The ELIANA Clinical Trial
Fact Sheet

The pivotal ELIANA clinical trial is a global study conducted to evaluate the safety and efficacy of CTL019 (tisagenlecleucel) in pediatric and young adult patients with relapsed or refractory (r/r) B-cell acute lymphoblastic leukemia (ALL).

The following updated, longer-term results from the ELIANA study were published in *The New England Journal of Medicine* in January 2018.

The ELIANA Trial (NCT02435849)

Novartis-sponsored global, multi-center Phase II study evaluating the safety and efficacy of CTL019 in pediatric and young adult patients with r/r B-cell ALL.

TRIAL DESIGN

Single-arm, open-label, international, multicenter, Phase II trial of **92 enrolled patients,** of which **75 were infused**[1]

Patients enrolled had r/r B-cell ALL, and had a median age of 11 (range **3-23 years**), with **>5%** lymphoblasts in bone marrow[1]

At enrollment, patients had a median of **3 prior therapies**, with **61%** of patients having received prior **allogeneic hematopoietic stem cell transplant (alloSCT)**[1]

ELIANA is the first global CAR-T cell therapy registration trial, with study enrollment having occurred across **25 centers in the US, Canada, EU, Australia** and **Japan**[1]

PRIMARY ENDPOINT: Overall remission rate, defined as best overall response of complete remission (CR) or CR with incomplete blood count recovery (CRi) within 3 months

SECONDARY ENDPOINTS: CR/CRi with undetectable minimal residual disease (MRD), duration of remission, event-free survival, overall survival, cellular kinetics and safety.

TRIAL RESULTS: The primary endpoint and all key secondary endpoints were met.

- In the updated analysis of 75 infused patients with median follow-up of 13.1 months, the overall remission rate (CR/CRi) was **81% (95% CI: 71%-89%; p<0.001)**[1].
- 60% of patients achieved CR and 21% of patients achieved CRi[1].
- All infused patients with best overall response of CR/CRi were MRD negative, 95% by day 28 following infusion[1].
- Kymriah was detected in patients **up to 20 months**[1].
- **24%** of patients were infused in the outpatient setting[1].
- Seventeen patients discontinued before infusion, with the majority due to rapid disease progression or deterioration of their clinical status, reflecting the acute and progressive nature of the disease[1].
- Seven patients could not be infused due to inability to manufacture, with the majority (n=6) due to poor cell growth, and one unrelated to cell growth[1].

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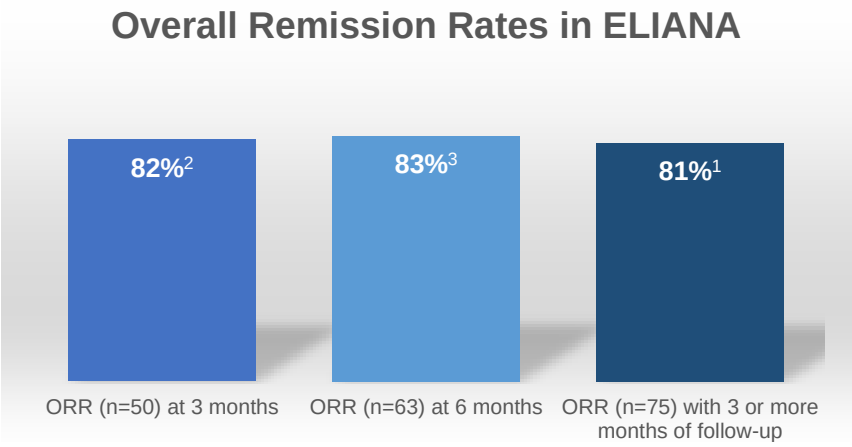
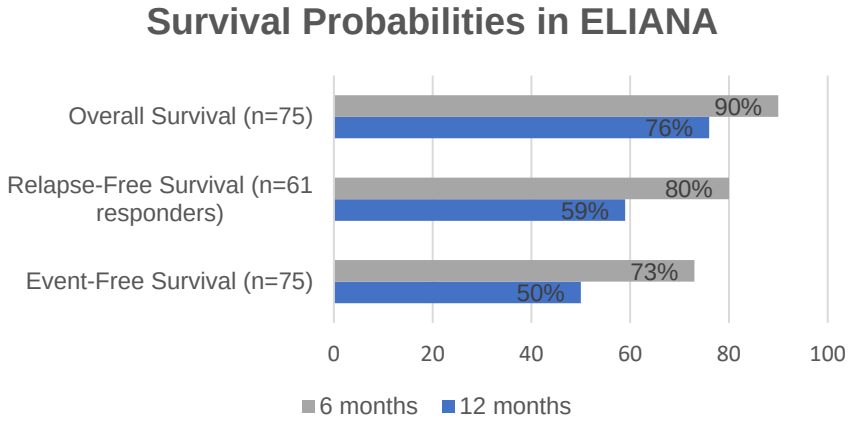
TRIAL RESULTS





SAFETY – Adverse events (AEs) of special interest include:

- Any grade treatment-related AEs occurred in 95% of patients, with the most common non-hematologic AEs being cytokine release syndrome (CRS; 77%), pyrexia (40%), decreased appetite (39%), febrile neutropenia (36%) and headache (36%). Seventy-three percent of patients experienced a grade 3/4 treatment-related AE.
- CRS, a known complication of CAR-T therapies that may occur when engineered cells become activated in the body, occurred in 77% of patients, with 46% of patients experiencing grade 3/4 CRS. CRS was managed globally using prior site education on implementation of the CRS treatment algorithm. Thirty-five of 75 infused patients (47%) were admitted to the intensive care unit for management of CRS.
- Neurological events occurred in 40% of patients within eight weeks of infusion, 13% of patients had grade 3 neurological events, which were managed with best supportive care after ruling out other potential causes of the symptoms. No incidence of grade 4 neurological events were reported.

About CTL019 (tisagenlecleucel): CTL019 is approved in the US as Kymriah™ suspension for intravenous infusion for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse[4]. An application is currently under review by the European Medicines Agency (EMA) for CTL019 for children and young adults with r/r B-cell ALL. The full prescribing information, including Boxed WARNING, for Kymriah can be found at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/kymriah.pdf

References:
1. Maude S L., et al. Tisagenlecleucel in Children and Young Adults with B Lymphoblastic Leukemia. N Engl J Med. February 1, 2018. doi: 10.1056/NEJMoa1709866. [Epub ahead of print].
2. Grupp, Stephen A. et al. Analysis of a Global Registration Trial of the Efficacy and Safety of CTL019 in Pediatric and Young Adults with Relapsed/Refractory Acute Lymphoblastic Leukemia (ALL). Session 614, Saturday, December 3, 5:00 p.m. PST. 58th American Society of Hematology Annual Meeting and Exposition: Abstract 221.
3. Buechner, Jochen Et Al. Global Registration Trial Of Efficacy And Safety Of Ctl019 In Pediatric And Young Adult Patients With Relapsed/Refractory (R/R) Acute Lymphoblastic Leukemia (All): Update To The Interim Analysis. June 24, 4:00 Pm CEST. European Hematology Association: Abstract S476.
4. Kymriah (tisagenlecleucel) Prescribing information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation. Accessed December 2017.

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