3565

Phenotype and functional state of endogenous T-cells support T-cell engager therapy in the post-CAR T therapy setting

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Objective

- To describe the phenotypic composition and assess the *ex vivo* functional response of T cells to CD3xCD20 bispecific antibodies before and after CAR T therapy

Conclusion

- Expansion of endogenous CD8 effector memory T-cells was independent of CAR T response, suggesting that this effect may be associated with lymphodepletion
- Epcoritamab response *ex vivo* was minimally impacted by prior CAR T therapy (failure at 3 to 6 months)

Epcoritamab use based on timing and reason for CAR T failure

Early Failure	Later Failure	
0–1 month	3–6 months	Relapse > 6 months
	Most patients post-CAR T	

- These data support the benefit of epcoritamab post-CAR T therapy, as evidenced by the high complete response rate observed in epcoritamab-treated CAR T-exposed patients[1]

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Disclosures

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References

1. Thieblemont C, et al. *Leukemia*. 2024;38(12):2653-2662.
2. Messéant O, et al. *Cancers (Basel)*. 2021;13(17):4274.
3. Broussais F, et al. *Bull Cancer*. 2021;108(10S):S143-S154.
4. Epling-Burnette PK, et al. (2025) https://app.biorender.com/illustrations/68d99504009c6f5a5259d767

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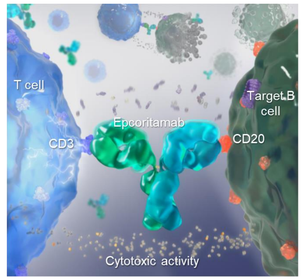
Introduction

- Several new therapies have been approved for the treatment of B-cell non-Hodgkin lymphoma in the relapsed/refractory (R/R) setting including T-cell engagers (TCE), such as the CD3xCD20 bispecific (bsAb) epcoritamab, and chimeric antigen receptor T cell (CAR T) therapies[1-3]
- Approved CAR T therapies rely on structural engineering and adoptive transfer of autologous T-cells following lymphodepletion, while TCEs are engineered antibodies that redirect the activity of endogenous T-cells against tumor cells[2]
  - Given the potential requirement for additional lines of therapy following CAR T infusion and the impact of CAR T therapy on the immune system, additional data on the composition and functionality of patients' T-cells following CAR T therapy are needed

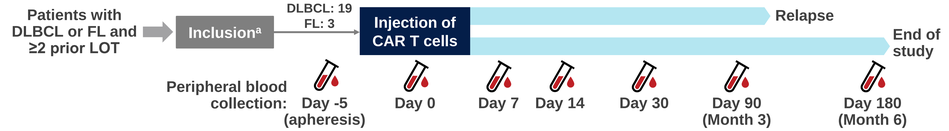
Epcoritamab Mechanism of Action



The aim of this study is to describe the phenotypic composition of endogenous T cells prior to and after CAR T-cell infusion and assess function of these cells *ex vivo* in response to epcoritamab treatment

Methods

Figure 1: Study Design[3]



CAR T Lymphodepletion Regimens	
Axicabtagen ciloleucel (Yescarta)	Cyclophosphamide 500 mg/m^2 + fludarabine 30 mg/m^2 on days -5, -4, -3 before CAR T-cell infusion
Tisagenlecleucel (Kymriah)	Cyclophosphamide 250 mg/m^2 + fludarabine 25 mg/m^2 for 3 days or bendamustine 90 mg/m^2 for 2 days

[a]All patients provided written informed consent in accordance with the Declaration of Helsinki and institutional research board approval.

CAR-T cell, chimeric antigen receptor T cell; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; LOT, lines of therapy.

