Navigating Uncertainty Within a Re-evaluation Process: Epidemiological Approach vs Real-World Data in a Budget Impact Analysis for CAR T-cell Therapies in Quebec

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BACKGROUND

In a constantly evolving environment, HTA agencies must adapt their methods to inform decision-makers regarding equitable and timely access to innovative therapies, even when evidence is limited. In this regard, the INESSS introduced a new type of reimbursement recommendation in 2018: *Caractère prometteur* (Promise of therapeutic value). This mechanism allows exceptional access to innovative therapies in cases where clinical data are limited or immature, with a requirement for re-evaluation when deemed appropriate by INESSS. CAR-T therapies were an appropriate case in this context, given their curative potential, which was uncertain at the time of initial assessment.

OBJECTIVES

This case study examines the methodology used by INESSS to re-evaluate CAR T-cell therapies (tisagenlecleucel and axicabtagene ciloleucel) and the challenges encountered when re-evaluating their budget impact analysis (BIA).

METHODS

- A reanalysis of the initial BIA, conducted in 2019 using an epidemiological approach, was performed to compare the initial estimations with up-to-date real-world data (RWD).
- A retrospective BIA was carried out using RWD and sales data from the IQVIA Canadian Drugstore and Hospital Purchase Audit database (CDH).
- The follow-up requirements inherent to this new reimbursement mechanism enabled certified centers to collect additional RWD over time. This data served to corroborate the CDH data.
- Various discrepancies emerged between the original and updated analyses, each based on a different approach, allowing INESSS to assess the variations and collaborate with Quebec clinicians to explore the underlying reasons.
- The collected RWD from CDH for both molecules was then used to conduct a prospective analysis and estimate the anticipated budget impact over the coming years.

RESULTS

OVERALL FINDINGS:

- While the initial estimations for axi-cel were overall accurate (74.1 M$ predicted vs. 70.1 M$ observed), market uptake was slower than anticipated. In contrast, the initial estimations for tisa-cel were significantly overestimated (94.5 M$ predicted vs. 35.3 M$ observed).

Table 1. Tisa-cel's Gross Budget Impact Results

Kymriah® (tisa-cel)		2019-2020	2020-2021	2021-2022	TOTAL	2022-2023
ESTIMATIONS (2020)	N of patients	64	68	78	210	n. a.
	Gross impact	$28 800 000	$30 600 000	$35 100 000	$94 500 000	n. a.
REAL-WORLD DATA (2024)	N of patients	22	31	21	74	23
	Gross impact	$10 503 791	$14 800 797	$10 026 346	$35 330 934	$10 981 236

Table 2. Axi-cel's Gross Budget Impact Results

Yescarta® (axi-cel)		2021	2022	2023	TOTAL
ESTIMATIONS (2020)	N of patients	41	42	47	130
	Gross impact	$22 825 000	$24 080 600	$27 155 900	$74 061 500
REAL-WORLD DATA (2024)	N of patients	22	45	67	134
	Gross impact	$11 508 089	$23 539 273	$35 047 362	$70 094 725

Figure 1. Cumulative Number of Patients Through Time (Predicted vs Actual)

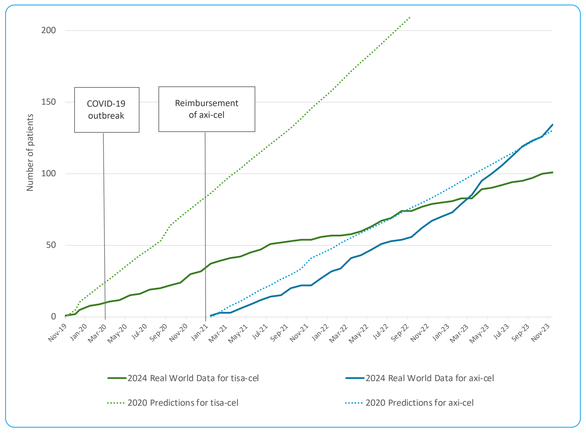
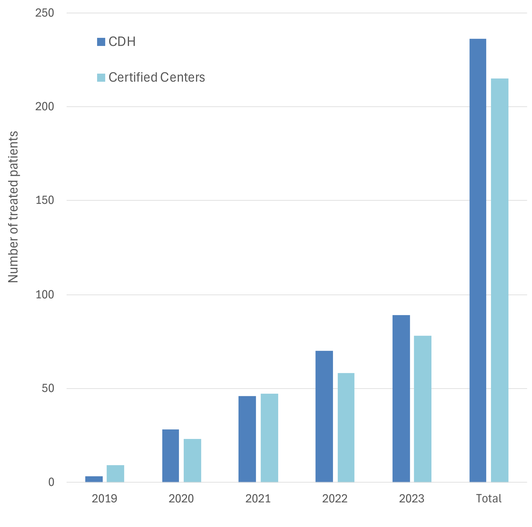


Figure 2. Data Comparison - CDH (IQVIA) vs Certified Centers



EFFECTIVENESS

In the real-world clinical setting in Quebec, the efficacy of axi-cel appears to be superior to that of tisa-cel. Consequently, the use of axi-cel has been favored for eligible patients. Some centers have recently discontinued tisa-cel altogether.

ACCESS/IMPLEMENTATION

Clinicians reported delays in the implementation of care pathways, as CAR-T therapies are innovative and resource-intensive treatments. Referral of patients to designated centers was also likely delayed.

REIMBURSEMENT DYNAMICS

The 2019 estimates for tisa-cel could not account for the arrival of axi-cel on the market. Indeed, axi-cel was listed in February 2021 during the second year of the tisa-cel reference analysis and its use quickly surpassed that of tisa-cel.

COVID-19

Tisa-cel was listed in October 2019, just months before the outbreak of the SARS-CoV-2 coronavirus pandemic. It contributed to delays in its implementation and restricted the capacity to administer the therapy.

CONCLUSION

In the absence of more robust data, the epidemiological approach is often the preferred method for conducting BIAs and informing decision-makers. However, this approach is subject to uncertainty and partly based on assumptions derived from clinicians' input. A retrospective analysis using RWD yields more accurate estimates and should be prioritized in a re-evaluation context whenever possible.

INESSS recommended maintaining the listing of both therapies based on updated clinical evidence, available RWD, identified health needs, and the results of the reanalysis of the economic data (CUA and BIA).

REFERENCES

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