Cost-effectiveness of Belantamab mafodotin (Belamaf) vs. Melphalan flufenamide in combination with dexamethasone (MEL+DEX) in heavily pre-treated relapsed/refractory multiple myeloma patients: a U.S. payer perspective

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BACKGROUND

> Multiple myeloma (MM) is a rare and incurable hematologic malignancy of plasma cells. [1]

> Despite recent advancements in the therapeutic landscape, MM remains incurable, and most patients eventually relapse or become refractory to classes of drugs.

> Belantamab mafodotin (belamaf) and Melphalan flufenamide in combination with dexamethasone (MEL+DEX) are both first-in-class medications recently approved by the FDA for heavily pre-treated patients with relapsed and refractory multiple myeloma (RRMM). [2-3]

> While both belamaf and MEL+DEX extend treatment options, belamaf and MEL+DEX come with hefty price tags, highlighting the need to evaluate the relationship between the costs and outcomes of these therapies.

OBJECTIVE

> To evaluate the cost-effectiveness of belamaf compared with MEL+DEX in RRMM patients who have received at least four prior lines of therapy, including immunomodulatory drugs (IMiD), proteasome inhibitors (PI), and anti-CD38 monoclonal antibodies (mAb).

METHODS

Study Design

> A three health state partitioned survival model was developed to estimate the overall survival (OS) and progression-free survival (PFS) based on the results from pivotal clinical trial data for belamaf (DREAMM-2) and MEL+DEX (HORIZON). [2-3] (Figure 1)

> The patient population of HORIZON and DREAMM-2 shared similar baseline clinical characteristics. DREAMM-2 enrolled patients who had received at least 3 prior therapies and were refractory to IMiD and PI and had been exposed to mAb. HORIZON enrolled patients who had received at least 2 prior therapies, including IMiD and PI, and were refractory to PI and/or mAb. [2-3]

> The best-fitting parametric distributions of OS and PFS for both populations were based on the visual assessment of the parametric distribution curves and the lowest Akaike's Information Criterion (AIC). (Figure 2)

> The analysis was performed from a U.S. commercial payer perspective and a monthly cycle was applied for a lifetime horizon. An annual discount rate of 3% and half-cycle corrections were applied to costs and health outcomes.

> Quality-adjusted life-year (QALY) was the main health outcome used in the model and the willingness-to-pay (WTP) threshold of $100,000 and $150,000 per QALY gained were used to evaluate the cost-effectiveness.

> Uncertainty in the model was tested through one-way sensitivity analysis (OWSA) and probabilistic sensitivity analyses (PSA).

Figure 1. Partitioned survival model with 3 health states

Notes: All patients were assumed to have started from PF state and patients could either remain in the state or progress to the PD state or Death state. All patients were assumed to not receive treatment beyond progression. PFS partitioned alive patients in PF and PD states and was used as a proxy for time to treatment discontinuation, progression, or death (TTDPD).

