An economic model comparing the costs associated with cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) among patients treated with chimeric antigen receptor (CAR) T-cell therapies for relapsed/refractory B-cell acute lymphoblastic leukemia (R/R B-ALL)

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INTRODUCTION

- CAR T-cell therapies have revolutionized treatment for R/R B-ALL,[1–3] but are associated with adverse events (AEs), including AEs of special interest such as CRS and ICANS,[4] which can substantially increase healthcare resource utilization (HCRU) and costs.[5]
- Obecabtagene autoleucel (obe-cel) is an autologous CD19-directed CAR T-cell therapy with a fast off-rate binding domain, a 4-1BB co-stimulatory domain, and tumor burden-guided dosing, designed to enhance persistence and reduce toxicity.[2,6]
- These unique features of obe-cel may potentially reduce the costs of CRS/ICANS. However, few studies have examined the costs of these AEs in R/R B-ALL or evaluated the potential cost-benefits of obe-cel.
- Obe-cel was approved in November 2024 by the U.S. Food and Drug Administration, [7] received conditional marketing authorization in April 2025 from the UK MHRA,[8] a positive EMA CHMP opinion in May 2025,[9] and marketing authorization from the European Commission in July 2025[10] for adult R/R B-ALL.

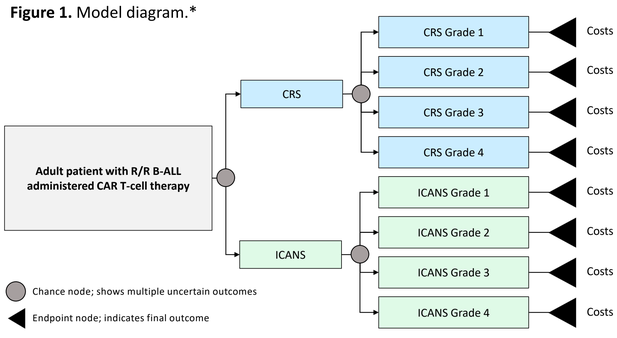
AIM

To estimate the per-patient weighted costs associated with managing CRS and ICANS in adults with R/R B-ALL who have been treated with CAR T-cell therapies (obe-cel, brexucabtagene autoleucel [brexu-cel]).

METHODS

- The cost of treatment for CRS and ICANS (also referred to as AEs herein) was estimated for two CAR T-cell products, obe-cel and brexu-cel, by developing a decision tree economic model (**Figure 1**).
- Probabilistic sensitivity analysis (PSA) was conducted using 1,000 Monte Carlo simulations to account for variability and uncertainty in model inputs.
- Costs are expressed in 2024 US dollars (USD) and weighted across the trial population, including patients with and without CRS and ICANS, to yield a mean ± standard deviation (SD) weighted cost per treated patient.

Figure 1. Model diagram.*



*CRS and ICANS may have occurred in the same patients but were modeled separately for this analysis.

Model design and analysis[5]

- The rate (%; **Table 1**) and median duration (days; **Table 2**) of each AE were obtained from the FELIX (NCT04404660; N=127) and ZUMA-3 (NCT02614066; N=55) clinical trials for obe-cel and brexu-cel, respectively.[1,11–13]
  - Severe (Grade 3/4) AEs were less frequently observed and resolved more quickly among adults who received obe-cel versus brexu-cel.

Table 1. CRS and ICANS rate (%) inputs.

AE* and severity, %	Obe-cel[12] (N=127)	Brexu-cel[1] (N=55)
CRS		
Grade 1	37.0	20.0
Grade 2	29.1	45.5
Grade 3	2.4	12.7
Grade 4	0	10.9
ICANS‡		
Grade 1	10.2	10.9
Grade 2	5.5	23.6
Grade 3	5.5	23.6
Grade 4	0.8	0

*AE rates are reported for 6 months post obe-cel and for a median of 16.4 months post brexu-cel.[1,13] As the median (range) time to onset for obe-cel was 8 (1–23) days for CRS (any grade) and 12 (1–31) days for ICANS (any grade),[13] this was expected to capture the majority of AEs. Grade 5 AEs (one event each in FELIX and ZUMA-3) were excluded from the model. ‡For brexu-cel, data for neurological events (including ICANS) were utilized for this model.

Table 2. CRS and ICANS median (range) AE durations.

AE and severity	Obe-cel (N=127)	Brexu-cel[11] (N=55)
CRS		
Any grade	5 (1–21) days[13]	8 (2–63) days
Grade 3/4	6 (5–7) days[12]	Not available*
ICANS‡		
Any grade	8 (1–53) days[13]	15 (1–397) days
Grade 3/4	11 (8–32) days[12]	Not available*

*In the absence of reported Grade 3/4 AE duration data for brexu-cel, any grade AE duration data were utilized for this model. ‡For brexu-cel, data for neurological events (including ICANS) were utilized for this model.

- AE-related healthcare costs were estimated by conducting a separate analysis of the FELIX trial datasets in which resource utilizations (drugs, procedures, labs, facility charges) associated with the management of each AE were quantified and monetized to arrive at mean costs per AE by severity (**Table 3**).[14]
  - Assuming that both FELIX and ZUMA-3 used standard AE management guidelines, cost estimates were applied uniformly across the trials using AE rates (**Table 1**) and durations (**Table 2**).

