EE265

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

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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-CEL) 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 and by the Evaluation & Reimbursement Committee for Medicines in Greece in June 2024.

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 payer perspective in Greece.

METHODS

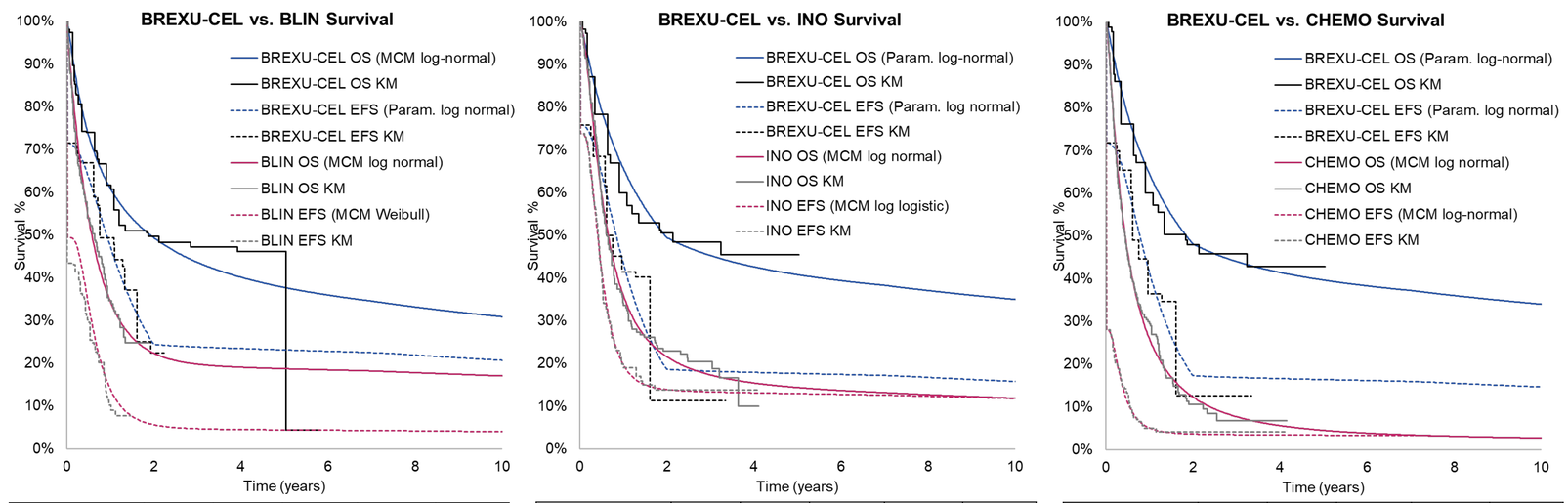
A partitioned-survival model comprising the health states 'event-free survival', 'progressed disease' and 'death' was used to estimate treatment-specific health outcomes and costs over a lifetime time horizon. Efficacy and safety data were obtained from ZUMA-3[2] for BREXU-CEL (median follow-up duration: 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 and mixture cure models were used to extrapolate EFS and OS for all treatments. When standard parametric models were used, patients alive at 2 years were assigned general population mortality to which a standardized mortality ratio of 4 was applied[5], national data on general population mortality were applied. Utilities for the EFS and PD health state were derived from ZUMA-3 data. Direct medical costs of pre-treatment, drug acquisition costs (ex-factory prices), treatment administration, monitoring, allogeneic stem-cell transplant, adverse event and end-of-life costs were derived from up-to-date national sources and published literature (€, 2023). Annual discount rate of 3.5% was applied on costs and health outcomes. 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
Survival extrapolation model for BREXU-CEL (MAIC vs. BLIN)	EFS: Param. log-normal OS: MCM log-normal	-
Survival extrapolation model for BLIN	EFS: MCM log-normal OS: MCM Weibull	-
Survival extrapolation model for BREXU-CEL (MAIC vs. INO, MAIC vs. CHEMO)	EFS: Param. log-normal OS: Param. log-normal	-
Survival extrapolation model for INO	EFS: MCM log-normal OS: MCM log-logistic	-
Survival extrapolation model for CHEMO	EFS: MCM log-normal OS: MCM log-normal	-
Time of cure (standard parametric models)	2 years	3 years
BREXU-CEL drug cost (list price per infusion)	€ 311,364[6]	-
BLIN drug cost (per cycle)	€ 36,773 (cycle 1)[6] € 42,902 (cycle 2+)[6]	-
BLIN number of cycles	4.43[7]	-
INO drug cost (per cycle)	€ 36,657[6]	-
CHEMO drug cost (per cycle)	€ 3,164[6]	-
BREXU-CEL pre-infusion cost (one-off)	€ 1,954[8]	
BREXU-CEL administration cost (one-off)	€ 6,577[9]	-
BLIN administration cost (one-off)	€ 9,000[9]	-
INO administration cost (per cycle)	€ 240[8]	-
CHEMO administration cost (per cycle)	€ 5,707[9]	-
EFS utility	0.822[10]	0.840[11]
PD utility	0.751[10]	0.350[11]
Cured patients' utility	0.860[11]	Same as gen pop.
Standardized mortality ratio (cured)	4[5]	1.09[12]