- Epcoritamab was tested in *ex vivo* experiments to assess functionality of the full cohort of PBMC samples collected 5 days before and 3 to 6 months after CAR T therapy
- Complete blood counts, phenotypic assessments of T cells, and CAR T levels were assessed by flow cytometry 2 to 3 days (based on the CAR T therapy) before and after the standard conditioning regimen containing cyclophosphamide and fludarabine and up to 300+ days post-CAR T therapy

Results

Patient response

- Complete response was observed in 81.8% (18/22) patients (**Figure 2**)

Figure 2: Patient Response and Sample Collection Following CAR T Infusion

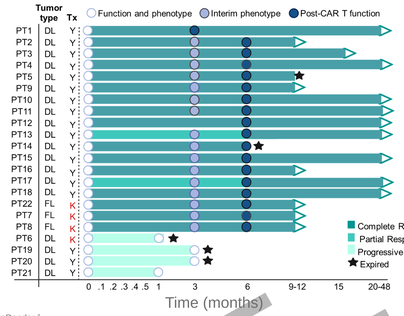


Figure created in BioRender.[4]

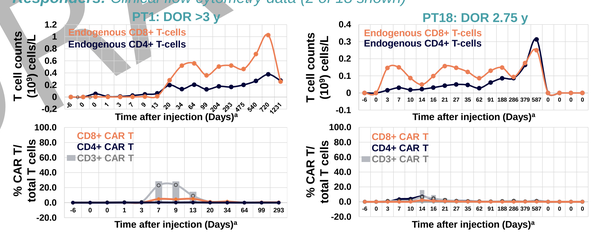
CAR T, chimeric antigen receptor T-cell; DL, diffuse large B cell lymphoma; FL, follicular lymphoma; K, Kymriah® (tisagenlecleucel); PT, patient; Tx, treatment; Y, Yescarta® (axicabtagen ciloleucel).

T-cell population analyses

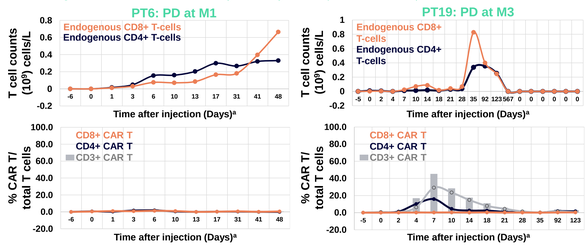
- Endogenous T-cell expansion peaks at 10–300+ days, while CAR T expansion peaks at day 7–14, regardless of clinical response (**Figure 3**)

Figure 3: Endogenous T-Cell and CAR T Expansion Following CAR T Infusion

Responders: *Clinical flow cytometry data (2 of 18 shown)*



Non-responders: *Clinical flow cytometry data (2 of 4 shown)*



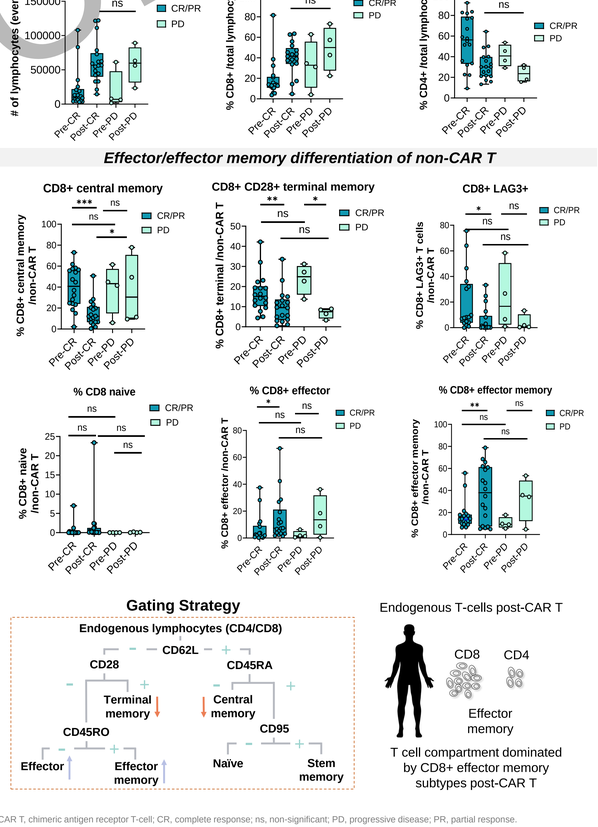
[a]Time 0 is 2 hours after CAR T injection.