Table 3. CRS and ICANS cost inputs (further details previously presented).[14]

AE and severity	Mean total cost (USD)	Model application*
CRS		
Grade 1	$5,781	Per event
Grade 2	$11,159	Per event
Grade 3	$9,922	Per day of event
Grade 4	$9,922	Per day of event
ICANS		
Grade 1	$2,322‡	Per event
Grade 2	$1,056‡	Per event
Grade 3	$7,943	Per day of event
Grade 4	$7,943	Per day of event

*Grade 1/2 AEs were assumed to be treated in an outpatient setting, and thus were estimated per event, whereas Grade 3/4 AEs were assumed to be treated in an inpatient setting and were estimated over the median duration of the AE. The mean cost per day of each AE was calculated over the entire duration of each AE, as reported in **Table 2**, to produce a conservative estimate of upper-level AE-related healthcare costs. ‡The increased cost of Grade 1 versus Grade 2 ICANS is likely due to the variance and small sample sizes (n=7 and n=3, respectively) when quantifying costs.

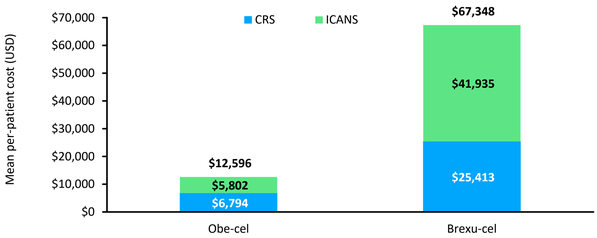
- PSA was conducted to estimate the typical total costs associated with managing CRS and ICANS for each CAR T-cell therapy, using the rates, durations, and costs reported herein.

RESULTS

AE-associated costs

- The lower rate and duration of AEs for obe-cel corresponded with reduced mean ± SD weighted costs relative to brexu-cel, even when conservatively assuming that patients were hospitalized for the entire duration of Grade 3/4 AEs (**Figure 2**).
  - For obe-cel, the weighted per-patient costs associated with CRS and ICANS were $6,794 ± $2,520 and $5,802 ± $3,343, respectively.
  - For brexu-cel, the weighted per-patient costs associated with CRS and ICANS were $25,413 ± $12,059 and $41,935 ± $18,386, respectively.
- Additional analyses that applied the actual known median length of inpatient stay (LOS) observed in the FELIX datasets (Grade 3/4 CRS: 2.5 days, Grade 3/4 ICANS: 7.0 days) further reduced the mean weighted per-patient costs of obe-cel by an additional 12% for CRS ($5,949 ± $1,907) and 34% for ICANS ($3,805 ± $2,270).
  - Actual known LOS data were not available for brexu-cel.
- Total AE-related costs were thus estimated between $9,754 to $12,596 for obe-cel, relative to $67,348 for brexu-cel.

Figure 2. Mean total weighted per-patient cost of CRS and ICANS (any grade) as calculated based on the entire duration of the AE.



LIMITATIONS

- This cost model was based on AE rates observed in the FELIX and ZUMA-3 clinical trials and assumed that AE management guidelines and associated costs were consistently implemented across CAR T-cell therapies. This may not account for potential variations in resource utilization or care delivery in real-world settings, limiting generalizability.
- This model assumed that rates of neurological events with brexu-cel were similar to rates of ICANS, despite differences in definitions.
- In the absence of reported Grade 3/4 AE duration data for brexu-cel, this model utilized duration data of any grade CRS and ICANS. Given that the duration of Grade 3/4 AEs was longer than any grade AEs in FELIX, using the duration from any grade AEs in ZUMA-3 is likely to underestimate the AE costs associated with Grade 3/4 AEs with brexu-cel.
- In accordance with the FELIX study protocol, all patients were hospitalized for 10 days following their first obe-cel infusion. However, this model assumed that Grade 1/2 AEs were all treated in an outpatient setting. Therefore, this could have resulted in underestimation of costs of these AEs.

CONCLUSIONS

- Obe-cel was associated with a 5-fold lower rate of severe CRS and a 4-fold lower rate of severe ICANS compared with existing CAR T-cell therapies (brexu-cel) for adult patients with R/R B-ALL.
- The reductions in AE severity reduced the costs associated with obe-cel relative to brexu-cel, with conservative estimates returning a mean weighted per-patient cost saving of $18,619 for CRS and $36,133 for ICANS.
- These findings highlight the value of obe-cel's fast off-rate CD19 binding domain (designed to mitigate immunotoxicity) in reducing the healthcare burden associated with CRS and ICANS, and the cost of care associated with CAR T-cell therapy.

PLAIN LANGUAGE SUMMARY

- We examined the cost of managing side effects in adults with relapsed or hard-to-treat B-cell leukemia who were treated with CAR T-cell therapy, with either obe-cel or brexu-cel.
- The side effects investigated in this study were CRS and ICANS, which are common with CAR T-cell treatments.
- Patients treated with obe-cel had fewer and less severe side effects compared with brexu-cel, which led to lower healthcare costs.
- Overall, obe-cel may offer a safer and more cost-effective option for CAR T-cell therapy in this patient population.

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DISCLOSURES

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