Canadian HTA and Early-Phase Evidence in Oncology: Current Trends and the Path Ahead

Coral Fairhead, HBSc, MBiotech, Tricia Waldron, BSc, MSc, and Luigi Formica, BA
GSK, Mississauga, ON, Canada

HTA162

Introduction

In September 2023, CADTH implemented a new Time-Limited Reimbursement (TLR) process aimed to enable earlier access to drugs that are associated with clinical uncertainty, for example, those submitted with early-phase evidence. To be eligible, the drugs must receive conditional regulatory approval (NOC/c), and the recommendation is contingent on a reassessment following completion of a phase III trial in the same patient population within three years.[1]

The pan-Canadian Pharmaceutical Alliance (pCPA) has proposed a Temporary Access Process that will inform the negotiation process and potential product listing agreements for drugs that follow CADTH's proposed TLR pathway; INESSS (Québec) subscribes to pCPA's principles, but no specific early-access health technology assessment (HTA) process has been announced to date.[2]

This review aims to compare Canada's oncology drug access with other HTA markets and identify factors influencing clinical success with early-phase evidence at CADTH.

Methods

CADTH's Reimbursement Reviews website was searched for files submitted with phase I or II evidence and issued final recommendations from January 2021 through May 2023.[3] Recommendations were analysed to identify clinical drivers of outcomes. Files were also assessed for eligibility under CADTH's TLR process[1] hierarchically, starting with conditional regulatory approval (Health Canada NOC database[4]), followed by phase III trial completion in the same patient population within three years (clinicaltrials.gov[5]). Websites of INESSS[6] and seven international HTA bodies with accessible English information[7-13] were searched (September 19, 2023) to compare recommendation outcomes for the identified CADTH files. HTA bodies with which CADTH is currently collaborating[14], and markets included in CADTH's recent environmental scan of HTA processes for TLRs[15] were considered for analysis. Two markets were excluded due to low file sample size (n<5). HTA recommendation outcomes were determined by two independent reviewers. Results are presented descriptively; no comparative analyses were conducted.

Results

- 27 CADTH files with early-phase data (phase I or II) were identified: 9 negative and 18 positive recommendations ***(Figure 1A)***. INESSS reviewed 26/27 CADTH files: 14 negative and 12 positive recommendations **(*Figure 1B*)**
- Clinical limitations cited were similar across negative and positive CADTH recommendations, with the exception of HRQoL, RCT feasibility, and subjective endpoints **(*Figure 2*)**
- ITCs were submitted in 24 (89%) of the files, with similar ITC limitations cited across positive and negative recommendations; 1/9 (11%) of the negative files and 6/15 (40%) of the positive files resulted in directional efficacy conclusions
- 6 (67%) negative and 15 (83%) positive recommendations cited a significant unmet medical need; only positive files (17/18, 94%) concluded that the drug addressed the need
- 24/27 (89%) CADTH files would not have been eligible for CADTH TLR[1] **(*Figure 3A*)**; reasons for ineligibility were consistent between positive and negative files **(*Figure 3B*)**
- For the CADTH files that were also reviewed by other HTA markets, SMC and NICE had lower rates of negative outcomes compared to Canadian HTA agencies ***(Figure 4)***

