White Paper

Access to oncology pharmaceutical innovations in Canada

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Cancer in Canada

The oncology market is growing, innovation in oncology is accelerating, and advancements in oncology are leading to improvements in patient outcomes. However, high unmet need persists for a large number of cancers which continue to have low response rates or limited available therapies. According to the Canadian Medical Association Journal, an estimated 233,900 new cancer cases will be diagnosed in Canada in 2022, with the four most common cancers — lung, breast, prostate, and colorectal — representing 46% of all cancers[1] and contributing to 54% of all cancer deaths. Furthermore, it is estimated that 43% of all Canadians will be diagnosed with cancer in their lifetime and cancer will continue to be the leading cause of death in this country[2].

These epidemiological trends are mirrored by trends in pharmaceutical sales in Canada. Oncology is the leading therapeutic class in this country as measured by retail and hospital purchases, totaling $4.8 billion in sales in 2021[3]. Many novel cancer medicines employ precision biomarkers to improve treatment outcomes. Cell and gene therapies also offer tremendous promise where traditional treatments may fall short[4]. Other advances in pharmaceuticals, such as the introduction of targeted therapies and the combination of these therapies, have led to decreasing mortality rates and improved survival rates among cancer patients[5]. However, despite their high value and the potential of precision medicine and advanced therapies, patient outcomes are hindered by barriers to access[6].

Historically, Canada has been one of the top countries for new oncology product launches in the world. However, recent data highlighted in this report shows a concerning trend of increased time to launch in Canada compared to global launches. In addition, oncology products also face health technology assessment (HTA) and reimbursement challenges. Innovative combination oncology products challenge cost-effectiveness frameworks and are faced with higher price reduction in HTA recommendations and longer price negotiations. Prior research has highlighted the substantial impact of launch and access delays on the quality of life of patients in Canada[7].

While drug development, evaluation, and funding processes for oncology drugs are robust in Canada, similar systems for evaluation, funding, and delivery for companion diagnostics (CDx) do not yet exist. Cell therapies realize the promise of precision medicine where therapy is customized to the individual, yet they are not accessible for all patients across Canada. Although CADTH, INESSS and Health Canada parallel review processes contribute to faster review, complexity of the current framework can delay launches and potentially impede timely access to innovative products for patients. This shows that the entire healthcare ecosystem needs to align in the objective of streamlining the HTA and reimbursement process as a national priority to meet the rapidly evolving cancer treatment landscape.

This IQVIA report examines Canada's current trends in oncology including its place in the global launch sequence, market access and pricing, developments in precision medicine and companion diagnostics, and referral patterns and awareness of cell therapies.

Canada's place in global launch sequencing for oncology products

IQVIA conducted a launch sequencing analysis to assess how Canada compared to international markets for time to launch of new active substances for oncology (oncology NAS) over the last 20 years. IQVIA's global launch and sales database (MIDAS) was used as a robust source of worldwide pharmaceutical sales data. Using MIDAS data, the top 25 countries by global pharmaceutical sales in 2021 were identified and assessed for the quality of launch data. Sweden and Austria were excluded from this analysis due to launch data quality, therefore the analysis was conducted on the remaining top 23 countries. Oncology NAS first launched, and globally available, within 2002-2021 were included for analysis based on the selection criteria highlighted in **Figure 1**.

Figure 1: Selection criteria - New active substances for oncology

Inclusion criteria

- Global first launch at the molecule level in 2002-2021
- For use in human therapy
- Has been approved by officially recognized governmental bodies (e.g. FDA)
- Is commercially available in at least one of these three regions (US, Europe or Canada) and available in more than one country
- Global first launched branded pharmaceutical
- Global first launch in oncology therapeutic area

Exclusion criteria

- Generics and biosimilars
- New indication of existing substance
- New combination of existing substance (aka fixed dose combos)
- New salt, hydrate, crystalline form, formulation, etc. of previously approved substance
- Not an active substance (e.g., drug delivery system)
- Natural tissue or plant extract with no identifiable therapeutic entity
- Blood products, vaccines, or natural health products/vitamins
- Products that launched in only one country
- Products/countries where data was not available