Figure 2. Parametric distributions of OS and PFS for belamaf and MEL+DEX
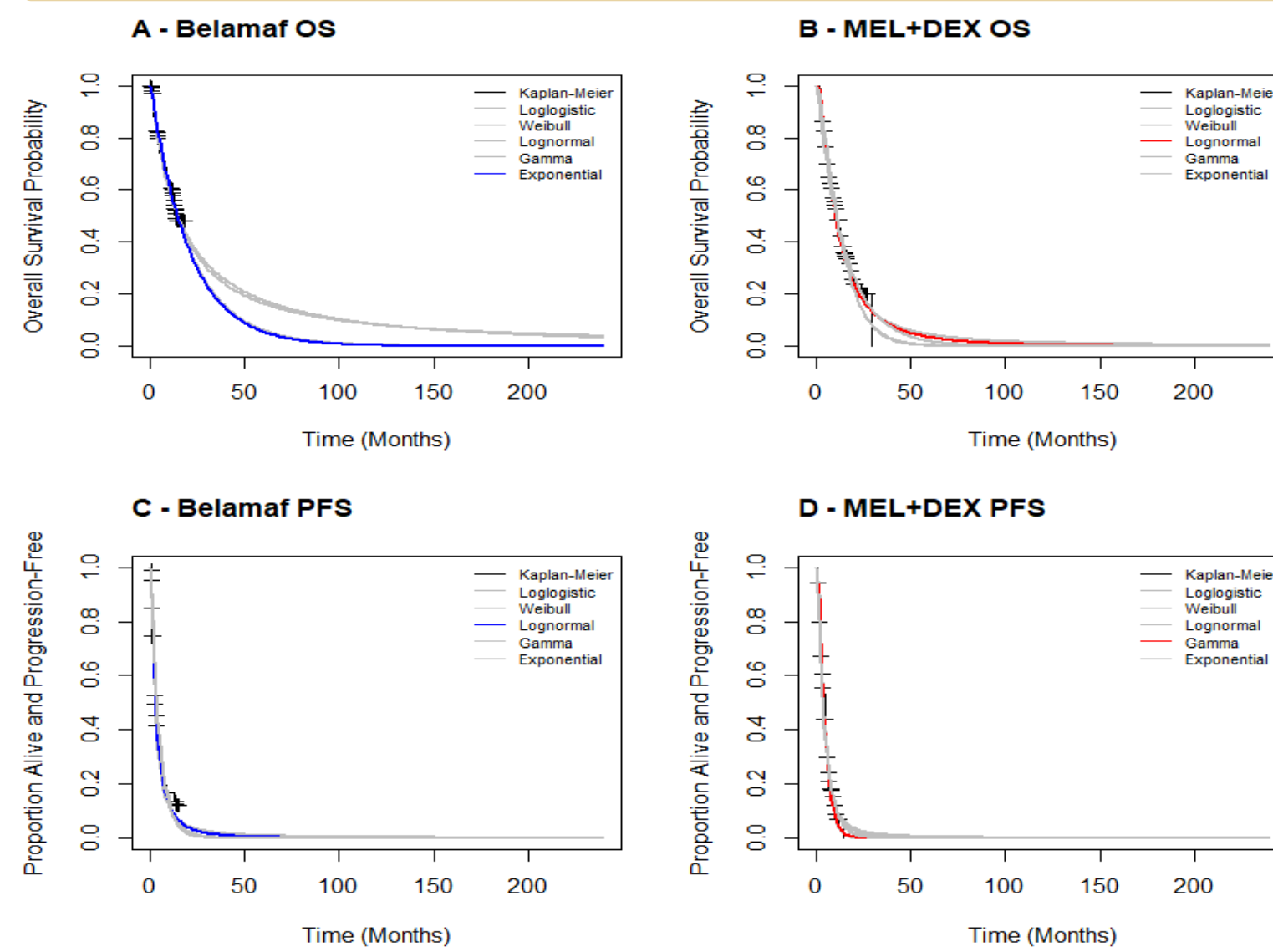
Notes: Parametric distribution curves in blue have been selected to estimate OS and PFS for belamaf and in red have been selected to estimate OS and PFS for MEL+DEX.

Model Inputs

> Health state utilities were obtained from a study that collected quality-of-life in DREAMM-2 and mapped it to the EuroQoL five-dimensions questionnaire (EQ-5D). [4] (Table 2)

> Unit cost inputs were derived from IBM Micromedex® Redbook and published cost-effectiveness analysis of belamaf compared to a different MM drug. Drug acquisition costs were estimated based on belamaf 2.5 mg/kg every 3-week and melphalan 40 mg once monthly IV infusion in combination with oral dexamethasone 40 mg once-weekly from HORIZON. [3-4] (Table 3)

> The incidence of grade 3 or 4 adverse events that occurred in > 5% of patients on both treatments was obtained from the FDA labels and converted to monthly probabilities to calculate adverse events related disutility and management costs. [4-7] (Table 3)

Table 2. Health state utilities values

Health State Utilities	Belamaf	MEL+DEX	Sources
Progression-Free	0.73	0.73	[4]
Progressed	0.66	0.66	[4]
Adverse Events-related Disutility [a]	-0.09	-0.29	[4,6,7]

