Canada's Drug Agency
L'Agence des médicaments du Canada
Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

quizartinib (Vanflyta)

(Daiichi Sankyo Pharma Canada)

Indication: Vanflyta (quizartinib) is indicated in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, and as continuation maintenance monotherapy following consolidation, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FMS-like tyrosine kinase 3 internal tandem duplication (FLT3-ITD) positive.

December 20, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CDA-AMC and do not necessarily represent or reflect the views of CDA-AMC. No endorsement by CDA-AMC is intended or should be inferred.

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CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Quizartinib (Vanflyta)

Indication: acute myeloid leukemia.
FDA: On July 20, 2023, the Food and Drug Administration approved quizartinib (Vanflyta, Daiichi Sankyo, Inc.) with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive, as detected by an FDA-approved test. Similar authorizations have been granted in Europe and Japan.

Name of Patient Group: Heal Canada

Author of Submission: Brigitte Leonard, Ph.D.

1. About Your Patient Group

Heal Canada is a registered not-for-profit organization that aims to empower patients, improve healthcare outcomes, and advocate for equitable access to quality healthcare across Canada. We are committed to fostering a patient-centred healthcare system that prioritizes every individual's well-being, dignity, and rights through:

- Patient Empowerment
- Patient Education and Awareness
- Advocacy for Equity
- Collaboration and Partnerships with the highest ethical standards.

During their career, the executive team of Heal Canada developed a strong expertise in rare hematological diseases, such as CML, myelofibrosis, Mastocytosis and AML.

Cheryl Petruk, MBA, B.Mgt / Founder and CEO

- Founder and former Executive Director of the Canadian MPN Network
- Founder and former Executive Director of the Canadian MPN Research Foundation

Brigitte Leonard, Ph.D./ Executive Director and Chief Scientific Officer

- MSL and Medical Advisor involved in the clinical development of nilotinib, ruxolitinib and midostaurin at Novartis Canada.

Website: https://healcanada.org/

2. Information Gathering

The methodology includes:

1. Online survey: Impact of diagnosis and treatments on patients' lives.
    - Enrolling period: November 16 to December 16
    - Canadian participants = 26, number of completed surveys = 22.
        - Completion rate: 77%
            - 5 participants didn't complete the survey:
                - 3 from the age cohort < 18 years old.
                - 2 from age cohort 50-64 years old.
    - Regional distribution: ON (38%), QC (18%), BC (12%), AB (9%), MB (3%), NS (3%), NB (3%), and SK (3%).
    - Age of participants:
        - 79% of participants are at the age of working (19-64 yo)
        - Only 12% are 65 or older, and 9% are younger than 18.
    - Duration of disease:
        - 44% of participants were diagnosed for less than a year.
        - 44% of participants were diagnosed for 1 to 2 years
        - 12% of participants were diagnosed for more than 2 years.

This observation is in line with the poor long-term outcomes of patients diagnosed with AML.

2. AML patient interviews

3. Information and international medical experts' quotes captured from ASH 2024 oral and poster presentations

4. Medical and scientific publications

3. Disease Experience

Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Patient's perspective regarding diagnosis and treatments

Based on the patient survey,

- 94% of patients received their diagnosis within a month, and 59% of participants received it within a week.
- 100% of participants have received mutation testing.
    - 40% of patients received their test results within a week
    - 60% of patients received their results after a week.
- 67% of participants said their treatments started before getting the mutation testing results.
    - Integrating new recommendations can take more than 3 years for the medical community.[1] With this mindset, it is unsurprising that only 33% of patients had mutation results before initiating their treatments.
    - During AML oral sessions at ASH 2024, several international experts stressed the importance of waiting for mutation results before initiating treatments. Mutations are part of the prognostic risk classification, and some treatment provides superior results in different patient populations based on their mutation profile. [2,3,4]
    - A Canadian panel of experts from CLSG/GCEL published guidelines in December 2023. They also recommend conducting an FLT-3 mutation test before initiating treatments.[5]
    - AML is an aggressive and fast-growing cancer; this new approach contrasts gravely with the old paradigm that the treatment needed to start as soon as possible. When the Ratify study (midostaurin trial) was enrolling patients, principal investigators were seriously worried about waiting a few days for FLT-3 testing results. More than a decade later, the perception remains. The situation can seriously impact patient outcomes. The CLSG/GCEL can play an essential role in harmonizing treatment standards for AML patients in Canada.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

1- AML patients have limited treatment options:

For patients with acute myeloid leukemia (AML), the ideal treatment scenario is to achieve complete remission (CR) after one cycle of intensive induction chemotherapy and subsequently receive allogeneic hematopoietic stem cell transplantation (aHSCT) and stay in remission. However, this scenario is far from the norm for most patients.

1) Not all patients are fit enough to receive an intensive chemo regimen.
2) Not all patients are eligible for an aHSCT due to health status and donor limitations.
3) Not all patients who achieve a CR and receive an aHSCT stay in remission

For patients who relapse, the survival rate is terrible.

2- AML treatments provide relatively poor long-term results:

Even for patients who are fit enough to receive an intensive chemotherapy regimen and lucky enough to receive an aHSCT, their long-term overall survival is relatively small. Even in QUANTUM-First, the median overall survival in the placebo group who receive aHSCT is 12.9 months (9.2-14.7).[6]

In the survey, treatments received are (Table 1):

- 100% of patients received IV chemotherapy (CxIV)
  - 38% of participants received IV chemotherapy only
- 38% of participants received a combination of Oral (CxO)and IV chemotherapy
  - 10% of participants had chemotherapy only
  - 24% of participants had chemotherapy and aHSCT (T).
- 52% of participants received an aHSCT (T).

Table 1: Treatment received by participants

Treatment received	29	Ratio
CxIV	11	38%
CxO,CxIV	3	10%
CxIV,T	8	28%
CxO,CxIV,T	7	24%

When we look at treatments received, we notice that 48% of patients did not receive an aHSCT. The survey highlights the limitations of aHSCT in the real-world setting. Patients need

a suitable donor to receive a transplant as well as being in shape. Based on several conversations, for most patients, transplantation is a very stressful procedure. They do it because there is no better treatment option; It is the price to pay to improve their odds of beating their cancer.

Transplantation has a negative impact on their QoL. Several severe complications are experienced, such as acute and chronic GVHD, infections, etc. They cannot function properly for several months and rely on their caregivers. Even if they are eligible for transplantation, not all patients accept the risk associated with the procedure. Some patients refuse the procedure.

