EE540

Cost-Effectiveness of Brexucabtagene Autoleucel for the Treatment of Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia in Patients Aged 26 Years or Older in the United Kingdom

Tomas Spousta[1], Chaoling Feng[2], Frank van Hees[1], Sally W. Wade[3], Brett Doble[2]

[1]Maple Health Group LLC, New York, NY, USA; [2]Kite, a Gilead Company, Santa Monica, CA, USA; [3]Wade Outcomes Research and Consulting, Salt Lake City, UT, USA

BACKGROUND

Adult B-cell acute lymphoblastic leukemia (B-ALL) is a rare and aggressive haematologic cancer. For patients who are refractory to, or relapse following, initial treatment, prognosis is poor: with currently available treatments median survival is approximately 7 months,[1] highlighting the need for new therapeutic strategies.

Brexucabtagene autoleucel (BREXU-cell) was approved for the treatment of relapsed or refractory (R/R) B-ALL by the European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA) in September 2022 and October 2021, respectively, and recommended by The National Institute for Health and Care Excellence (NICE) through the Cancer Drugs Fund in April 2023.

OBJECTIVES

To estimate the cost-effectiveness of BREXU-CEL versus blinatumomab (BLIN), inotuzumab ozogamicin (INO), and salvage chemotherapy (CHEMO) for patients aged 26 years or older with R/R B-ALL from a United Kingdom (UK) National Health Service and Personal Social Services perspective.

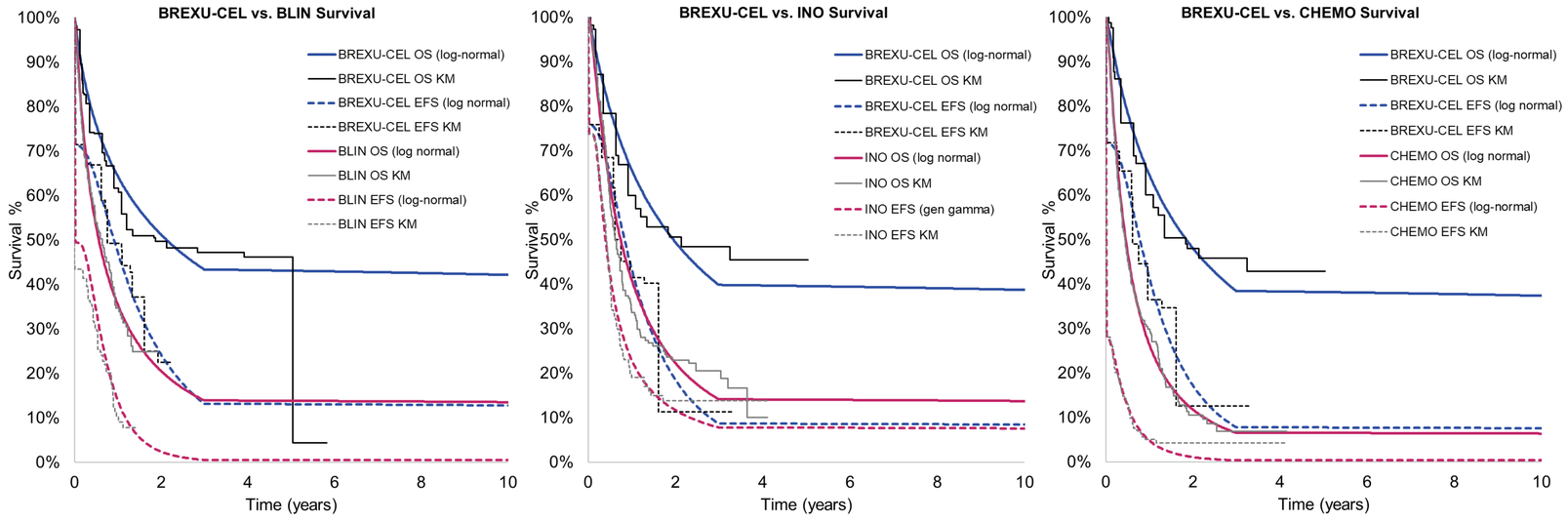
METHODS

A partitioned-survival model comprising the health states 'event-free survival', 'progressed disease' and 'death' was used to estimate treatment-specific health outcomes and costs over a lifetime time horizon. Efficacy and safety data were obtained from ZUMA-3[2] for BREXU-CEL (median follow-up duration: 37.3 months), TOWER[3] for BLIN, and INO-VATE[4] for INO and CHEMO. Matching-adjusted indirect comparisons were conducted to adjust BREXU-CEL event free survival (EFS) and overall survival (OS) for differences between the ZUMA-3, TOWER, and INO-VATE study populations. For BREXU-CEL, we used data from patients aged 26 years or older only, in line with the EMA label. In the BREXU-CEL arm, patients who received infusion were assigned EFS and OS as observed for patients who received infusion in ZUMA-3; patients who did not receive infusion were assigned EFS and OS as modelled for the comparator treatments. Standard parametric models were used to extrapolate EFS and OS for all treatments. Patients alive at 3 years were assigned general population mortality to which a standardized mortality ratio of 1.09 was applied[5]. Utilities for all arms were derived from ZUMA-3 data. Unit costs were obtained from public databases or the literature. List prices were used for all treatments. Costs and health outcomes were discounted at 3.5% annually. Key model inputs are summarized in Table 1. EFS and OS KM data and the extrapolations used in the base case analysis are shown in Figure 1.

