Cost-effectiveness of ibalizumab versus routine clinical care in heavily treatment-experienced (HTE) people with HIV in the United States (US)

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Background and objectives

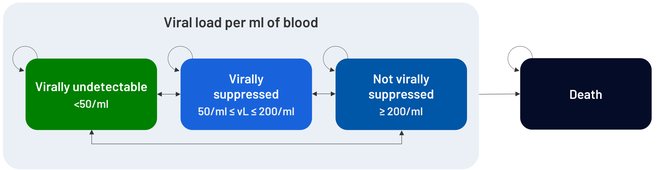
- Heavily-treatment experienced (HTE) patients with multi-drug resistant (MDR) HIV are a rare subset of HIV patients with limited treatment options due to resistant viral strains.[1]
- Ibalizumab is a monoclonal antibody antiretroviral (ARV) approved in the US for HTE patients with HIV with ongoing viral replication.[2]
- Clinical evidence demonstrates that ibalizumab is effective in reducing and suppressing viral load (VL) in HTE people with HIVd, which may have an economic benefit to US payers.
- A cost-effectiveness analysis was conducted to assess the addition of ibalizumab to routine clinical care (e.g optimized background regimens [OBR]) from a US payer perspective.

Methods

Structure

- A Markov model was developed to estimate the cost per quality-adjusted life year (QALY) gained following the addition of ibalizumab to OBR from a US payer perspective over lifetime horizon (Figure 1).
- The model considered HTE people with HIV as per ibalizumab's trials (TMB-202 and TMB-301/311).[3,4,5]
- Model health states were: virally undetectable (vL<50 copies/ml), virally suppressed (50 ≤vL≤ 200 copies/ml), and virally unsuppressed (vL>200 copies/ml). A 12-week cycle length was used.
- All patients entered the model in the virally undetectable health state.

Figure 1: Model schematic



Comparative effectiveness

- Transition probabilities for achieving viral suppression or viral undetectability for ibalizumab patients were informed by Phase 2 and 3 clinical trials (TMB-202 and TMB-301/311). Data is available for 96 weeks.
- Estimates of comparative effectiveness were derived through a standardized mortality rate (SMR)-weighting analysis of TMB-202 and TMB-301/311 data to non-ibalizumab-containing regimens in routine clinical care from the OPERA® cohort (Table 1).[6]
- After 96 weeks (end of the observed data), long-term transition matrices were derived from the average of the transition probabilities from weeks 1-96.

Table 1: Mean risk ratio (Ibalizumab + OBR vs OBR) for the virally undetectable and virally suppressed health states over time[7]

	Time period (weeks), HR (95% CI)				
	1-25	25-48	48-60	60-96	96+
Virally undetectable	1.50 (1.01, 2.22)	2.09 (1.24, 3.54)	2.33 (1.08, 5.03)	1.49 (0.95, 2.24)	1.49 (0.95, 2.24)
Virally suppressed	0.92 (0.73, 1.17)	0.90 (0.70, 1.15)	1.07 (0.71, 1.60)	1.64 (0.45, 5.94)	1.64 (0.45, 5.94)

Costs

- Costs were derived from appropriate US sources and included treatment acquisition (Table 2) and administration, monitoring, adverse events, opportunistic infections, and terminal care.
- Costs and outcomes were discounted at 3% per annum, in line with the Institute for Clinical and Economic Review (ICER) reference case.[7] A 2022 price year was used.

Table 2: Annual treatment acquisition costs*

	Ibalizumab + OBR	OBR
Year 1	$157,465.00	$69,445.05
Year 2+	$148,876.00	$69,445.05

*Unit costs sourced from RedBook, WAC prices.

Mortality and utilities

- Mortality assumptions (Table 3) and health-state utility values were based on disease-specific published literature and clinical trial data.[8,9]
- Utility values were 0.778, 0.773, and 0.771 for the virally undetectable, virally suppressed, and not virally suppressed health states, respectively.[9]

Table 3: Mortality hazard ratios for ibalizumab + OBR and OBR for each health state

	Virally undetectable	Virally suppressed	Not virally suppressed
Ibalizumab + OBR	1.00	2.20	6.75*
OBR	1.00	2.20	7.70
Relative to:	General population mortality	Undetectable	Undetectable

*It is assumed that ibalizumab will manage VL in the unsuppressed cohort more effectively than OBR and hence a lower HR is applied in the base case to the ibalizumab arm.