During interviews, some participants mentioned:

- I had my BMT a year ago, I do NOT feel capable of driving yet … wondering if I ever will?
- My judgment was compromised; I'm 2 ½ years post-SCT and just getting back to where I once was.
- Tacrolimus meds make my hands so shaky I couldn't even write.
- The transplant itself is very harsh on the body. After the BMT it's GVHD, to treat this, you need a strong heart and mind.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families differ if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

- As part of the treatment discussion, only 86% of participants recalled having been informed about the risk of relapse by their treating HCPs. The concept that the disease can reappear after an initial treatment is stressful for most participants.
- When we asked the participants this question: How stressful is it to think that your cancer can come back? Their answers can vary from 0 (not stressful at all) to 100, representing severe stress and anxiety (Table 2).
    - The average response is 76.1%, ranging from 20 to 100.
    - The median response is 87%, ranging from 20 to 100.
    - When split into categories, only 1 participant rated their stress below 25%, while 97% rated their stress at 25% or more
        - 83% rated their stress ≥ 50%
        - 66% rated their stress ≥ 75%
        - 33% rated their stress at 100%

The stress seems, in general, inferior in participants who did not recall discussing with their treating HCP about the risk of relapse (Table 2)

Table 2: Level of stress regarding the potential risk of relapse			**Discussion about risk of progression**			
			No		**Yes**	
How stressful is to think that your cancer can come back? 100 being severe stress and anxiety	**29**	**Ratio**	**5**	**Ratio**	**24**	**Ratio**
Number of person with 100%	8	28%	0	0%	8	33%
Number of person with ≥ 75%	19	66%	3	60%	16	67%
Number of person with ≥ 50%	24	83%	3	60%	21	88%
Number of person with ≥ 25%	28	97%	5	100%	23	96%
Number of person with < 25%	1	3%	0	0%	1	4%
Average	76.1	(20-100)	63.4	(25-90)	78.7	(20-100)
Median	87.0	(20-100)	87.0	(25-90)	87.5	(20-100)

- 89% of participants think that receiving treatment in maintenance to reduce their risk of relapsing and prolong their survival would alleviate some of the stress related to their cancer. This data contrasts with some medical experts' opinions who think that having a maintenance therapy could be perceived negatively by patients. Now, several

hematological cancers have become chronic conditions. In general, patients are concerned about survival and QoL. They prefer a long-term treatment as long it is efficient and relatively well-tolerated compared to traditional chemotherapy associated with high short-term adverse reactions and long-term increased risk of secondary cancer and cardiac complications.

- When we asked the participants this question: How important is it for you to prolong the response to your treatment and avoid the disease coming back? Their answers can vary from 0 (not important) to 100 (extremely important) (Table 3).
    - The average response is 94%, ranging from 59 to 100.
    - The median response is 100%, ranging from 59 to 100.
    - When split into categories, only 1 participant rated the importance below 75%, while 97% rated the importance ≥ 75%.
        - 62% rated the importance at 100% (extremely important)
- The importance seems, in general, inferior in participants who did not recall discussing with their treating HCP about the risk of relapse (Table 3).

Table 3: Importance to prolong response and avoid relapse			**Discussion about risk of progression**			
			No		**Yes**	
How important is to prolong treatment response and avoid the disease coming back? From 0 (not important) to 100 (extremely important)	**29**	**Ratio**	**5**	**Ratio**	**24**	**Ratio**
Number of person with 100%	18	62%	0	0%	18	75%
Number of person with ≥ 75%	28	97%	5	100%	23	96%
Number of person with ≥ 50%	29	100%	5	100%	23	96%
Number of person with ≥ 25%	29	100%	5	100%	24	100%
Number of person with < 25%	0	0%	0	0%	0	0%
Average	93.9	(59-100)	88.4	(59-100)	95.1	(59-100)
Median	100.0	(59-100)	94.0	(59-100)	100.0	(59-100)

Quizartinib fulfills current needs in this poor-prognosis patient population:

In QUANTUM-FIRST,

1) The median duration of CR in patients who achieved CR during induction is 3 times the one with placebo (38.6m vs 12.4m).

2) The median relapse-free-survival is almost 3 times longer in quiz group vs placebo (39.3m vs 13.6m)

3) The median overall survival is two times longer in the quiz group vs placebo (31.9m vs 15.1m)

The importance of FLT-3 inhibitors in maintenance:

When patients have a mutation like FLT-3, maintenance therapy has been proven effective and is recommended by ELN and NCCN guidelines. Patients with FLT3-ITD mutated AML have a particularly poor prognostic; unsurprisingly, Quizartinib was approved in the United States and Europe for maintenance of patients with newly diagnosed FLT3-ITD AML.

Why is maintenance therapy so important?

As discussed earlier, the stress related to relapse is high in AML patients.

- Intensive chemotherapy regimens and aHSCT are difficult treatments impacting severely QoL for a long period of time.
- For patients who need a second induction or who couldn't receive transplantation, the stress is even higher.

Having access to targeted therapy with a well-tolerated profile improves patients' QoL and addresses the most stressful aspect of their disease. Avoiding relapse and prolonging their response and survival are the most important objectives for them. Quizartinib, added to the standard treatment and provided in monotherapy as maintenance, fulfills their current unmet needs.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families. How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

- One person interviewed finished his first round of Vanflyta. He was okay, and it was well tolerated.
- One person was on AZA+Ven +Glit post-transplant with MRD+; he switched to quizartinib to improve his response. It is well-tolerated, and his response improved.
- One person participates in QUANTUM-First. He got CR at the first induction, went to BMT, had no residual disease 90 days post-transplantation, and continued with a quiz for maintenance therapy. The treatment is well-tolerated, so his oncologist continues with maintenance as per protocol.

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments. What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

- In the USA, the FDA approved a companion diagnostic test for FLT3-ITD mutation in line with quizartinib approval. However, this companion test is not necessary in Canada. FLT-3 mutation testing has been integrated into clinical practices since the approbation of midostaurin. FLT-3 testing has become an essential part of the AML workup. It is also now recommended by medical experts to conduct mutation testing before initiating the treatment in AML. Therefore, FLT3 mutation testing should not be an issue for AML patients in Canada
- In 2023, a Canadian CLSG/GCEL panel of eight experts published guidelines in December 2023 regarding FLT3 mutation testing.[5] The panel followed an evidence-based approach, taken together with Canadian clinical and laboratory experience and expertise, to create a consensus document to facilitate a more uniform approach to AML diagnosis and treatment across Canada. The CLSG/GCEL panel recommends that all AML patients be tested for *FLT* mutation (ITD and TKD) at the time of initial diagnosis, regardless of age. They also provide technical details about the appropriate way of conducting the test. The latest is part of their mission to harmonize the AML standard care in Canada.
- Why testing for FLT-3 mutation is clinically relevant to maximize patient outcomes:
    - FLT-3 mutation is detected in 20 to 30% of patients.
    - FLT-3-ITD mutation is associated with a poor prognosis.
    - FLT-3 inhibitor added with intensive chemotherapy or venetoclax/HMA regimen improves response rate, relapse-free survival and overall survival
- It is well-known that bone marrow (BM) biopsy is relatively invasive and not the preferred diagnostic procedure for patients. For now, it is recommended that the mutation test be done on the BM aspirate sample. However, a blood sample should be enough in most cases due to the high number of blast cells in peripheral blood (PB). Even if clinicians prefer a BM sample for now, mutation testing will not present an additional burden for patients because a BM biopsy is mandatory to confirm the diagnosis and determine the severity by pathologists.

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8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

Abbreviations :

aHSCT: allogeneic hematopoietic stem cell transplantation
CLSG/GCEL : *Canadian Leukemia Study Group / Groupe Canadian d'étude sur la leucémie*
Cx : Chemotherapy
CxIV : IV chemotherapy
CxO : Oral chemotherapy
T : Transplantation
Quiz : quizartinib

References:

1- *Daniel J. Zheng,* Near Universal National Uptake of Dexrazoxane in the Real-World Setting Associated with Reduced Cardiac ICU Care Requirements in Pediatric Acute Myeloid Leukemia, ASH2024; Abstract 116

2- Panel of experts during pre-ASH 2024 Friday Symposium titled AML Bridging Evidence to practice in AML: Naval G. Daver, Jessica Altman, Amir T. Fathi, Gail J. Roboz, Joshua Zeidner.

