Can chimeric antigen receptor T-cell therapy be a definitive treatment for adult relapsed/refractory B-cell acute lymphoblastic leukemia without stem cell transplant? Long-term findings and predictors of sustained remission for obecabtagene autoleucel

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Poster ALL-712

INTRODUCTION

- Obecabtagene autoleucel (obe-cel), an autologous fast off-rate 4-1BB-ζ CD19-directed chimeric antigen receptor (CAR) T-cell therapy,[1] received approval from the US FDA in November 2024,[2] conditional marketing authorization from the UK MHRA in April 2025,[3] a positive EMA CHMP opinion in May 2025,[4] and marketing authorization from the European Commission in July 2025[5] for adult relapsed/refractory B-cell acute lymphoblastic leukemia (R/R B-ALL).
  - FDA and EC approval was based on results from the FELIX Phase Ib/II study (NCT04404660), where 78% of patients achieved remission following treatment with obe-cel.[1]
- Patient outcomes at a median follow-up of 21.5 months were previously reported:[6]
  - 40% of responders were in ongoing remission without consolidative stem cell transplant (SCT) or other anti-cancer therapies, excluding maintenance tyrosine kinase inhibitors (TKIs) in patients with Philadelphia chromosome-positive (Ph+) disease.

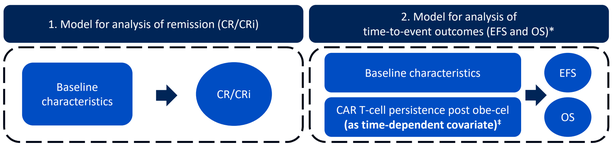
AIM

Here, we present efficacy data at a median follow-up of ~3 years (additional 11.3 months compared with last data cut) in obe-cel-infused patients and investigate which clinical factors may predict long-term outcomes.

METHODS

- The Phase Ib/II FELIX study investigated the efficacy and safety of obe-cel, administered using a tumor-burden guided dosing strategy to a total target dose of 410×10^6 CAR T-cells in adult patients (≥18 years) with R/R B-ALL.
- A univariate analysis (UVA) on complete remission (CR) or complete remission with incomplete hematologic recovery (CRi), event-free survival (EFS), and overall survival (OS) was performed to pre-select baseline characteristics; those significant (p-value <0.1) in any of the three UVAs were fed into two multivariate analysis (MVA) models (**Figure 1**).
- Stepwise variable selection was performed to identify the list of important factors in the final MVA model; the significance level for entry and stay was 0.25 and 0.2, respectively.

Figure 1. MVA models.

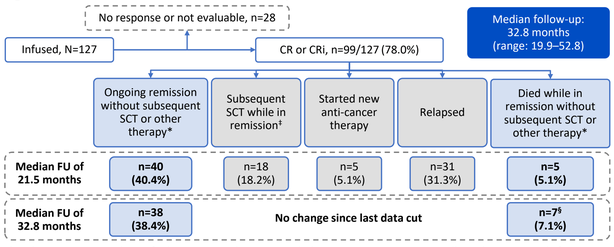


*Deep MRD-negative remission by NGS was not considered because of sample size limitation, as not all patients had NGS calibration. ‡Change in CAR T-cell persistence status (ongoing versus loss) over time, rather than at a specific timepoint, was analyzed. MRD, measurable residual disease; NGS, next-generation sequencing.

RESULTS

- After ~3 years of follow-up, 38.4% of responders remain in remission without subsequent treatment (**Figure 2**).

Figure 2. Patient status at extended follow-up.

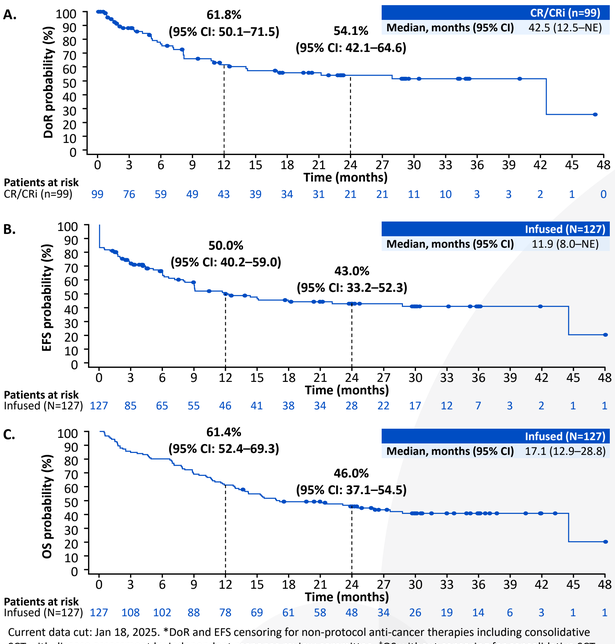


*Without non-protocol specified anti-cancer therapies, including SCT; maintenance TKIs allowed per protocol after two months post obe-cel infusion in patients with Ph+ disease. ‡All patients who received consolidative SCT were in MRD-negative remission ($<10^{-4}$ leukemic cells) at the time of transplant. §Two deaths while in remission observed since the last data cut (reasons: pneumonia and sepsis). FU, follow-up.

Efficacy outcomes

- At 24 months, the probability for duration of remission (DoR), EFS, and OS was 54.1%, 43.0% and 46.0%, respectively, with a potential for long-term plateau in EFS and OS (**Figure 3**).

Figure 3. Kaplan-Meier plots. (A) DoR,* (B) EFS,* and (C) OS.‡



Current data cut: Jan 18, 2025. *DoR and EFS censoring for non-protocol anti-cancer therapies including consolidative SCT with disease assessment by independent response review committee. ‡OS without censoring for consolidative SCT. CI, confidence interval; NE, not estimable.

