Oncology drugs without Phase III data: Comparison of reimbursement recommendations issued by the Canadian Agency for Drugs and Technologies in Health (CADTH), and the National Institute for Health and Care Excellence (NICE)

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Background

Introduction

- Regulatory agencies are increasingly approving promising oncology therapies in the absence of phase III trials, resulting in potential challenges for HTA agencies tasked with developing reimbursement recommendations. Previous research has shown that the likelihood of a positive recommendation from CADTH's pan-Canadian Oncology Drug Review (pCODR) is lower for submissions with phase II data as the highest level of evidence versus submissions with phase III data[1]. Here, we compare recommendation outcomes between pCODR and NICE for submissions supported by phase II data.

Objectives

- Examining trends in the number of phase-II-informed pCODR recommendations over time
- Describing the overall degree of agreement between pCODR and NICE

Methods

Methods

- Recommendation reports were reviewed from pCODR inception (2012) to May 2021
  - Submissions with phase II data as the highest level of clinical evidence for which a final recommendation was issued were documented
- NICE recommendations for the same product and indication pairs were identified and documented (if available)
- Descriptive statistics were generated for pCODR submissions and recommendation agreement between pCODR and NICE

Results

Trends over Time

- Since its inception in 2012 to May 2021, pCODR received 219 submissions, 35 (16.5%) of which were submitted with phase II data as the highest level of evidence. Over time, there has generally been an increase in the number of such submissions (**Figure 1**)**.**
  - Of the 35 submissions, nearly 40% were for hematological malignancies.
- 19/35 submission (54%) received a recommendation to Reimburse, most with Conditions.

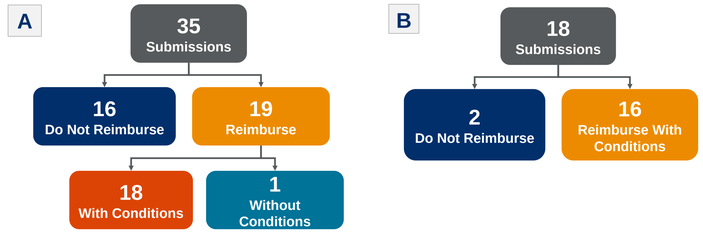
Results Cont'd

Figure 1: Number of final recommendations with phase II data as the highest level of evidence issued by pCODR each year since agency inception.

Agency Agreement

- Of the 35 phase II pCODR submissions, 22 (63%) had a corresponding NICE recommendation. Of these NICE recommendations, 18 (82%) were based on phase II data as the highest level of clinical evidence (**Figure 2**).

Figure 2: (**A**) Recommendations made for phase-II-informed pCODR submissions; (**B**) Recommendations made for corresponding NICE submissions



- Among the 18 overlapping submissions between pCODR and NICE, the proportion of positive recommendations was 10/18 (56%) and 16/18 (89%), respectively (Chi-squared test p = 0.026).
  - 7/16 (44%) positive NICE recommendations were for funding under the Cancer Drugs Fund (CDF), with requirements for additional data collection to reduce uncertainty, and future re-assessment.
  - There was agreement between agencies for 10 (56%) recommendations. 9/10 (90%) received positive recommendations from both pCODR and NICE and 1/10 (10%) received a negative recommendation from both (**Figure 3**).
  - 7/8 (88%) submissions given a negative recommendation by pCODR were given a positive recommendation by NICE. 3/7 (43%) of these were for funding under the CDF, with a requirement for additional data collection and re-assessment.

Results Cont'd

Figure 3: Recommendations made for corresponding submissions to pCODR and NICE

		NICE	
	Recommendation	Reimburse with Conditions	Do not Reimburse
pCODR	Reimburse with Conditions	**9***	**1**
	Do not Reimburse	**7**	**1**

*** For 1 submission (pembrolizumab for classical relapsed/refractory Hodgkin's lymphoma), NICE recommended reimbursement under CDF for patients that have had brentuximab vedotin (BV) but cannot undergo autologous stem cell transplant (ASCT), but not for patients that have had ASCT and BV. pCODR recommended reimbursement for both subpopulations.**

- Some reasons for issuing negative recommendations were common to pCODR/CADTH and NICE, such as the lack of comparative data, or lack of data on key outcomes such as overall survival.
  - Unique to pCODR, 6/35 (17%) recommendations discussed that a phase III trial was feasible; all of these were negative recommendations.

Conclusions

- Over time, progressively more submissions have been made to pCODR with phase II data as the highest level of clinical evidence. 13/35 (37%) product-indication pairs with a pCODR recommendation did not have an associated NICE recommendation.
- For submissions supported by phase II trials as the highest level of evidence at both pCODR and NICE, the level of agreement between the two agencies was modest (56%). pCODR tended to issue more negative recommendations than NICE, potentially reflecting a lower tolerance for the uncertainty in clinical evidence when phase III data are lacking.
- Several positive NICE recommendations were for reimbursement under the CDF, with requirements for additional data collection and reassessment. It will be important to monitor whether the positive recommendation rate for pCODR submissions with phase II data increases in the future as Canadian initiatives to gather real-world data in oncology evolve.

References & Funding

1. Li YYR, Mai H, Trudeau ME, Mittmann N, Chiasson K, Chan KKW, & Cheung MC. Reimbursement recommendations for cancer drugs supported by phase II evidence in Canada. *Curr Oncol.* 2020; 27(5): 495-500.

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