In the last 20 years, Canada has experienced a median time to launch of 1.1 years from first global launch, ranking fourth compared to other international markets (**Figure 2**). Seventy-one percent of all globally launched oncology NAS were launched in Canada putting it seventh in comparison with other international markets in terms of proportion of oncology NAS launched within each country in the last 20 years (**Figure 3**). The yearly trend of the number of oncology NAS launches and median time to launch does not show any specific patterns from 2007-2021. However, in the last three years, the median time to launch oncology NAS in Canada showed a consistent increase. (**Figure 4**)

IQVIA's global launch planning experts cited market opportunity, regulatory and market access environment, and organizational priority as some of the key factors considered by the pharmaceutical industry in launch sequencing at an international level. The experts indicated that the complexity introduced by sub-national markets, lengthy processes, low net public prices, and relatively small and diverse populations are important challenges that impact Canada's position in the global market. Other markets that are characterized by high market potential with predictable regulatory and market access environments, and that reward innovation, seem to have higher priority in launch timing decisions by pharmaceutical companies. Delays in each step of the HTA and reimbursement pathway in Canada contribute to the overall delay in launch which, in turn, results in longer wait times for patients to access new medicines.

Figure 2: Median time from global launch to local country launch (Data period: 2002-2021; global oncology NAS launches = 146)*

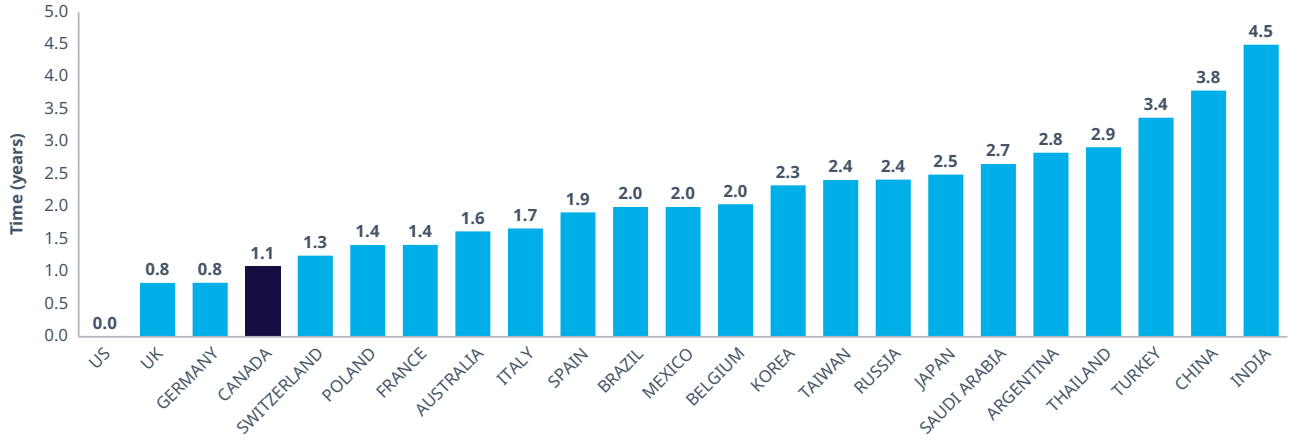


Figure 3: Proportion of oncology NAS launch by country (Data period: 2002-2021; Global oncology NAS launches = 146)*

