<tr>
<td>ORR(^a)</td>
<td>65 (82)</td>
</tr>
</tbody>
</table>

- 98% of patients who achieved remission were MRD– at Month 3

\(^a\)Only patients who achieved BOR of CR or CRi within 3 months are included. \(^b\)MRD % <0.01.
BOR, best overall response; CR, complete remission; CRi, CR with incomplete blood count recovery; CNS, central nervous system; IRC, independent review committee; MRD, minimal residual disease; ORR, overall remission rate.
Median RFS Was 43 Months

RFS for Patients With a CR/CRi within 3 months

5-year RFS: 44% (95% CI, 31%-56%)

Note: RFS is without censoring for SCT and other cancer therapies
*1 patient who died at Month 17 while in CR was censored as the event happened after at least 2 missing assessments.
CR, complete remission; CRi, CR with incomplete blood count recovery; NE, not estimable; RFS, relapse-free survival; SCT, stem cell transplant.
Median Time to B-cell Recovery Was 39 Months in Responders

- The probability of B-cell aplasia at
  - Month 6 was 83% (95% CI, 71%-91%)
  - Month 12 was 71% (95% CI, 57%-82%)
- Patients with B-cell recovery experienced a 2-year cumulative incidence of relapse of 40%

Note: B-Cell recovery is censored for HSCT.
(H)SCT, (hematopoietic) stem cell transplantation; NE, not estimable.
Post Tisagenlecleucel Infusion, 25% of Patients Underwent AlloSCT

<table>
<thead>
<tr>
<th>Patients Who Achieved Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=69</td>
</tr>
<tr>
<td>No. of patients who received post infusion alloSCT, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>AlloSCT in remission</td>
</tr>
<tr>
<td>17 (25)</td>
</tr>
<tr>
<td>AlloSCT after relapse</td>
</tr>
<tr>
<td>10 (14)</td>
</tr>
<tr>
<td>7 (10)</td>
</tr>
</tbody>
</table>

*Four patients had alloSCT within 3 months post infusion and the remaining had alloSCT after 3 months post infusion. alloSCT, allogeneic stem cell transplantation.*
Median EFS was 15 Months

EFS Without Censoring for alloSCT
5-year EFS: 36% (95% CI, 25%-47%)

EFS With Censoring for alloSCT
5-year EFS: 34% (95% CI, 23%-45%)

Kaplan-Meier medians
All patients: 15 months, 95% CI [10-45]

Censoring times
All patients (N=79)
Number of events (n)
Patients: 46
Kaplan-Meier medians
All patients: 13 months, 95% CI [9-35]

allesCT, allogeneic stem cell transplantation; EFS, event-free survival; NE, not estimable.
Median OS Was Not Reached

Overall Survival

5-year OS: 55% (95% CI, 43%-66%)

Note: OS is without censoring for alloSCT.
alloSCT, allogeneic stem cell transplantation; NE, not estimable; OS, overall survival.
OS And EFS Were Comparable Between Pediatric And Young Adult (18-25 years-old) Patients

OS Without Censoring for AlloSCT

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>Number of patients still at risk</th>
<th>Censoring times</th>
<th>Number of events</th>
<th>Kaplan-Meier medians</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18 years</td>
<td>65 61 58 54 51 48 46 46 42 41 38 36 36 35 35 34 31 29 24 16 4 3 1 0</td>
<td>&lt;18 years (N=65)</td>
<td>&lt;18 years (N=26)</td>
<td>&lt;18 years NE months, 95% CI [44-NE]</td>
</tr>
<tr>
<td>≥18 years</td>
<td>14 12 12 12 9 9 7 7 7 7 7 7 7 6 6 5 5 4 1 0</td>
<td>≥18 years (N=14)</td>
<td>≥18 years (N=7)</td>
<td>≥18 years 15 months, 95% CI [3-NE]</td>
</tr>
</tbody>
</table>