3- *Jennifer Marvin-Peek*[1]A Phase Ib/II Study of Ivosidenib with Venetoclax ± Azacitidine in IDH1-Mutated Hematologic Malignancies: A 2024 Update; 219 :

4- *Richard M Stone,* 10-Year Follow-up of CALGB 10603/Ratify: Midostaurin Versus Placebo Plus Intensive Chemotherapy in Newly Diagnosed FLT3 Mutant Acute Myeloid Leukemia Patients Aged 18-60 Years; 218

5- Bergeron J. et al, The Clinical Utility of FLT3 Mutation Testing in Acute Leukemia: A Canadian Consensus, *Curr. Oncol.* **2023**, *30*(12), 10410-10436;

6- Erba HP. et al, Quizartinib plus chemotherapy in newly diagnosed patients with FLT3-internal-tandem-duplication-positive acute myeloid leukaemia (QuANTUM-First): a randomised, double-blind, placebo-controlled, phase 3 trial; Lancet. 2023 May 13;401(10388):1571-1583.

7- Sadia Ansar, FLT3 Inhibitors As Maintenance Therapy Post Allogenic Hematopoietic Stem Cell Transplantation in Acute Myeloid Leukemia Patients with FLT3 Mutations; A Systematic Review and Meta-Analysis | Blood | American Society of Hematology; 5197

8- Real World Experience of FLT3-Inhibitor Post-Transplant Maintenance with Sorafenib Demonstrating Superior Overall- and Relapse-Free Survival Following Allogeneic Hematopoietic Stem Cell Transplantation in FLT3-ITD Mutated Acute Myeloid Leukemia | Blood | American Society of Hematology; 3589

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No help was provided or requested from outside of the organization to develop this submission.

   The content of this submission is derived from the presentation of international medical experts (ASH 2024), the scientific literature and from the patients` survey conducted by Heal Canada.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No help was provided or requested from outside of the organization to develop this submission.

   The content of this submission is derived from the presentation of international medical experts (ASH 2024), the scientific literature and from the patients` survey conducted by Heal Canada.

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have a direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis Canada			X	
SOBI USA			X	X
GSK Canada			X	
Servier Canada			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Brigitte Leonard
Position: Executive Director and Chief Scientific Officer
Patient Group: Heal Canada
Date: 20-12-2024

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: quizartinib (Vanflyta®)
Indication: In combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, and as continuation maintenance monotherapy following consolidation, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FMS-like tyrosine kinase 3 internal tandem duplication (FLT3-ITD) positive.
Name of Patient Group: The Leukemia & Lymphoma Society of Canada (LLSC)
Author of Submission: Colleen McMillan

1. About Your Patient Group

The Leukemia & Lymphoma Society of Canada - bloodcancers.ca

LLSC is a national charitable status organization dedicated to finding a cure for blood cancers and its ability to improve the quality of life of people affected by blood cancers and their families by funding life-enhancing research and providing educational resources, services, and support. The Leukemia and Lymphoma Society of Canada is the largest charitable organization in Canada dedicated to blood cancer, our focus includes:

- Funding research from bench to bedside.
- Rethinking how a person navigates their blood cancer experience
- Providing targeted blood cancer information
- Offering tools for psychological and emotional support
- Empowering Canadians to take charge of their blood cancer experience through practical support and advocacy

2. Information Gathering

One online survey **(Survey #1)** was created for this input submission through SurveyMonkey. Information was gathered from November-December 2024. The survey was developed and distributed by LLSC, in English only. The survey was distributed by email.

The survey asked for input from patients and caregivers who have lived experience with AML.

245 respondents participated in this survey. The majority of respondents (72.42%) indicated that they were the AML patient (past or present). 26.75% of respondents indicated that they were a caregiver of an AML patient (past or present). 2 respondents answered, “none of the above” and were disqualified from the survey.

Respondents were asked to identify the age range of the person diagnosed with AML at the time of diagnosis. 9 respondents answered “0-17 years of age” and were disqualified from the survey.

31 respondents indicated that the patient’s AML is/was FLT3-ITD positive

224 respondents identified their primary residence:

Ontario (94), British Columbia (52), Alberta (29), Nova Scotia (12), Quebec (10), Manitoba and Saskatchewan (8 in each province), New Brunswick (7), PEI (2), Newfoundland and Labrador (1). 1 respondent was International.

Input from this population of patients and/or caregivers regarding their disease experience and experience with currently available treatments has been previously gathered and submitted to the CDA (formerly CADTH) for consideration.

To prevent emotional exhaustion and undue burden on this affected population, the most recent survey ***(Survey #1)*** *focused specifically on patients' and/or caregivers' experience with the treatment under review, quizartinib (Vanflyta), for the treatment of AML, as well as the meaning of the potential for longer remission that this maintenance therapy may offer.*

Additionally, some of the previously gathered input from a separate survey and two one-on-one interviews with patients and caregivers affected by AML has been incorporated into this submission (ONLY in Sections 3 – Disease Experience and 4 – Experience with Currently Available Treatments). Further details about this previous survey and interviews can be found here*: https://www.cda-amc.ca/sites/default/files/DRR/2024/PC0349-Tibsovo_Patient_Clinician_Group_Input.pdf*

For the purposes of this submission, any information from the earlier input will be referred to as "Survey #2."

3. Disease Experience

The AML treatment journey can vary greatly from person to person.

In **Survey #1** Respondents were asked, Which types of AML treatment have you or your loved one received? Select all that apply. 223 respondents answered this question.

Chemotherapy – 207/223 (92.83%)
Stem Cell Transplant – 125/223 (56.05%)
Targeted Therapy – 23/223 (10.31%)
Immunotherapy – 22/223 (9.87%)
48 respondents (21.52%) answered "other". Some respondents commented and listed: Radiation, Transfusions, Bone marrow transplant

ALL SUBSEQUENT INFORMATION UNDER THIS SECTION HAS BEEN PREVIOUSLY SUBMITTED AND IS FROM "SURVEY #2"

Many AML patients require a high degree of caregiver support throughout their AML experience and need assistance with various day-to-day tasks.

64% of those surveyed indicated that they needed caregiver support. This can be an enormous drain on the AML patient who struggles with not being able to do things independently and has to rely on their caregivers. This creates an enormous burden on the caregivers as well. The mental, physical and financial effects of the AML experience have significant impact on the lives of patients and caregivers alike.

Respondents were asked, do/did you require caregiver support to manage your AML symptoms? 67 respondents answered this question.

43/67 (64.18%) -- Yes, I had/have caregiver support
22/67 (32.84%) -- No, I manage(d) fine on my own
2/67 (2.99%) -- Yes, but I was/am unable to access a caregiver (due to cost, no available family member etc.)

Caregivers expanded on their experiences caring for their loved ones with AML:

- “Life completely changes. You worry about work, your own health and being there for the patient. There is no family life, or should I say a negative family life as it revolves around the patient. Taking care of their needs, talking about their illness and praying for recovery. That goes for social life as well. If anything there is guilt for going out and possibly enjoying yourself when a loved one is so restricted, ill and could be dying! Guilt for being alive and healthy! Romantic relationships are put on hold. Who can focus on someone else? There's already too much to deal with”
- “As a caregiver, the care for my dying mother is overwhelming and also trying to be supportive for my father. All this and full-time work, and my own three children and wife. Lots fell through the cracks during the last six months of life”
- “Not only was it my mother, the patient that was affected but also my father who did not do well with this at all. I had to take an extended period off work to spend with both of them in a strange city, staying in hotels, eating meals at restaurants (or not at all). The caretaking was for all 3 of us!”

Over 65% of patients reported a negative impact of AML on their mental health. Fear, anxiety, devastation and worry can take over and add to fatigue and exhaustion already exacerbated by the illness. The mental affects can have an impact on the patient’s overall health and ability to properly care for themselves.