Table 1. Key Inputs

Parameter	Base case	Alternative scenario
Efficacy source	MAIC	Naïve comparison
OS extrapolation model for BREXU-CEL and comparators	Log-normal	All other standard extrapolation models
Time of cure for BREXU-CEL and comparators	3 years	2 years, 4 years
BREXU-CEL drug cost (list price per infusion)	£316,118	-
BLIN drug cost (per cycle)	£36,306 (cycle 1)[6] £42,357 (cycle 2+)[6]	-
INO drug cost (per cycle)	£32,192[6]	-
CHEMO drug cost (per cycle)	£4,437[6,7]	-
BREXU-CEL pre-infusion cost (one-off)	£7,615[8]	£41,101[9]
BREXU-CEL administration cost (one-off)	£13,210[8]	
BLIN administration cost (per cycle)	£7,362[8]	-
INO administration cost (per cycle)	£777[8]	-
CHEMO administration cost (per cycle)	£12,730[8]	-
EFS utility	0.822[10]	0.910[11]
PD utility	0.751[10]	0.750[11]
Cured patients' utility	Same as gen pop.	0.760[12]
Standardized mortality ratio (cured)	1.09[5]	1, 4[13]

Figure 1. EFS and OS Extrapolations



Number at risk	0 months	6 months	12 months	18 months	24 months
BREXU-CEL (MAIC)	63	24	17	5	2
BLIN	271	55	11	2	0

Number at risk	0 months	6 months	12 months	18 months	24 months
BREXU-CEL (MAIC)	63	21	13	7	1
INO	164	59	23	15	9

Number at risk	0 months	6 months	12 months	18 months	24 months
BREXU-CEL (MAIC)	63	23	13	6	1
CHEMO	162	17	4	1	0

KM = Kaplan-Meier, EFS = Event-free survival, OS = Overall survival; KM curves for BREXU-CEL are MAIC-adjusted; best fitting curves were selected based on AIC/BIC and visual to the KM data.
Note: Patients receiving BREXU-CEL and all comparator treatments alive at 3 years were assigned general population mortality to which a standardized mortality ratio of 1.09 was applied.

RESULTS

Table 2. Base Case Results

Technology	Total LYs	TOTAL QALYs	Total cost	Incremental LYs	Incremental QALYs	Incremental cost	ICER (£/QALYs)
BREXU-CEL vs. BLIN							
BREXU-CEL	8.98	6.53	£368,223	-	-	-	-
BLIN	3.32	2.24	£273,789	5.67	4.29	£94,433	**£22,011**
BREXU-CEL vs. INO							
BREXU-CEL	8.40	6.03	£370,274	-	-	-	-
INO	3.47	2.38	£214,657	4.93	3.65	£155,617	**£42,623**
BREXU-CEL vs. CHEMO							
BREXU-CEL	8.13	5.83	£369,420	-	-	-	-
CHEMO	1.88	1.21	£97,197	6.25	4.62	£272,223	**£58,897**

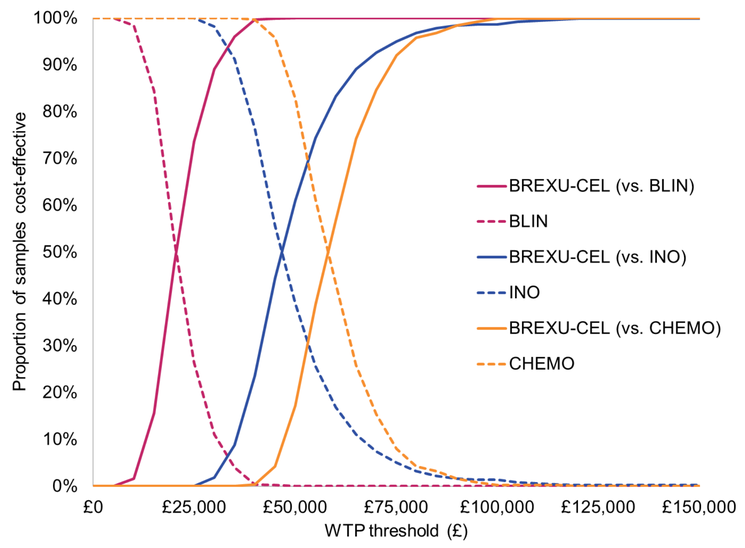
LY = Life year, QALY = Quality-adjusted life year, ICER = Incremental cost-effectiveness ratio; Note: LYs, QALYs, and costs are discounted at 3.5% annually; MAIC data were used for BREXU-CEL

