Remission first. Durability next.

Tisagenlecleucel (KYMRIAH) | Relapsed / refractory B-cell precursor ALL

The clinical problem

ELIANA studied children and young adults with B-cell acute lymphoblastic leukemia that had relapsed or resisted treatment. It asked whether an engineered cellular therapy could produce remission in this heavily pretreated population. [2]

The mechanism

Patient-derived T cells receive a CD19-directed CAR with CD3-zeta and 4-1BB signaling domains. After infusion, antigen recognition can activate cytotoxic function and expansion. CD19 is also present on normal B cells. [1; Figure 1]

The evidence needs two time horizons

The initial study measured remission within three months. Follow-up then examined whether disease control persisted. An early remission rate and a three-year survival estimate answer different questions; neither should stand in for the other. [2,3]

A living therapy can induce remission and persist. The evidence must also show who reached infusion, how long benefit lasted and what treatment required.

Continue the story

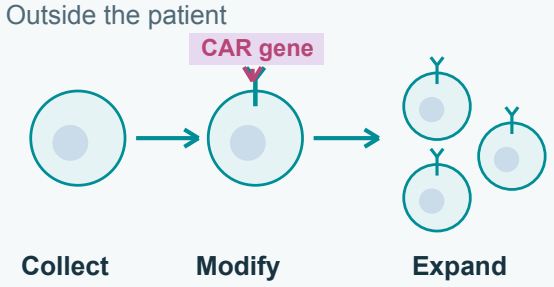
Watch the film and explore the mechanism

The animation explains biology. The following pages examine measured patient outcomes.

Figure 1. CAR-T: recognition to target-cell killing

Follow the mechanism from left to right, then down each row.

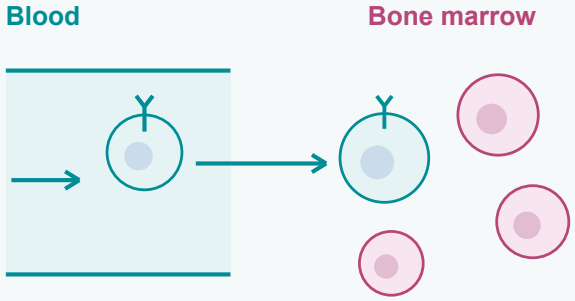
A Collect and engineer



Patient T cells receive a CD19-directed CAR. [1]

The engineered cells are expanded for infusion.

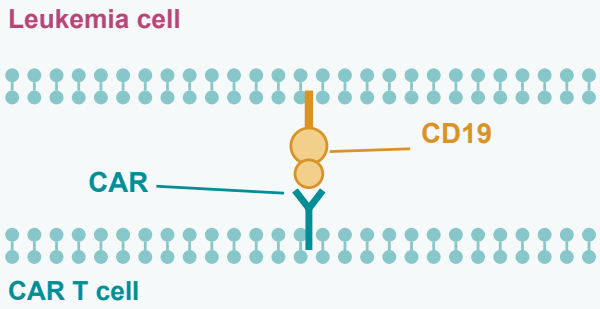
B Infuse and encounter



After lymphodepletion, CAR T cells are infused. [1]

They encounter CD19-positive leukemia cells.

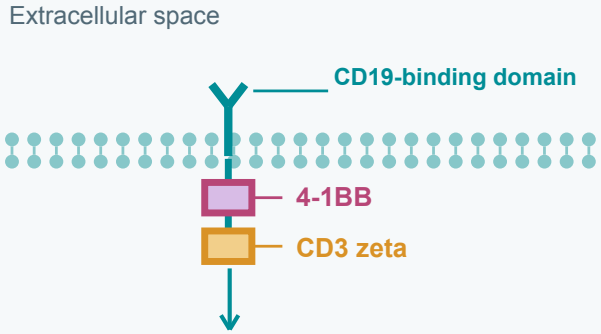
C Recognize CD19



CAR binds CD19 across the cell-cell contact. [1]

Normal B cells also express CD19.

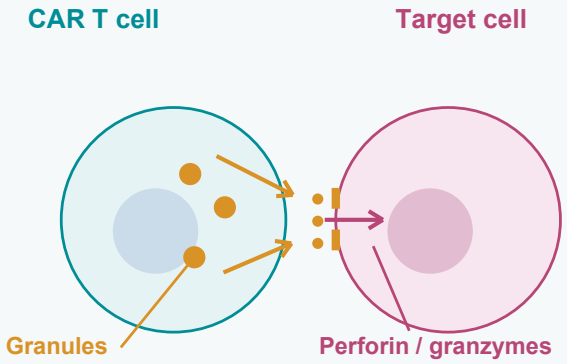
D Activate the T cell



CD3 zeta activates; 4-1BB supports persistence. [1]

Both signaling domains lie inside the T cell.

