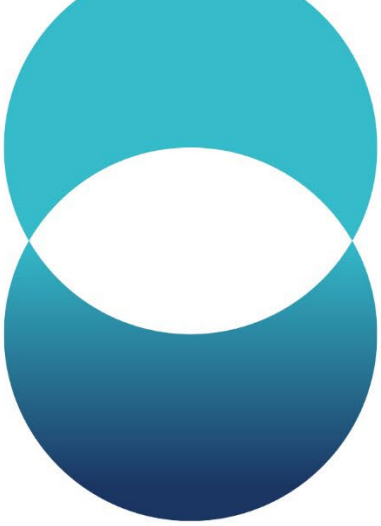
The Conference Board of Canada



The Value of Access: Modelling Outcomes for New Blood Cancer Therapies

Methodology and Bibliography

Prepared by
The Conference Board of Canada

Contents

Methodology

Literature search

Phase one consisted of a comprehensive review of both white and grey literature to more thoroughly understand the baseline status of pandemic-related impacts including the following:

- What was the impact of the pandemic on the cancer care continuum, cancer (both blood and solid tumour) patient outcomes, and treatments?

Inclusion criteria focused on publications from 2019–23 to ensure timely relevance of the subject area. Additionally, articles were limited to a Canadian-based population or one of similar origin (e.g., United States, Europe) in the event local data was not available.

Once the background and model were established, we performed a secondary search to contextualize the modelling results surrounding access to newly developed or applied therapies, and to provide additional information to complement the results of the expert interviews:

- Which mechanisms may improve timely access to newly developed or applied therapies?
- Which factors (enabling or hindering) influence equitable access to newly developed or applied therapies?
- What effect do newly developed or applied therapies have on system capacity for other cancer cohorts?

Therapy inclusion criteria

- Health Canada must have approved the therapy.
- There must be a positive CDA recommendation:
- “Reimburse without conditions”
- “Reimburse with clinical criteria and/or conditions”
- There must be approval for a therapeutic area that includes MM, HL, or NHL.
- Therapy must have a reported progression-free survival (PFS).
- Therapy must have a calculatable incidence for its intended therapeutic population.
- Therapies cannot be listed as a comparator for newer therapies in CDA recommendation (e.g., an earlier therapy was replaced by a newer therapy as a standard of care).

Model methodology

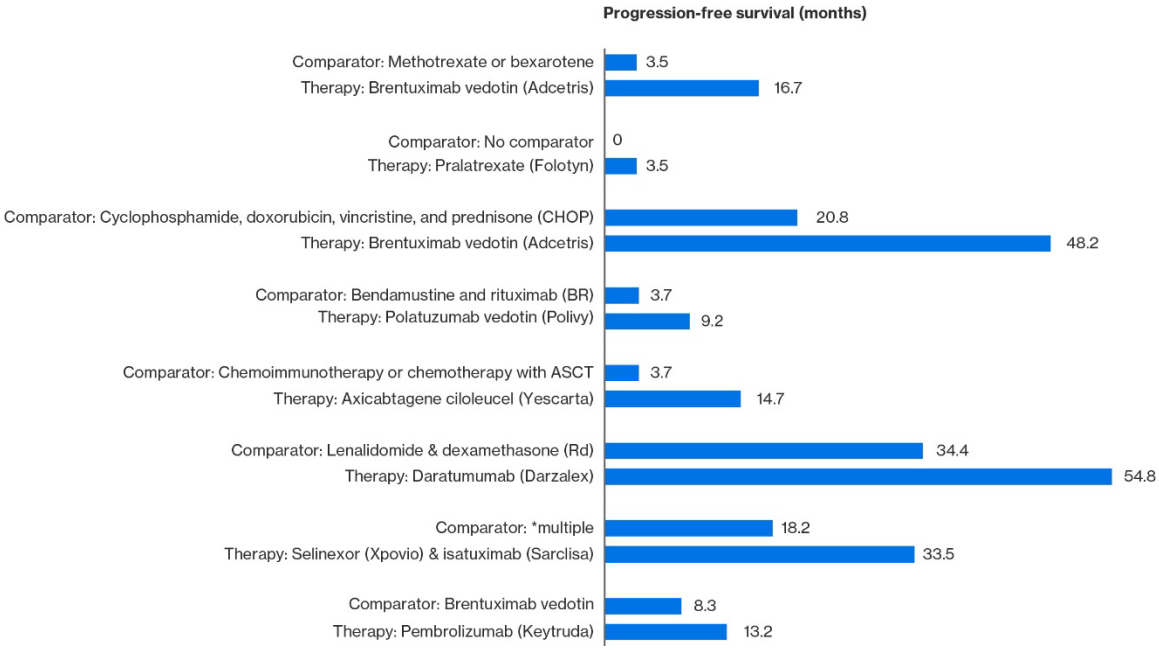
These therapies, along with Canadian health and economic data, were explored to identify the following inputs for model calculations:

