# The effect of obecabtagene autoleucel (obe-cel) on adult patients with relapsed/refractory B-cell acute lymphoblastic leukemia (R/R B-ALL) and extramedullary disease (EMD)

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**Poster number ALL-777**

## INTRODUCTION

- Obe-cel is an autologous chimeric antigen receptor (CAR) T-cell therapy designed to mimic natural T-cell engagement, improve persistence and reduce severe immunotoxicity.[1–3]
- Obe-cel demonstrated long-term efficacy and had single-digit incidence of severe immunotoxicity in adult patients with R/R B-ALL in the FELIX study (NCT04404660);[3,4] these data formed the basis for its approval by the U.S. Food and Drug Administration.[5]
- Patients with R/R B-ALL and EMD have limited treatment options and are a population of unmet need.[6]

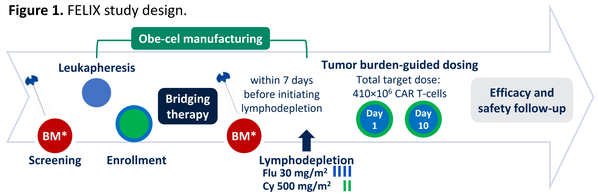
## AIM

To explore efficacy and safety outcomes with obe-cel in adult patients with R/R B-ALL, by EMD status at lymphodepletion (LD).

## METHODS

- In FELIX, adult patients (aged ≥18 years) with R/R B-ALL underwent LD, followed by tumor burden-guided dosing infusions of obe-cel to a total target dose of $410\times10^6$ CAR T-cells (**Figure 1**).
- Patients with central nervous system (CNS) 3 disease or CNS 2 disease with neurological changes were excluded (exclusion criteria for FELIX); patients developing CNS 3 disease or symptomatic CNS 2 disease at any time after enrollment were also excluded until they no longer met these criteria.
- The primary endpoint was overall remission rate (ORR), defined as the proportion of patients achieving complete remission (CR), or CR with incomplete hematologic recovery (CRi), with disease assessment by an independent response review committee.
- Secondary endpoints included: duration of remission (DoR), event-free survival (EFS), overall survival (OS), and safety.

**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

- Among 127 obe-cel-infused patients in FELIX, there were 27 patients with EMD at LD, and 100 patients without EMD at LD. **Table 1** shows baseline patient and disease characteristics for these patients.
  - A total of 36 patients had <5% bone marrow (BM) blasts at LD; of these, seven had EMD and 29 did not have EMD at LD.

**Table 1.** Baseline characteristics of all infused patients in FELIX (N=127), by EMD status at LD.

| Patient and disease characteristics | With EMD at LD (n=27) | Without EMD at LD (n=100) |
|---|---|---|
| **Age in years, median (range)** | 36.0 (20–73) | 50.5 (20–81) |
| **Male / female, %** | 48.1 / 51.9 | 53.0 / 47.0 |
| **Hispanic or Latino, n (%)** | 11 (40.7) | 27 (27.0) |
| **Ph+ disease at LD, n (%)** | 6 (22.2) | 30 (30.0) |
| **Prior lines of therapy, median (range)** | 3.0 (1–6) | 2.0 (1–6) |
| ≥3 prior lines, n (%) | 16 (59.3) | 29 (29.0) |
| **Refractory to all prior lines of anti-cancer therapy, n (%)** | 2 (7.4) | 11 (11.0) |
| **Refractory to first-line therapy, n (%)** | 6 (22.2) | 26 (26.0) |
| **Refractory to last prior line of therapy, n (%)** | 16 (59.3) | 50 (50.0) |
| **Relapsed to first-line therapy within 12 months, n (%)** | 12 (44.4) | 48 (48.0) |
| **Prior blinatumomab, n (%)*** | 19 (70.4) | 34 (34.0) |
| **Prior InO, n (%)*** | 12 (44.4) | 28 (28.0) |
| **Prior blinatumomab and InO, n (%)*** | 8 (29.6) | 13 (13.0) |
| **Prior blinatumomab or InO, n (%)*** | 23 (85.2) | 49 (49.0) |
| **Prior allogeneic SCT, n (%)** | 12 (44.4) | 44 (44.0) |
| **BM blast % at screening, median (range)** | 30.0 (0–100) | 40.0 (0–100) |
| **BM blast % at LD, median (range)** | 54.0 (0–100) | 39.0 (0–100) |
| **BM blast % at LD, n (%)** | | |
| >75% | 11 (40.7) | 29 (29.0) |
| >20%–≤75% | 6 (22.2) | 29 (29.0) |
| ≥5%–≤20% | 3 (11.1) | 13 (13.0) |
| <5% | 7 (25.9) | 29 (29.0) |
| **EMD at screening, n (%)** | 23 (85.2) | 6 (6.0) |

