EE489

Cost-effectiveness of Zanubrutinib + Obinutuzumab for Treatment of Relapsed or Refractory Follicular Lymphoma in the United States

Sameh Gaballa,[1] Mei Xue,[2] Shilpi Swami,[3] Anuja Bhardwaj,[4] Radha Sharma,[5] Leyla Mohseninejad,[6] Marjan Massoudi,[2] Keri Yang[2]

[1]Moffitt Cancer Center, Tampa, FL, USA; [2]BeiGene USA, San Mateo, CA, USA; [3]ConnectHEOR, UK; [4]ConnectHEOR, India; [5]ConnectHEOR, Montreal, Canada; [6]BeiGene Netherlands B.V.

INTRODUCTION

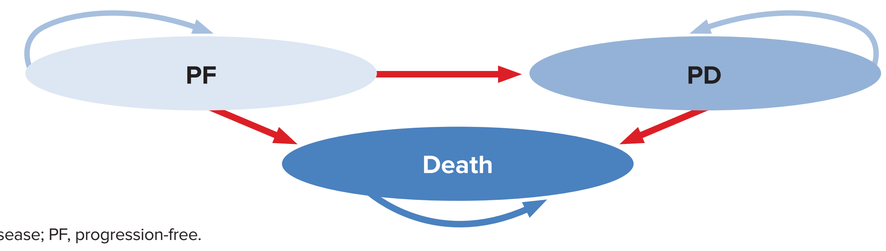
- Follicular lymphoma (FL) is a slow-growing type of non-Hodgkin lymphoma (NHL) that accounts for approximately 20% to 30% of NHL cases and originates in B lymphocytes within the lymphoid tissue[1]
- Despite its slow progression, around 20% of FL patients are expected to experience disease relapse within two years of treatment, with the disease often becoming increasingly refractory with each successive line of therapy[2]
- In March 2024, the United States (US) Food and Drug Administration granted accelerated approval to the combination of zanubrutinib (BeiGene U.S., Inc.) and obinutuzumab for the treatment of relapsed or refractory (R/R) FL following two or more lines of systemic therapy[3]
- Clinical trials, including phase 1b and phase 2 studies, demonstrated that zanubrutinib + obinutuzumab achieved a meaningful activity and a manageable safety profile in patients with third-line or higher (3L+) R/R FL.[4] This study aims to evaluate the cost-effectiveness of zanubrutinib + obinutuzumab compared to mosunetuzumab for the treatment of 3L+ R/R FL from the US healthcare payer perspective

METHODS

Model Framework

- The study used a three-state partitioned-survival model (cohort-based) comprising the health states of 'progression-free' (PF), 'progressive disease' (PD), and death **(Figure 1)**
- The base case model used a lifetime time horizon (40 years) with a cycle length of one week; costs and benefits were discounted at 3% annually

Figure 1. Model Structure



PD, progressive disease; PF, progression-free.