Respondents were asked, what kind of impact has AML had on the mental health status of the patient and/or caregivers? 70 respondents answered this question. Responses are reflected in the chart below:

ANSWER CHOICES	RESPONSES	
Extremely Negative Impact	18.57%	13
Negative Impact	48.57%	34
Neutral	21.43%	15
Positive Impact	7.14%	5
Extremely Positive Impact	4.29%	3
TOTAL		70

Respondents reflected on their thoughts, feelings and mental wellness through AML:

- “It was and is a very scary time for us. Too many unknown factors. We were away from our home and had many challenges to overcome”
- “Depression, feelings of losing hope”
- “Having survived AML (two years now), the biggest negative impact on my mental health is the impact from living with the threat of a recurrence”
- “I have PTSD, anxiety and trouble sleeping”
- “Dealing with major depressive disorder and PTSD since diagnosis but especially after treatment. Dealing with worrying every single day about my family and myself”

Over 60% of patients report negative impact of AML on personal life. It affects all aspects of the lives of patients and caregivers including home and family life, social life and personal relationships. The physical impacts and risks of the disease as well as the overwhelming mental load can limit the ability to go out of the house and participate in activities as one may have before diagnosis. Maintaining relationships and routines can be difficult, sometimes impossible for patients with fatigue, low energy levels, pain, mental health struggles, and other symptoms and side effects.

Respondents were asked, what kind of impact has AML had on your personal life/home life? 70 respondents answered this question. Responses are reflected in the chart below:

ANSWER CHOICES	RESPONSES	
Extremely Negative Impact	20.00%	14
Negative Impact	41.43%	29
Neutral	22.86%	16
Positive Impact	12.86%	9
Extremely Positive Impact	2.86%	2
TOTAL		70

Respondents commented on the changes to their home and family life due to AML:

- "We adapted to [redacted] fatigue with chairs placed in certain places around the home, grab bars, use of a cane, wheelchair as necessary. He often felt cold so warm blankets, fireplace, higher room temperature helped. The day's timetable was what worked at the time, depending on how he was feeling"
- "I can't go to get togethers, dinners, missed out on Christmas! Feel alone a lot"
- "No sports activity"
- "My father lived alone, so I was his primary caregiver during his cancer journey. Spare time and work hours were spent trying to get clear information, coordinate appointments, understand next steps and prognosis. My father would have never been able to navigate on his own"

Respondents were asked, what kind of impact has AML had on your social life? 59% reported a negative impact on social life. Responses are reflected in the chart below:

ANSWER CHOICES	RESPONSES	
Extremely Negative Impact	18.57%	13
Negative Impact	40.00%	28
Neutral	30.00%	21
Positive Impact	8.57%	6
Extremely Positive Impact	2.86%	2
TOTAL		70

Respondents gave examples of some of the changes they have had to make to their social activities due to AML:

- “Used to go to the gym, parties, friends. Not anymore”
- “Seeing less people due to physical changes”
- “Only focused on caregiving and work. No socializing, travel or fitness”
- “Hospital twice a week so no travel, home bound”

4. Experiences With Currently Available Treatments

ALL INFORMATION UNDER THIS SECTION HAS BEEN PREVIOUSLY SUBMITTED AND IS FROM “SURVEY #2”

This patient population is difficult to treat and currently have very few treatment options. Current treatments that are available cause various concerns for patients including toxicities and unstable blood counts, creating the need for blood product transfusions due to anemia, neutropenia, and thrombocytopenia. Often, dosages have to be decreased, or treatment has to be stopped completely because patients’ side effects are intolerable, or patients just do not respond to treatment. If available treatments fail the patient, and stem cell/bone marrow transplant is not an option, the only alternative is often best supportive care until death.

Respondents were asked, which types of AML treatment have you or your loved one received? (Select all that apply) 69 respondents answered this question.

46 (66.67%) – Chemotherapy
28 (40.58%) -- AZA+VEN (Azacitidine + Venetoclax)
2 (2.9%) -- Immunotherapy
1 (1.45%) – Radiation
11 (15.94%) – Other (“other” responses included: Azacitidine, ATRA/Mercaptopurine/Methotrexate, ATRA/Arsenic Trioxide, Sorafenib (Nexavar), Dictabene/Venetoclax, Onureg Oral tablets, Ivosidenib)

One respondent commented, “The cycles of azacitidine treatments are demanding. The treatment causes pain and severely limits activity. Low neutrophils are also limiting. Usually there is a week+ when things are better but then the next treatment cycle begins.”

Respondents were asked to identify the top 5 side effects of AML treatment that had the most effect on them. 69 respondents answered this question. The top answers were as follows:

Fatigue – 50/69 (72.46%)

Neutropenia – 39/69 (56.52%)

Thrombocytopenia – 37/69 (53.62%)

Anemia – 30/69 (43.48%)

Some respondents listed other serious side effects they experienced such as: Heart muscle damage, Cerebellar damage, Aneurysm exacerbated by blood infection

Over 50% of those living with AML found the side effects bothersome or severe.

Respondents were asked, overall, how would you rate the side effects of your AML treatments? 69 respondents answered this question. The top 2 answers were:

Bothersome -- 21/69 (30.43%) Severe -- 17/69 (24.64%)

The desire to live was a key driver to tolerating the side effects.

Several respondents forthrightly answered that their driver was the desire to live or the hope of survival. Respondents were asked why they, as the patient or caregiver, were willing to tolerate these side effects and continue with AML treatment? Others stated that they had no other choice, this was their only chance, and there were no other alternatives. Below are some more of their responses…

- "Promise of some remission, even if we knew it was not a cure"
- "Not ready to die yet. Still much to see and do with our lives"
- "I'm not that old, I would like to have more time with my family"
- "I thought it would work"
- "Can't give up"
- "Hopefully live until a cure is available"
- "My baby was 5 months old and I wanted to get home to him"
- "Only tolerated until death by suicide"

70% of patients felt that AML had a significant impact on their ability to continue with normal or future plans. Respondents were asked, what impact, if any, did AML treatment have on the patients' or caregivers' ability to continue with normal routines and future plans (example – work, travel, etc)? 70 respondents answered this question.

49/70 (70%) of respondents answered - Significant change
19/70 (27.14%) of respondents answered - Minor change
2/70 (2.86%) of respondents answered - No change

One respondent noted, "Not able to do many of the things I had planned for my retirement"

30/70 (42.86%) respondents stated that they experienced a loss of income due to AML treatment. Others mentioned throughout the survey that this was not an issue that applied to them as they were retired.

The ability to remain independent throughout treatment is important to patients' mental well-being. Patients want to be able to participate meaningfully in their lives and keep as much of a sense of normalcy as possible while managing treatment of their disease. Patients do not want to be a burden on their loved ones and see their independence as a signal that in spite of their disease they still have an acceptable quality of life.

Respondents were asked, did AML treatment have an impact your ability to care for yourself independently? 70 respondents answered this question.

29/70 (41.43%) -- Some negative impact

21/70 (30%) -- Significant negative impact

Many patients needed assistance with even the simplest day-to-day tasks from walking, to going to the washroom, to cooking, and completing household chores. Many other activities were limited or made impossible due to the patient's inability to function at a pre-treatment level.

- "My husband has gained increased independence, but it is limited. He needs support and consistent supervision"
- "Can't do car maintenance when your belly is inflamed by aza. Severely limits exercise. Severely limits travel and social activity"
- "At the beginning of my disease I was unable to do anything such as cook, eat, walk any distance, difficult to go up and down stairs. I was unable to work as I had major fatigue. My caregiver did everything for me"
- "I needed to be driven to day appointments daily. In the early days I could not look after myself - going to the washroom, not being able to walk without help"
- "I needed help with household chores, cooking, laundry etc."