EFS Without Censoring for AlloSCT

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>Number of patients still at risk</th>
<th>Censoring times</th>
<th>Number of events</th>
<th>Kaplan-Meier medians</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18 years</td>
<td>65 51 41 36 33 29 28 27 25 25 24 24 23 20 19 18 16 13 13 11 7 0</td>
<td>&lt;18 years (N=65)</td>
<td>&lt;18 years (N=38)</td>
<td>&lt;18 years NE months, 95% CI [10-NE]</td>
</tr>
<tr>
<td>≥18 years</td>
<td>14 11 11 11 7 7 7 6 6 6 6 6 6 5 5 5 4 4 4 4 3 0</td>
<td>≥18 years (N=14)</td>
<td>≥18 years (N=9)</td>
<td>≥18 years 15 months, 95% CI [9-48]</td>
</tr>
</tbody>
</table>

alloSCT, allogeneic stem cell transplantation; EFS, event-free survival; NE, not estimable; OS, overall survival.
Adverse Events of Special Interest >1 Year Post Infusion

- 82% of patients received IVIG at any time post-infusion; 33% >1 year and 16% >2 years post-infusion
  - 88% of patients in remission received IVIG during persistent B-cell aplasia

<table>
<thead>
<tr>
<th>AESI occurring &gt;1 y post infusion</th>
<th>Any Grade, n (%)</th>
<th>Grade ≥3, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with at least 1 event</td>
<td>27 (39)</td>
<td>15 (21)</td>
</tr>
<tr>
<td>Hemophagocytic lymphohistiocytosis/CRS</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Serious neurological events</td>
<td>2 (3)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Infection</td>
<td>23 (33)</td>
<td>14 (20)</td>
</tr>
<tr>
<td>Hematological disorders, including cytopenias</td>
<td>7 (10)</td>
<td>4 (6)</td>
</tr>
<tr>
<td>Secondary malignancy</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

AESI, adverse events of special interest; CRS, cytokine release syndrome; IVIG, intravenous immunoglobulin.

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*a Includes patients who achieved response at any time, including > Month 3. **If a patient received multiple treatments of IVIG, the duration of each treatment was derived and summed to provide the total duration of IVIG treatment for the patient.

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Conclusions

- These long-term follow-up data demonstrate continued durable efficacy of tisagenlecleucel in heavily pretreated pediatric and young adult patients with r/r B-ALL.
- No new long-term treatment-related safety events were observed in this longer-term >5-year follow-up.
- Long-term remission rates up to 5.9-years of follow-up from ELIANA demonstrate that tisagenlecleucel may be a curative treatment option for heavily pretreated pediatric and young adult patients with r/r B-ALL.
Acknowledgments

• The authors sincerely thank
  – The patients enrolled in the ELIANA study and their families
  – The principal investigators and support staff
  – SSC, DMC, IRC members
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• Medical writing support was provided by Nitya Venkataraman, PhD, of Healthcare Consultancy Group, LLC, and was funded by Novartis Pharmaceuticals Corporation
BACK UP
EFS by Age Group (<18 years and ≥18 years)

EFS with Censoring for Antineoplastic Therapies

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>Number of patients still at risk</th>
<th>Number of events</th>
<th>Kaplan-Meier medians</th>
<th>Censoring times</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;18 years (N=31)</td>
<td>≥18 years (N=8)</td>
<td>&lt;18 years 37.4 months, 95% CI [8.87-NE]</td>
<td>&lt;18 years (N=65) ≥18 years (N=14)</td>
</tr>
<tr>
<td></td>
<td>≥18 years (N=10)</td>
<td></td>
<td>≥18 years 18.7 months, 95% CI [2.79-NE]</td>
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</tbody>
</table>

EFS With Censoring for AlloSCT

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>Number of patients still at risk</th>
<th>Number of events</th>
<th>Kaplan-Meier medians</th>
<th>Censoring times</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;18 years (N=37)</td>
<td>≥18 years (N=9)</td>
<td>&lt;18 years 14.3 months, 95% CI [8.34-34.73]</td>
<td>&lt;18 years (N=65) ≥18 years (N=14)</td>
</tr>
<tr>
<td></td>
<td>≥18 years (N=10)</td>
<td></td>
<td>≥18 years 11.6 months, 95% CI [2.79-NE]</td>
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</tbody>
</table>

alloSCT, allogeneic stem cell transplantation; EFS, event free survival; NE, not estimable.