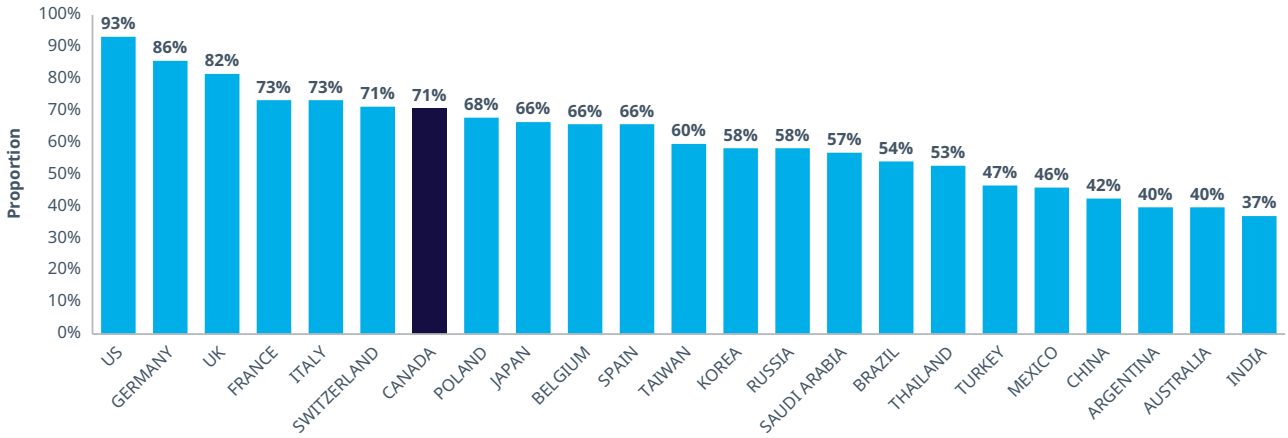
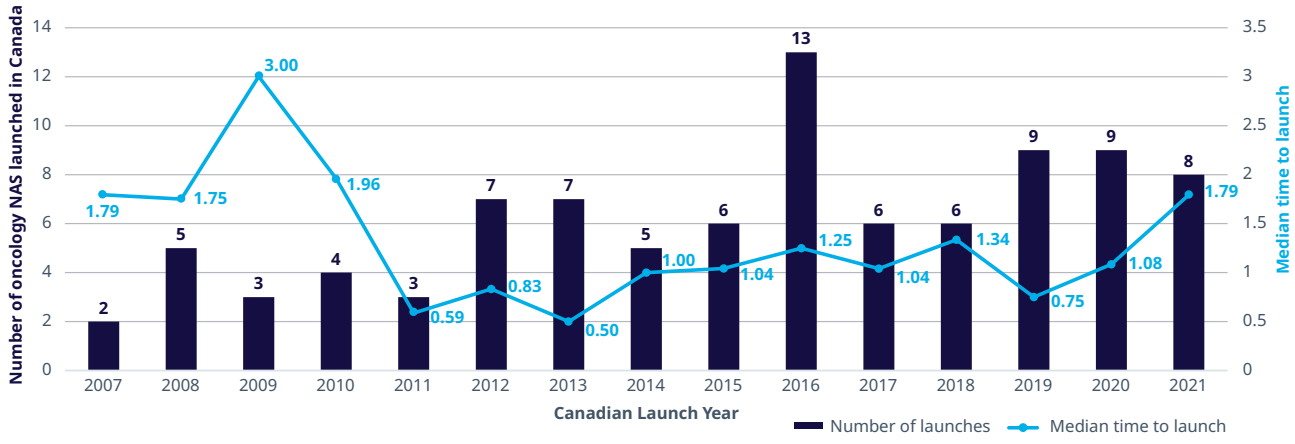


Figure 4: Yearly trend of number of launches and median time to launch in Canada (Data period: 2007-2021; Canadian oncology NAS launches = 93)**



* Data source: IQVIA MIDAS Database, all new oncology launches within Jan 1, 2002 – Dec 31, 2021 (Data extracted on Mar 21, 2022). Top 25 countries based on 2021 sales. Austria and Sweden were excluded due to launch data quality. Abbreviation: NAS, New active substance.

** Data source: IQVIA MIDAS Database, all new oncology launches within Jan 1, 2007 – Dec 31, 2021 in Canada (Data extracted on Mar 21, 2022). Abbreviation: NAS, New active substance

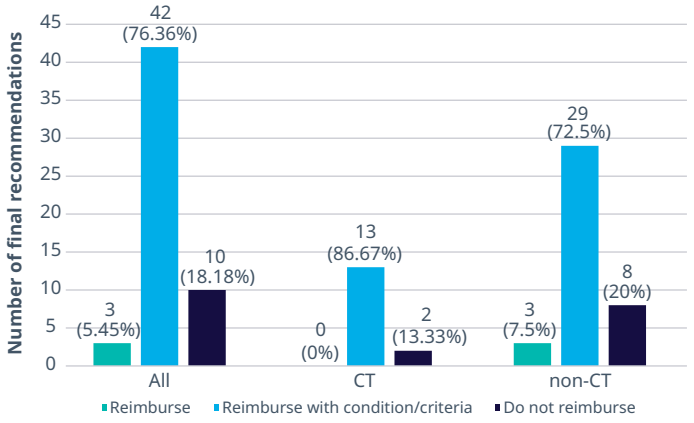
Market access and pricing of combination oncology products in Canada

In recent years, targeted therapies in combination have become the standard of care, as new products target cancers through multiple mechanisms of action. Combination therapies (CT), especially where all molecules are on-patent, are often expensive and present challenges in terms of HTA, value for outcomes, and affordability. Additionally, molecules within combination therapy regimens are often manufactured by different sponsors, making it difficult to appropriately price and negotiate these new products. Despite the burden of regulations, combination treatments carry a net improvement for patient outcomes.