Patients have various challenges accessing available treatments for AML. These treatments are often not available in community cancer centres and require that patients attend specialized centres. This often means that patients and caregivers have to travel a far distance which creates a significant barrier. A lack of locally accessible treatment options can have various impacts on patients' ability to access the care they need (including physical, mental and financial impacts). Patients are not feeling generally well and often require caregiver support to travel to these appointments, which may not always be an option for

all patients. If patients are unable to travel, often their only recourse is an admittance to hospital which comes with its own set of problems including mental impact, financial impact, impact on family and social life, and increased risk of infections. Many patients have to leave their home communities, uproot their entire lives and relocate permanently, solely so that they can access treatment for their disease.

Respondents were asked, If AML treatment were available within your home community, how would this impact the treatment experience? 66 respondents answered this question.

29/66 (43.94%) – Significant positive impact

24/66 (36.36%) – Some positive impact

Respondents expanded on potential impacts of treatment being available close to home:

- “Being close to home for the patient as well as family would ease the anxiety of not only the disease but being in a strange environment with nothing familiar. Also, if the patient would be able to stay home, in their own surroundings, much more reassuring and comfortable for them”
- “Instead of going to the hospital 11 times a month I would only have to go 3 times a month for blood work”
- “I was an in-patient for months and being home is the best!! I feel we heal quicker and are happier”

Many respondents relayed, in detail, the burden and stress of having to travel for treatment while already going through this difficult time and trying to manage their symptoms and feelings around their AML. Having to travel for treatment and being away from home, loved ones and a sense of familiarity and community contributes to the mental and physical burdens that patients and caregivers are already dealing with, and negatively affects various areas of their lives. Patients who live in rural communities are especially impacted.

- “Driving in rush hour traffic across town anywhere from daily to twice a week is a real drain, and will get worse when I can no longer drive, as will happen”
- “Victoria BC Cancer Clinic is unable to deal with AML patients. No choice but to go to Vancouver BC”
- “I received my chemo treatment 5 hours away from my hometown. The cost of being away from home was extreme and being away from my family was awful”
- “We live a distance from the hospital in which I spent a long time and my spouse had to travel back and forth for a year”
- “Our home is 8 hrs away from treatment. It has been a tremendous burden for us”

- “Due to the isolated community my dad lives in, he had to travel 6 hours each way to receive treatments. The travel cost alone was substantial and minimal assistance was available to cover these costs”
- “My husband had to receive treatment in a different city (4 hours travel each way, including a ferry). Financial stress was extreme. We are classed as low/mid income. They told me to liquidate all our belongings. Give up my home. If it wasn't for donations from our co-workers, I would have been sleeping in our car”

Several respondents described that they had to pick up their lives and relocate to be closer to treatment centres in order to access treatment for their disease

- “I was diagnosed in Iqaluit and had to move to Ottawa for treatment and lost my job and had to move permanently”
- “Travel distance from home. Had to relocate to the city for treatment”
- “Lived remote in Alberta, had to move to Ontario to have a caregiver so I could get blood regularly”

5. Improved Outcomes

When evaluating new treatment options for AML, patients and caregivers prioritize improved outcomes in long-term side effects, the risk of relapse, and how side effects may impact daily life. They also place great importance on quality of life, the severity and frequency of side effects, and, crucially, the duration and potential for sustained remission.

Respondents were asked, What concerns, if any, do you have about trying a new treatment for AML that aims to extend remission? Select all that apply. 184 respondents answered this question.

Unknown long-term effects or side effects – 125/184 (67.93%)
Fear of relapse or treatment failure -116/184 (63.04%)
Managing side effects and their impact on daily life – 116/184 (63.04%)
Concerns about the effectiveness of the new treatment – 111/184 (60.33%)
Potential impact on quality of life during treatment – 110/184 (59.78%)
Cost of treatment and potential financial burden – 100/184 (54.35%)
Need for frequent medical visits or monitoring – 65/184 (35.33%)
Uncertainty about the treatment process or protocol – 58/184 (31.52%)
Availability of support and resource is during treatment – 57/184 (30.98%)

Respondents were asked, Please choose the top three factors that are most important to you when considering new treatment options. 177 respondents answered this question. The top 3 answers were:

Quality of life during treatment – 132/177 (74.58%)
Number/severity of side effects – 107/177 (60.45%)
length of time and potential remission – 96/177 (54.24%)

Extended remission offers more time with loved ones, reduced stress, and the opportunity to travel, engage in hobbies, and return to work or school. Longer remission helps individuals pursue life goals, spend time with family, and maintain normalcy. Overall, the potential for longer remission brings hope for better quality of life, less anxiety about relapse, and greater participation in daily activities. Introducing treatments that provide longer remission periods can greatly improve the quality of life in all areas for patients and caregivers

Respondents were asked, What would a longer remission period mean for you and your quality of life? Please consider the following aspects: personal, professional, family, (Please elect all that apply). 187 Respondents answered this question.

More time with family and friends – 163/187 (87.17%)
Reduced stress and improved emotional well-being – 136/187 (72.73%)
Opportunity to travel or explore new experiences – 120/187 (64.17%)
More time for hobbies and personal interests – 117/187 (62.57%)
Ability to return to work or school – 70/187 (37.43%)

Some respondents commented:

- “A long remission period (20 years to date) has meant all of the above for me, so for anyone currently undergoing treatment this would definitely be the goal.”
- “My Mother would have liked more time with her husband, children and grandchildren.”
- “It would mean everything - if there was quality of life. If the side effects do not allow a person to have a life then it probably isn't worth it.”
- “More time for me to achieve some of my research goals.”
- “Longevity of life - when diagnosed I wanted to see my children go from adolescents to adults- now I want to see my grandchildren become adolescents”
- “Hopefully be in remission long enough to get a stem cell transplant”
- “Be here for my children as long as possible. Until they're at least adults”

Respondents were asked the open-ended question, Ideally, what desired improvements to quality of life would you like to see from new AML treatments? 148 respondents answered this question. Some common themes among their answers were:

- **Longer remission**
    - “Remission without the need for a BMT/SCT”
    - “Longer remissions in order to be able to spend more time with loved ones and friends.”

- “Long term remission is a huge factor.”

- **Reducing the fear/risk of disease recurrence**
  - “For me just being in remission and less anxiety about relapse improves my quality of life. Hope for new, better treatments increases my quality of life too. Ability to return to work as well (which I have).”
  - “Eliminate the fear and stress of relapsing.”

- **Cure**
  - “Complete remission and a cure once and for all, a final drug”
  - “Permanent cure”

- **Improved quality of life - Respondents value being able to resume regular daily activities and participate meaningfully in everyday life despite disease or treatment**
  - “Just being able to go about daily activities like playing with my kids and basic light housework.”
  - “Ability to have a life, not linked to medical appointments and side effects. Have a future.”
  - “To be healthy enough to return to work”
- **Limited side effects**
  - “Ability to live a normal life without pain”
  - “Not being nauseous/vomiting. No skin reactions, no infections, less vulnerable to other disease (flu, covid etc.)”
  - “Shortened side effects length, I will be off work for 2 years with a 1-year-old at home. It will cripple me financially.”

- **Outpatient treatment/Less time in hospital - the convenience of being treated as an outpatient, rather than requiring hospitalization, is valued for its impact on daily life**
  - “I am from Abbotsford so it would have been more convenient to have received the outpatient treatment program at the Abbotsford Hospital than at Vancouver General.”