*Therapies administered prior to screening. BM, bone marrow; EMD, extramedullary disease; InO, inotuzumab ozogamicin; LD, lymphodepletion; Ph+, Philadelphia chromosome-positive; SCT, stem cell transplant.

- In the 27 patients with EMD at LD, the sites of EMD were: lymph node (n=13; 48.1%), bone (n=9; 33.3%), liver (n=3; 11.1%), CNS (n=1; 3.7%), testis (n=1; 3.7%), and other (n=9; 33.3%).
  - Other sites included: skin (n=1), muscle (n=1), spleen (n=2), salivary glands (n=1), breast (n=1), pharynx/tonsil (n=1), pancreas (n=1), kidney (n=1), and non-CNS (unclassified; n=3).
- Most patients had EMD involvement in one (n=18; 66.7%) or two organs (n=4; 14.8%). One patient (3.7%) had EMD involvement in three organs, and two patients (7.4%) had EMD involvement in an unknown number of organs.
- Two patients (7.4%) had EMD involvement in four organs: one patient had involvement in the testis, liver, spleen, and lymph node; the other patient had involvement in the spleen, pancreas, kidney, and bone.

### Efficacy outcomes

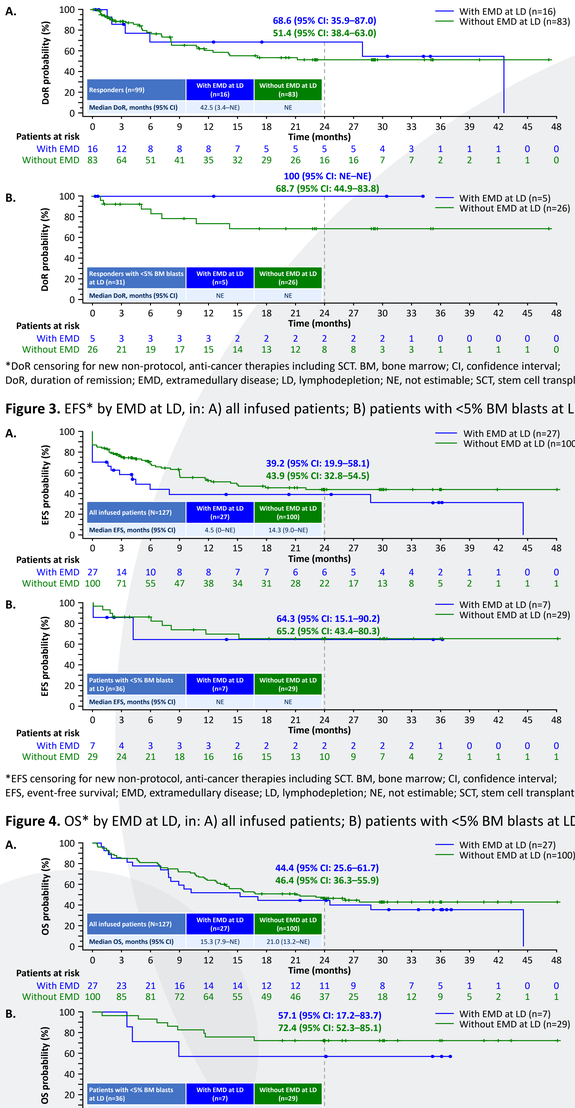
- At a median follow-up of 32.8 months (range: 19.9–52.8; data cut-off: January 18, 2025), the ORR was higher in patients with EMD and <5% BM blasts versus all infused patients with EMD (71.4% vs 59.3%; **Table 2**).
- Patients with EMD benefit from obe-cel treatment (**Figures 2–4**).