In Canada, the Canadian Agency for Drugs and Technologies in Health (CADTH) and the Institut national d'excellence en santé et en services sociaux (INESSS) conduct HTA reviews for new oncology products, which serves to inform subsequent negotiations that happen with the Pan-Canadian Pharmaceutical Alliance (pCPA) and provincial health ministries. This ultimately impacts on patient access.

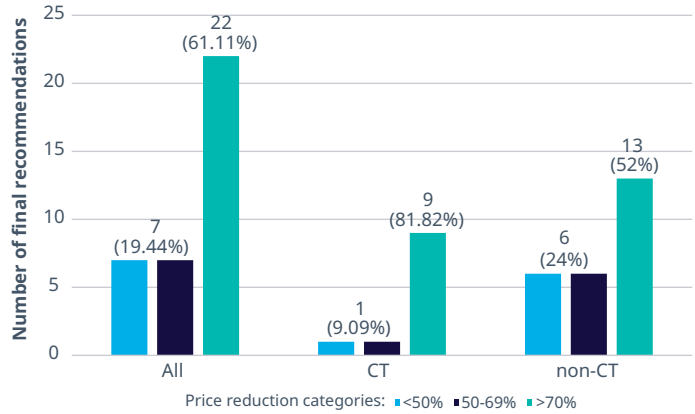
IQVIA's Market Access Metrics database was used to identify final recommendations for sponsor-initiated submissions of oncology products in the last two years. Fifty-five final recommendations have been issued by CADTH for oncology products from January 2020 to December 2021. Fifteen (27%) of these recommendations were for combination therapy products, which were defined as either a new combination of targeted therapies or a new targeted therapy being added to an existing backbone therapy (or therapies). Thirteen of the 15 CTs (87%) received a recommendation to "reimburse with condition/criteria" as depicted in **Figure 5**. The remaining 40 (73%) recommendations were for oncology products not identified as CT (non-CT). Three of the 40 non-CTs (8%) received a recommendation to "reimburse" and 29 (72%) received a recommendation "to reimburse with condition/criteria".

Figure 5: Recommendation outcome*



"Percentage of price reduction" was stated in 11 of 13 CTs with "reimburse with condition/criteria" and in 25 of 32 non-CTs with "reimburse or reimburse with condition/criteria". On average, CADTH requested a price reduction of 76% for CTs and 67% for non-CTs. As shown in **Figure 6**, it was requested that 82% of CTs reduce their price by 70% or more, while 52% of non-CTs were requested to reduce price by 70% or more. For nine CTs that had concluded pCPA negotiations it took approximately 10 months from CADTH recommendation to letter of intent (LOI). In contrast, it took an average of 7.5 months from CADTH recommendation to LOI for 26 non-CTs that had concluded pCPA negotiations.

Figure 6: Percentage price reduction in "Reimburse" or "Reimburse with condition/criteria" recommendations*



*Data source: IQVIA's Market Access Metrics database. Abbreviation: CT, Combination therapy

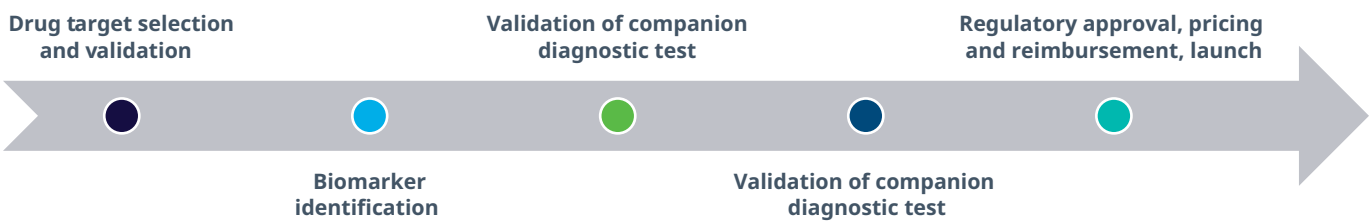
Recent research[4] has studied the impact of launch delay and access to medicines on potential life-years lost in Canada. The study analyzed 15 publicly funded oncology drugs that underwent HTA review between 2011 and 2016 and found the median time from proof of efficacy to first public funding was 26.6 months. The access delays translated to 39,067 overall life-years lost and 48,037 progression-free life-years lost. These findings highlight the substantial impact on patients' quality of life because of launch and market access delays for innovative oncology products in Canada.