- “Less time in hospital and after-care. Quicker recovery from treatment.”
- “Closer to home - no hospital stay”

- **Reduced need for transfusions**
  - “Less frequent blood transfusions”
  - “Less transfusions, hospital visits”

- **Access to care - better availability of care in smaller communities which reduces the need for travel is seen as a beneficial improvement. Being treated closer to home.**
  - “Improved access to family and friends for out of province patients.”
  - “Ability to maintain lifestyle away from Vancouver. Ability to receive treatment in other cancer centers around the province, such as Kelowna and Prince George.”
  - “Less time travelling back & forth to London.”

When choosing new therapies for AML, patients, caregivers, and families face difficult trade-offs between the potential benefits of longer remission and the risks or side effects of treatment. While many are willing to tolerate mild or moderate side effects for the chance at extended remission, fewer are open to severe or high-risk options. Ultimately, most prioritize longer remission, but there is a clear and delicate balance between treatment benefit and quality of life.

Respondents were asked, What risks or side effects would you be willing to tolerate for the chance of a longer remission? 185 respondents answered this question.

Mild side effects – 59/185 (31.89%)
Moderate side effects – 56/185 (30.27%)
Severe but manageable side effects -- 27/185 (14.59%)
Uncertain or unknown risks if the potential benefits are significant – 22/185 (11.89%)
High risk for longer term benefits (eg. risk of serious complications or new health issues) – 12/185 (6.49%)
Not willing to tolerate any additional risks or side effects – 9/185 (4.86%)

One respondent commented: “I would be willing to suffer short term in order to survive long term”

Remission is important to over 95% of respondents.

Respondents were asked, How important is it to you to achieve longer remission, even if the new treatment might come with increased risks or uncertainties? 185 respondents answered this question.

Very important – 98/186 (52.97%)

Somewhat important – 80/185 (43.24%)
Not important – 7/185 (3.78%)

6. Experience With Drug Under Review

As quizartinib is a relatively new drug and a targeted therapy, it hasn't been widely used in AML treatment, particularly among Canadians. However, 13 respondents reported having experience with quizartinib and shared their insights on this treatment.

Respondents were asked, Did you or the person you care(d) for receive treatment with quizartinib (Vanflyta) for AML? 218 respondents answered this question.

13/218 (5.96%) answered - Yes

The remainder of the information in this section was provided by respondents who indicated they had received treatment with quizartinib (Vanflyta). A total of 7 respondents answered this set of questions.

Respondents were asked, How did you get access to quizartinib (Vanflyta)?

4/7 (57.14%) – Clinical Trial
2/7 (28.57%) -- Compassionate use program (through pharmaceutical company)
1/7 (14.29%) answered “other” and stated – “Trillium”
0/7 – Paid for by Private Insurance
0/7 – Paid for out-of-pocket

Respondents were asked, Were there any out of pocket costs associated with quizartinib treatment?

6/7 (85.71%) – No

1/7 (14.29%) – Yes. *(This respondent commented: “Extra 100+ km travel to/from hospital. Fuel, meals for extra monitoring and biopsies.”)*

Overall, respondents found quizartinib (Vanflyta) to be a gentle treatment with limited, mild side effects.

Many reported that it was less difficult than other AML treatments, and most felt that quizartinib improved their quality of life compared to other therapies. All respondents indicated they would be willing to take quizartinib again if recommended by their doctor and would recommend it to others with AML.

Respondents were asked to rate the severity of the side effects of quizartinib treatment they experienced. Weighted average was used to measure their collective responses. According to their answers, the most severe side effects were:

Thrombocytopenia – 2.33/5
Anemia – 2.14/5

100% of the respondents found quizartinib to the same or less difficult compared to other treatments they have had for AML.

Respondents were asked, Overall, how does quizartinib compare to other treatments you have had for AML?

Same – 4/7 (57.14%)
Less difficult – 2/7 (28.57%)
Much less difficult – 1/7 (14.29%)
More difficult – 0/7
Much more difficult – 0/7

Over 80% felt that quizartinib improved their quality of life compared to other treatments.
Respondents were asked, If applicable, please rate how much you agree or disagree with the following statement: "quizartinib improved my quality of life compared to other treatments I have received."

4/7 (57.14%) -- Strongly agree
2/7 (28.57%) – Agree
1/7 (14.29%) – Neutral
0/7 – Disagree
0/7 – Strongly Disagree

One respondent commented: “I am convinced quiznartinib has prevented relapse. I am 6 years in remission.”

100% would choose quizartinib again if it was offered and would recommend it to others.
Based on your experience with quizartinib, would you take this again if your doctor recommended it for you?

7/7 (100%) answered Yes

Respondents were asked, Based on your experience with quizartinib, would you recommend it to others with AML?

7/7 (100%) answered Yes

7. Companion Diagnostic Test

8. Anything Else?

The financial burden of AML treatment, especially when it requires travel to specialized centers, can be overwhelming for patients and their families. Patients often face significant costs for housing, travel, and living expenses, particularly if they need to be close to a treatment facility for extended periods. Additionally, the inability to work due to the illness or treatment, combined with caregiving responsibilities, further strains financial resources. The financial stress of managing treatment, maintaining basic living expenses, and supporting loved ones can be a heavy burden, making it clear that the financial impact of AML can be as challenging as the disease itself.

“We were in shock about the unexpected financial burdens of this disease. If my son had been solely responsible for his treatment plan it would have overwhelmed him and his financial resources. His Dad and I were able to pay for a place to him to live (twice, as he relapsed) because he had to be within 15 minutes of Vancouver General Hospital, and we live 90 minutes away. My son also did not work for 2 years, and we supported him financially as his caregivers. His fiancé also was off work to care for him. The financial stress is real and overwhelming.”

Respondents’ answers and comments throughout our survey underscore the deep emotional, physical, and financial challenges faced by AML patients and their families. A common thread is the hope for longer remission periods without active disease, which would allow patients more time with their loved ones and a better quality of life. The impact of AML goes beyond the individual, affecting caregivers and families in profound ways. As we look to the future, it is essential that new treatments achieve prolonged remission with minimal side effects, offering patients and their families the time and peace they deserve.

“My husband was diagnosed was AML in June 2020 and died in Feb. 2021. He did 3 rounds of chemotherapy and had a stem-cell transplant. It failed after one month. We came back and the doc thought he’d have a few months to a year left. 13 days later, he died. When all was said and done, in 8.5 months he was gone. He was young (44) and in great shape. So I’d say more time with them would be the most important thing to see from new treatments.”

“Would like to have more energy. I would like to live to see my daughter get married. I just want to live.”

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Daiichi Sankyo		X		

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Colleen McMillan
Position: Advocacy Lead
Patient Group: The Leukemia & Lymphoma Society of Canada (LLSC)
Date: December 17, 2024

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0359
Generic Drug Name (Brand Name): quizartinib (Vanflyta)
Indication: In combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, and as continuation maintenance monotherapy following consolidation, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FMS-like tyrosine kinase 3 internal tandem duplication (FLT3-ITD) positive.
Name of Clinician Group: OH (CCO) Hematology Cancer Drug Advisory Committee
Author of Submission: Dr. Tom Kouroukis

1. About Your Clinician Group

OH(CCO)'s Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Information was gathered by videoconferencing.

3. Current Treatments and Treatment Goals

Current treatments include midostaurin with induction chemotherapy (i.e., 3+7), allogeneic stem cell transplant.