Table 3. Cost inputs (2021 US Dollars)

Costs per Month (Base Case)	Belamaf	MEL+DEX	Sources
Drug Acquisition	$25,393	$19,159	[3-5]
Drug Administration	$825	$825	[4]
Concomitant Medication	$5.64	$6.85	[4,5]
Adverse Events Management [a]	$1,953	$4,901	[4,6,7]
Treatment Monitoring	$580	$318	[4,6,7]
Disease management – On treatment [b]	$984	$984	[4]
Disease management – Off treatment [c]	$1,224	$1,224	[4]
One-off Terminal care [d]	$5,732	$5,732	[4]

a Estimated adverse-events related utility decrements and management costs were applied to the patients remaining in the PF state for each cycle
b Applied to the patients remaining in the PF state for each cycle
c Applied to the patients in the PD state for each cycle
d Applied to all new deaths for each cycle

RESULTS

> Over a lifetime horizon, belamaf was associated with higher incremental life-years and QALYs by 0.33 and 0.30 compared to MEL+DEX. Total treatment costs were higher in patients receiving belamaf with the incremental cost of $37,959. The incremental cost-effectiveness ratio (ICER) for belamaf versus MEL+DEX was $130,723 per QALY gained. (Table 4)

> The one-way sensitivity analysis demonstrated that the model was the most sensitive to variations in PFS estimates of MEL+DEX and belamaf, followed by drug acquisition costs of both drugs. (Figure 3)

> The results from the probabilistic sensitivity analysis demonstrated that belamaf had 46% probability of being cost-effective compared to MEL+DEX at a WTP threshold of $100,000 and 62% probability at a WTP threshold of $150,000 per QALY gained. (Figure 4)

**Table 4.** Base-case results – lifetime horizon

	Belamaf	MEL+DEX	Differences, belamaf vs. MEL+DEX
Life Years (LY)	**1.63**	**1.30**	**0.33**
Progression-Free LY	0.42	0.32	0.10
Progressed LY	1.21	0.93	0.28
QALY	**1.07**	**0.77**	**0.30**
Progression-Free QALYs	0.31	0.27	0.04
Progressed QALYs	0.80	0.61	0.19
QALY Loss due to Adverse Event	**-0.04**	**-0.11**	**0.07**
Costs (2021 US Dollars)	$172,231	$134,272	$37,959
Drug Acquisition	$127,217	$84,178	$43,039
Drug Administration	$4,133	$3,625	$508
Concomitant Medications	$28	$30	-$2
Treatment Monitoring	$2,906	$1,397	$1,509
AE Management	$9,784	$21,533	-$11,749
Disease Management – On Treatment	$4,930	$4,323	$607
Disease Management – Off Treatment	$17,777	$13,676	$4,101
Death (Terminal Care)	$5,456	$5,510	-$54
ICER per LY			**$114,723**
ICER per QALY			**$130,723**