Figure 1: Canadian HTA recommendations

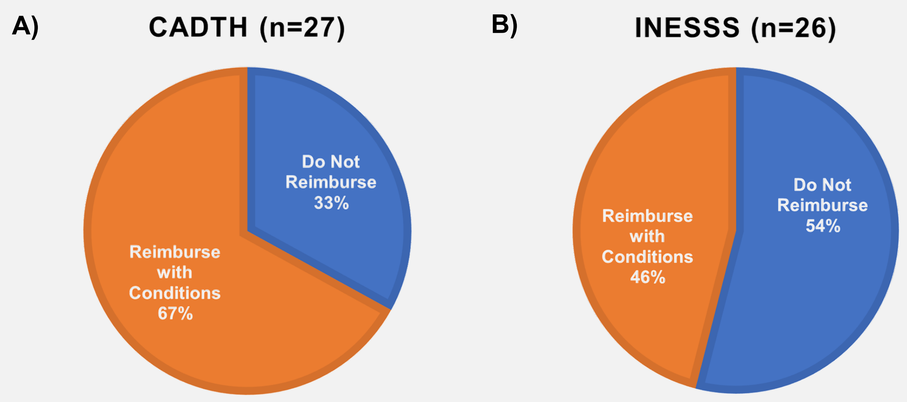
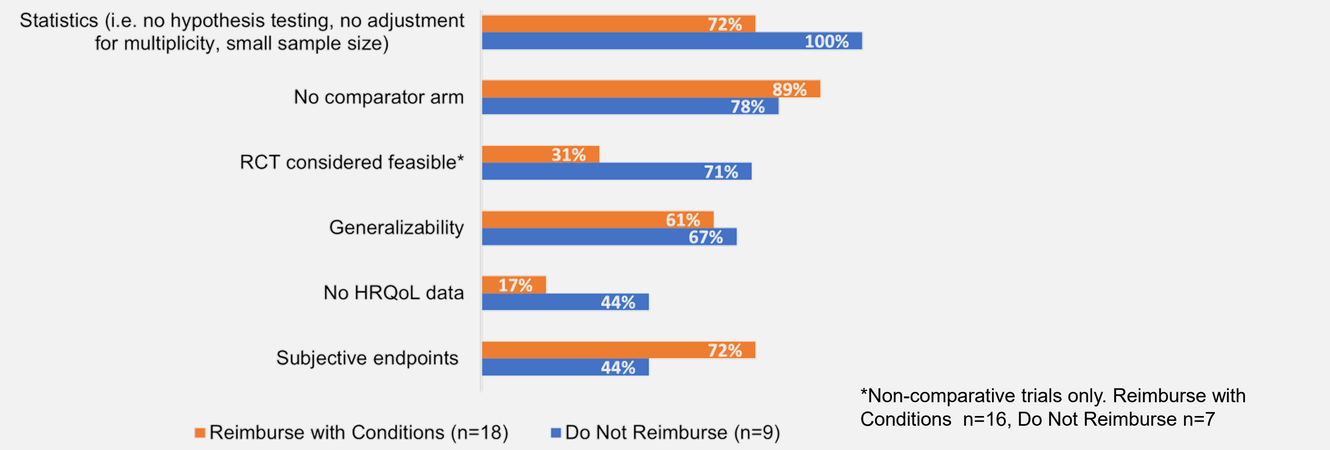


Figure 2: Clinical limitations cited across positive and negative recommendations



*Non-comparative trials only. Reimburse with Conditions n=16, Do Not Reimburse n=7

Figure 3: Eligibility for CADTH Time-Limited Reimbursement

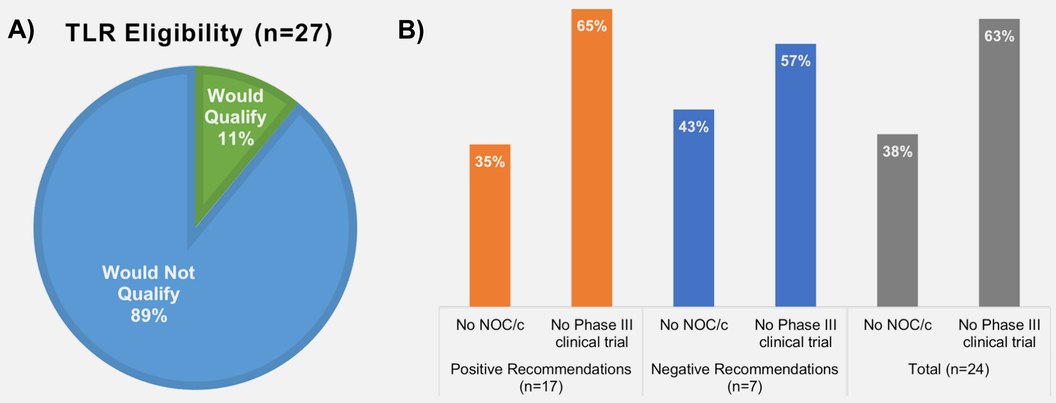
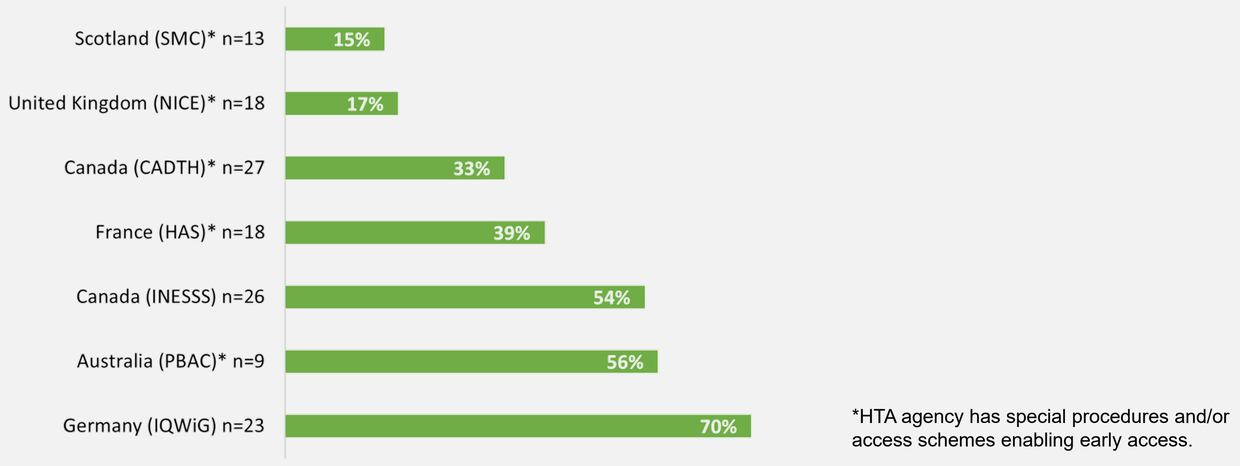


