LONG-TERM EFFICACY AND SAFETY OF OBECABTAGENE AUTOLEUCEL (OBE-CEL) IN ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA ([R/R B-ALL]; POOLED ANALYSIS OF ALLCAR19 AND FELIX PHASE IB STUDIES) OR OTHER B-CELL MALIGNANCIES (ALLCAR19 EXTENSION STUDY)

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1. INTRODUCTION

- The autologous CD19 chimeric antigen receptor (CAR) T-cell product, obe-cel, has a fast off-rate CD19 binding domain designed to reduce toxicity and improve persistence.[1–3]
- Obe-cel has been investigated in adults with R/R B-ALL, R/R B-cell chronic lymphocytic leukemia (B-CLL), and R/R B-cell non-Hodgkin lymphoma (B-NHL) in the Phase I ALLCAR19 (NCT02935257) and Phase Ib/II FELIX (NCT04404660) studies.[1–5]
- Here, we report long-term obe-cel data from a pooled analysis of the ALLCAR19 and FELIX Phase Ib studies in R/R B-ALL, and from the ALLCAR19 extension phase.

2. METHODS

- ALLCAR19 is a multicenter, non-randomized, open-label Phase I study in patients aged ≥16 years with B-cell malignancies (data cut-off: November 01, 2023).[1,2,4]
- FELIX is a global, open-label, single-arm Phase Ib/II study enrolling patients aged ≥18 years with R/R B-ALL (data cut-off: September 13, 2023).[3,5]
- Obe-cel was administered as a split dose in patients with B-ALL (target dose: 410 x 10^6 CAR T-cells) and B-CLL (target dose: 230 x 10^6 CAR T-cells) and as a single infusion (200 x 10^6 CAR T-cells) in patients with B-NHL.[1,4,5]

3. RESULTS: R/R B-ALL

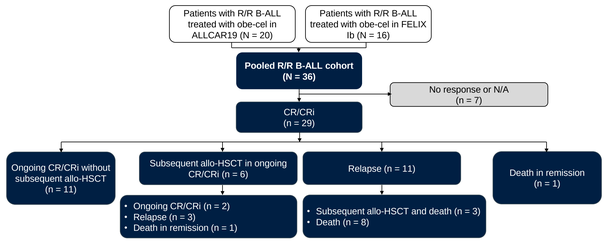
Baseline characteristics and outcomes in R/R B-ALL

Table 1. Baseline characteristics for patients with R/R B-ALL.

Characteristic	N = 36
Age years, median (range)	42 (18–74)
Sex male/female, n	23/13
Philadelphia chromosome-positive, n (%)	10 (28)
Prior therapies, median (range)	3 (2–6)
≥3 prior lines, n (%)	20 (56)
Prior allo-HSCT, n (%)	22 (61)
Prior blinatumomab, n (%)	14 (39)
Prior inotuzumab, n (%)	15 (42)
Prior blinatumomab and inotuzumab, n (%)	5 (14)
BM blasts % at pre-conditioning, median (range)	46 (0–98)
Extramedullary disease at pre-conditioning, n (%)	6 (17)

Allo-HSCT, allogeneic hematopoietic stem cell transplant; BM, bone marrow.

Figure 1. Disposition of patients with R/R B-ALL.



Investigator-assessed disease evaluations were performed locally by CT and BM biopsy for B-ALL. Allo-HSCT, allogeneic hematopoietic stem cell transplant; B-ALL, B-cell acute lymphoblastic leukemia; BM, bone marrow; CR/CRi, complete remission/complete remission with incomplete hematologic recovery; CT, computed tomography; N/A, not available; obe-cel, obecabtagene autoleucel; R/R, relapsed/refractory.

Safety and B-cell function

- There were no deaths related to obe-cel in patients with R/R B-ALL.

Table 2. Safety and B-cell function in patients with R/R B-ALL.

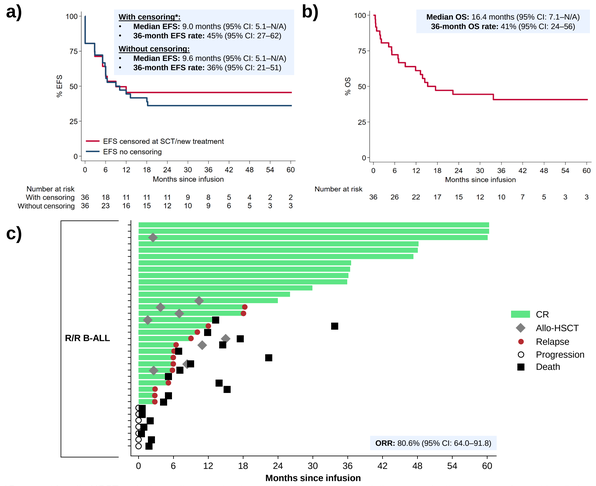
Parameter	R/R B-ALL (N = 36)
Ongoing B-cell aplasia at last assessment, n/N (%)	9/11 (82)*
IVIG replacement at any point post-infusion, n (%)	15 (42)
Grade 3/4 CRS, n (%)	0
Grade 3/4 ICANS, n (%)	4 (11)†