Developments in precision medicine and companion diagnostics

The increase in the development and clinical implementation of targeted therapies in recent decades has led to a concurrent growth in the development of companion diagnostics (CDx) which guide the choice and/or dosing of a drug to improve efficacy and safety. This precision medicine approach has the potential to improve patient outcomes and reduce healthcare system burden[8].

Health Canada established the Personalized Medicine Working Group (PMWG) in 2019 to facilitate a coordinated policy approach to precision medicine. This led to the development of a pharmacogenomics guidance document, regulatory modernization, and participation in the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) E15 and E16 initiatives[9,10]. Currently, CDx are regulated as Class III in vitro diagnostic devices (IVD) by Health Canada and require a medical devices license application. When testing of a biomarker is required prior to prescribing a treatment, the submission for the regulatory approval of the CDx can be sent with the associated drug but each is reviewed by a separate directorate within Health Canada and is subject to different regulation (**Figure 7**). A CDx can also be developed and approved after market approval of the associated therapy if a new indication requires identification of a biomarker prior to use of therapy. However, there is no formal process for HTA evaluation and reimbursement of CDx in Canada, including a lack of standardized processes for determining clinical utility and reimbursement rates and lack of formal coordination between reimbursement processes of diagnostics and drugs[9]. Instead, coverage and reimbursement rate decisions are typically made case-by-case. In the absence of standardized processes for HTA review across jurisdictions, the pressure is often on hospitals to evaluate and provide genetic tests. Some pharmaceutical companies also provide access to companion tests, but this method of access is usually only available for a limited time and may be associated with other conditions.

Figure 7: Companion diagnostic test development process



Based on data from IQVIA's Oncology Patient Outcomes, which examined mutational testing practices in advanced colorectal and melanoma cancers, it was determined that the majority of physicians test advanced cancer patients for mutations to make informed treatment decisions. This includes testing for BRAF, NRAS, KRAS mutations and microsatellite instability (MSI) and DNA mismatch repair deficiency (dMMR) (**Figure 8**).

Figure 8: Timing of mutation testing for patients with metastatic colorectal cancer by practice type

	BRAF*		NRAS		KRAS		MSI		dMMR	
Total patients tested	**Community (n=42)**	**Academic (n=34)**	**Community (n=42)**	**Academic (n=34)**	**Community (n=42)**	**Academic (n=34)**	**Community (n=42)**	**Academic (n=34)**	**Community (n=42)**	**Academic (n=34)**
Not tested	0%	0%	48% (20)	9% (3)	36% (15)	3% (1)	50% (21)	32% (11)	55% (23)	29% (10)
At diagnosis	79% (33)	82% (28)	31% (13)	76% (26)	40% (17)	85% (29)	21% (9)	59% (20)	26% (11)	62% (21)
Prior to initiating 1L*	14% (6)	0%	14% (6)	0%	17% (7)	6% (2)	24% (10)	3% (1)	14% (6)	3% (1)
After 1L but prior to initiating 2L	7% (3)	15% (5)	7% (3)	15% (5)	7% (3)	6% (2)	5% (2)	6% (2)	5% (2)	6% (2)
After 2L but prior to initiating 3L	0%	3% (1)	0%	0%	0%	0%	0%	0%	0%	0%

*Physicians were required to have treated at least three BRAF positive metastatic colorectal cancer patients to be eligible to participate in this study.
Data source: IQVIA Oncology Patient Outcomes – Metastatic Colorectal Cancer Report Q1 2022

In 2022, at least 12 oncology pharmaceuticals with market authorization in Canada require CDx testing. There are 14 commercially available diagnostic tests approved for use with companion drugs[5] and there are a growing number of available diagnostic tests in development for oncology. One of these, the Oncotype DX breast cancer assay, is publicly reimbursed in Ontario, Quebec, and Saskatchewan with other provinces considering public funding[5].

