Clinical outcomes in adult patients with relapsed/refractory acute lymphoblastic leukemia (R/R B-ALL) who achieved remission following treatment with obecabtagene autoleucel (obe-cel) in the FELIX study

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INTRODUCTION

- Obe-cel is a novel, autologous 4-1BB-ζ CD19-directed chimeric antigen receptor T-cell therapy (CAR T) with a fast off-rate target antigen binding domain that mimics natural T-cell engagement.[1–3]
- The CD19-targeting (CAT) single-chain variable fragment (scFv) has a lower affinity for CD19 than the FMC63-derived scFv; this was designed to minimize severe immunotoxicities, such as cytokine releases syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).[1–3]
- Obe-cel is approved by the U.S. Food and Drug Administration for the treatment of adults aged ≥18 years with R/R B-ALL.[4]

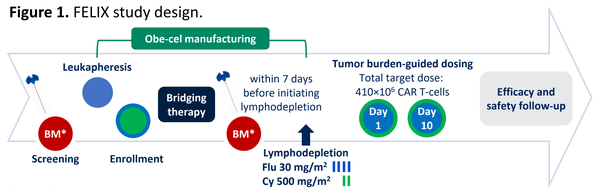
AIM

To explore long-term clinical outcomes in patients who achieved remission, stratified by best overall response (BOR), in a post-hoc analysis of the FELIX study, to further characterize durability of response and post-CAR T management.

METHODS

- In FELIX (NCT04404660), adults (aged ≥18 years) with R/R B-ALL underwent lymphodepletion, followed by infusion with obe-cel via a tumor burden-guided split dosing strategy to a total target dose of 410×10^6 CAR T-cells (**Figure 1**).
- Primary endpoint: overall remission rate defined as BOR of complete remission (CR) or CR with incomplete hematologic recovery (CRi), by an independent response review committee.
  - CR criteria were: <5% blasts in the bone marrow (BM), no extramedullary disease, no circulating lymphoblasts in peripheral blood, absolute neutrophil count (ANC) >1,000/μL, platelet count >100,000/μL, no platelet transfusions in the last seven days and no administration of short-acting granulocyte colony-stimulating factor (G-CSF) and long-acting G-CSF in the last three and 14 days, respectively.
  - CRi criteria was defined as: CR criteria, with recovery of platelets to ≤100,000/μL and/or recovery of ANC to <1,000/μL.
- Secondary endpoints included event-free survival (EFS) and overall survival (OS).
- A landmark analysis was also performed in patients with ongoing remission at Month (M) 3 to evaluate the impact of achieving BOR within 3 months post infusion on EFS and OS.

Figure 1. FELIX study design.



*While FELIX required two bone marrow biopsies, this is not mandated in routine clinical practice. BM, bone marrow; CAR, chimeric antigen receptor; Cy, cyclophosphamide; Flu, fludarabine; obe-cel, obecabtagene autoleucel.

RESULTS

- Of the 99 responders in FELIX, 73 (73.7%) achieved CR and 26 (26.3%) achieved CRi.
- Baseline patient and disease characteristics are shown in **Table 1**.
  - Disease burden at screening was higher in patients who achieved CRi than in those who achieved CR (median BM blast percentage at screening: 78.5% vs 30.0%, respectively).
  - Similarly, a higher proportion of patients who achieved CRi (50.0%) had >75% BM blasts at screening, compared with patients who achieved CR (23.3%).