**Table 2.** Overall remission rates, by EMD status at LD.

| | All infused patients | | Patients with <5% BM blasts at LD | |
|---|---|---|---|---|
| | With EMD at LD (n=27) | Without EMD at LD (n=100) | With EMD at LD (n=7) | Without EMD at LD (n=29) |
| **ORR, % (95% CI)** | 59.3 (38.8–77.6) | 83.0 (74.2–89.8) | 71.4 (29.0–96.3) | 89.7 (72.6–97.8) |
| **CR / CRi, %*** | 44.4 / 14.8 | 61.0 / 22.0 | 42.9 / 28.6 | 62.1 / 27.6 |

*CR criteria: <5% BM blasts, no EMD (if additional assessments are performed, results must show remission status), no circulating lymphoblasts in peripheral blood, ANC >1,000/μL, platelet count >100,000/μL, and no platelet transfusions in the last seven days and no administration of short-acting G-CSF and long-acting G-CSF in the last three and 14 days, respectively. CRi was defined as: CR criteria with recovery of platelets to ≤100,000/μL and/or recovery of ANC to <1,000/μL. ANC, absolute neutrophil count; BM, bone marrow; CI, confidence interval; CR, complete remission; CRi, CR with incomplete hematologic recovery; EMD, extramedullary disease; G-CSF, granulocyte colony-stimulating factor; LD, lymphodepletion; ORR, overall remission rate.

**Figure 2.** DoR* by EMD at LD in: A) responders; B) responders with <5% BM blasts at LD.




*DoR censoring for new non-protocol, anti-cancer therapies including SCT. BM, bone marrow; CI, confidence interval; DoR, duration of remission; EMD, extramedullary disease; LD, lymphodepletion; NE, not estimable; SCT, stem cell transplant.

**Figure 3.** EFS* by EMD at LD, in: A) all infused patients; B) patients with <5% BM blasts at LD.




*EFS censoring for new non-protocol, anti-cancer therapies including SCT. BM, bone marrow; CI, confidence interval; EFS, event-free survival; EMD, extramedullary disease; LD, lymphodepletion; NE, not estimable; SCT, stem cell transplant.

**Figure 4.** OS* by EMD at LD, in: A) all infused patients; B) patients with <5% BM blasts at LD.




*OS without censoring SCT. BM, bone marrow; CI, confidence interval; EMD, extramedullary disease; LD, lymphodepletion; NE, not estimable; OS, overall survival; SCT, stem cell transplant.

### Safety outcomes

- Patients with EMD and <5% BM blasts had no Grade ≥3 cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS; **Table 3**).

