COST-EFFECTIVENESS ANALYSIS OF LENVATINIB VS KEY COMPARATORS IN FIRST-LINE UNRESECTABLE HEPATOCELLULAR CARCINOMA IN CANADA

Poster No.
EE372

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BACKGROUND

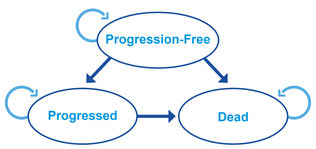
- Liver cancer is the 13th most common cause of cancer in Canada,[1] and the majority of liver cancers are hepatocellular carcinomas (HCCs). Liver cancer was estimated to cost the Canadian health system $421M in 2024[2]
- Lifestyle factors, along with increased prevalence of chronic hepatitis B and C infection, are believed responsible for the increasing incidence and mortality of HCC[3]
- Lenvatinib (LEN), an orally administered, once a day, second generation multiple receptor tyrosine kinase inhibitor, was approved for first-line treatment of unresectable HCC (uHCC) in Canada in 2018[4]
- Approval of LEN was based on results from the REFLECT trial which demonstrated non-inferiority in overall survival (OS) compared with sorafenib (SOR) (13.6 months for LEN vs 12.3 months for SOR; hazard ratio [HR] 0.92; 95% confidence interval [CI] 0.79, 1.06) and improved progression-free survival (PFS; 7.4 months for LEN vs 3.7 months for SOR; HR 0.66; 95% CI 0.57, 0.77)[5]
- Previous analyses have found LEN to be a cost-effective use of resources versus SOR in Canada for the treatment of uHCC[6]
- More recently, both tremelimumab plus durvalumab (TREM+DURV)[7] and atezolizumab plus bevacizumab (ATEZO+BEV)[8] have been approved in Canada for first-line treatment of uHCC
- Since REFECT, LEN has also been compared against a combination of LEN plus pembrolizumab for the first-line treatment of uHCC in the LEAP-002 trial[9]
- The trial failed to achieve its primary outcome of improved OS in patients treated with LEN plus pembrolizumab,[9] but did show longer median OS for patients receiving LEN monotherapy (18.9 months) when compared with previous data from REFLECT[5]

Purpose

- Leveraging data from LEAP-002, we evaluated the cost-effectiveness of LEN with SOR, TREM+DURV and ATEZO+BEV in a Canadian setting
- Health economic evaluations enable efficient use of health care resources and are recognized as important inputs in guiding treatment recommendations in Canada[10]

METHODS

- Patient outcomes were simulated using a partitioned survival model with health states representing progression-free disease, progressed disease and death
- The model was parameterized using data on PFS and OS for LEN, and for each of the three comparators: SOR, TREM+DURV and ATEZO+BEV



Partitioned survival model

- Parametric modelling of PFS and OS for LEN from LEAP-002 was undertaken to estimate health state occupancy over a time horizon for patients treated with LEN
- Health state occupancy over a lifetime time horizon for patients treated with each of the comparators was estimated by applying a HR to the appropriate curve for LEN
- HRs for each of the comparators were determined from a network meta-analysis (NMA) which in the base-case pooled RELECT and LEAP-002 data, using inverse probability of treatment weightings to adjust for imbalances at baseline. A two-stage estimator was further used to adjust for the use of subsequent immuno-oncotherapies
- Health outcomes were measured in quality-adjusted life years (QALYs), after applying health state utility values (0.774 in the progression-free state and 0.743 in the progressed state) determined from EQ-5D data collected in LEAP-002
- Resource use in the progression-free and progressed states was taken from a previously reported resource use, and valued using unit costs taken from Canadian sources[11]
- Costs and health outcomes were discounted at a rate of 1.5% per year, consistent with Canada's Drug Agency (CDA-AMC) guidelines
- Uncertainty was explored using one-way sensitivity analysis, scenario analysis and probabilistic sensitivity analysis, with parameter distributions chosen to reflect the natural bounds on parameters and ranges reflecting published values or set to ±20% of the mean value
- The impact of structural elements of the model was explored in scenario analysis

Scenario 1: Use of societal perspective
Scenario 2: Use of utility estimates based on proximity to death
Scenario 3: 10-year time horizon