Figure 4: Scotland and the UK have lower rates of negative HTA outcomes



*HTA agency has special procedures and/or access schemes enabling early access.

Discussion

Identifying success factors at CADTH was challenging due to inconsistencies across files, though RCT feasibility and HRQoL assessment seem influential towards CADTH decisions. The results suggest that CADTH's TLR process may not be fit for purpose, with the majority of both positive and negative files not meeting eligibility criteria. One key limitation of the eligibility criteria is the requirement to perform a phase III trial[1], which may be particularly challenging for rare diseases. In disease settings where there may be no available efficacious therapy and where clinically meaningful tumour response rates can be presumed to be attributed to the tested drug, single arm and early-phase data should be accepted.[16] In the UK, NICE can recommend drugs for inclusion in the Cancer Drug Fund, which enables early access to innovative therapies. Similarly, SMC (Scotland) can issue an acceptance on an interim basis. The utilization of a Managed Access Agreement (MAA) in the UK, which in 60% of files (9/15) incorporates the collection of real-world evidence (RWE),[7] may contribute to the lower negativity rate. The utilization of RWE is not formally included in the CADTH TLR reassessment process. The authors acknowledge that this review is limited by the fact that the results are reported descriptively without comparative statistical analysis.

Conclusion

Do Not Reimburse HTA outcomes are common in Canada for files with early-phase clinical evidence and there is inconsistency in decision making. Scotland and the UK have lower rates of negative HTA outcomes. A consistent deliberative framework among Canadian HTAs and a funding mechanism for early-phase evidence, which includes the effective use of RWE to fill evidence gaps, could enhance transparency, reduce regional disparities, and improve patient access, while addressing clinical uncertainty for public payers.

Abbreviations

CADTH: Canadian Agency for Drugs and Technologies in Health (Canada ex Quebec); HAS: Haute Autorité de Santé (High Authority for Health, France); HRQoL: health-related quality of life; HTA: health technology assessment; INESSS: Institut national d'excellence en sante et en services sociaux (Québec, Canada); IQWiG: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care, Germany); ITC: indirect treatment comparison; MAA: Managed Access Agreement; NICE: National Institute for Health and Care Excellence (UK); NOC: Notice of Compliance; NOC/c: Notice of Compliance with Conditions; PBAC: Pharmaceutical Benefits Advisory Committee (Australia); RCT: randomized controlled trial; RWE: real-world evidence; SMC: Scottish Medicines Consortium (Scotland); TLR: Time-Limited Reimbursement; UK: the United Kingdom

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Disclosures

This research and work was conducted by GSK. The authors declare the following real or perceived conflicts of interest during the past 3 years in relation to this presentation: CF, TW and LF are employees of, and hold stocks in, GSK. TW was previously employed by CADTH prior to February 2022.

ISPOR Europe | 12-15 November 2023 | Copenhagen, Denmark

Presenting author: Coral Fairhead, coral.e.fairhead@gsk.com

gsk.com