**Table 3.** Safety outcomes, by EMD status at LD.

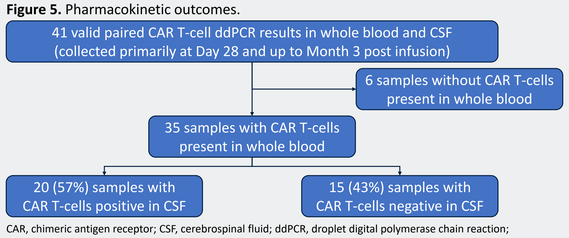
| | All infused patients | | Patients with <5% BM blasts at LD | |
|---|---|---|---|---|
| | With EMD at LD (n=27) | Without EMD at LD (n=100) | With EMD at LD (n=7) | Without EMD at LD (n=29) |
| **Any-grade CRS, n (%)** | 21 (77.8) | 66 (66.0) | 3 (42.9) | 14 (48.3) |
| **Grade ≥3 CRS, n (%)** | 1 (3.7) | 2 (2.0) | 0 | 0 |
| **Time to onset of CRS in days,* median (range)** | 6.0 (2–13) | 9.0 (1–23) | 7.0 (3–12) | 7.0 (1–23) |
| **Duration of CRS in days, median (range)** | 6.0 (2–11) | 5.0 (1–21) | 6.0 (4–8) | 4.5 (1–12) |
| **Any-grade ICANS, n (%)** | 9 (33.3) | 20 (20.0) | 1 (14.3) | 2 (6.9) |
| **Grade ≥3 ICANS, n (%)** | 5 (18.5) | 4 (4.0) | 0 | 0 |
| **Time to onset of ICANS in days,* median (range)** | 11.0 (1–26) | 12.5 (1–31) | 18.0 (18–18) | 10.0 (8–12) |
| **Duration of ICANS in days, median (range)** | 8.0 (1–53) | 8.5 (2–42) | 3.0 (3–3) | 5.5 (2–9) |
| **Any-grade infections, n (%)** | 22 (81.5) | 81 (81.0) | 5 (71.4) | 25 (86.2) |
| **Grade ≥3 infections, n (%)** | 13 (48.1) | 57 (57.0) | 3 (42.9) | 19 (65.5) |

*Time to onset (days) = ([date of start of CRS/ICANS – date of first obe-cel infusion] +1). BM, bone marrow; CRS, cytokine release syndrome; EMD, extramedullary disease; ICANS, immune effector cell-associated neurotoxicity syndrome; LD, lymphodepletion; obe-cel, obecabtagene autoleucel.

### Pharmacokinetic outcomes: CNS

- Obe-cel crosses the blood-brain barrier (**Figure 5**).

**Figure 5.** Pharmacokinetic outcomes.




CAR, chimeric antigen receptor; CSF, cerebrospinal fluid; ddPCR, droplet digital polymerase chain reaction; obe-cel, obecabtagene autoleucel.

## CONCLUSIONS

- Obe-cel had beneficial therapeutic effect in adult patients with R/R B-ALL with EMD.
  - DoR, EFS, and OS were favorable regardless of EMD presence at LD.
- Patients with EMD and with <5% BM blasts at LD did not reach median DoR, EFS, and OS.
- Grade ≥3 CRS/ICANS were not observed in patients with <5% BM blasts regardless of EMD presence at LD.
- Obe-cel was detected in the cerebrospinal fluid, suggesting that it can cross the blood-brain barrier.
- Evidence from this exploratory post-hoc analysis supports obe-cel as a treatment in patients with R/R B-ALL and EMD at LD, including in those with EMD and <5% BM blasts.
- Overall, these findings support a positive benefit–risk profile for obe-cel, regardless of EMD presence at LD.

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### ACKNOWLEDGMENTS

This study was sponsored by Autolus Therapeutics PLC. Third-party medical writing assistance, under the direction of authors, was provided by Emily Fang, MPharm, of Ashfield MedComms, an Inizio company, and was funded by Autolus Therapeutics PLC. Previously presented at the 2026 ASCO Annual Meeting, May 29–June 02, 2026, Chicago, IL, USA (Publication number: 6517), and the 2026 EHA Congress, June 11–14, 2026, Stockholm, Sweden (Publication number: PS1484).

### DISCLOSURES

Dr Jae H Park has stock/ownership in CuroCell; has acted in a consulting or advisory role for Adaptive Biotechnologies, Affylmmune, Allogene, Amgen, Artiva Biotherapeutics, Ascentage, Autolus Therapeutics, Bright Pharmaceutical Services, Bristol Myers Squibb, Caribou Biosciences, CuroCell, Galapagos, Gilead Sciences, Intellia, Iovance, Jazz Pharmaceuticals, Kite, Novartis, Pfizer, Servier, Sobi, Synthekine, and Takeda; and has received research funding from Autolus Therapeutics, Fate Therapeutics, Genentech Inc., Servier, Sobi, and Takeda.

**Presented at the 14th Society of Hematologic Oncology (SOHO) Annual Meeting, September 9–12, 2026; Houston, TX, USA**