Reimbursement recommendations of conditionally-approved cancer drugs:
Comparing pCODR recommendations for files receiving NOC/c or NOC from Health Canada

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ABSTRACT

Background
Health Canada's Notice of Compliance with Conditions (NOC/c) pathway is designed to facilitate early access to drugs that treat serious diseases with high unmet need, or which demonstrate a significant improvement in the benefit/risk profile relative to currently-available therapies. Cancer therapies must also have their clinical and health economic evidence evaluated by the pan-Canadian Oncology Drug Review (pCODR) to receive reimbursement recommendations prior to public funding. This analysis aims to understand how the pCODR review process manages drugs approved through the NOC/c pathway.

Methods
pCODR recommendations available before mid-June 2020 were evaluated to identify drug submissions reviewed under the NOC/c pathway. Recommendations were categorized as either "positive" or "negative" and compared using a χ^2 test.

Results
pCODR issued 156 recommendations for unique drug-indication combinations. 35 (22.4%) of those files were reviewed under the NOC/c pathway. Files reviewed under this pathway were statistically less likely to receive a positive reimbursement recommendation compared to files reviewed under the traditional NOC pathway (62.9% vs. 81.8%; p=0.02). Clinical uncertainty was the primary rationale for negative recommendations, with resubmissions leveraging additional trial data often being recommended.

Conclusions
The NOC/c pathway was designed to enable access to drugs with promising clinical data, while establishing mechanisms for the early data to be verified following market authorization. However, this uncertainty is the rationale often cited in these drugs receiving negative reimbursement recommendations. Alternative reimbursement models may be needed to ensure temporary access for patients while additional data is reviewed by pCODR.

BACKGROUND

- Health Canada's Notice of Compliance with Conditions (NOC/c) pathway is designed to facilitate early access to drugs that treat serious diseases with high unmet need, or which demonstrate a significant improvement in the benefit/risk profile relative to currently-available therapies[1].
- The pan-Canadian Oncology Drug Review (pCODR) process assesses anti-cancer drugs based on clinical and economic evidence to provide funding recommendations to the Canadian provinces (excepting Quebec)[2].
- As the process is aimed at expediting review timelines for potentially high-benefit drugs, those products reviewed under the NOC/c pathway are often approved with less mature data than those undergoing the standard NOC file review. To account for this greater uncertainty, NOC/c approvals are contingent on conditions requiring the submitter to gather or continue gathering trial data.
- Previous research on NOC/c files in pCODR has explored the impact of data maturity, NOC/c conditions, and Health Canada decision-making on the likelihood of these files receiving a positive recommendation[5,6,7].
- With these factors in mind, this analysis aims to understand how the pCODR review process manages drugs approved through the NOC/c pathway compared to the traditional NOC pathway and provide conclusions that combine and update the results of previous analyses by looking at the frequency of positive recommendations, time spent under review, and reason for recommendations given to files in both pathways.

METHODS

- NOC/c file data were retrieved from the NOC database[3] and pCODR final recommendations were retrieved from the pCODR website[4] as of June 12, 2020, and pCODR files associated with an NOC/c were identified. pCODR recommendations were categorized as either positive or negative, with conditional positive recommendations considered positive.
- Focus was on submissions associated with a new drug or new indication for an existing drug (referred to as "unique drug-indication pairings") to remain consistent with previous analyses and to exclude resubmitted files.
- The portion of positive recommendations, time from pCODR submission to recommendation, and phase of clinical study data for NOC and NOC/c New Drug and New Indication files was determined and compared using a χ^2 test.

RESULTS

- 156 pCODR recommendations for unique drug-indication pairings were available as of June 12, 2020, 35 (22.4%) of which were associated with an NOC/c.
- Files reviewed under the NOC/c pathway were statistically less likely to receive a positive reimbursement recommendation compared to files reviewed under the traditional NOC pathway (62.9% vs. 81.8%; p=0.02). **Table 1** outlines the volume of positive NOC and NOC/c recommendations by year from 2012 to 2020.
- More specifically, New Drug files receiving NOC/c were statistically less likely to receive positive compared to NOC (56.5% vs. 85.1%; p=0.009), while New Indication files showed no significant difference in positive outcomes of NOC/c and NOC files (75.0% vs. 79.7%; p=0.71).
- **Table 2** and **Figure 2** illustrate the difference between the portion of positive NOC and NOC/c New Drug and New Indication pCODR recommendations.