Safety outcomes

- During the additional 11.3 months of follow-up, no new safety signals were observed; rates of Grade ≥3 cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome remained at 2% and 7%, respectively.
- Since the previous data cut, new Grade ≥3 infections and malignancies were observed in four and zero patients, respectively.

UVA outcomes

- Characteristics identified as important for remission and/or survival by UVA are shown in **Table 1**; these characteristics were fed into the MVA models.

Table 1. Baseline characteristics selected by UVA for the MVA models.

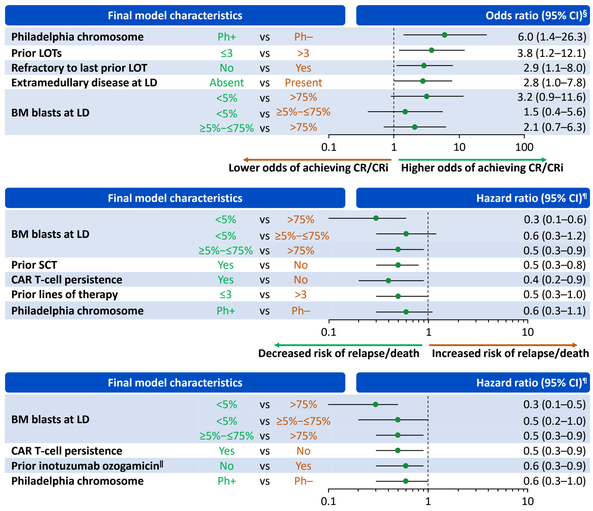
Characteristics with a UVA p-value <0.1	Associated with CR/CRi, EFS, and/or OS			
	Better outcome (% of patients)		Worse outcome (% of patients)	
Age	≥55 years	(37.8%)	<55 years	(62.2%)
Ethnicity	Not Hispanic/Latino/unknown	(70.1%)	Hispanic or Latino	(29.9%)
Philadelphia chromosome	Ph+	(28.3%)	Ph–	(71.7%)
Prior LOTs	≤3	(85.0%)	>3	(15.0%)
Response to first-line therapy	Relapse after 12M	(27.6%)	R/R within 12M	(72.4%)
Refractory to last prior LOT	No	(48.0%)	Yes	(52.0%)
Prior allogeneic stem cell transplant	Yes	(44.1%)	No	(55.9%)
Prior inotuzumab ozogamicin*	No	(68.5%)	Yes	(31.5%)
Extramedullary disease at LD	Absent	(78.7%)	Present	(21.3%)
BM blasts at LD‡	<5% (28.3%)		≥5% – ≤75% (40.2%) >75%	(31.5%)

*Prior to screening; inotuzumab ozogamicin used as bridging therapy in FELIX was not included in these analyses. ‡Categorical variable with three groups. BM, bone marrow; LD, lymphodepletion; LOT, line of therapy; M, months.

MVA outcomes

- By MVA, the following characteristics were associated with remission and survival:
  - Ph+ disease, earlier obe-cel use, and less refractory disease correlated with achieving CR/CRi (**Figure 4A**).
  - Low BM blasts, prior SCT, ongoing persistence, and earlier obe-cel use correlated with better EFS (**Figure 4B**).
  - Low BM blasts, ongoing persistence, and no prior inotuzumab ozogamicin correlated with better OS (**Figure 4C**).

Figure 4. MVA models of baseline characteristics associated with efficacy outcomes. Model 1: (A) CR/CRi; Model 2: (B) EFS,* and (C) OS.‡



*EFS censoring for non-protocol anti-cancer therapies including consolidative SCT with disease assessment by independent response review committee. ‡OS without censoring for consolidative SCT. §A logistics regression analysis of patients achieving CR/CRi was performed against baseline characteristics. ¶An MVA Cox regression model was used to identify key factors for survival using baseline characteristics and CAR T-cell persistence as a time-dependent covariate. ‖Prior to screening; inotuzumab ozogamicin used as bridging therapy in FELIX was not included in these analyses.

CONCLUSIONS

- At a median follow-up of ~3 years, there is a sustained benefit for DoR, EFS, and OS.
  - The 24-month probability of remaining in remission was 54.1% and 38.4% of responders are in long-term remission without consolidative SCT or other therapies, excluding maintenance TKIs in patients with Ph+ disease.
  - EFS and OS had no substantial difference since last data cut and showed a potential for long-term plateau.
- No new safety signals were observed at the long-term follow-up.
- Ph+ disease, earlier obe-cel use, and less refractory disease correlated with achieving higher remission rates; lower disease burden at LD and ongoing CAR T-cell persistence were independent factors associated with long-term remission and survival.
- These results suggest that a proportion of patients may not need further therapy; however, longer follow-up, further analyses, and independent validation are needed to confirm results.

PLAIN LANGUAGE SUMMARY

- Here, we looked at how well obe-cel worked and how safe it was after nearly 3 years of follow-up; we also looked at which patient or disease factors influenced how well the treatment worked, and how long patients lived.
- The probability of a patient living at 24 months after treatment with obe-cel, without events (i.e. their condition worsening, their treatment ceasing to be effective, or death) was 43% in all patients. The probability of a patient living overall at 24 months following treatment with obe-cel, was 46% in all patients.
- No new side effects were observed in patients after nearly 3 years of follow-up (additional 1 year of follow-up compared with previous reports).
- Use of obe-cel in earlier lines of treatment was identified as a factor that may benefit remission, while the amount of obe-cel in a patient's blood over time and less severe disease before obe-cel treatment were factors that may benefit survival outcomes.
- These results suggest that a proportion of patients with R/R B-ALL may not need further therapy following treatment with obe-cel.

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DISCLOSURES

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