Table 1: Selected model inputs

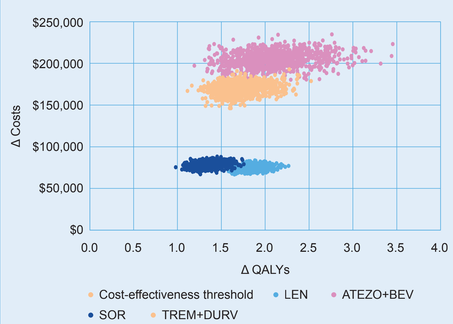
Drug acquisition costs (per cycle)					
LEN	$2,234				
SOR	$4,320				
DURV	$11,733				
ATEZO+BEV	$10,576				
TREM (one cycle only)	$34,320				
Medical resource use costs (per cycle)	**Progression-free health state**		**Progressed health state**		
Physician contacts	$151		$131		
Nurse contacts	$39		$32		
Laboratory tests	$30		$15		
Radiological tests	$81		$17		
Hospitalization	$67		$206		
Most common Grade 3 or 4 treatment-emergent adverse events	**Cost per event**	**Events per patient**			
		LEN	**SOR**	**ATEZO + BEV**	**TREM + DURV**
Aspartate aminotransferase increased	$10,052	0.05	0.07	0.09	0.12
Blood bilirubin increased	$10,052	0.07	0.10	0.05	0.01
Diarrhea	$4,697	0.05	0.07	0.05	0.01
Gamma-glutamyl transferase increased	$10,052	0.06	0.08	0.04	0
Hypertension	$13,068	0.26	0.33	0.16	0
Palmar-plantar erythrodysesthesia	$6,874	0.03	0.04	0.13	0
Weight decreased	$7,699	0.08	0.10	0.03	0

Abbreviations: ATEZO+BEV, atezolizumab plus bevacizumab; DURV, durvalumab; LEN, lenvatinib; QALYs, quality-adjusted life years; SOR, sorafenib; TREM, tremelimumab; TREM+DURV, tremelimumab plus durvalumab.

RESULTS

- When evaluated at a willingness-to-pay threshold considered acceptable to the Canadian healthcare system, LEN was the most cost-effective option, and LEN dominated (was cheaper and more effective than) both SOR and TREM+DURV
- The QALY gain for LEN compared to SOR and TREM+DURV was 0.52 and 0.14, respectively; the cost saving for LEN compared to SOR and TREM+DURV was $3,299 and $95,724, respectively
- ATEZO+BEV generated a QALY gain of 0.20 and an additional cost of $130,603 compared to LEN resulting in an ICUR of $642,499 per QALY
- The likelihood that LEN is cost-effective, as a function of joint uncertainty in input parameters was 100% if a QALY is valued at $100,000 and 88% if a QALY is valued at $200,000

Figure 1: Cost effectiveness plane



Abbreviations: ATEZO+BEV, atezolizumab plus bevacizumab; LEN, lenvatinib; QALYs, quality-adjusted life years; SOR, sorafenib; TREM+DURV, tremelimumab plus durvalumab.

Table 2: Base-case and scenario analysis results for LEN

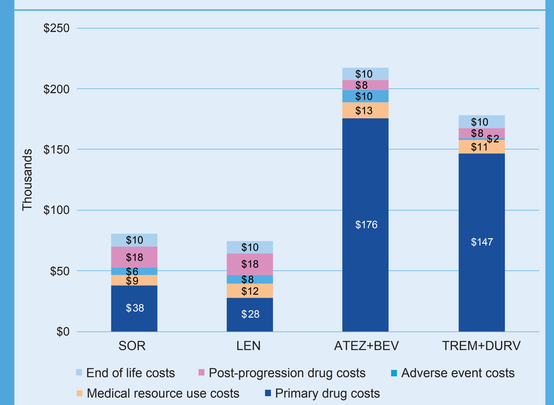
Scenario	**ICUR vs SOR**	**ICUR vs TREM+DURV**	**ICUR vs ATEZO+BEV**
Base-case	Dominant	Dominant	SW: $642,499
#1 Societal perspective	$31,066/QALY	Dominant	$583,749/QALY (SW)
#2 Utility scores based on proximity to death	Dominant	Dominant	$506,516/QALY (SW)
#3 10-year time horizon	Dominant	Dominant	$751,345/QALY (SW)

Abbreviations: ATEZO+BEV, atezolizumab plus bevacizumab; ICUR, incremental cost-utility ratio; LEN, lenvatinib; SW, South-West quadrant (i.e. higher ICER implies LEN is more cost-effective); TREM+DURV, tremelimumab plus durvalumab.