Table 1. Patient and disease characteristics of responders.*

Patient and disease characteristics	Patients who achieved CR (n=73)	Patients who achieved CRi (n=26)	Responders (CR/CRi; n=99)
Age in years, median (range)	50.0 (20–81)	54.5 (22–73)	50.0 (20–81)
Male / female, %	58.9 / 41.1	42.3 / 57.7	54.5 / 45.5
Ethnicity, n (%)			
Hispanic or Latino	18 (24.7)	7 (26.9)	25 (25.3)
Not Hispanic or Latino	50 (68.5)	17 (65.4)	67 (67.7)
Unknown	5 (6.8)	2 (7.7)	7 (7.1)
Prior lines of therapy, median (range)	2.0 (1–5)	2.0 (1–5)	2.0 (1–5)
≥3 prior lines, n (%)	22 (30.1)	11 (42.3)	33 (33.3)
Refractory to all prior lines of anti-cancer therapy, n (%)	8 (11.0)	0	8 (8.1)
Refractory to first-line therapy, n (%)	21 (28.8)	5 (19.2)	26 (26.3)
Refractory to last prior line of therapy, n (%)	31 (42.5)	15 (57.7)	46 (46.5)
Prior blinatumomab, n (%)	26 (35.6)	12 (46.2)	38 (38.4)
Prior inotuzumab ozogamicin, n (%)	17 (23.3)	9 (34.6)	26 (26.3)
Prior blinatumomab and inotuzumab ozogamicin, n (%)	11 (15.1)	4 (15.4)	15 (15.2)
Prior blinatumomab or inotuzumab ozogamicin, n (%)	32 (43.8)	17 (65.4)	49 (49.5)
Prior allogeneic SCT, n (%)	34 (46.6)	13 (50.0)	47 (47.5)
Ph+ at lymphodepletion, n (%)	25 (34.2)	8 (30.8)	33 (33.3)
BM blast % at screening, median (range)	30.0 (0–100)	78.5 (0–100)	38.0 (0–100)
BM blast % at screening, n (%)			
>75%	17 (23.3)	13 (50.0)	30 (30.3)
>20% to ≤75%	21 (28.8)	6 (23.1)	27 (27.3)
≥5% to ≤20%	21 (28.8)	4 (15.4)	25 (25.3)
<5%	14 (19.2)	3 (11.5)	17 (17.2)
BM blast % at lymphodepletion, median (range)	30.0 (0–99)	23.5 (0–100)	30.0 (0–100)
BM blast % at lymphodepletion, n (%)			
>75%	18 (24.7)	8 (30.8)	26 (26.3)
>20% to ≤75%	24 (32.9)	5 (19.2)	29 (29.3)
≥5% to ≤20%	10 (13.7)	3 (11.5)	13 (13.1)
<5%	21 (28.8)	10 (38.5)	31 (31.3)
EMD at screening, n (%)	14 (19.2)	5 (19.2)	19 (19.2)
EMD at lymphodepletion, n (%)	12 (16.4)	4 (15.4)	16 (16.2)
Neutrophil count (10^9/L) at lymphodepletion, n (%)			
<0.5	12 (16.4)	7 (26.9)	19 (19.2)
≥0.5	59 (80.8)	19 (73.1)	78 (78.8)
Platelet count (10^9/L) at lymphodepletion, n (%)			
<50	15 (20.5)	10 (38.5)	25 (25.3)
≥50	58 (79.5)	16 (61.5)	74 (74.7)

*Infused patients who achieved remission following treatment with obe-cel. BM, bone marrow; CR, complete remission; CRi, CR with incomplete hematologic recovery; EMD, extramedullary disease; obe-cel, obecabtagene autoleucel; Ph+, Philadelphia chromosome-positive; SCT, stem cell transplant.

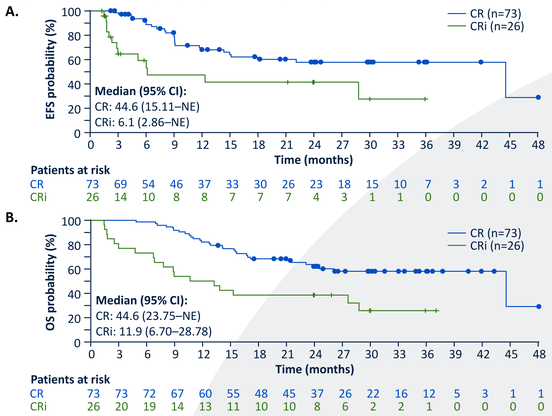
EFS and OS by BOR at any time post infusion

- As of January 18, 2025, the median study follow-up was 32.8 months (range: 19.9–52.8).
- Median EFS (95% confidence interval [CI]) was 44.6 months (15.1–not estimable [NE]) in the CR group and 6.1 months (2.9–NE) in the CRi group.
- Obe-cel appeared to deliver a plateau in EFS and OS, regardless of BOR (**Figure 2**): the 24-month EFS probability was 57.9% for CR and 41.5% for CRi; the 24-month OS probability was 62.1% for CR and 38.5% for CRi.

EFS and OS by BOR at M3 (landmark analysis)

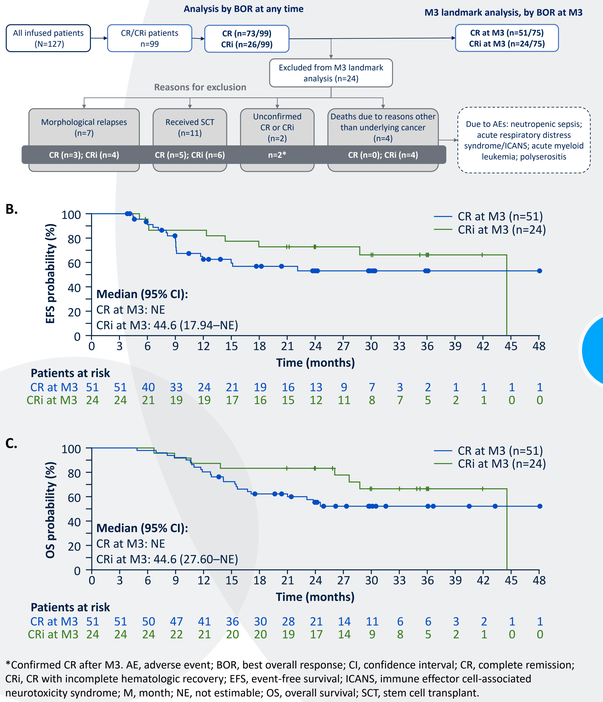
- Of the 99 responders, 24 were excluded from the M3 landmark analysis; reasons for exclusion are shown in **Figure 3A.**
- At M3, 51/75 patients (68.0%) had achieved CR and 24/75 patients (32.0%) had achieved CRi.
- By M3, 32 patients converted from CRi at M1 to CR, representing 63% (32/51) of patients with CR by M3.
- The 24-month EFS probability was 53.2% for CR and 72.9% for CRi (**Figure 3B**); the 24-month OS probability was 55.5% for CR and 83.3% for CRi (**Figure 3C**).