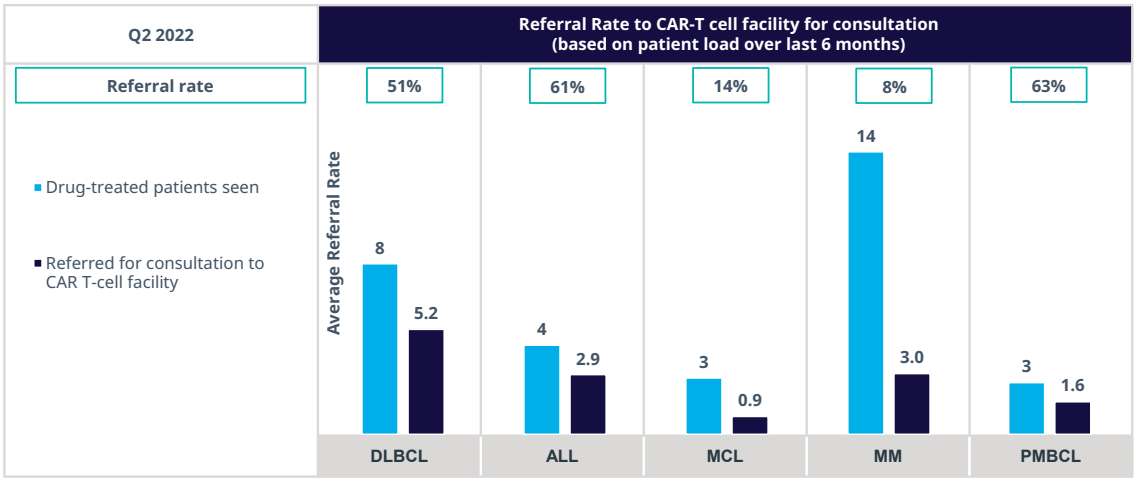
The value of the global oncology precision market in 2019 was $46.9 billion and is expected to triple to $148.7 billion by 2030[7]. IQVIA's Oncology Patient Outcomes provides support to regulatory submission payer negotiations by providing a snapshot of the treatments patients receive in each line of therapy and also collects information on the frequency, timing, and results of mutational testing. The data also provide insights on the uptake of pharmaceuticals and CDx in a variety of cancer types.

Referral patterns and awareness of CAR T-cell therapies in Canada

Chimeric antigen receptor T-cell (CAR-T) therapy represents a new class of treatment currently available for some types of leukemia and lymphoma, with early phase testing in other hematological and solid cancers. This adoptive T-cell immunotherapy uses a person's own reprogrammed immune cells to find and attack the cancer. Production and delivery of CAR-T is complex and provinces across Canada currently have limited capacity, hence, can only treat a limited number of patients. Kymriah (September 2018) and Yescarta (February 2019) were the first CAR-T therapies to be approved in Canada. Their approval resulted in a specific review process for cell and gene therapies in January 2020 by CADTH. Kymriah is now publicly funded in Quebec (October 2019), Ontario (December 2019), and Alberta (August 2020). Access to non-resident patients is limited to out-of-province or out-of-country programs. Furthermore, access is strictly controlled and only oncologists, hematologists, or CAR-T specialists can enroll patients in treatment.

IQVIA conducted a physician survey between April 1, 2022 and June 30, 2022 to better understand the CAR-T referral process in Canada. Based on this data, despite multiple myeloma (MM) having the highest patient load, referral rates were highest for primary mediastinal B-cell lymphoma (PMBCL) followed by diffuse large B-cell lymphoma (DLBCL) (**Figure 9**). The key barrier to referring patients for CAR-T treatment was patient health (i.e., performance status, patient fitness) but lengthy time between the referral and start of CAR-T treatment was also a deterrent (**Figure 10**). This means that the patient is unable to start treatment within a clinically appropriate timeframe, which is a key eligibility criterion for referral to CAR-T therapy. Approximately 78% of physicians indicated that the primary factors influencing their decision to refer a patient for treatment at a CAR-T treatment facility were limited treatment options outside CAR-T therapy, the patient's performance status, and the results of clinical trials. While 56% of the survey's respondents felt well-informed about CAR-T therapy, overall, 44% felt they could use more information, particularly about patient profile (88%) for CAR-T eligibility as well as more information about CAR-T products (63%). Physician awareness of Kymriah, Yescarta, and Abecma was high; however, awareness of Tecartus, Breyanzi and Cilta-cel was low (**Figure 11)**. IQVIA has multiple ongoing studies that provide a comprehensive overview of the CAR-T market and its dynamics in Canada through IQVIA's Canadian CAR-T Monitor.