*Patients with ongoing CR/CRi without subsequent allogeneic hematopoietic stem cell transplant. †Grade 3 was the highest reported grade. Safety assessments were conducted according to NCI-CTCAE 4.03/5.0 and ASTCT/ASBMT criteria.[6–8] B-cell aplasia was assessed using flow cytometry and defined as <20 B-cells/μL. ASBMT, American Society for Blood and Marrow Transplantation; ASTCT, American Society for Transplantation and Cellular Therapy; B-ALL, B-cell acute lymphoblastic leukemia; CR/CRi, complete remission/complete remission with incomplete hematologic recovery; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IVIG, intravenous immunoglobulin; NCI-CTCAE, National Cancer Institute common terminology criteria for adverse events; R/R, relapsed/refractory.

Efficacy

- Median follow-up: 36.5 months (range 23.9–60.3).
- Overall response rate (ORR): 80.6% (95% CI: 64.0–91.8).
- Median duration of response (DOR): Not reached (95% CI: 5.1–NA).
- All patients in ongoing remission were MRD-negative at last assessment.

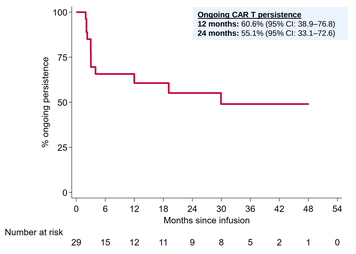
Figure 2. EFS (a), OS (b), and swim plot (c) for patients with R/R B-ALL.



*Censored for allo-HSCT and other anti-cancer treatment. Investigator-assessed disease evaluations were performed locally by CT and BM biopsy for B-ALL. Allo-HSCT, allogeneic hematopoietic stem cell transplant; B-ALL, B-cell acute lymphoblastic leukemia; BM, bone marrow; CI, confidence interval; CR, complete remission; CT, computed tomography; DOR, duration of response; EFS, event-free survival; N/A, not available; ORR, overall response rate; OS, overall survival; R/R, relapsed/refractory.

Persistence

Figure 3. Obe-cel persistence in responding patients with R/R B-ALL.



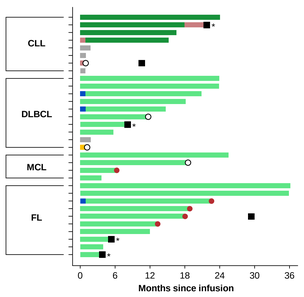
Loss of CAR T persistency was defined as the time from first obe-cel infusion to undetectable CAR T transgene (copies/μg DNA) in peripheral blood. Patients who proceeded to allo-HSCT with ongoing CAR T persistency were censored at the last result prior to receiving allo-HSCT.
Allo-HSCT, allogeneic hematopoietic stem cell transplant; B-cell acute lymphoblastic leukemia; CAR T, CD19 chimeric antigen receptor (CAR) T-cell; CI, confidence interval; DNA, deoxyribonucleic acid; obe-cel, obecabtagene autoleucel; R/R, relapsed/refractory.

4. RESULTS: R/R B-CLL/B-NHL

Efficacy

- Median follow-up: 20.9 months (range 0.9–36.2).
- Patients infused and evaluable for response: CLL, n = 5; DLBCL, n = 9; MCL, n = 4; FL, n = 10.

Figure 4. Swim plot and response data for patients with R/R B-CLL/B-NHL.



Subtype	ORR, n/N (%)
R/R CLL	4/5 (80)
R/R DLBCL	8/9 (89)
R/R MCL	4/4 (100)
R/R FL	10/10 (100)

*Patient death unrelated to obe-cel and without relapse or disease progression (COVID-19 [DLBCL and FL, n = 1 each]; grade 5 appendicitis on a background of myelodysplastic syndrome [FL, n = 1]; unrelated esophageal cancer [CLL, n = 1]). Investigator-assessed disease evaluations were performed locally by CT and BM biopsy for B-CLL, and by FDG-PET-CT imaging per Lugano criteria[9] for B-NHL. MRD status was determined using flow cytometry or IgH PCR/NGS (MRD-negative: $<10^{-4}$ [<0.01%]). BM, bone marrow; CLL, chronic lymphocytic leukemia; CMR, complete metabolic remission; CT, computed tomography; FDG-PET-CT, fluorodeoxyglucose-positron emission tomography-computed tomography; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MCL, mantle cell lymphoma; MRD, measurable residual disease; NGS, next-generation sequencing; PCR, polymerase chain reaction; PR, partial remission; R/R, relapsed/refractory; SD, stable disease.