- **PFS:** The PFS reported in the CDA Recommendation and Reasons, or clinical trial cited in the CDA Recommendation and Reasons, for both the newly approved therapy and comparator were used as the patient survival value. (See Chart 1.)
- **Incidence:** The age group (20–29, 30–39, 40–49, 50–59, 60–69, and 70+) incidence was acquired for the therapeutic populations for which the newly developed or applied therapy was indicated. Therapies that outlined population subgroups in the indication had incidence for the years 2024–30 calculated based on projected population data obtained from Statistics Canada and forecasting using data from 2016–20. Incidence rates were represented as a proportion of the total cancer incidence.
- **Market share:** For select therapies that had potential crossover where populations may be eligible for both therapies, market share was estimated based on expert recommendation.
- **Economic societal contribution (Total Income):** Similar to productivity, we calculated economic societal contribution by considering the percentage of the population with reported total income and the median total income in 2021 using data obtained from Statistics Canada.

Increased access to therapies: Our model assumes that all eligible individuals within each therapeutic population have access to the designated therapy. Therefore, there is an assumption of no access restrictions such as lack of provincial funding, geographical barriers, health human resources, or additional mechanisms.

Chart 1

Newly approved or applied therapy and current comparator progression-free survival comparison
(number of months)



Source: The Conference Board of Canada.

Modelling assumptions

Due to lack of data, comparator specificity, or the stage of clinical trial, several assumptions/estimates were made to model the clinical and economic impact most accurately. First, selinexor and isatuximab were the only models that contained crossover in therapeutic population, and therefore both therapies along with their comparator were modelled together using weighted market share. The weighted PFS for the new therapies was 33.5 months, and the comparator was 18.2 months. Next, Pralatrexate did not include a comparator and, after reviewing all available documentation and undergoing expert review, it was deemed there was no alternative therapy for this indication in Canada. Therefore, we listed this comparator at a PFS of zero. In the Brentuximab Vedotin report for ALCL, the comparator was noted as the “Standard of Care.” After both a literature and expert review, we included methotrexate or bexarotene as the comparator with a PFS of 3.5 months. For therapies where the PFS was not reached (e.g., there are patients involved in the clinical trial and who have been administered the therapy who have not experienced disease progression or death), we used the lower bound of the reported 95 per cent confidence interval to ensure the model was not over estimated.

Lastly, we assumed open therapy access to all eligible therapeutic populations for our model. While this does not reflect current therapy access restrictions, it highlights the potential impact should these barriers be reduced.

Selinexor and isatuximab treatment line

Due to the indication of selinexor and isatuximab, we are unable to predict what proportion of patients received the treatment at second, third, or fourth line. Furthermore, we are unable to acknowledge which of these patients received autologous stem-cell transplantation (ASCT) prior to the therapy. Therefore, results for selinexor and isatuximab are presented separately for ASCT and non-ASCT subgroups, as well as by each specific line of therapy to meet the product indication.