Figure 3. Tornado diagram of one-way sensitivity analysis
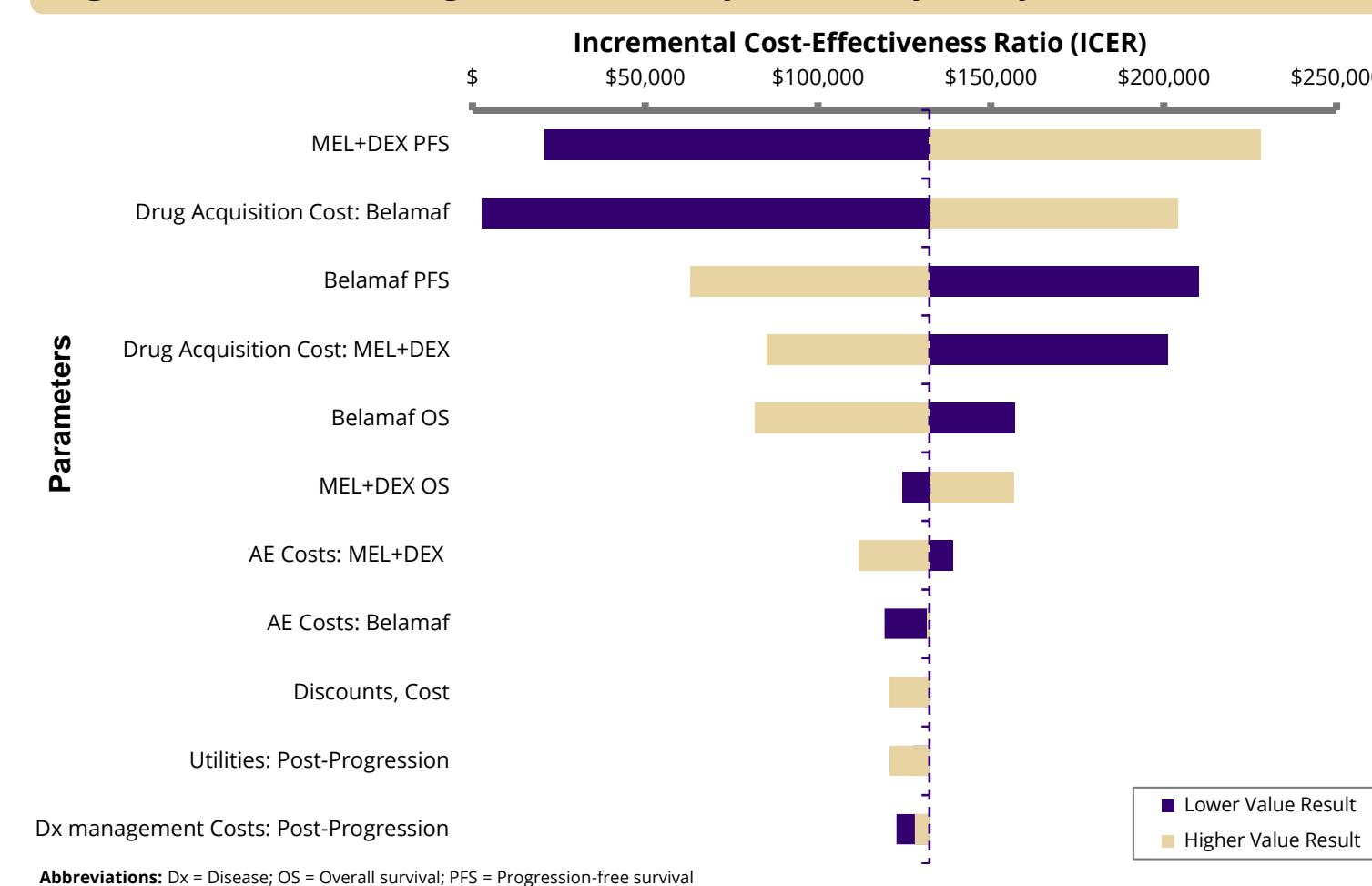
Abbreviations: Dx = Disease; OS = Overall survival; PFS = Progression-free survival