The treatment goals are to improve survival, attain remission.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

This can be an alternate option to midostaurin. Quizartinib has the additional benefit of being used as maintenance therapy.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

For first line therapy along with 3+7 induction and with consolidation and maintenance.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

For newly diagnosed AML with *FLT3*-ITD mutation.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Standard leukemia response measures. Post-induction bone marrow to confirm remission.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Significant intolerance or disease progression.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Induction phase is inpatient and consolidation phase may be as an outpatient.

Physicians with expertise in leukemia.

6. Additional Information

Patients who received midostaurin as part of induction or consolidation therapy should be eligible for quizartinib for maintenance on a time-limited basis.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   OH (CCO) provided a secretariat function to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Tom Kouroukis
Position: Lead, OH (CCO) Hematology Cancer DAC
Date: 20-06-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Selay Lam
Position: Member, OH (CCO) Hematology Cancer DAC
Date: 20-06-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Lee Mozessohn
Position: Member, OH (CCO) Hematology Cancer DAC
Date: 20-06-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Jordan Herst
Position: Member, OH (CCO) Hematology Cancer DAC
Date: 20-06-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 4: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Dr. Christopher Cipkar
Position: Member, OH (CCO) Hematology Cancer DAC
Date: 20-06-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				

Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0359-000
Generic Drug Name (Brand Name): Quizartinib (Vanflyta)
Indication: Newly-diagnosed *FLT3*-ITD-positive acute myeloid leukemia (AML)
Name of Clinician Groups:

- Canadian Leukemia Study Group (CLSG)/Groupe Canadien d'Étude Sur La Leucémie (GCEL), and
- Cell Therapy Transplant Canada (CTTC)

Author of Submission: Andre Schuh

1. About Your Clinician Groups

CLSG/GCEL

- CLSG/GCEL is a cross-Canada collective of acute leukemia treating physician representing all major leukemia centres in all provinces. The CLSG incorporation documents of 23.10.2019 define the purpose of CLSG/GCEL:
- 'To improve the diagnosis and treatment of leukemia in Canada, by identifying diagnostic and management best practices, promoting Canada-wide standards-of-care, fostering clinical and basic leukemia research, and improving new drug access.'
- The CLSG/GCEL website: https://www.clsg.ca/

CTTC

- CTTC is a member-led, Canada-wide, multidisciplinary professional organization providing leadership and promoting excellence in patient care, research and education, in the field of hematopoietic stem cell transplant and cell therapy.

2. Information Gathering

CLSG and CTTC board members are all leukemia physicians working in an academic, university-based treatment setting. The CLSG and CTTC memberships includes leukemia physicians from ALL of the major leukemia centres across Canada, including non-university-based cancer clinics and hospitals. Thus our members would be responsible for administering intensive induction chemotherapy to > 95% of patients undergoing such treatment in Canada. CLSG and CTTC opinions are evidence- and literature-based, and are buttressed by extensive collective experience. CLSG and CTTC opinions and positions are defined via ongoing group discussions and polling of members, with input requested from other international experts, as appropriate. Written opinions are reviewed, edited, and approved by the groups.

3. Current Treatments and Treatment Goals

Disease and Drug Background:

FMS-like tyrosine kinase 3 internal tandem duplication (*FLT3*-ITD) genetic abnormalities are found in ~30% of adult AMLs. The presence of a *FLT3*-ITD abnormality is associated with a higher white blood cell (WBC) count at presentation, higher post-remission disease relapse rates, and with inferior overall survival. Due to this 'higher risk' status conferred by the presence of a *FLT3*-ITD abnormality, specific treatment is required (see below) including the addition of a FLT3 inhibitor to intensive induction and consolidation chemotherapy, and allogeneic hematopoietic stem cell transplantation (alloSCT), if at all possible, once complete remission (CR) is obtained.

Prior to the publication of the RATIFY Trial in 2017 (Stone R *et al. N Engl J Med.* 2017; 377: 454-464), *FLT3*-ITD positive AML was treated as was traditional for all AMLs, with the '7 + 3' protocol (7 days of cytarabine plus 3 days of an anthracycline [usually daunorubicin or idarubicin]), but with inferior outcomes. The RATIFY Trial demonstrated that addition of the FLT3 inhibitor midostaurin (a 1st generation, Type I inhibitor) to 7 + 3 -based induction and consolidation chemotherapy, dramatically improved both event free survival (EFS) and overall survival (OS) in *FLT3*-ITD positive AML. The addition of midostaurin in this manner thus became a new standard of care for *FLT3*-ITD positive AML.

The EFS and OS benefit conferred by midostaurin was not sufficient, however, to prevent disease relapse, or the need for alloSCT. While every attempt was (and is) made to permit such patients proceed to alloSCT, this was/is not possible in all cases. Some patients were/are excluded from alloSCT for reasons of age or comorbid illness, and in some cases suitable donors could not/cannot be found. And notably, alloSCT while reducing the risk of relapse, does not eliminate relapse. Thus, *FLT3*-ITD positive patients may relapse prior to alloSCT, in the absence of an alloSCT (if excluded for one of the reasons above), or after alloSCT.

Therefore, there remains a great need for *FLT3*-ITD-specific maintenance therapy not just for patients excluded from alloSCT, but also for transplant-eligible patients both before and after alloSCT.

Consistent with this need, the RATIFY Trial (see above) actually included maintenance therapy, but the small numbers of patients that reached the maintenance phase of the study precluded statistically-meaningful analysis. As a result, midostaurin was not approved for maintenance therapy by the FDA or by Health Canada. It was approved for this indication, however by the EMA.

Midostaurin is a non-specific 1st generation multi-kinase inhibitor. It is likely that more potent and specific FLT3 1st and 2nd generation inhibitors will show greater efficacy at all stages of AML treatment - induction, consolidation, and maintenance. Consistent with this notion, a number of other FLT3 inhibitors have been proposed for AML therapy, including for maintenance:

1. Sorafenib (a 1st generation, Type 2 inhibitor) was in studied in this context in 2 studies (Burchert A *et al. , J Clin Oncol* 2020; 38:2993–3002, and Röllig C *et al. Lancet Oncol* 2015; 16:1691–1699).

- Despite the positive results of these clinical trials, sorafenib has not been approved in Canada for FLT3 maintenance.
- However, based on these studies, Sorafenib could temporarily be accessed in Canada via a compassionate access program. This program has been discontinued as of December 2023, so Sorafenib is no longer available.

2. Gilteritinib (a 2nd generation, Type 1 inhibitor) was studied in the post-alloSCT maintenance setting in two studies (Perl A *et al. N Engl J Med* 2019;381:1728-1740, and Levis M *et al. J Clin Oncol* 2024; 42:1766-1775.)
    - The former dealt with patients transplanted in CR2, and thus is beyond the scope of this discussion.
    - The latter dealt with patients in CR1, but did not reach its overall primary study end-point, although it was a positive study if only North American or MRD +ve patients were considered. Nevertheless, it is unlikely that Gilteritinib will become available in Canada for maintenance.

3. Quizartinib (a 2nd generation, Type 2 inhibitor), is the focus of the current application.

    The Quantum-First study of up-front Quizartinib in *FLT3*-ITD positive AML was published recently (Erba H *et al. Lancet* 2023; 401:1571-1583).

    This study included patients with *FLT3*-ITD positive AML aged 18-75 years (the RATIFY study [see above] included patients only up to age 59, and also included patients with *FLT3*-TKD mutations, which are recognized to confer LESS chemotherapy resistance than the *FLT3*-ITD mutation). The Quantum-First study showed that the addition of Quizartinib to standard induction/consolidation chemotherapy +/- alloSCT, followed by continuation monotherapy (maintenance) for up to 3 years, resulted in statistically-significant improved overall survival in adults aged 18-75 years with *FLT3*-ITD-positive newly diagnosed AML.

