



A Total Cost of Care Analysis of Immune-Oncology (IO) Treatments for Unresectable Hepatocellular Carcinoma (uHCC): A Canadian Payer Perspective

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Objective

- Tremelimumab + durvalumab (STRIDE) and atezolizumab + bevacizumab are the NCCN and ESMO recommended first-line (1L) IO treatment options for uHCC. This study aimed to quantify the total economic burden associated with treating uHCC patients with STRIDE compared to atezolizumab + bevacizumab from the Canadian payer perspective.

Conclusions

- From a Canadian payer perspective, there was an average cost savings of \$16,869 per patient per year when patients were treated with STRIDE compared to atezolizumab + bevacizumab. The incremental cost offset to the health plan was \$4,174,158 per year when treated with STRIDE.
- This study suggests that STRIDE offers cost savings for uHCC treatment in the Canadian healthcare system. This is the first study that holistically captures the cost of treating uHCC patients over one year. However, additional real-world evidence studies are warranted to capture the long-term survival benefits and associated treatment costs.

Plain language summary



Why did we perform this research?

- To understand the impact of two immunotherapy regimens, STRIDE (tremelimumab + durvalumab) and atezolizumab + bevacizumab, on the Canadian public payer's budget following the introduction of STRIDE as a first-line treatment option for uHCC patients



How did we perform this research?

- We developed a total cost of care model that compared direct medical costs of treating newly diagnosed uHCC patients with STRIDE versus atezolizumab + bevacizumab over one year
 - Data from the HIMALAYA⁴ and IMbrave150⁵ clinical trials and unit costs from local and commercial sources were used for inputs



What were the findings of this research and what are the implications?

- The model suggests STRIDE offers cost savings for uHCC treatment in the Canadian healthcare system compared to atezolizumab + bevacizumab, largely because of lower drug acquisition costs

Introduction

- In North America, more than 50% of HCC patients are diagnosed at advanced stages of disease, with approximately 80% of HCC patients being ineligible for curative therapies^{1,2}
 - These patients rely on systemic treatment, such as immunotherapy, as patients may not be eligible for available locoregional therapies which are often ineffective for those patients³
- Two immunotherapy combinations, (1) single tremelimumab regular interval durvalumab (STRIDE), and (2) atezolizumab + bevacizumab, have demonstrated clinical benefit in their respective clinical trials, HIMALAYA and IMbrave150^{4,5}
- Previous indirect treatment comparison analysis showed similar efficacy outcomes between treatments until two years, while STRIDE demonstrated favorable safety⁶. Comparison after two years was not feasible due to absence of data for IMbrave150 after 26.9 months (maximum length of follow-up for sorafenib). However, the costs associated with STRIDE and atezolizumab + bevacizumab have not yet been compared.

Methods

Model Structure and Population

A cost of care model was developed, which followed uHCC patients eligible for first-line systemic therapy over the course of one year, considering direct medical costs. The model was used to estimate the total cost of care among eligible uHCC patients using STRIDE versus atezolizumab + bevacizumab from a Canadian payer perspective. Costs considered in the model included treatment acquisition and administration, endoscopy, healthcare resource use, and cost for treating grade ≥3 treatment-emergent adverse events (TEAEs).

- The population eligible to receive first-line systemic therapy in Canada was estimated as shown in Figure 1. Briefly, eligible patients are those with newly diagnosed uHCC and (1) Barcelona Clinic Liver Cancer (BCLC) stage C with Child-Pugh A or (2) BCLC stage B with Child-Pugh A that would be ineligible for locoregional treatment

Methods

Model Inputs

Clinical Data

- Data from the HIMALAYA⁴ and IMbrave150⁵ trials were used to extract the rate of TEAEs (Table 2) and treatment regimens (Table 4) of STRIDE and atezolizumab + bevacizumab.
- Weekly resource use** rates for atezolizumab + bevacizumab were sourced from NICE Technology appraisal guidance [TA666]¹⁰, based on progression-free health state data from the IMbrave150 clinical trial (atezolizumab + bevacizumab). Rates for STRIDE were assumed equal to atezolizumab + bevacizumab due to lack of real-world data for STRIDE patients at the time of the analysis. Healthcare resource use accounted for physician visits, laboratory and radiological tests, and hospitalization.