Figure 9: Physician referral rates to CAR T-cell therapy treatment facility by cancer type



*Data source: IQVIA CAR-T Monitor Report Q2 2022. Abbreviation: DLBCL, diffuse large B cell lymphoma; ALL, acute lymphoblastic leukemia; MCL, mantle cell lymphoma; MM, multiple myeloma; FL, follicular lymphoma; PMBCL, primary mediastinal large B-cell lymphoma.
Note: FL not included due to low sample size

Figure 10: Physician identified barriers to referring patients to a CAR T-cell therapy treatment facility

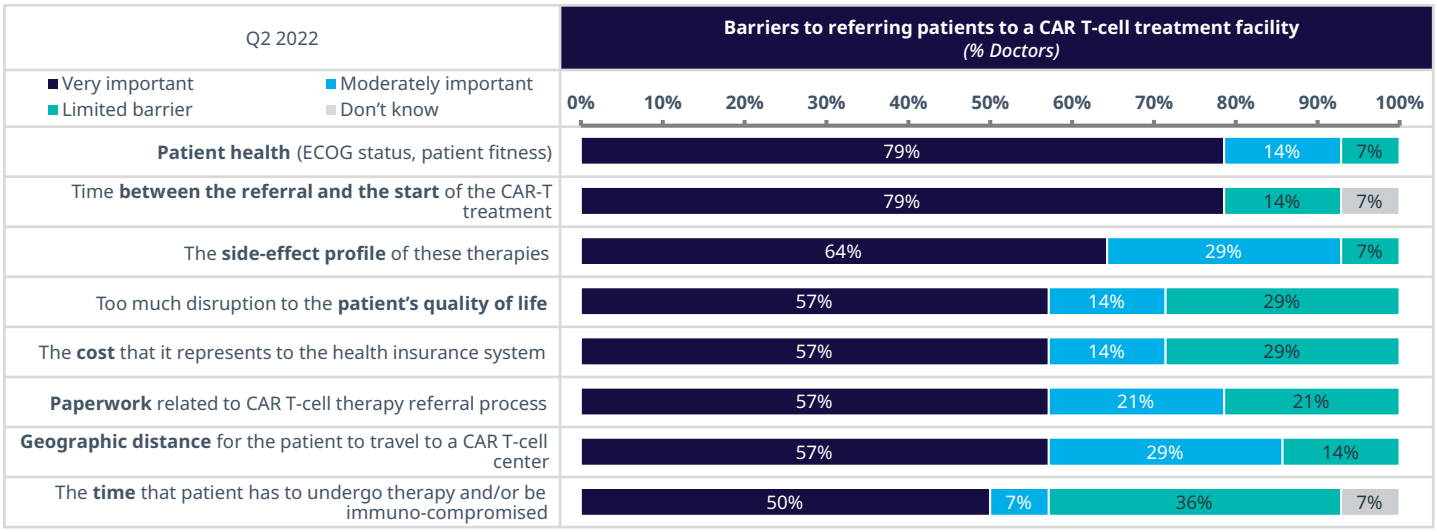
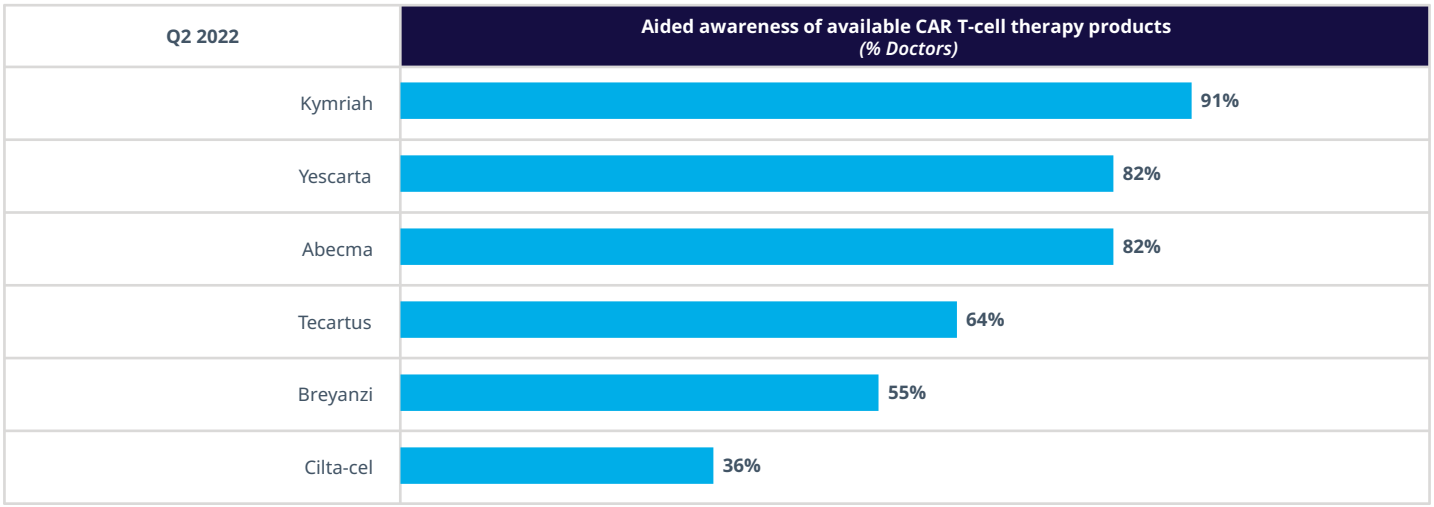