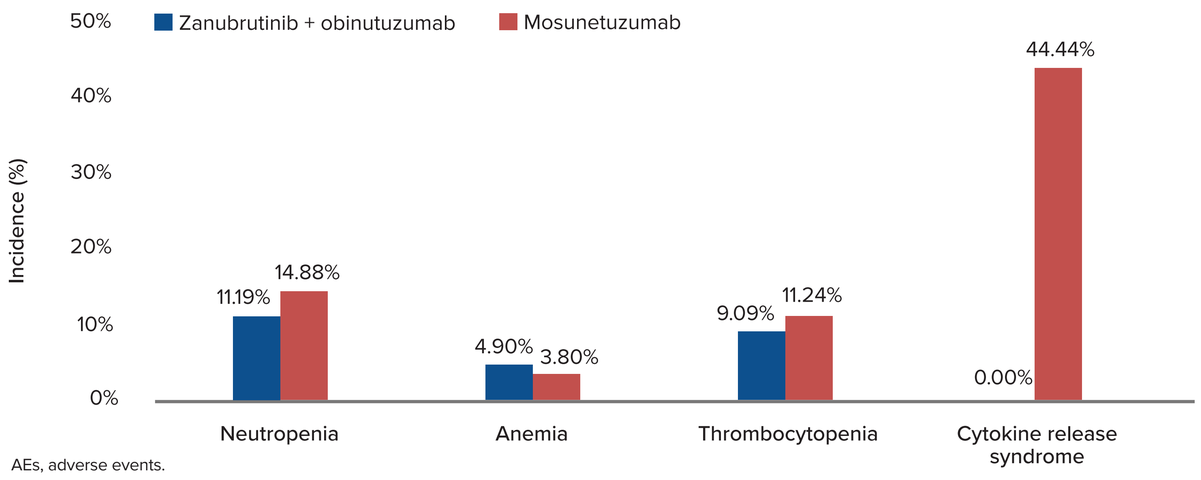
Treatment Efficacy

- PF survival (PFS), overall survival (OS), and time to treatment discontinuation (TTD) for zanubrutinib + obinutuzumab were extrapolated using parametric models based on patient-level data from the phase 2 ROSEWOOD trial (NCT03332017)
- PFS in the model was based on independent review committee assessments
- Unanchored matching-adjusted indirect comparisons (MAIC) of PFS data and safety outcomes were performed (since a network meta-analysis was not feasible due to the lack of a linked network) for zanubrutinib + obinutuzumab vs mosunetuzumab
- As OS was immature, an assumption of equal OS (vs mosunetuzumab) was incorporated following feedback from a US key opinion leader
- TTD for zanubrutinib + obinutuzumab was calculated based on the treatment until progression of each of the components (zanubrutinib and obinutuzumab) for a comprehensive analysis
- To calculate TTD for mosunetuzumab, an approach of treatment until progression with a maximum treatment duration of 24 weeks was used[5]
- The parametric distribution selected for extrapolation was chosen for its 'goodness of fit' to the data, as evaluated using the Akaike information criterion, Bayesian information criterion, and visual inspection

Adverse Events and Healthcare Resource Utilization (HCRU)

- Grade 3+ MAIC adjusted adverse events (AEs) with incidence ≥5% in any treatment arm were included. All grades of cytokine release syndrome (CRS) were included in the analysis due to cost factors. The AEs considered in the model were neutropenia, anemia, thrombocytopenia, and CRS **(Figure 2)**
- The frequency of HCRU was categorized into pre- and post-progression phases and was assumed to be similar across the treatments

Figure 2. Incidence of AEs (%)



AEs, adverse events.

Utility

- In the base case, utility data were sourced from the GO29781 trial[6] and were adjusted for disutility associated with increasing age (as outlined in Ara et al. [2010]),[7] as well as for AEs

Costs

- Direct costs included drug acquisition and administration, subsequent therapies, AE management, healthcare resource use, and terminal care
- All costs were referenced or inflated to 2024 cost

Model Output

- The primary outputs of the cost-effectiveness analyses included costs, life years (LYs) gained, quality-adjusted life years (QALYs), the incremental cost-effectiveness ratio (ICER), and net monetary benefit (NMB)
- In the base case, the model results were discounted using 3% for both costs and benefits, and no cycle correction was applied due to the short cycle length of one week
- Deterministic sensitivity analyses (DSAs), probabilistic sensitivity analyses (PSAs) and scenario analyses were performed to address elements of uncertainty in the model and to explore the robustness of the results

RESULTS

Base Case Results (Table 1)

- Total costs (in US dollars) of zanubrutinib + obinutuzumab were slightly higher compared to mosunetuzumab (by $7,515)
- The largest component of total costs was drug acquisition, followed by HCRU and subsequent treatments
- Notably, zanubrutinib + obinutuzumab demonstrated lower AE costs of $4,961, compared to mosunetuzumab at $14,862
- Total LYs generated by zanubrutinib + obinutuzumab and mosunetuzumab were equal (based on the assumption of equal OS due to data immaturity)
- However, zanubrutinib + obinutuzumab resulted in higher total QALYs than mosunetuzumab by 0.21. The QALY gain was driven by lower AEs and resulting lower disutility due to AEs
- At a willingness-to-pay (WTP) threshold of $150,000/QALY, zanubrutinib + obinutuzumab is highly cost-effective compared to mosunetuzumab, with an ICER of $35,819/QALY and a positive NMB of $23,963