Costs

- Weekly healthcare resource use costs were calculated by multiplying rate with unit costs obtained from local sources¹¹⁻¹³ (Table 1). The annual cost-of-care per patient was calculated by multiplying weekly resource use by 52 (weeks).
- The cost of treating grade ≥3 TEAEs were calculated by multiplying the cost of treatments^{8,13} with the mean frequency of TEAEs associated with STRIDE and atezolizumab + bevacizumab (Table 2).
- An **endoscopy** is required before initiating atezolizumab + bevacizumab to assess the bleeding risk and appropriately manage gastric varices.⁵ Endoscopy is not required before initiating STRIDE as there is no increase in bleeding risk with this treatment.⁴ The cost was derived from a local source¹¹. The one-time pre-treatment monitoring cost of **\$158.56** for endoscopy is applied only to patients receiving atezolizumab + bevacizumab.
- Drug administration** costs were estimated based on IV infusion time and frequency^{11,14-17} (Table 3). **Drug acquisition costs** were estimated based on the cost of each drug and the mean treatment frequency and duration^{14,18,19,20} in the HIMALAYA and IMbrave150 clinical trials.^{4,5} (Table 4).
- Adverse events, treatment acquisition and administration are assumed to be annual costs.
- Unit costs were collected from public and commercial sources and inflated to 2023 Canadian dollars. The total annual burden from the plan perspective was calculated by multiplying the annual cost-of-care per patient with the number of eligible patients (n = 247) (Figure 1)

Table 1. Weekly healthcare resource use rates and costs

Resource Use		Unit Cost (2023 CAD)	Frequency per week	Cost per year (2023 CAD)	
				STRIDE	Atezolizumab + bevacizumab
Physician visits	Appointment with oncologist	\$162.01	0.248	\$482.91	\$482.91
	Appointment with hepatologist	\$162.01	0.002	\$4.67	\$4.67
	Appointment with gastroenterologist	\$162.01	0.000	\$0.00	\$0.00
	Appointment with radiologist	\$157.26	0.013	\$23.59	\$23.59
	Appointment within clinician nurse specialist	\$87.14	0.315	\$329.40	\$329.40
Laboratory tests	Appointment with palliative care physician/nurse	\$33.23	0.035	\$14.03	\$14.03
	AFP test	\$10.26	0.230	\$28.32	\$28.32
	Liver function test	\$27.74	0.240	\$79.90	\$79.90
	INR	\$2.93	0.240	\$8.44	\$8.44
	Complete blood count	\$4.39	0.230	\$12.11	\$12.11
Radiological tests	Biochemistry*		0.240	\$0.00	\$0.00
	Abdominal CT	\$100.61	0.126	\$152.12	\$152.12
	Abdominal MRI	\$75.69	0.059	\$53.41	\$53.41
Hospitalization	Hospitalisation	\$8,172.91	0.014	\$1,333.82	\$1,333.82
	Hospital follow-up: Specialist	\$162.01	0.023	\$45.49	\$45.49
	Hospital follow-up: General Practitioner	\$87.14	0.021	\$21.86	\$21.86
	Hospital follow-up: Nurse	\$87.14	0.031	\$32.21	\$32.21