CAR T, chimeric antigen receptor T-cell; DOR, duration of response; M#, month #; PD, progressive disease; PT, patient.

T-cell population analyses (continued)

- Analysis of T cells in samples collected pre- and post-CAR T infusion showed that CD8+ T-cells expanded and CD4+ T-cells decreased in both responders (n=17) and nonresponders (n=4; **Figure 4**)
  - In patients with CR, expansion of endogenous CD8+ effector memory T-cells was observed without increase in LAG3 (Figure 3), PD-1, or TIM3 (data not shown)

Figure 4: Expansion and Differentiation of Endogenous CD8+ T-Cells Following CAR T/Lymphodepleting Regimens



Gating Strategy

Endogenous T-cells post-CAR T

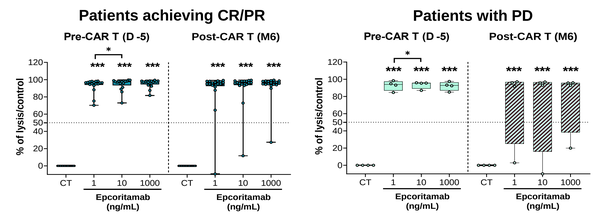
T cell compartment dominated by CD8+ effector memory subtypes post-CAR T

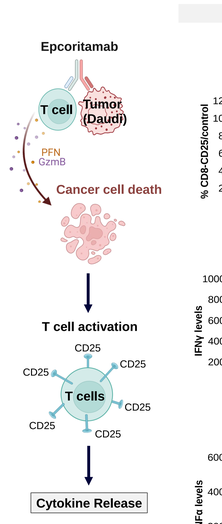
CAR T, chimeric antigen receptor T-cell; CR, complete response; ns, non-significant; PD, progressive disease; PR, partial response.

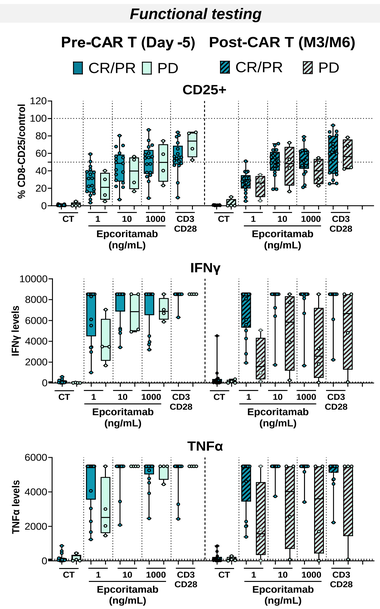
Ex vivo T cell cytotoxicity and functionality analyses

- *Ex vivo* treatment with epcoritamab induced comparable tumor cell lysis in matched patient samples pre- and post-CAR T cell infusion, in both responders (n=17) and nonresponders (n=4; **Figure 5**)
- Epcoritamab induces CD8 activation (CD25) and cytokine production (INFγ and TNFα) in the same samples when tested functionally

Figure 5: Cytotoxicity and T Cell Functionality in Response to *Ex Vivo* Epcoritamab Treatment in Pre- and Post-CAR T PBMC Samples







Cytotoxicity performed at 48 hours with 10:1 PBMC to Daudi tumor ratio using labeled Daudi tumor cells as targets.

CAR T, chimeric antigen receptor T-cell; CR, complete response; CT, control; D-5, 5 days before treatment; DLBCL, diffuse large B-cell lymphoma; GzmB, granzyme B; M#, month #; PBMC, peripheral blood mononuclear cell; PFN, perforin; PD, progressive disease; PR, partial response.

*P < 0.05, **P < 0.001 compared to CT by ANOVA.