Figure 2. A) EFS and B) OS, by BOR at any time post infusion.



BOR, best overall ; CI, confidence interval; CR, complete remission; CRi, CR with incomplete hematologic recovery; EFS, event-free survival; NE, not estimable; OS, overall survival.

Figure 3. A) Patient disposition, B) EFS and C) OS, by BOR at M3 (landmark analysis).

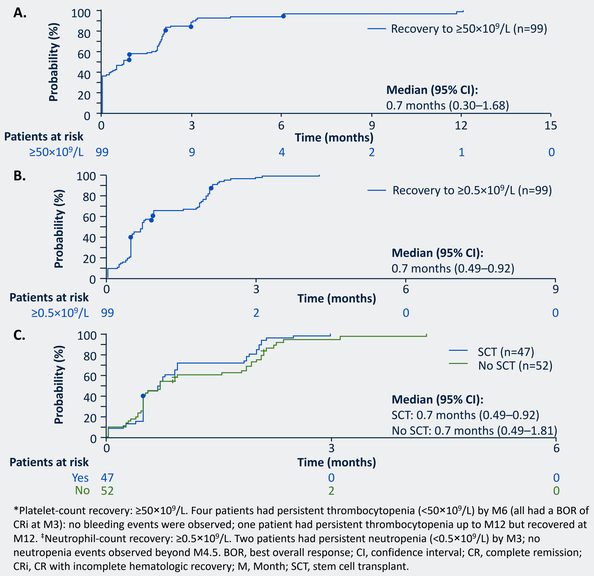


*Confirmed CR after M3. AE, adverse event; BOR, best overall response; CI, confidence interval; CR, complete remission; CRi, CR with incomplete hematologic recovery; EFS, event-free survival; ICANS, immune effector cell-associated neurotoxicity syndrome; M, month; NE, not estimable; OS, overall survival; SCT, stem cell transplant.

Cytopenia recovery in responders

- Median time to platelet-count recovery (≥50×10^9/L) and median time to neutrophil-count recovery (≥0.5×10^9/L) were observed within 1 month post obe-cel (**Figures 4A and 4B**).
- Time to neutropenia recovery did not appear to be impacted by prior SCT (**Figure 4C**).
- Three patients who achieved remission died due to infection prior to relapse or subsequent SCT.
  - BOR of CRi: n=2; due to sepsis in both cases (1 within 3 months of treatment; 1 in the long-term follow up).
  - BOR of CR: n=1; due to pneumonia (in the long-term follow up).

Figure 4. Time to: A) platelet-count recovery,* B) neutrophil-count recovery,‡ and C) neutrophil-count recovery, by prior SCT.



*Platelet-count recovery: ≥50×10^9/L. Four patients had persistent thrombocytopenia (<50×10^9/L) by M6 (all had a BOR of CRi at M3): no bleeding events were observed; one patient had persistent thrombocytopenia up to M12 but recovered at M12. ‡Neutrophil-count recovery: ≥0.5×10^9/L. Two patients had persistent neutropenia (<0.5×10^9/L) by M3; no neutropenia events observed beyond M4.5. BOR, best overall response; CI, confidence interval; CR, complete remission; CRi, CR with incomplete hematologic recovery; M, Month; SCT, stem cell transplant.

CONCLUSIONS

- Most patients with R/R B-ALL who achieved remission following obe-cel, achieved CR (n=73/99; 74%).
  - Most patients in CRi recover their blood counts to achieve CR within 3 months.
  - 32 patients converted from CRi at M1 to CR by M3, representing 63% (32/51) of patients with CR by M3.
- A substantial number of patients who responded to obe-cel treatment had a sustained survival benefit, regardless of BOR.
  - 24-month EFS probability: 57.9% for CR and 41.5% for CRi.
  - 24-month OS probability: 62.1% for CR and 38.5% for CRi.
- The M3 landmark analysis suggests that patients who achieved CRi have similar outcomes to patients who achieved CR.
- Late platelet count recovery after 3 months was not associated with any bleeding events.
- In this post-hoc analysis, obe-cel demonstrated meaningful and durable clinical benefit in patients with R/R B-ALL, regardless of BOR.

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DISCLOSURES

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