Table 2. Frequency and cost of grade ≥3 TEAEs

Grade ≥3 TEAEs	Cost (2023 CAD)	Frequency		Total costs per year	
		STRIDE	Atezolizumab + Bevacizumab	STRIDE	Atezolizumab + Bevacizumab
ALT increased	\$495.16	2.6%	3.6%	\$12.87	\$17.83
AST increased	\$8,176.26	5.2%	7.0%	\$425.17	\$572.34
Blood bilirubin increased	\$2,184.06	0.8%	2.4%	\$17.47	\$52.42
Diarrhea	\$429.21	4.4%	1.8%	\$18.89	\$7.73
Fatigue	\$505.22	2.1%	0.0%	\$10.61	\$0.00
Hypertension	\$538.75	0.0%	15.2%	\$0.00	\$81.89
Hyperthyroid events	\$4,999.65	1.8%	2.4%	\$89.99	\$119.99
Proteinuria	\$467.22	0.0%	3.0%	\$0.00	\$14.02
Rash, pruritis	\$7,387.14	1.5%	0.0%	\$110.81	\$0.00
Upper GI bleeding	\$9,831.64	0.0%	6.4%	\$0.00	\$629.22

Table 3. Treatment administration frequency and costs

Treatment	Infusion time	Number of administrations	Cost of IV infusion (2023 CAD)		Annual cost of administration (2023 CAD)
			For initial hour	For additional hour	
Atezolizumab	60 min; 30 min for subsequent infusions	10	\$58.26	\$58.26	\$582.59
Bevacizumab	(a) First: 90 min (b) second: 60 min (c) subsequent: 30 min	10	\$58.26	\$58.26	\$640.85
Durvalumab	60 min	5	\$58.26	\$58.26	\$291.30
Tremelimumab	60 min	1	\$58.26	\$58.26	\$58.26

Table 4. Treatment regimen and acquisition costs

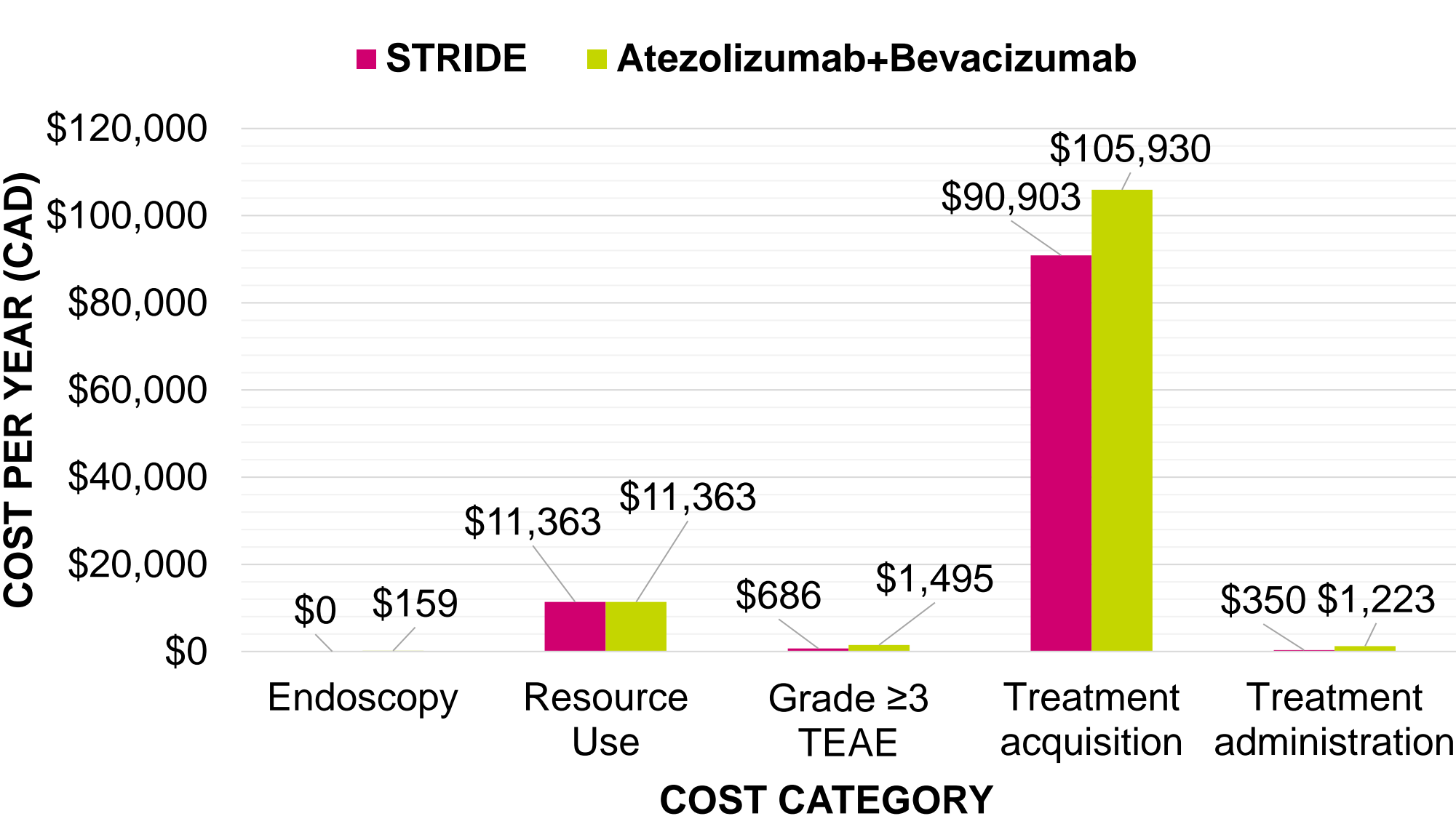
Drug acquisition	Atezolizumab	Bevacizumab	Durvalumab	Tremelimumab
Dose per vial (mg)	1200	100	500	300
Drug dose (mg)	1200	1063.5	1500	300
Dose frequency (per week)	0.33	0.33	0.25	N/A
Mean treatment duration (days)	225.24	210.02	167.41	N/A
Number of vials used per administration	1	11	3	1
Total number of administrations per patient per year	10	10	5	1
Total number of drug vials used per patient per year	10	110	15	1
Cost per vial (2023 CAD) – list prices considered	\$6,776.00	\$347.00	\$3,911.11	\$32,236.00