CONCLUSIONS

- This study demonstrates that zanubrutinib + obinutuzumab is a cost-effective treatment option for 3L+ R/R FL in the US compared to mosunetuzumab, with an ICER of $35,819 per QALY
- At a WTP threshold of $150,000/QALY, zanubrutinib + obinutuzumab yields a positive NMB of $23,963
- In the base case analysis, zanubrutinib + obinutuzumab was slightly more expensive than mosunetuzumab, but it provided an additional 0.21 QALYs gain, driven by fewer AEs
- Sensitivity analyses confirmed the robustness of the results, with zanubrutinib + obinutuzumab being more cost-effective in 72.19% of the iterations

Table 1. Detailed Costs-effectiveness Results

	Zanubrutinib + obinutuzumab	Mosunetuzumab
Total Costs	**$ 455,831**	**$ 448,314**
Drug Acquisition Cost	$ 204,239	$ 178,630
Administration Cost	$ 547	$ 582
Subsequent Treatment Cost	$ 68,385	$ 74,922
HCRU Cost – PF	$ 74,964	$ 66,031
HCRU Cost - PD	$ 94,782	$ 105,334
AE Cost	$ 4,961	$ 14,862
Terminal Care Cost	$ 7,953	$ 7,953
Total Life Years	**7.03**	**7.03**
Progression-free	3.40	2.99
Progressive Disease	3.63	4.04
Total QALYs	**5.15**	**4.94**
Progression-free	2.63	2.33
Progressive Disease	2.59	2.87
AE Disutility	**0.07**	**0.26**
Incremental Costs	**$ 7,517**	**-**
Incremental QALYs	**0.21**	**-**
Incremental Cost-effective Ratio	**$ 35,819**	**-**
Net Monetary Benefit	**$ 23,963**	**-**

AE, adverse event; HCRU, healthcare resource utilization; PD, progressive disease; PF, progression-free; QALYs, quality-adjusted life years.

Sensitivity Analysis

- In the DSA, the model was most sensitive to HCRU frequencies in both the PF and PD states, followed by inputs relating to CRS, including its incidence and disutility (data not shown)
- When the WTP threshold exceeded $54,000/QALY, the probability of zanubrutinib + obinutuzumab being cost-effective surpassed that of mosunetuzumab **(Figure 3)**
- The PSA confirmed the robustness of the results, with zanubrutinib + obinutuzumab being more cost-effective in 72.19% of the iterations **(Figure 4)**

