Poster
EE298

Cost-effectiveness of Brexucabtagene Autoleucel (brexu-cel, CAR-T) for the Treatment of Relapsed/Refractory Mantle Cell Lymphoma in Greece

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BACKGROUND

- Mantle Cell Lymphoma (MCL) is a rare, but aggressive form of Non-Hodgkin lymphoma (NHL) having an incidence of <1 per 100,000 persons and accounting for approximately 5-7% of newly diagnosed NHL cases in Europe [1, 2].
- Clinical experts in Greece estimate that there are approximately 100-110 new cases of MCL annually, which accounts for 7% of all new cases of NHL.
- Overall, 5-year relative survival in MCL is estimated at approximately 30-60% and is significantly lower than other hematological cancers and lymphomas and the lowest among the different NHL subtypes [3, 4].
- Survival curves with current therapy show no plateau, thus suggesting that virtually all patients die from the disease [5].
- Responses to therapy, progression-free survival (PFS) and overall survival (OS) all decrease with increasing lines of treatment and progression of disease or eventually death is inevitable [6,7].
- Patients with relapsed/refractory (R/R) MCL post-bruton tyrosine kinase inhibitors (BTKi) failure currently have no recognized clinical standard of care (SoC).
- Brexucabtagene autoleucel (brexu-cel) is a novel cell therapy (CAR-T) with promising outcomes. In ZUMA-2 study, which included heavily pre-treated patients who were either relapsed or refractory to up to 5 previous regiments for MCL, including a BTKi, displayed very high response rate (ORR 93%) with 83% of patients in the study alive at 12 months [8].

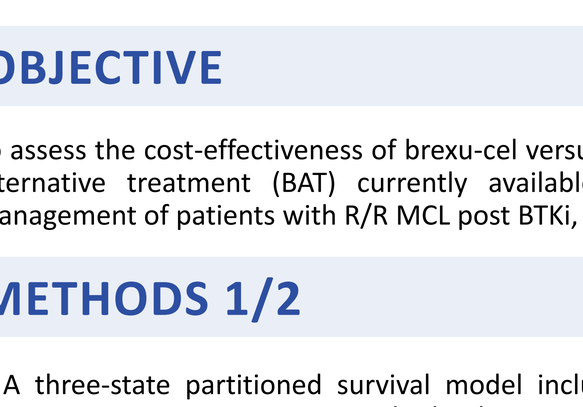
OBJECTIVE

To assess the cost-effectiveness of brexu-cel versus the best alternative treatment (BAT) currently available for the management of patients with R/R MCL post BTKi, in Greece.

METHODS 1/2

- A three-state partitioned survival model including pre-progression, progression, and death, was used for projecting lifetime costs and outcomes for patients with R/R MCL post-BTKi, from a public payer perspective (Figure 1).
- Patients entered the model in the pre-progression health state and could transition to progression and/or death.
- All survival data concerning brexu-cel were extracted from the ZUMA-2 18-month, ITT set (N=74). Survival estimates for BAT were sourced from a literature-based meta-analysis and the respective MAIC [9].

Figure 1. Model structure



- According to the literature, BAT for R/R MCL post-BTKi therapy includes the treatments presented in Table 1, either as monotherapies or in combination. The proportion of patients receiving each treatment was derived from a meta-analysis, dosing scheme was sourced from the relevant summaries of product characteristics (SmPCs) issued by European Medicines Agency (EMA).
- Utilities were sourced from the literature and NICE submission of ibrutinib and were assigned to each health state, irrespective of the treatment arm.

METHODS 2/2

- Mortality rate of the general population in Greece were used in the analysis, as obtained by WHO national lifetables.
- Costs considered in the model included: drug acquisition (based on ex-factory prices), drug administration, hospitalization, disease management per health state, AE management and end of life care. All costs reflect the year 2022 (€). All future outcomes were discounted at 3.5 % per annum. The list of all cost inputs used in the model as well as their sources are presented in Table 1.
- Adverse event (AE) rates for brexu-cel were derived from ZUMA-2 and their management was considered to be part of the hospitalization diagnostic related group (DRG) needed for brexu-cel infusion. For the management of cytokine release syndrome (CRS) and neutropenia, administration of high cost- severe diseases drugs were required based on current clinical practice, which are not included in the respective DRG.
- Main outcomes of the model were discounted and undiscounted patient life years (LYs) and Quality-adjusted life-years (QALYs), total costs, incremental LYs, costs and QALYs as well as ICERs.
- A willingness-to-pay (WTP) threshold of €100,000 per QALY gained per patient was used in the current analysis. This assumption was based on published studies that recommend this threshold to be used for orphan drugs or rare diseases, in absence of a local WTP threshold [10-11].