Discontinuation

- Due to the chronic nature of HIV and the reduced expectancy of patients entering the analysis, patients were assumed to remain on OBR treatment indefinitely.
- Ibalizumab discontinuation was based on the number of discontinuations that occurred during the TMB-301/311 trials.

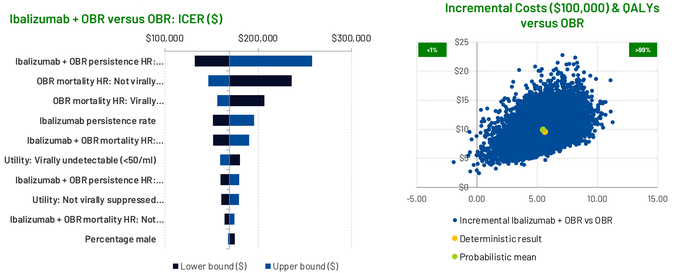
Results

- Over a lifetime horizon, the addition of ibalizumab to OBR increased the time patients spent virally undetectable or suppressed and extended a patient's QALYs compared to OBR alone.
- The addition of ibalizumab to OBR was associated with an incremental cost-effectiveness ratio (ICER) of $169,103 (Table 4). These results should be considered in context of rare diseases, with a cohort study identifying only 2,277 patients in the US living with HTE HIV.[10] The Institute for Clinical and Economic Review increase their WTP threshold to $175,000 for rare diseases,[11] indicating that ibalizumab can be considered cost-effective in its target population.
- Results were robust to deterministic and probabilistic sensitivity analyses (over 10,000 iterations) (Figure 2).

Table 4: Base case results

	OBR	Ibalizumab + OBR	Incremental
Total costs ($)	706,145	1,660,015	953,871
Total LYs	9.655	16.824	7.169
Total QALYs	7.409	13.050	5.641
ICER ($)	-	-	**169,103**

Figure 2. *Left*: One-way sensitivity analysis tornado. *Right*: Probabilistic sensitivity analysis incremental cost-effectiveness plane



Conclusion

The addition of ibalizumab to OBR resulted in increased costs and QALYs. The ICER fell below an acceptable WTP threshold for rare diseases and demonstrates that the addition of ibalizumab to routine clinical care may provide payers with a cost-effective treatment option that can substantially improve outcomes for HTE people with HIV.

Acknowledgements

Theratechnologies, Inc funded this work.

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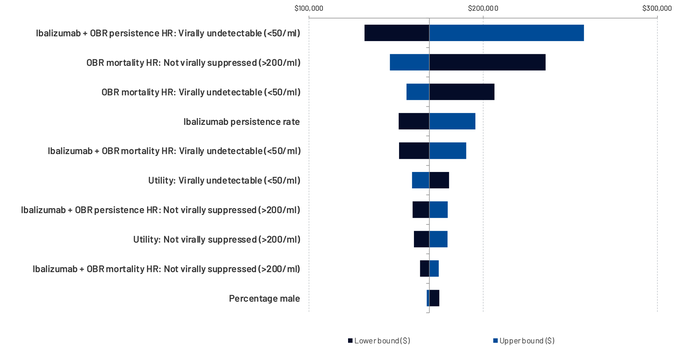
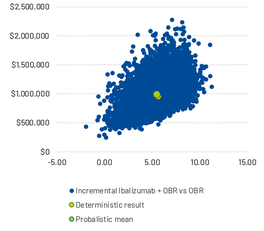
Abbreviations CI - confidence interval; HIV – Human immunodeficiency virus; HR – hazard ratio; HTE – heavily treatment-experienced; ICER – Incremental cost-effectiveness ratio; ICER – Institute for Clinical and Economic Review; vL – viral load; MDR – multi-drug resistant; OBR – optimized background regimens; QALY – quality-adjusted life year; SMR – standardized mortality ratio; US – United States; vL – viral load; WAC - Wholesale Acquisition Cost; WTP – willingness-to-pay

Ibalizumab + OBR versus OBR: ICER ($)



Incremental Costs ($) & QALYs versus OBR



Incremental Costs ($) & QALYs versus OBR