CONCLUSION

- The economic model demonstrates that LEN is the cost-effective treatment for first-line uHCC
- LEN is more effective than either SOR or TREM+DURV and results in overall cost savings
- The modest additional health gains associated with ATEZO+BEV compared to LEN are insufficient to justify the additional costs associated with ATEZO+BEV
- LEN results in lower primary drug costs than any of the comparators, and this is sufficient to ensure overall costs are also lower than any of the comparators
- The analysis uses an NMA which incorporates additional data from LEAP-002.[12] This NMA found that LEN was associated with comparable or significantly longer OS compared with key comparators. However subsequent therapy will vary across studies, with participants in later studies having more treatment options available to them post-progression, and this is a limitation of the analysis
- Findings were robust to parameter uncertainty and to structural assumptions applied in the modelling of event data for LEN or in the estimation of comparative effectiveness undertaken using NMA
- These findings support the selection of LEN as a cost-effective use of healthcare resources in the first line treatment of patients with uHCC

Figure 2: Cost breakdown across comparators



Abbreviations: ATEZO+BEV, atezolizumab plus bevacizumab; LEN, lenvatinib; SOR, sorafenib; TREM+DURV, tremelimumab plus durvalumab.

Acknowledgment

This study was funded by Eisai Limited, Ontario, Canada. Medical writing and editorial assistance were provided by Source Health Economics, UK. This assistance was funded by Eisai Inc., Woodcliff Lake, NJ, USA.

Presented at ISPOR 2025
May 13th -16th 2025
Montreal Convention Centre
Montreal, QC, Canada

References

1 Brenner, DR, et al., Projected estimates of cancer in Canada in 2024. Cmaj. 2024 May; 13;196(18):E615-23.
2 Canadian Cancer Society. Canadian Cancer Statistics: A 2024 special report on the economic impact of cancer in Canada. Available from: https://cancer.ca/en/cancer-information/resources/publications/canadian-cancer-statistics-a-2024-special-report-on-the-economic-impact-of-cancer-in-canada (last accessed: 27 Mar 2025). 2024.
3 Kudo, M., et al., Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. The Lancet, 2018. 391(10126): p. 1163-1173.
4 Government of Canada. Drug and Health Product Portal. Summary Basis of Decision for Lenvima. Available at: https://dhpp.hpfb-dgpsa.ca/review-documents/resource/SBD00209 (last accessed: 20 Mar 2025). Updated: 2025.
5 Cheng, ALF, et al., Phase III trial of lenvatinib (LEN) vs sorafenib (SOR) in first-line treatment of patients (pts) with unresectable hepatocellular carcinoma (uHCC) [abstract]. J Clin Oncol. 2017;35:15_Suppl: 4001.
6 Meyers, BM, et al., The cost-effectiveness of lenvatinib in the treatment of advanced or unresectable hepatocellular carcinoma from a Canadian perspective. Can J Gastroenterol Hepatol. 2021;23;2021:8811018.
7 Canadian Drugs Agency, durvalumab and tremelimumab. Available at: http://cda-amc.ca/durvalumab-and-tremelimumab (last accessed 20 Mar 2025). 2024.
8 Canadian Drugs Agency, Atezolizumab-Bevacizumab. Available at: https://www.cda-amc.ca/atezolizumab-bevacizumab (last accessed: 20 Mar 2025). 2025.
9 Llovet, J. M., et al., Lenvatinib plus pembrolizumab versus lenvatinib plus placebo for advanced hepatocellular carcinoma (LEAP-002): A randomised, double-blind, phase 3 trial. Lancet Oncol., 2023;24(12), 1399-1410.
10 Canada's Drug Agency. Methods and Guidelines. Available at: https://www.cda-amc.ca/methods-and-guidelines (last accessed: 20 March 2025). 2025.
11 National Institute for Health and Care Excellence. Atezolizumab with bevacizumab for untreated unresectable or advanced hepatocellular carcinoma - Committee papers. Available at: https://www.nice.org.uk/guidance/ta666/documents/committee-papers (last accessed: 20 March 2025). 2020.
12 Trueman, D., et al., Network meta-analyses (NMA) of lenvatinib vs key comparators in first-line unresectable hepatocellular carcinoma (uHCC). Ann Oncol, 2024;34, S615-S616.