RESULTS (CONT'D)

Table 1: Recommendation type and HTA duration of pCODR files by year, 2012-2020

	Year	Total	2012	2013	2014	2015	2016	2017	2018	2019	2020
NOC/c	pCODR Recommendations	35	1	2	0	8	5	4	7	6	2
	Positive Recommendations	22	0	2	0	6	2	3	6	2	1
	% Positive	62.9%	0.0%	100%	--	75.0%	40.0%	75.0%	85.7%	33.3%	50.0%
	Average HTA Duration (months)	7.3	6.3	6.8	--	6.7	6.3	7.9	6.6	7.8	7.1
NOC	PCODR Recommendations	121	9	14	10	13	13	10	14	22	16
	Positive Recommendations	99	7	12	8	11	11	7	10	19	14
	% Positive	81.8%	77.8%	85.7%	80.0%	84.6%	84.6%	70.0%	71.4%	86.4%	87.5%
	Average HTA Duration (months)	7.0	6.0	6.8	7.4	6.3	6.4	6.5	6.9	6.9	7.9

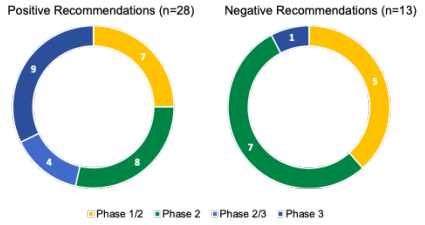

Figure 1: Clinical study phase of NOC/c pCODR recommendations

Table 2: Comparison of % positive pCODR recommendations for NOC and NOC/c files by submission type

File Type	NOC	NOC/c	p
New Drug	85.1%	56.5%	0.009
New Indication	79.7%	75.0%	0.709
All Unique Submissions	81.8%	62.9%	0.018

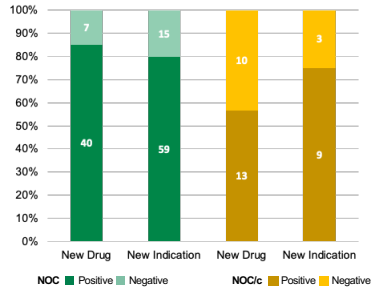

Figure 2: Portion of positive and negative pCODR recommendations by submission type

RESULTS (CONT'D)

- There was no statically significant difference in time from pCODR submission to recommendation between NOC and NOC/c files, with NOC files spending an average of 7.0 months under pCODR review compared with 7.3 months for NOC/c files. **Table 1** outlines the average review duration by year from 2012-2020.
- Positive pCODR recommendations for NOC/c files typically cited net positive clinical benefit despite uncertainty, while negative recommendations cited clinical uncertainty as the rationale behind the recommendation.
- NOC/c files submitted to pCODR with phase 2/3 or 3 study data were about 6 times more likely to receive a positive recommendation than those with phase 1/2 or 2 data. **Figure 1** shows the clinical study phase of positive and NOC/c recommendations, including those files that were resubmitted with more mature data.
- 51.4% of unique drug-indication files met the conditions of NOC/c, with an average time of 37.3 months from NOC/c to conditions met. No file met the conditions of its conditional market authorization prior to receiving a pCODR recommendation.

DISCUSSION

Factors Influencing pCODR Recommendations
- The NOC/c pathway was designed to enable accelerated access to drugs with promising clinical data.
- The most common condition given to NOC/c files was that the manufacturer continue to gather additional clinical data.
- These files were then submitted to pCODR and evaluated under the same pathway as traditional NOC files.
- New Drug pCODR files reviewed under the NOC/c pathway were significantly less likely to receive a positive reimbursement recommendation than those reviewed under the traditional NOC pathway.
- Negative pCODR recommendations for NOC/c files often cited data immaturity as a rationale and suggested resubmitting with more mature data.
- Alternative reimbursement models may be needed to ensure temporary access for patients while additional data is reviewed by pCODR.

Comparison to Previous Analyses
- Previous analyses investigating NOC/c file handling through pCODR focused on individual aspects that this analysis combined, with the aim of providing a comprehensive view of the pathway.
- When looking at recommendations up to 2017, no significant difference was found in pCODR outcome of NOC/c vs. NOC files for unique drug-indication pairings[5], while this analysis found a very significant difference particularly in New Drug files.
- Results of this analysis were consistent with previous studies when looking at the value of higher phase clinical data, as pCODR may value phase 3 data when determining net clinical benefit[7].

REFERENCES

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