Key informant interviews

We followed Key Informant interview guidelines from the University of California, Los Angeles, Center for Health Policy Research.[1] Leveraging the first component of phase two of the literature review (model contextualization), we identified what additional information was needed to fully understand and define access in terms of newly developed or applied therapies for HL, NHL, and MM. The target population of hematologic oncologists was decided through discussions with our Research Advisory Board due to their extensive knowledge of this specialized topic. Sample size was not predetermined for these interviews; however, the focus was to incorporate interviewee representation from across Canada to provide insight into the current landscape of blood cancer therapy access. The pan-Canadian interviewee list (n = 6) included oncologists from British Columbia, Saskatchewan, Manitoba, Ontario, and Nova Scotia. An interview guide was developed based on the objectives outlined in the “Literature Review” section. Interviews were conducted on Microsoft Teams (approximately one hour per interview), recorded, and transcribed using NVivo 14. Key terms and themes were compiled. A total of 141 pages and 41,428 words of interview transcripts were generated from this research. Results were represented in the thematic categories expressed in the thematic analysis that underwent internal validation, and a final literature scan was utilized for supplementary information and evidence for each theme.

Research ethics was not obtained for these interviews due to the key informants sharing information in the ordinary course of their employment regarding professional practice as a hematological oncologist.

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[1] UCLA Center for Health Policy Research, “Section 4: Key Informant Interviews.”

Model limitations

While many rigorous steps were taken to ensure model accuracy, there are several limitations that warrant mention.

COVID data

Incidence calculation modelling for the years 2024–30 was performed using pre-COVID-19 data (prior to 2020). While these estimates did not account for the impact of the pandemic on cancer rates, they provide a more accurate trajectory for the post-pandemic time frame. Furthermore, we were able to compare our modelled incidence with the current reported estimates for validation. Future work with additional post-COVID-19 incidence for MM, HL, and NHL would be advantageous for the most precise trajectory.

Market share estimates

Both selinexor (Xpovio) and isatuximab (Sarclisa) contained therapeutic population overlap and were therefore modelled in a single output while accounting for market share. Due to the extensive therapy review for this project, we were unable to identify this requirement until midway through the research. Therefore, we leveraged the experts (Research Advisory Board, Key Informants, and external sources) nationwide who specialized in the MM field to illustrate the observed market share of these two therapies in the Canadian market. While this expert review provided an on-the-ground report of therapy use, future research should include a market share analysis utilizing appropriate data sets that capture this information.

Incidence estimates

All therapies required a calculation to determine population incidence for each therapy. To determine the proportion of overall incidence, we performed an extensive literature review of available sources to identify translatable and recent population data. In cases where Canadian data was unavailable, American data was utilized, which provides similar population attributes. We recognize that these incidence rates do not provide exact population estimates.

However, due to the unavailability of these data points, we feel these estimates closely depict the true values, and all underwent confirmation by expert review.

Efficacy interpretations

Measures of efficacy were PFS for the clinical model and total income for the economic model. While these values provide insight into the potential impacts of newly developed or applied therapies, there are several key discussion points that should be raised. First, PFS is defined by the National Cancer Institute as "the length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease, but it does not get worse."[2] For many clinical trial and CDA recommendation reports, PFS is used almost exclusively to measure therapeutic efficacy; however, it does not effectively capture QOL. Experts noted that, for many of these therapies, particularly in later lines of treatment, patients have reduced QOL due to the therapy toxicity and the advanced state of disease. Therefore, while PFS measures a component of drug efficacy, it does not necessarily translate to the individual's having increased functional health status.[3] For these reasons, we opted to use "Total income" as the measure of economic contribution as it accounts for various sources of income (e.g., employment, investments, pension).[4] Therefore, if an individual is unable to return to employment during or after their treatment, this marker accounts for additional societal contributions. In summary, the life-years and economic impact calculated in our models do not account for the QOL years gained and/or the direct passive income source participation. Future modelling should include overall survival when possible as a measure of therapeutic efficacy, as well as a validated measure of health-related QOL.

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2 National Cancer Institute, "Progression-free survival. Definition"

3 Kovic and others, "Evaluating Progression-Free Survival as a Surrogate Outcome for Health-Related Quality of Life in Oncology."

4 Statistics Canada, "Total income of person."

Bibliography

Canada's Drug Agency. "pCODR Expert Review Committee (pERC) Final Recommendation – Axicabtagene Ciloleucel." February 3, 2023. https://www.cda-amc.ca/axicabtagene-ciloleucel.

