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A Cost-effectiveness Analysis of Mosunetuzumab for Treatment of Third- or Higher-line Relapsed or Refractory (R/R) Follicular Lymphoma (FL) in the United States (US)

Matthew Matasar,[1] Javier Sanchez Alvarez,[2] Hélène Parisé,[3] Eric Zuk,[3] Danilo Di Maio,[2] Sheila Shapouri,[4] Eunice Kim,[4] Shih-Wen Lin[4]

Summary

Mosunetuzumab (Mosun) has received accelerated approval from the US Food and Drug Administration (FDA) for the treatment of patients with R/R (3L+) FL. An analysis was conducted to assess the cost-effectiveness of Mosun from a US-payer perspective

A three-state partitioned survival model was developed to simulate the lifetime costs and benefits of Mosun; these were compared with a range of approved regimens for the treatment of patients with R/R (3L+) FL

Mosun is projected to be a cost-effective treatment compared with most approved regimens for patients with R/R (3L+) FL

Mosun either dominated, with greater quality-adjusted life years (QALYs) and lower costs, or was cost-effective against all comparators except rituximab + lenalidomide (R-Len) in the base case

Background

- FL accounts for approximately 35% of all non-Hodgkin lymphomas in the US and, despite being indolent, is considered incurable with current therapies.[1]
- Most patients with FL eventually develop resistant disease that can transform into a more aggressive lymphoma, which is associated with poor outcomes.[1,2]
- Mosun, a CD20xCD3 T-cell engaging bispecific antibody, received approval by the US FDA for the treatment of adult patients with R/R FL after two or more lines of systemic therapy.[3,4]
- Approval was based on the results of the Phase II GO29781 study (NCT02500407), which showed frequent and durable responses to fixed-duration Mosun, and a favorable safety profile.[3,5]
- This analysis aimed to assess the cost-effectiveness of Mosun for the treatment of R/R (3L+) FL from a US-payer perspective.

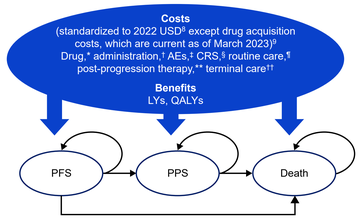
[1]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; [2]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [3]Medicus Economics LLC, Boston, MA, USA; [4]Genentech, Inc., South San Francisco, CA, USA

Methods

Model overview

- A three-state partitioned survival model was developed to simulate the lifetime (60-year) costs and benefits of Mosun vs relevant comparators in adults with R/R (3L+) FL (**Figure 1**).
- Comparators were tazemetostat (taz, EZH2 wild-type patients only), axicabtagene ciloleucel (axi-cel), tisagenlecleucel (tisa-cel), 3L+ FL treatments used in routine care by a retrospective real-world cohort (RW, data derived from Flatiron Health database), obinutuzumab + bendamustine (O-Benda), rituximab + bendamustine (R-Benda), and R-Len.[6]
- Cost components accounted for: drug, administration, adverse events (AEs), cytokine release syndrome (CRS), routine care, post-progression therapy, and terminal care.
- Benefits (health effects) were primarily measured by QALYs based on US-specific health state utilities derived from the EQ-5D-5L scores collected in the NCT02500407 study.[6]
- Cost and health benefits (life years [LYs] and QALYs) were discounted at an annual rate of 3%.[7] A half-cycle correction was applied to the model.

Figure 1. Model overview.



Drug	Cost per mg‡‡
Mosun	$594.06
Taz	$0.39
Axi-cel	$424,000
Tisa-cel	$427,048
Obinutuzumab	$7.78
Bendamustine	$16.00
Rituximab	$8.24
Lenalidomide	$41.66

PFS, progression-free survival; PPS, post-progression disease; USD, United States Dollars.