Safety and B-cell function

- There were no deaths related to obe-cel in patients with R/R B-CLL/B-NHL.

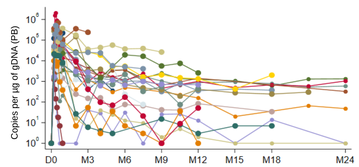
Table 3. Safety and B-cell function in patients with R/R B-CLL/B-NHL.

Parameter	R/R B-CLL (N = 8)	R/R DLBCL (N = 10)	R/R MCL (N = 4)	R/R FL (N = 10)
Ongoing B-cell aplasia at last assessment, n/N (%)	5/5 (100)*	5/7 (71)*	2/2 (100)*	3/4 (75)*
IVIG replacement at any point post-infusion, n (%)	1 (13)	1 (10)	1 (25)	5 (50)
Grade 3/4 CRS, n (%)	0	0	0	0
Grade 3/4 ICANS, n (%)	0	0	0	0

*Patients currently alive without progression. Safety assessments were conducted according to NCI-CTCAE 4.03/5.0 and ASTCT/ASBMT criteria.[6–8] B-cell aplasia was assessed using flow cytometry and defined as <20 B-cells/μL. ASBMT, American Society for Blood and Marrow Transplantation ASTCT; American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IVIG, intravenous immunoglobulin; NCI-CTCAE, National Cancer Institute common terminology criteria for adverse events.

Persistence

Figure 5. Post-infusion kinetics of obe-cel in the peripheral blood of patients with R/R B-CLL/B-NHL.



Cmax (CAR transgene per μg gDNA)	
Mean	284646.6
CV%	153.0
Time to Cmax (days)	
Median	11
Range	7–28
Time last measurable in blood (days)	
Median	365
Range	21–731

qPCR data were available for n = 26 patients. Loss of CAR T persistency was defined as the time from first obe-cel infusion to undetectable CAR T transgene (copies/μg DNA) in peripheral blood. B-CLL, B-cell chronic lymphocytic leukemia; B-NHL, B-cell non-Hodgkin lymphoma; Cmax, maximum concentration; CV%, coefficient of variation; D, day; gDNA, genomic deoxyribonucleic acid; M, month post-infusion; obe-cel, obecabtagene autoleucel; PB, peripheral blood; qPCR, quantitative polymerase chain reaction; R/R, relapsed/refractory.

5. CONCLUSIONS

R/R B-ALL (pooled ALLCAR19 and FELIX Ib)

- Obe-cel can result in durable remissions in adults with R/R B-ALL.
- Prolonged persistence of obe-cel is seen in most long-term responders.
- A role for consolidative HSCT allograft is not clear.

R/R B-CLL and B-NHL (ALLCAR19 extension)

- High response rates with durable remissions were observed in patients with R/R B-CLL/B-NHL.
- Notably, in patients with DLBCL, 8/9 evaluable patients entered CMR; 6 patients are in ongoing CMR with one relapse at 12 months and one unrelated death.

All cohorts

- As expected, B-cell aplasia was common among patients in long-term ongoing remission following obe-cel therapy (R/R B-ALL, 9/11 [without allo-HSCT]; R/R B-CLL, 5/5; R/R B-NHL, 10/13), but without a corresponding increase in serious late infections.
- Obe-cel is consistently associated with low levels of grade ≥3 CRS and ICANS across indications and dosing regimens.
- **These data demonstrate the long-term efficacy and safety of obe-cel in patients with B-cell malignancies.**

6. REFERENCES

[1]Roddie C, et al. *J Clin Oncol* 2021;39(30):3352–63; [2]Roddie C, et al. *Blood* 2022;140(Suppl 1):7452–3; [3]Roddie C, et al. *J Clin Oncol* 2023;41:16_suppl, 7000; [4]NCT02935257; [5]NCT04404660; [6]National Cancer Institute. CTCAE v4.03. 2010; [7]National Cancer Institute. CTCAE v5.0. 2017; [8]Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25(4):625–38; [9]Cheson BD, et al. *J Clin Oncol* 2014;32(27):3059–68.

7. ACKNOWLEDGMENTS

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