Table 1. Cost inputs used in the cost-effectiveness analysis

	Cost inputs parameters		Cost input	Source
Brexucel Arm	**Administration costs**			
	Drug acquisition cost (one-time)		€ 360,000	Drug Price bulletin (ex-factory), MoH
	Hospitalization cost for infusion and conditioning chemotherapy		€ 8,384	DRG code: E08M, Government gazette
	Apheresis cost		€ 471	DRG code: Σ21A, Government gazette
	Conditioning chemotherapy (cost per administration)	Fludarabine	€ 90	Drug Price bulletin (ex-factory), MoH
		Cyclophosphamide	€ 26	IFET A.E.
	Adverse events & End-of-life costs			
	CRS		€ 847.70	
	Neutropenia		€ 421.24	
BAT arm	**Cost per administration (% of patients receiving treatment*)**			
	Venetoclax (12.7%)		€ 1.08	Drug Price bulletin (ex-factory), MoH
	Rituximab (56.7%)		€ 649.15	
	Bendamustine (35%)		€ 260.78	
	Cytarabine (32.5%)		€ 8.61	
	Lenalidomide (15.9%)		€ 25.77	
	Bortezomib (6.4%)		€ 23.27	
	Doxorubicin (3.2%)		€ 1.28	
	Cost per IV administration		€ 80	Cost of one-day clinic, Government gazette
	Monitoring cost per health state			
	Cost (per cycle) associated with resource use in pre-progression health state		€ 73	
	Cost (per cycle) associated with resource use in post-progression health state		€ 404	
Both arms	End-of- life cost (one-off)		€ 1,243	DRG tariff, MoH & Expert opinion

Abbreviations: DRG, Diagnostic related group; IV, intravenous; AE, Adverse events; CRS, Cytokine release syndrome; MoH, Ministry of Health

RESULTS 1/2

- Brexu-cel was associated with both significantly higher median survival (7.48 vs 1.61 years) and QALYs gained (5.42 vs. 1.19) than BAT at an additional cost of €368,851.
- The incremental cost-effectiveness ratio (ICER) was estimated at €62,763 and €87,281 per LY and QALY gained respectively.
- The most influential model parameters were proportion retreated and PFS utilities beyond five years, that is pre-progression and cure utility value (Figure 2).
- At a willingness to pay threshold of €100,000/QALY gained, as indicated for life-threatening diseases, the probability for brexu-cel to be cost-effective was 87% (Figure 3).

RESULTS 2/2

- When applying the respective pricing provisions for supply of medicinal products in public hospitals, ICER is further reduced to €54.291 and €75.499 per LY and QALY gained, respectively and the respective probability to be cost-effective is increased to >95%

Table 2. Model results

	Brexu-cel	BAT	Incremental
LYs	7.48	1.61	5.88
QALYs	5.42	1.19	4.23
Cost	€ 412,880	€ 44,029	€ 368,851
Incremental cost per LY gained			**€ 62,763**
Incremental cost per QALY gained			**€ 87,281**

Figure 2. Cost-effectiveness analysis: Tornado diagram of brexu-cel versus BAT

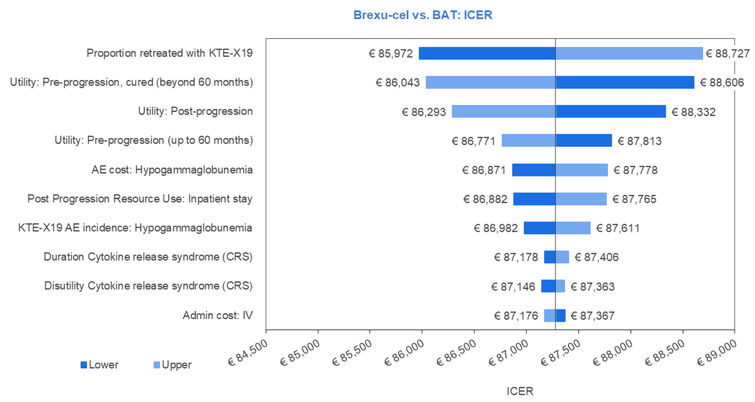
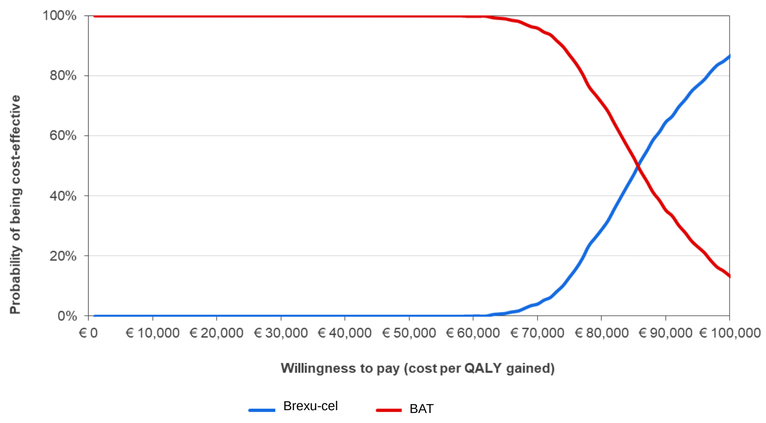


Figure 3. Cost–effectiveness acceptability curves of brexu-cel versus BAT



CONCLUSIONS

Considering the lack of established clinical SoC and the recognized insufficient outcomes for patients with R/R MCL post-BTKi failure, brexu-cel provides a valuable and potentially cost-effective alternative to current BAT in Greece, deriving its value from incremental survival and health-related quality-of-life benefits.

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ACKNOWLEDGMENTS

Authors would like to thank Gilead for funding this research.