*Assume biochemistry costs are included in liver function tests
Abbreviations: AFP: alpha-fetoprotein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; CAD: Canadian dollars; CT: computerized tomography; ; GI: gastrointestinal; INR: international normalized ratio; IV: intravenous; MRI: magnetic resonance imaging; STRIDE: single tremelimumab regular interval durvalumab

Blue cells represent inputs, grey cells represent calculations

Results and interpretation

Figure 2. Annual drug and non-drug costs per patient



- The total annual cost of care for STRIDE and atezolizumab + bevacizumab was estimated at \$103,301 and \$120,171 per patients, respectively.
- There was an **average cost savings of \$16,869 per patient per year when patients were treated with STRIDE** compared to atezolizumab + bevacizumab.
- The main driver of cost savings was treatment acquisition (-\$15,027, -14%), though lower costs were also associated with treatment administration (-\$873, -71%), TEAE management (\$809, -54%) and endoscopy (-\$159, -100%)

Table 5. Annual burden to the plan

Cost Category	STRIDE	Atezolizumab+ Bevacizumab	Incremental
Endoscopy	\$0	\$39,234	-\$39,234
Resource use	\$2,811,693	\$2,811,693	\$0
Grade ≥3 TEAEs	\$169,696	\$370,028	-\$200,332
Treatment acquisition	\$22,492,888	\$26,211,245	-\$3,718,357
Treatment administration	\$86,494	\$302,729	-\$216,235
TOTAL	\$25,560,771	\$29,734,929	-\$4,174,158



Patients receiving 1L systemic therapy = 247

- The total burden to the health plan was estimated at \$25,560,771 when all patients were treated with STRIDE, and \$29,734,929 when treated with atezolizumab + bevacizumab.
- The incremental cost offset to the health plan was \$4,174,158 per year when treated with STRIDE, with treatment acquisition accounting for 89% of cost savings (-\$4,174,158).

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