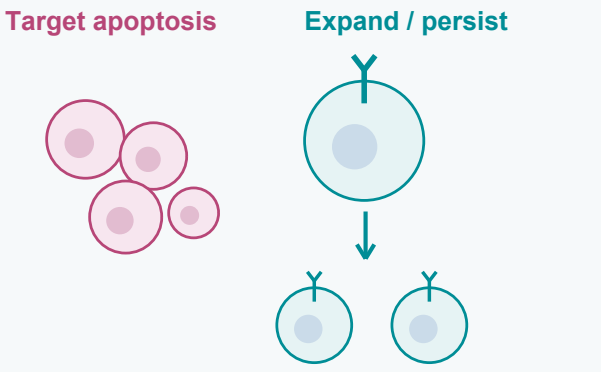
E Direct granule release



Cytotoxic contents are released at the contact. [2]

Granzymes can trigger target-cell apoptosis.

F Kill and persist



CAR T cells can expand and remain after infusion. [1]

Persistence does not guarantee lasting remission.

[1] KYMRIAH prescribing information, sections 11–12.1.
[2] Davenport et al., PNAS (2018), doi:10.1073/pnas.1716266115.

Schematic, not to scale. Mechanism does not predict an individual clinical response.

From infusion to longer follow-up.

ELIANA | Global, single-arm phase 2 | Pediatric / young-adult relapsed or refractory B-cell ALL. Primary analysis cutoff: 25 April 2017. [2]

Primary analysis | The denominator matters [2]

Enrolled / infused	**92 / 75 patients** 17 did not receive infusion; not all were manufacturing failures
CR + CRi within 3 months	**61 / 75 = 81%** 95% CI 71-89; independent review
Same remissions / enrolled	**61 / 92 = 66%** 95% CI 56-76; enrolled-population analysis

45 complete remissions and 16 with incomplete blood-count recovery (CRi). CRi is not partial remission. All 61 responders were MRD-negative by flow cytometry.

Three-year update | 79 infused patients [3]

Event-free survival at 3 years	**44% (95% CI 31-57)** Kaplan-Meier estimate
Overall survival at 3 years	**63% (95% CI 51-73)** Kaplan-Meier estimate

Median follow-up 38.8 months. The later analysis includes four additional infused patients; its survival estimates are not simple counts among the original 75.

What the evidence means.

Benefit, uncertainty and safety belong in the same clinical story.

What this study establishes

The study supports antileukemic activity and shows that some patients maintained disease control for years. Without a concurrent randomized comparator, it cannot estimate superiority over another CAR-T product, transplantation or a different treatment strategy. [2,3]

Treatment access is part of the evidence

Of 17 enrolled patients not infused in the primary report, seven had product-related issues, seven died and three had adverse events. Reporting only infused patients omits this attrition. [2]

Long-term estimates need context

At three years, relapse-free survival among responders was 52% with censoring for subsequent therapy and 48% without it. These differ from event-free survival in all infused patients. Subsequent treatment and censoring affect the question being answered. [3]

Benefit comes with substantial acute risk

In the primary report, cytokine release syndrome occurred in 77% and neurologic events in 40% of infused patients. [2] The current label includes boxed warnings for cytokine release syndrome, neurological toxicities and secondary hematological malignancies; other risks include infections and prolonged cytopenias. [1]

Keep this case specific

This story concerns pediatric / young-adult B-cell ALL. It should not be used as an outcome claim for adult lymphoma or solid tumors. Normal B-cell depletion, monitoring and long-term follow-up remain part of the clinical journey. [1]

Sources you can follow.

Numbered citations on pages 1, 3 and 4 refer to this list. Figure 1 retains its own source key.

[1] KYMRIAH US prescribing information.

Novartis | Current US label

Regulatory source. Indications, boxed warnings, precautions and mechanism.

[2] Maude SL et al. Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. NEJM (2018).

DOI: 10.1056/NEJMoa1709866 | Full text

Peer-reviewed ELIANA primary report. Enrollment, infused denominator, remission and acute safety.

[3] Laetsch TW et al. Three-year update of tisagenlecleucel in the ELIANA trial. JCO (2023).

DOI: 10.1200/JCO.22.00642 | Full text

Peer-reviewed follow-up. 79 infused patients; survival estimates and handling of subsequent therapy.

[4] Davenport AJ et al. CAR-T immune synapse and target-cell killing. PNAS (2018).

DOI: 10.1073/pnas.1716266115

Experimental mechanism supporting Figure 1; not a patient efficacy study. Its figure citations use a separate key.

How this brief was prepared

Selected primary publications, prescribing information and clearly identified conference material were checked on 7 September 2026. Data are not pooled across trials or cutoffs. This is a focused evidence summary, not a systematic review, prescribing guide or health-economic analysis.