Canada's Drug Agency. "pCODR Expert Review Committee (pERC) Final Recommendation – Brentuximab Vedotin (Adcetris) for Peripheral T-Cell Lymphoma." June 4, 2020. https://www.cda-amc.ca/brentuximab-vedotin.

Canada's Drug Agency. "pCODR Expert Review Committee (pERC) Final Recommendation – Brentuximab Vedotin (Adcetris) for Primary Cutaneous Anaplastic Large Cell Lymphoma or CD30-Expressing Mycosis Fungoides." December 3, 2020. https://www.cda-amc.ca/brentuximab-vedotin.

Canada's Drug Agency. "pCODR Expert Review Committee (pERC) Final Recommendation – Folotyn for Peripheral T-Cell Lymphoma." April 4, 2019. https://www.cda-amc.ca/folotyn-peripheral-t-cell-lymphoma.

Canada's Drug Agency. "pCODR Expert Review Committee (pERC) Final Recommendation – Isatuximab," January 28, 2022. https://www.cda-amc.ca/isatuximab.

Canada's Drug Agency. "pCODR Expert Review Committee (pERC) Final Recommendation – Pembrolizumab (Keytruda) Classical Hodgkin Lymphoma," January 5, 2018. https://www.cda-amc.ca/pembrolizumab.

Canada's Drug Agency. "pCODR Expert Review Committee (pERC) Final Recommendation – Polatuzumab Vedotin (Polivy) for DLBCL," April 21, 2021. https://www.cda-amc.ca/polatuzumab-vedotin.

Canada's Drug Agency. "pCODR Expert Review Committee (pERC) Final Recommendation – Selinexor," July 29, 2022. https://www.cda-amc.ca/selinexor.

Canadian Agency for Drugs and Technologies in Health. "Reimbursement Review Reports." Accessed April 10, 2024. www.cda-amc.ca/reimbursement-review-reports.

Canadian Agency for Drugs and Technologies in Health. "Reimbursement Review Reports." Accessed April 10, 2024. https://www.cadth.ca/reimbursement-review-reports.

Garaszczuk, Roxanne, Jean H. E. Yong, Zhuolu Sun, and Claire de Oliveira. "The Economic Burden of Cancer in Canada from a Societal Perspective." *Current Oncology* 29, no. 4 (April 2022): 2735–48. https://doi.org/10.3390/curroncol29040223.

Kovic, Bruno, Xuejing Jin, Sean Alexander Kennedy, Mathieu Hylands, Michał Pędziwiatr, Akira Kuriyama, Huda Gomaa, et al. “Evaluating Progression-Free Survival as a Surrogate Outcome for Health-Related Quality of Life in Oncology: A Systematic Review and Quantitative Analysis.” *JAMA Internal Medicine* 178, no. 12 (December 1, 2018): 1586–96. https://doi.org/10.1001/jamainternmed.2018.4710.

Malagón, Talía, Jean H. E. Yong, Parker Tope, Wilson H. Miller Jr., Eduardo L. Franco, and McGill Task Force on the Impact of COVID-19 on Cancer Control and Care. “Predicted long-term impact of COVID-19 pandemic-related care delays on cancer mortality in Canada.” *International Journal of Cancer* 150, no. 8 (2022): 1244–54. https://doi.org/10.1002/ijc.33884.

McMaster Health Forum. “Identifying models and approaches to enhance the role of pharmacists in cancer care.” Hamilton: McMaster University, March 2023. https://www.mcmasterforum.org/aboutus/products/project/identifying-models-and-approaches-to-enhance-the-role-of-pharmacists-in-cancer-care.

National Cancer Institute. “Progression-free Survival. Definition.” nciAppModulePage, 2024. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/progression-free-survival.

Statistics Canada. “Total Income of Person.” Ottawa: Statistics Canada, May 18, 2016. Last modified October 19, 2023. https://www23.statcan.gc.ca/imdb/p3Var.pl?Function=DEC&Id=100736.

UCLA Center For Health Policy Research. “Section 4: Key Informant Interviews.” Health DATA Program – Data, Advocacy and Technical Assistance, n.d. https://healthpolicy.ucla.edu/sites/default/files/2023-08/tw_cba23.pdf.

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