Figure 3. Cost-effectiveness Acceptability Curve

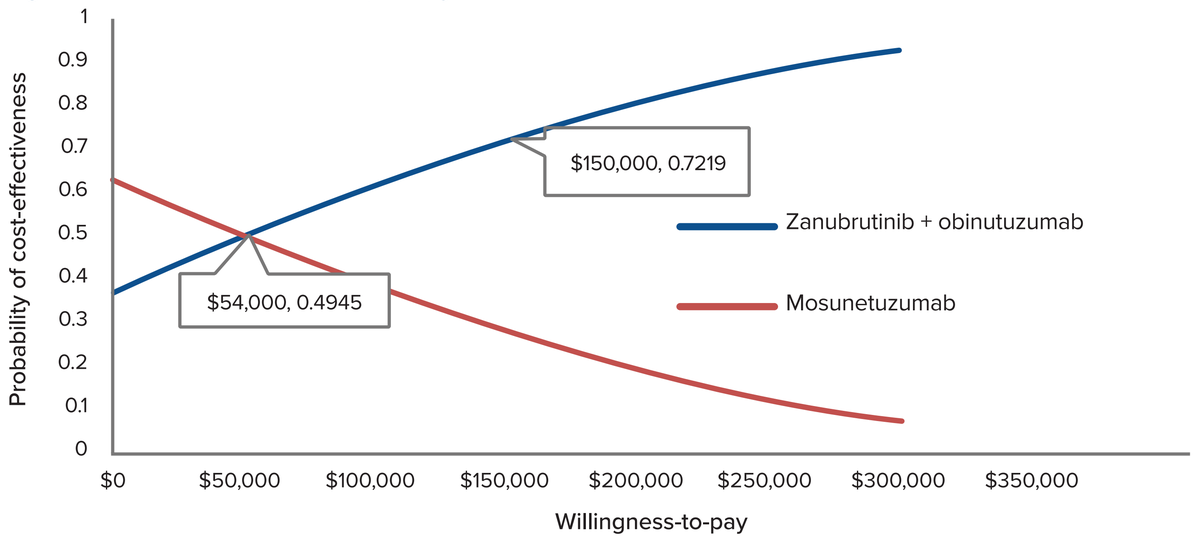
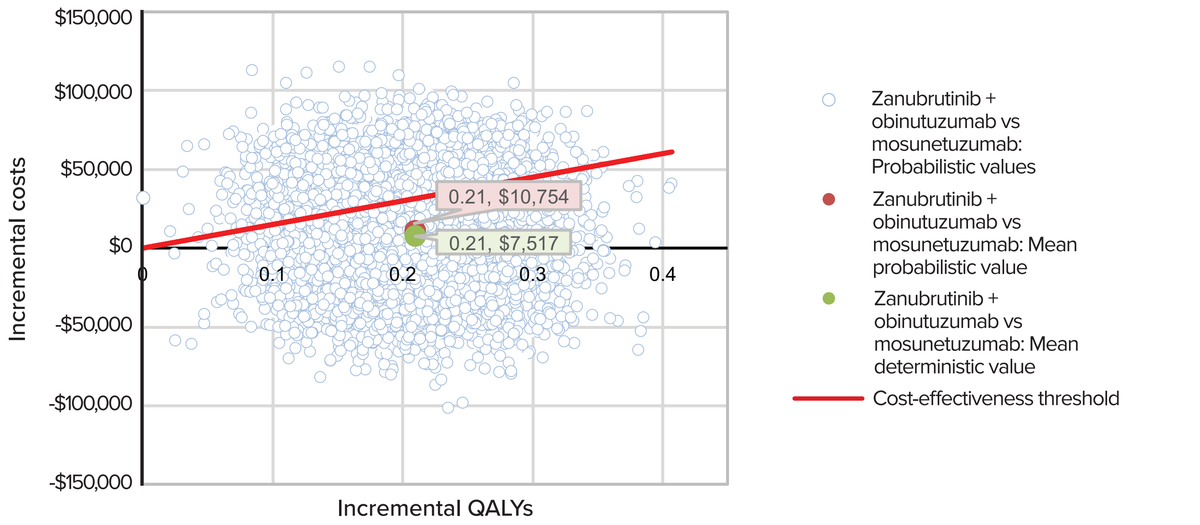


Figure 4. Cost-effectiveness Scatter Plot



QALYs, quality-adjusted life years.

REFERENCES

1. Carbone A, et al. *Nat Rev Dis Primers*. 2019;5:83
2. Kanters S, et al. *BMC Cancer.* 2023;23:74.
3. US Food and Drug Administration. FDA grants accelerated approval to zanubrutinib for relapsed or refractory follicular lymphoma. 7 March 2024. Accessed 9 September 2024. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-zanubrutinib-relapsed-or-refractory-follicular-lymphoma
4. Zinzani PL, et al. *JCO*. 2023;41:5107-5117.
5. Budde LE, et al. *Lancet Oncol.* 2022;23:1055-1065.
6. ClinicalTrials.gov. NCT02500407. Access date: 9 September 2024.
7. Ara R, et al. *Value Health.* 2010;13(5):509-518.

DISCLOSURES

SG: Consulting Fees: Genentech, Ipsen, ADC Therapeutics, AstraZeneca, BeiGene, Gilead, Genmab; Honoraria: ADC Therapeutics, Eli Lilly. **MX, LM, MM, KY**: Employment: BeiGene USA; Stock Ownership: BeiGene USA. **SS, AB, RS**: Employment: ConnectHEOR Ltd; Consulting/Service Fees: BeiGene USA (institutional).

ACKNOWLEDGEMENTS

This study was sponsored by BeiGene, Ltd. Editorial assistance was provided by SNELL Medical Communication, Inc. and was supported by BeiGene.

CORRESPONDENCE: Keri Yang, keri.yang@beigene.com

Presented at ISPOR Europe 2024; November 17-20, 2024; Barcelona, Spain