Table 3. Scenario analysis

Scenario	ICER vs BLIN	ICER vs. INO	ICER vs CHEMO
Base case	**£22,011**	**£42,623**	**£58,897**
Efficacy source (naïve comparison)	£28,903	£51,657	£66,018
OS extrapolation model (exponential)	£18,541	£38,748	£53,726
OS extrapolation model (Weibull)	£18,956	£40,116	£53,683
OS extrapolation model (log-logistic)	£22,380	£41,060	£60,002
OS extrapolation model (Gompertz)	£24,052	£46,415	£60,009
OS extrapolation model (gen gamma)	£27,843	£44,421	£59,036
Time of cure 2 years	£22,109	£45,491	£52,728
Time of cure 4 years	£24,212	£46,126	£66,218
BREXU-CEL delivery cost (NHS tariff)	£23,916	£44,958	£60,803
EFS utility source (TISA-CEL SMC)	£21,730	£42,375	£58,102
PD utility source (TISA-CEL SMC)	£22,029	£42,687	£58,962
Cured patients' utility (TA 541 SMC)	£23,171	£42,799	£60,556
Standardized mortality ratio = 1	£21,816	£42,260	£58,352
Standardized mortality ratio = 4	£26,533	£50,984	£71,427

Compared with BLIN, INO, and CHEMO, BREXU-CEL resulted in 5.67, 4.93, and 6.25 life-years gained, and 4.29, 3.65, and 4.62 quality-adjusted life-years (QALYs) gained per patient, respectively (Table 2). The incremental costs of BREXU-CEL versus BLIN, INO, and CHEMO were £94,433, £155,617, and £272,223, respectively. At list prize, BREXU-CEL's incremental cost-effectiveness ratios were £22,011/QALY versus BLIN, £42,623/QALY versus INO, and £58,897/QALY versus CHEMO. Results were robust to scenario analyses performed as shown in Table 3. At list prize, BREXU-CEL has a probability of being cost effective of 100%, 61%, and 17% compared to BLIN, INO, and CHEMO at a willingness to pay threshold of £50,000/QALY gained, respectively (Figure 2).

Figure 2. Cost-effectiveness acceptability curve



CONCLUSIONS

BREXU-CEL substantially improves the life-expectancy of patients with R/R B-ALL compared to BLIN, INO, and CHEMO and added life-years are spent in good health. Moreover, BREXU-CEL is cost-effective at list price versus BLIN and INO and borderline cost-effective versus CHEMO in the UK at a willingness-to-pay (WTP) threshold of £50,000/QALY, which is the WTP threshold that should be used for decision making given the end-of-life criteria apply.

REFERENCES

1. KITE. Meta-analysis of response outcomes in relapsed/refractory acute lymphoblastic leukemia with standard-of-care therapies: Technical Report. January 27th, 2001.
2. KITE. A study evaluating brexucabtagene autoleucel (KTE-X19) in adult subjects with relapsed/refractory B-precursor acute lymphoblastic leukemia (ZUMA-3).
3. Kantarjian H, Stein A, Gökbuget N, Fielding AK, Schuh AC, Ribera J-M, et al. Blinatumomab versus Chemotherapy for Advanced Acute Lymphoblastic Leukemia. New England Journal of Medicine. 2017;376(9):836-47.
4. Kantarjian HM, DeAngelo DJ, Stelljes M, Liedtke M, Stock W, Gökbuget N, et al. Inotuzumab ozogamicin versus standard of care in relapsed or refractory acute lymphoblastic leukemia: Final report and long-term survival follow-up from the randomized, phase 3 INO-VATE study. Cancer. 2019;125(14):2474-87.
5. National Institute for Health and Care Excellence. Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more systemic therapies [TA559]. 2019.
6. Monthly Index of Medical Specialties. [Available from: https://www.mims.co.uk/]
7. Drugs and pharmaceutical electronic market information (eMIT) [Available from: https://www.gov.uk/government/publications/drugs-and-pharmaceutical-electronic-market-information-emit.]
8. Calculation, costs based on publicly available sources.
9. NHS England. Cost of CAR T-cell therapy delivery. [Available from: https://www.nice.org.uk/guidance/ta893/chapter/committee-discussion#car-t-cell-delivery-costs-of-41101-are-most-appropriate-for-decision-making]
10. KITE. A study evaluating brexucabtagene autoleucel (KTE-X19) in adult subjects with relapsed/refractory B-precursor acute lymphoblastic leukemia (ZUMA-3) - EQ-5D-3L analysis
11. NICE - National Institute for Health and Care Excellence. Tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people aged up to 25 years. [TA554]. 2018.
12. National Institute for Health and Care Excellence. Inotuzumab ozogamicin for treating relapsed or refractory B-cell acute lymphoblastic leukaemia [TA541]. 2018.
13. Martin PJ, Counts GW, Appelbaum FR, Lee SJ, Sanders JE, Deeg HJ, et al. Life expectancy in patients surviving more than 5 years after hematopoietic cell transplantation. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2010;28(6):1011-6.

DISCLOSURES

This research was funded by Kite, a Gilead Company, Santa Monica, CA, USA.