*Calculated based on wholesale acquisition costs, dosing schedule, and mean treatment duration from US package inserts (PIs) and clinical trial data. †For intravenous drugs, based on administration time, using information available from US PIs. For axi-cel and tisa-cel, these accounted for leukapheresis, drug administration, conditioning chemotherapy, and hospitalization. ‡Calculated based on AE rates of Grade ≥3 severity occurring in ≥5% of patients treated with any comparator as reported in US PIs, clinical trial data, and unit costs from the Healthcare Cost and Utilization Project. §For Mosun, axi-cel, and tisa-cel, these were based on CRS rates of any severity and associated resources (hospitalization and tocilizumab treatment). Frequencies and cost sourced from US PIs, clinical trial data, and literature. ¶Comprised of FL management costs associated with typical clinical practice routine. Frequencies were sourced from expert opinion and costs were extracted from the Centers for Medicare & Medicaid Services fee schedules. **Computed as weighted average costs of a basket of therapies using market share from the NCT02500407 trial and associated mean treatment duration. ††Estimated from published data. ‡‡March 2023 wholesale acquisition costs per mg except for axi-cel and tisa-cel where the package cost was tabulated.

Treatment efficacy

- Clinical efficacy data for Mosun (PFS and overall survival [OS]) were taken from the NCT02500407 trial.
- The relative efficacy of Mosun vs comparators was estimated from indirect treatment comparisons (ITCs) due to a lack of comparator arm:
  - For R-Benda, O-Benda, and the retrospective RW cohort, inverse-probability of treatment weighting (IPTW) from an internal trial or Flatiron Health data were used
  - For all other comparators, a matching-adjusted indirect treatment comparison (MAIC) was used, which accounted for differences in trial population baseline characteristics.
- Extrapolation curves were fitted to PFS and OS for Mosun and comparators using ITC results, which determined patients' distribution among health states over time.
- Waning of the relative treatment effect was not considered on the basis that patients had not received Mosun treatment for a substantial amount of time at the end of follow-up in the NCT02500407 study.

Outputs

- Key outcomes of the cost-effectiveness analysis were: total costs, total LYs, and total QALYs (absolute and incremental), incremental cost-effectiveness ratios (ICERs), and net monetary benefit (NMB).
- Results are presented for each pairwise comparison owing to the ITCs (MAIC or IPTW).
- Probabilistic sensitivity analyses (PSA) with 1000 simulations were conducted for each pairwise comparison to account for uncertainty in model parameters.
- Due to immature OS data for R-Len, uncertainty in OS extrapolation exists and was tested by fitting an alternative parametric distribution chosen for its 'goodness of fit' to the data as assessed by Akaike information criterion, Bayesian information criterion, and visual inspection (base case: exponential; scenario: log-logistic).

Results

Base case results

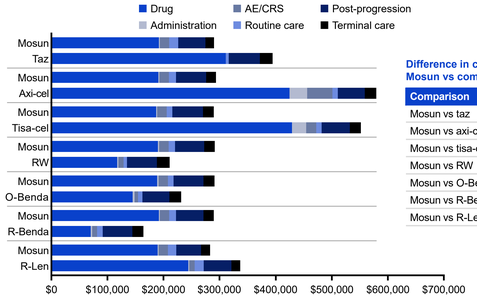
- All newer therapies resulted in higher total costs than Mosun, with axi-cel and tisa-cel accruing the highest costs (**Table 1**). The largest components of total costs were those associated with the drug (**Figure 2**).
- Mosun generated higher LYs and QALYs in all pairwise comparisons except R-Len (**Table 1**).
- Mosun dominated taz, axi-cel, and tisa-cel with greater QALYs and lower costs, and was cost-effective against RW, O-Benda, and R-Benda with ICERs of $21,434, $42,731, and $78,607, respectively (**Table 1**).
- At a willingness-to-pay (WTP) threshold of $150,000 per QALY, the NMB results showed that Mosun was cost-effective against all comparators except R-Len (**Figure 3**).

Table 1. Cost-effectiveness base case results.

