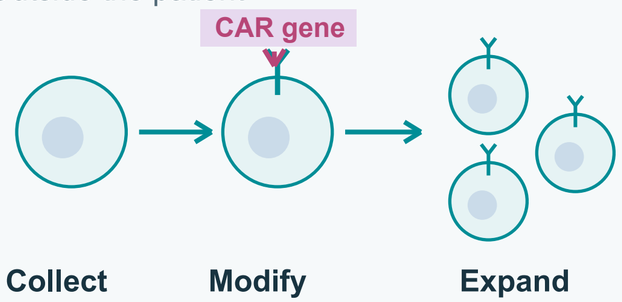
Tisagenlecleucel: from T-cell engineering to target-cell killing

CD19-positive B-cell acute lymphoblastic leukemia | Engineering, recognition and cellular action

A Collect and engineer

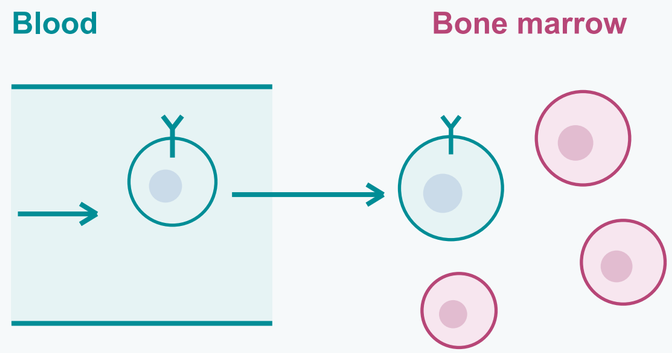
Outside the patient



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

The engineered cells are expanded for infusion.

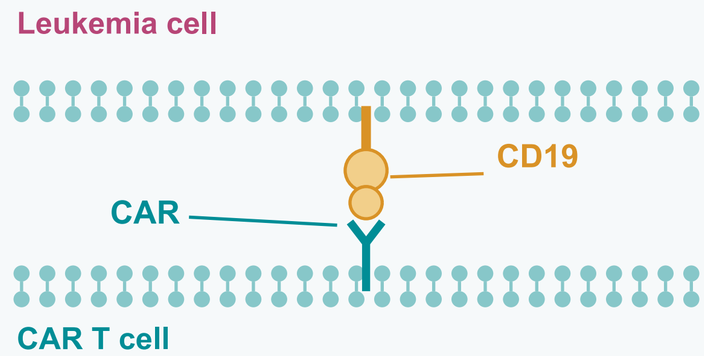
B Infuse and encounter



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

They encounter CD19-positive leukemia cells.

C Recognize CD19

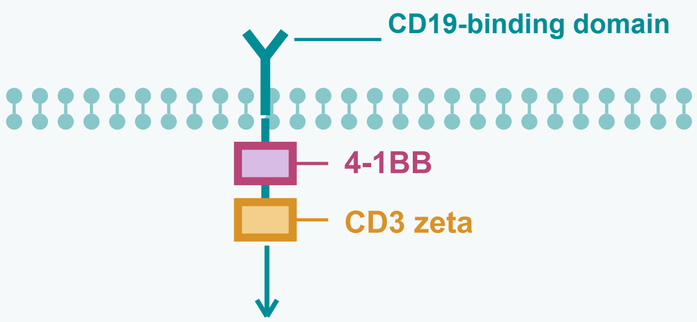


CAR binds CD19 across the cell-cell contact. [1]

Normal B cells also express CD19.

D Activate the T cell

Extracellular space

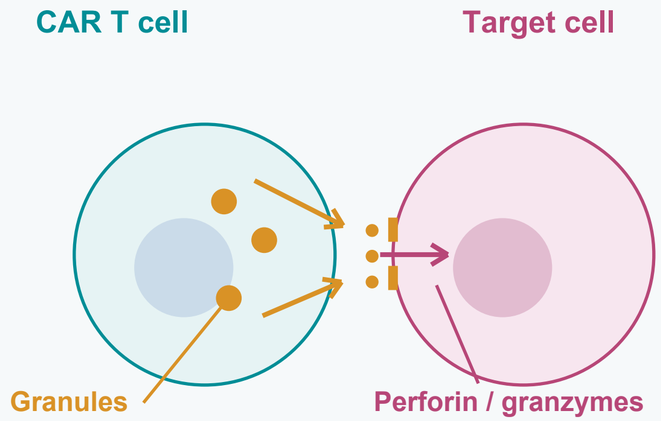


Activation and expansion

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

Both signaling domains lie inside the T cell.

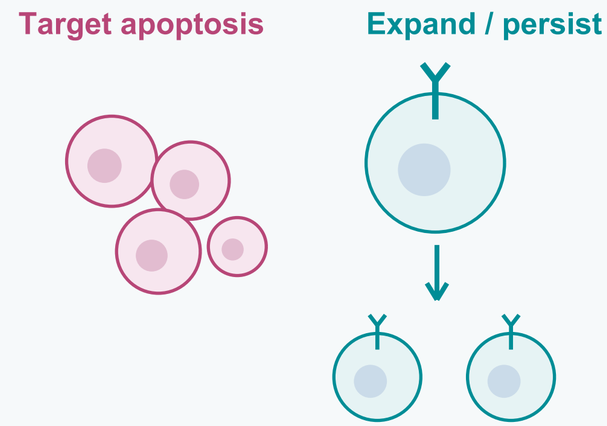
E Direct granule release



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.

Key: teal = CAR / T cell; magenta = target B cell; gold = CD19 or cytotoxic granules. Schematic, not to scale.

[1] KYMRIAH prescribing information, sections 2, 11 and 12.1-12.3. [2] Davenport et al., PNAS (2018), doi:10.1073/pnas.1716266115.

Panel E depicts a general experimental CAR-T mechanism. No transport rates or patient response probabilities are inferred.