CDA-AMC 'Do Not Reimburse' Oncology Recommendations from 2019-2024: Trends and Submission Characteristics

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Background and Objectives

- A positive Canada's Drug Agency-L'Agence des médicaments du Canada (CDA-AMC, formerly CADTH) recommendation is required for public reimbursement of novel oncology therapies in Canada (except for Quebec).
- We sought to:
  - Determine the frequency of "Do Not Reimburse Recommendations" (DNRR) issued by CDA-AMC over a five-year period (January 2019 to January 2024).
  - Assess the characteristics of submissions receiving DNRR, including cancer types and evidentiary limitations.

Methods

- A total of 158 pan-Canadian Oncology Drug Review (pCODR) reimbursement recommendations issued between January 2019 and January 2024 were evaluated.
- Recommendations, and sections related to the rationale or reasons for each DNRR, were extracted. The outcome of Reconsiderations and Resubmissions following a DNRR were recorded.
- Positive recommendations and DNRRs were compared with respect to trial phase and whether submitted studies were single-arm or controlled. As well, specific evidentiary limitations identified by pan-Canadian Oncology Drug Review Expert Committee (pERC) in DNRRs were recorded.
- The Chi-square test was applied to assess the statistical significance of observed trends, with Yates correction applied to account for smaller sample sizes.

Results

- The overall DNRR rate was 27/158 (17%).
- Unmet need was acknowledged by pERC in 22/27 (82%) DNRR submissions.
- 26/27 (96%) DNRR submissions underwent Reconsideration; the DNRR was maintained in all cases. One DNRR, in small-cell lung cancer, subsequently received a positive recommendation upon resubmission.
- Lung cancer submissions represented over one-quarter of all DNRRs, while breast cancer, leukemia, and lymphoma each represented 11% of DNRRs (**Figure 1**).

Evidentiary Gaps & Limitations Identified in DNRRs

- Key evidentiary limitations and gaps cited by pERC in DNRRs are summarized in Table 1.
- The clinical evidence consisted of Non-Phase III studies for 16/27 (59%) DNRR submissions (**Figure 2a**). 14/27 (52%) DNRR submissions were supported by single-arm studies (**Figure 2b**). Both study types were over-represented in DNRRs versus positive recommendations.

Table 1: Evidentiary limitations and gaps cited in pCODR DNRRs

Submission characteristic	Number of submissions (%)
Single-arm evidence	15 (56%)
Non-Phase III trial	19 (70%)
Uncertainty regarding presence/magnitude of clinical benefit	22 (82%)
Uncertain clinical significance of benefit	4 (15%)
Lack of QoL data	15 (56%)
Use of surrogate outcomes	8 (30%)
Concerns regarding quality and/or maturity of data*	19 (70%)

* Includes issues such as high degree of censoring, lack of adjustment for multiplicity, small sample sizes, lack of statistical significance testing, data immaturity.

Figure 1: Distribution of DNRRs across cancer types

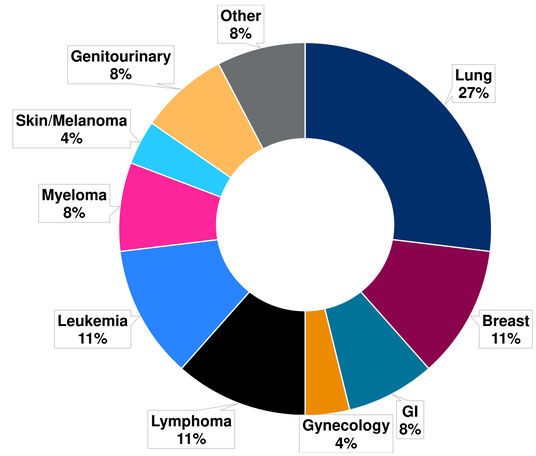


Figure 2a: Distribution of Phase III vs. Non-Phase III trials in negative and positive CDA-AMC oncology reimbursement recommendations

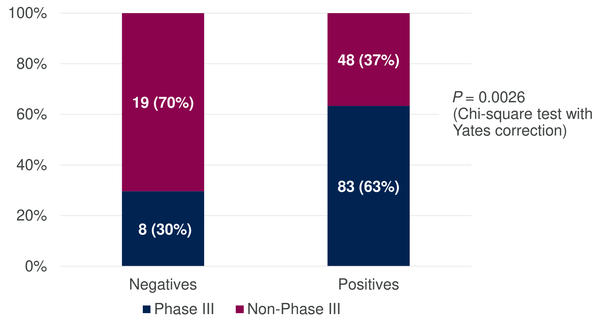
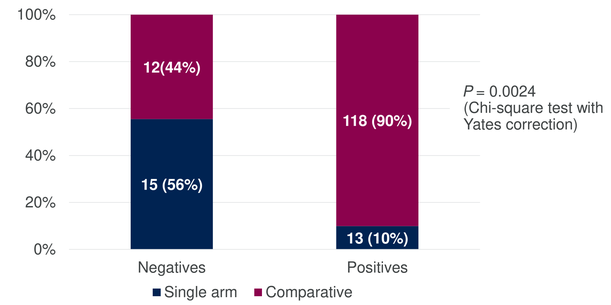


Fig 2b: Distribution of single-arm vs. comparative trials in negative and positive CDA-AMC oncology reimbursement recommendations



Discussion

- **Approximately 1 in 6 CDA-AMC oncology recommendations issued between January 2019 and January 2024 were DNRRs. Notably, unmet need was acknowledged by pERC for the majority of DNRR files.**
- **Uncertainty regarding the presence or magnitude of clinical benefit, often due to the limitations of Non-Phase III trials (particularly single-arm studies), as well as a variety of data limitations such as small sample sizes, data immaturity, and lack of QoL information, were among the most frequently cited reasons for DNRRs.**
- **These findings have important implications for the future reimbursement of novel oncology therapies in Canada given the increasing trend towards regulatory approvals based on trial designs that do not provide the level of certainty of phase III trials.[1]**

Abbreviations CDA-AMC = Canada's Drug Agency-L'Agence des médicaments du Canada; DNRR = Do Not Reimburse Recommendations; GI = gastrointestinal; pCODR = pan-Canadian Oncology Drug Review; pERC = pan-Canadian Oncology Drug Review Expert Committee; QoL = quality of life.

References

1. US Food & Drug Administration (2023). Clinical Trial Considerations to Support Accelerated Approval of Oncology Therapeutics Guidance for Industry. Available online at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trial-considerations-support-accelerated-approval-oncology-therapeutics. Accessed: August 21, 2024.

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