Figure 4. Probabilistic sensitivity analysis – Incremental cost-effectiveness scatter plot
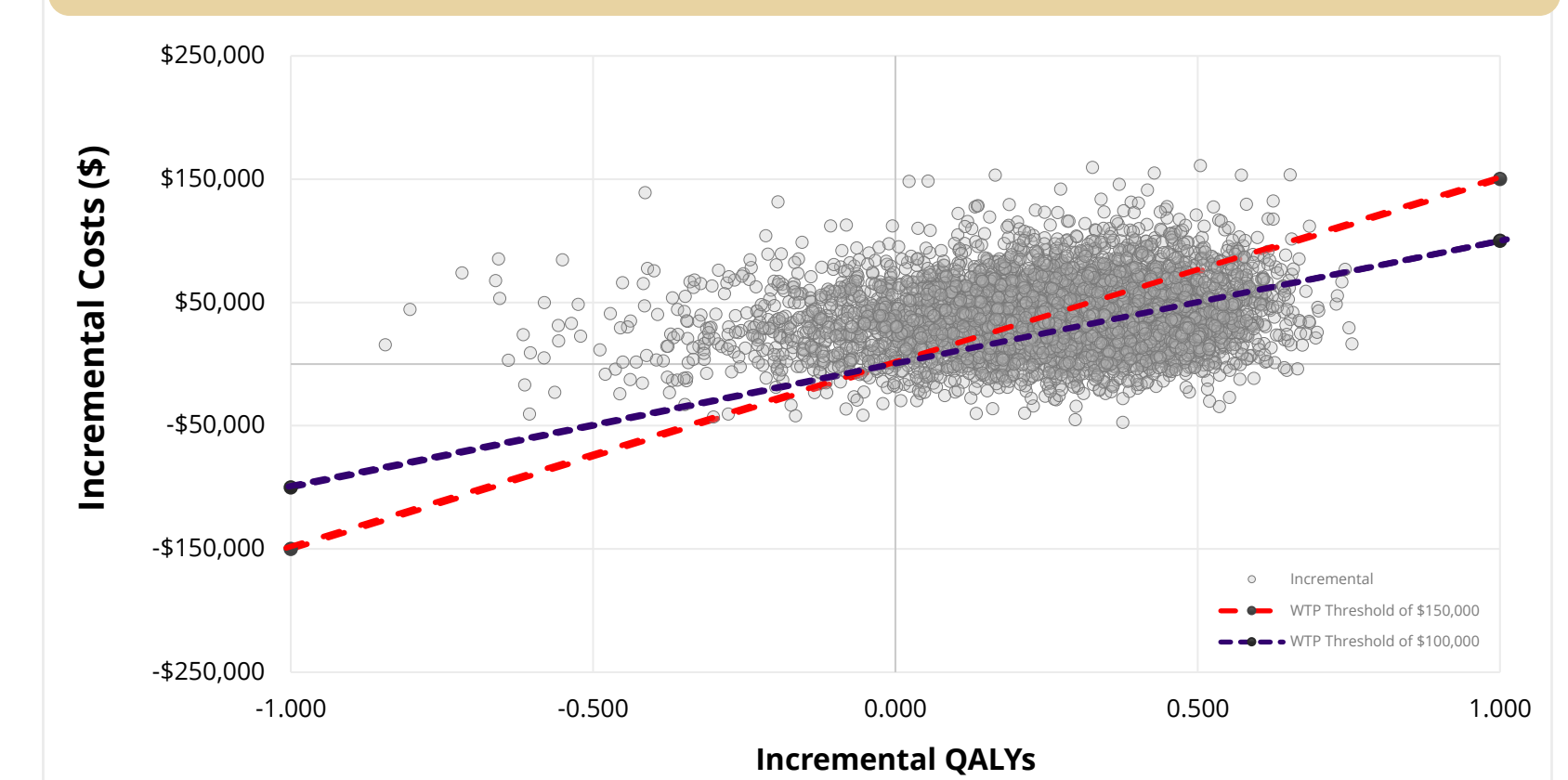
DISCUSSION

> The results of the model demonstrated incremental benefits of belamaf compared to MEL+DEX, in terms of safety and efficacy.

> The longer PFS associated with belamaf suggests that a higher proportion of patients will remain on treatment, which contributed to higher treatment-related costs. Consistent with this, the longer OS of belamaf contributed to higher overall disease management costs while on and off the treatment.

> There are several limitations to note in this study.
- First, this naïve indirect comparison was conducted in the absence of a head-to-head randomized clinical trial.
- Second, the sources of the cost inputs in the model were primarily published literature, which limits the precision in estimating the true healthcare resource utilization and costs.
- Lastly, there was limited data and great uncertainty in estimating the long-term survival outcomes based on short-term data.

CONCLUSION

> The study results suggest that belamaf is potentially a cost-effective therapy compared to MEL+DEX in heavily pretreated RRMM patients with limited treatment options under the commonly used WTP threshold range of $100,000 to $150,000 in the U.S.

> Future research should consider conducting a matching adjusted indirect comparison (MAIC) to adjust for trial differences and reduce the bias in the treatment effect estimates inherent in a naïve indirect comparison.

ACKNOWLEDGEMENTS

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