MAIC = Matching-adjusted indirect comparison, MCM = Mixture-cure model, BLIN = blinatumomab, INO = inotuzumab ozogamicin, CHEMO = salvage chemotherapy

Figure 1. EFS and OS Extrapolations



Number at risk (OS)	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 (OS)	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 (OS)	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: When standard parametric models were used, patients receiving BREXU-CEL and all comparator treatments alive at 2 years were assigned general population mortality to which a standardized mortality ratio of 4 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	6.10	4.63	€ 300,501	-	-	-	-
BLIN	3.41	2.37	€ 168,813	2.68	2.25	€ 131,688	**58,442 €/QALY**
BREXU-CEL vs. INO							
BREXU-CEL	6.72	4.99	€ 302,123	-	-	-	-
INO	2.78	1.97	€ 190,416	3.94	3.02	€ 111,706	**36,971 €/QALY**
BREXU-CEL vs. CHEMO							
BREXU-CEL	6.56	4.85	€ 301,891	-	-	-	-
CHEMO	1.23	0.79	€ 53,109	5.32	4.06	€ 248,781	**61,248 €/QALY**

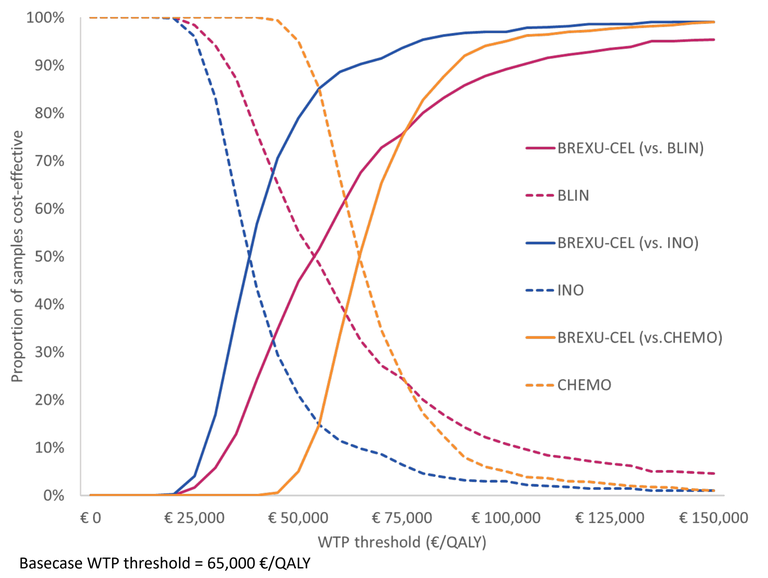
LY = Life year, QALY = Quality-adjusted life year, ICER = Incremental cost-effectiveness ratio; Note: LYs, QALYs, and costs are discounted at 3.5% annually; MAIC data were used for BREXU-CEL

Table 3. Scenario analysis

Scenario	ICER vs BLIN	ICER vs. INO	ICER vs CHEMO
Base case	**€58,442**	**€ 36,971**	**€ 61,248**
Efficacy source (naïve comparison)	€ 42,695	€ 31,584	€ 52,991
Time of cure 3 years	€ 63,234	€ 46,054	€ 71,635
EFS utility source (BLIN SMC)	€ 58,451	€ 37,195	€ 61,170
PD utility source (BLIN SMC)	€ 55,344	€ 59,647	€ 83,539
Cured patients' utility (same as gen. population)	€ 57,631	€ 36,667	€ 60,912
Standardized mortality ratio = 1.09	48,314	€ 29,631	€ 48,584

Compared with BLIN, INO, and CHEMO, BREXU-CEL resulted in 2.68, 3.94, and 5.32 life-years gained, and 2.25, 3.02, and 4.06 quality-adjusted life-years (QALYs) gained per patient, respectively. The incremental costs of BREXU-CEL versus BLIN, INO, and CHEMO were €131,688, €111,706, and €248,781, respectively. BREXU-CEL's incremental cost-effectiveness ratios were €58,442/QALY versus BLIN, €36,971/QALY versus INO, and €61,248/QALY versus CHEMO. Scenario analysis showed consistent results as presented in Table 3. At list prize, BREXU-CEL has a probability of being cost effective of 68%, 90%, and 51% compared to BLIN, INO, and CHEMO at a willingness to pay threshold of €65,000/QALY gained (3 times GDP per capita in 2023 prices[13]), respectively (Figure 2).

Figure 2. Cost-effectiveness acceptability curve



Basecase WTP threshold = 65,000 €/QALY

CONCLUSIONS

Considering the high unmet need in this patient population due to limited survival outcomes of existing therapeutic alternatives, BREXU-CEL provides a valuable and potentially cost-effective alternative to current treatments, deriving its value from incremental survival and health-related quality of life benefits.

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DISCLOSURES

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