Figure 11: Physician awareness of CAR T-cell therapy products



Data source: IQVIA CAR-T Monitor Report Q2 2022

In summary, emerging combination strategies and next-generation therapies have shown the potential for better outcomes for cancer patients. But they also bring with them more complex development paths and HTA review and reimbursement challenges. As the oncology landscape in Canada continues to evolve, it will be important to monitor both the challenges and opportunities in this space. Through advanced analytics and in-house oncology expertise, IQVIA can leverage the power of real-world data to accelerate time to insights and help drive business decisions which ultimately impact patient care.

For questions about IQVIA real-world oncology solutions, please contact **canadainfo@iqvia.com**

References

1. Brenner DR, Poirier A, Woods R, et al. Projected estimates of cancer in Canada in 2022. CMAJ. 2022; 194(17): E601-E607. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9067380/
2. Statistics Canada. Cancer incidence and mortality trends, 1984 to 2020. Release 2022-02-04. Available from https://www150.statcan.gc.ca/n1/daily-quotidien/220204/dq220204b-eng.htm
3. IQVIA 2021 Canadian Pharmaceutical Market Highlights. Available from https://www.iqvia.com/-/media/iqvia/pdfs/canada/2021-trends/2021-canadian-pharmaceutical-trends.pdf?_=1662648534009
4. Elverum, Kris, and Maria Whitman. “Delivering cellular and gene therapies to patients: solutions for realizing the potential of the next generation of medicine.” Gene Therapy 27.12 (2020): 537-544.
5. Brenner, Darren R., et al. “Projected estimates of cancer in Canada in 2022.” Cmaj 194.17 (2022): E601-E607.
6. Bonter, Katherine, et al. “Personalised medicine in Canada: a survey of adoption and practice in oncology, cardiology and family medicine.” BMJ open 1.1 (2011): e000110.
7. Gotfrit J, Shin JJW, Mallick R, Stewart DJ, Wheatley-Price P. Potential Life-Years Lost: The Impact of the Cancer Drug Regulatory and Funding Process in Canada. The Oncologist 2019;25:e130-e7.
8. Kasztura M, Richard A, Bempong NE, Loncar D, Flahault A. Cost-effectiveness of precision medicine: a scoping review. International journal of public health. 2019 Dec;64:1261-71.
9. Cowling T, Boucher M, Fitzsimmons H. CADTH Environmental Scan. Issue 57. Pharmaceuticals requiring companion diagnostics: 2014 [partially updated 2016]. Available from https://www.cadth.ca/pharmaceuticals-requiring-companion-diagnostics#references
10. Sarrazin P. Regulatory oversight of genetic testing in Canada. Health Canada perspective [presentation on the Internet]. Ottawa: Health Canada; 2010. Available from: http://www.slideshare.net/webgoddesscathy/patrice-sarrazin-health-canada
11. Global oncology precision medicine market (2020 to 2030). Intrado Global Newswire, Jan. 5, 2021. https://bit.ly/3B5m9DD

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