Comparison	Intervention (Mosun)			Comparator			Incremental			ICER (Cost/QALYs)
	Cost	LYs	QALYs	Cost	LYs	QALYs	Cost	LYs	QALYs	
Mosun vs taz	$290,097	13.96	11.06	$394,683	4.25	3.35	−$104,586	9.71	7.72	**Mosun dominant**
Mosun vs axi-cel	$293,659	11.06	8.63	$579,112	7.89	6.46	−$285,453	3.17	2.18	**Mosun dominant**
Mosun vs tisa-cel	$289,213	9.18	7.18	$552,338	8.21	6.61	−$263,125	0.97	0.57	**Mosun dominant**
Mosun vs RW	$290,794	10.26	8.09	$210,510	5.45	4.35	$80,284	4.81	3.75	**$21,434**
Mosun vs O-Benda	$290,925	8.88	6.95	$231,769	6.77	5.57	$59,156	2.10	1.38	**$42,731**
Mosun vs R-Benda	$289,584	10.70	8.54	$163,774	8.80	6.94	$125,810	1.90	1.60	**$78,607**
Mosun vs R-Len	$283,028	12.76	10.33	$336,467	14.04	11.09	−$53,439	−1.28	−0.76	**Less cost, less QALYs***

*Mosun is less costly but has lower QALYs than R-Len; therefore, R-Len is cost-effective vs Mosun.

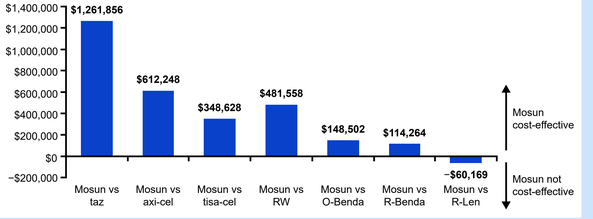
Figure 2. Cost breakdown in the base case.



Difference in cost, Mosun vs comparators

Comparison	Difference
Mosun vs taz	−$104,586
Mosun vs axi-cel	−$285,453
Mosun vs tisa-cel	−$263,125
Mosun vs RW	$80,284
Mosun vs O-Benda	$59,156
Mosun vs R-Benda	$125,810
Mosun vs R-Len	−$53,439

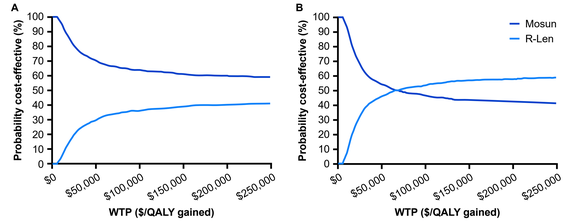
Figure 3. NMB associated with Mosun (WTP per QALY of $150,000).



Sensitivity analyses

- PSA simulations confirmed the robustness of the base case results to parameter uncertainty.
- Mosun was cost-effective at the WTP of $150,000/QALY in 100%, 98%, 96%, 87%, 66%, 61%, and 43% of the simulations against taz, axi-cel, RW, tisa-cel, O-Benda, R-Benda, and R-Len, respectively.
- For the OS extrapolation scenario, using a different parametric curve led to Mosun being cost-effective vs R-Len (NMB = $115,000) at a WTP of $150,000/QALY. In PSA simulations, Mosun was cost-effective in 61% of simulations compared with 43% if the log-logistic vs the exponential distribution was chosen, respectively (**Figures 4A** and **4B**).

Figure 4. Cost-effectiveness acceptability curve of Mosun vs R-Len using alternative (A) and base case (B) OS parametric curve.



Limitations

- Discounts on drug list prices were excluded, which may impact the results.
- There is some uncertainty around the OS extrapolation used in the model.
- Due to the lack of comparator arm in the NCT02500407 study, the model relied on ITCs where residual bias from substantial differences in study design and population across trials persisted, despite efforts to adjust for cross-study heterogeneity.
- Model inputs were obtained from multiple data sources and assumptions in some cases that led to uncertainties. However, extensive sensitivity analyses were conducted to assess the importance of these uncertainties.

Conclusions

- Fixed-duration treatment with Mosun is projected to be a cost-effective option for patients with R/R (3L+) FL compared with most approved regimens.
- Mosun may lead to cost savings for US payers.

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