    While comparison between studies is problematic, these positive results have not been shown previously when analyzed in the more resistant *FLT3*-ITD-positive AML population. Furthermore, there has been no prior study evidence to date supporting the use of a FLT3 inhibitor for maintenance therapy in *FLT3*-ITD-positive AML in patients who have had a FLT-3 inhibitor with their prior chemotherapy.

    These data strongly indicate that the addition of Quizartinib to *FLT3*-ITD-positive AML treatment should define a new standard of care, to be used both up-front, and for maintenance. Of course, *FLT3*-TKD-mutated patients would continue to be eligible for up-front midostaurin, as these patients were excluded from the Quantum-First study. *FLT3*-TKD mutations occur in ~5% of AMLs.

<u>Do current treatments modify the underlying disease mechanism? Target symptoms?</u>

- conventional cytotoxic chemotherapy preferentially kills leukemia cells in a leukemia-specific, but largely leukemia-genetics-independent manner.
- in contrast, FLT3-inhibitors target one of the most common AML ‘driver’ mutations, thereby targeting/modifying the underlying disease mechanism

- while not targeting symptoms directly, control of the underlying disease will dramatically influence symptoms

What are the most important goals that an ideal treatment would address?

- the goal of AML treatment is generally curative; in much older patients, the goal would be more palliative.
- overall goals would be to prolong life, delay disease progression, reduce the severity of symptoms, minimize adverse effects, improve health-related quality of life, increase the ability to maintain employment, maintain independence, reduce burden on caregivers.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Despite improvements in care over the last two decades, AML treatment outcomes remain quite poor, and current treatment approaches remain extremely toxic. There remains a huge need to improve AML treatment outcomes overall. And the patient subgroup that is the focus of this application - *FLT3*-ITD positive patients - is emblematic of this unmet need. Despite advances in care, *FLT3*-ITD positive AML is still associated with high relapse rates and inferior overall survival. There is much room for improvement.

In particular to this patient subgroup…

- more FLT3-specific, 2nd generation inhibitors such as Quizartinib will be more efficacious than is midostaurin (and at all phases of treatment); this will reduce rates of relapse and will prolong survival.
- there is currently no FLT3 inhibitor approved for maintenance therapy. Such therapy is desperately required for patients awaiting alloSCT, patients not proceeding to alloSCT, and for transplanted patients post-alloSCT.
- taken together these two considerations are substantial from patient, caregiver, institution, and province/country points of view.

Limitations associated with current treatments:

- sub-optimal outcomes; a large treatment gap
- no drug available for a major part of the *FLT3*-ITD positive patient treatment trajectory (maintenance post complete remission) that is the major cause of failure and death in this population.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Quizartinib would be used in first line during induction and consolidation, as well as for post-consolidation maintenance therapy (both for chemotherapy-only, and for chemotherapy + alloSCT consolidations). For induction and consolidation, Quizartinib is likely superior to the currently approved drug, midostaurin

(comparisons between studies are problematic). In the post-consolidation setting (with or without alloSCT), there is a huge need for maintenance therapy, and at present, there is no available drug.

Quizartinib would be added to first line induction and consolidation chemotherapy as in the Quantum-First study (and as is the case currently for midostaurin). For maintenance, Quizartinib would be used as a single agent.

Quizartinib will target a key driver mutation underlying the behaviour of *FLT3*-ITD positive AML. But by controlling the underlying disease, Quizartinib will also provide symptom control.

Quizartinib would be used up-front for all *FLT3*-ITD positive patients. There would be no other treatments to try first.

The availability of a more efficacious FLT3 inhibitor during induction/consolidation in FLT3-ITD positive patients will define a new standard of care. The availability of a FLT3-inhibitor in maintenance for FLT3-ITD positive patients will define a new standard of care.

One minor issue is that midostaurin is approved for both *FLT3*-ITD and *FLT3*-TKD mutated patients, while Quizartinib is just for *FLT3*-ITD positive patients. This distinction is clear-cut, but will require physician education. *FLT3*-TKD mutations occur in ~5% of patients.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Quizartinib is restricted to *FLT3*-ITD positive patients. It is unlikely that other patients will respond to this treatment.

At present, all FLT3-ITD positive patients require an intervention, both up-front (induction and consolidation) and for maintenance.

Patients would be identified by up-front molecular testing that is performed routinely at leukemia centres across Canada. Patients would not be identified by clinician choice, but rather by specific lab testing.

There are no issues related to diagnosis. Up-front *FLT3* testing is routine in all leukemia centres. The notion of misdiagnosis does not apply here. It is not possible to identify which *FLT3*-ITD positive patients are most likely to respond. And in any case, all *FLT3*-ITD positive patients should receive drug.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

The outcomes metrics used in the Quantum-First study are identical to the outcomes measures we use in clinical practice.

A clinically meaningful response to therapy would be absence of disease relapse, and prolonged remission and overall survival. It is possible that MRD response could act as an outcomes surrogate, but at present, the appropriate *FLT3*-ITD MRD test is not available in Canada. The response should not vary across physicians.

In the absence of disease relapse, one would expect patient performance and QoL etc. to return to pre-disease baseline in most patients.

Depending on the phase of treatment, patients would be reassessed weekly, q2weekly, monthly, q2-3monthly.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

During induction and consolidation, drug should be continued as defined by the protocol unless there is disease relapse or intolerable toxicity. The latter was rare at this early timepoint in the Quantum-First study.

The duration of treatment in the maintenance setting is unclear. Longer Quantum-First study follow-up will help clarify this question. At present, and as defined in the Quantum-First study, at least 3 years of maintenance would be recommended, in the absence of disease relapse or intolerable toxicity.

5.5 What settings are appropriate for treatment with Quizartinib? Is a specialist required to diagnose, treat, and monitor patients who might receive Quizartinib?

Quizartinib treatment would be initiated and monitored (at least initially) at a leukemia centre, which is usually but not always a university-associated academic centre. With longer-term maintenance (particularly in the absence of alloSCT), patients could be followed incrementally at a closer-to-home shared care site.

Specialists involved would be mostly Hematologists, but also some Oncologists.

6. Additional Information

Despite AML treatment advances over the last decade, there remain huge gaps in treatment. While modern diagnostics have identified *FLT3*-ITD positive patients up front, treatment advances have not followed in step. *FLT3*-ITD positive patients are currently being treated up-front with midostaurin, but this approach remains quite inadequate. There is much room for up-front treatment improvement. Also, there is currently no drug available for maintenance in *FLT3*-ITD positive patients. Such therapy is desperately required for patients awaiting alloSCT, patients not proceeding to alloSCT, and for transplanted patients post-alloSCT. Quizartinib can meet this need.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   NO

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   NO

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

CADTH

Declaration for Clinician 1

Name: Andre Schuh
Position: Professor of Medicine, University of Toronto; and Hematologist, Princess Margaret Cancer Centre, Toronto
Chair, CLSG
Date: 16.12.24

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AbbVie		x		
Amgen		x		
Astellas	x			
AZD	x			
BMS	x			
GlycoMimetics	x			
Jazz	x			
J&J	x			
Kite/Gilead	x			
Loxo	x			
Novartis	x			
Paladin	x			
Pfizer	x			
Servier		x		
Syndax	x			
Teva	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Yasser Abou Mourad
Position: Associate Professor, Medicine, UBC; Hematologist, VGH, Vancouver; and Board Member, CLSG
Date: 16.12.24

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Pfizer		x		
Amgen		x		
Paladin	x			
Jazz		x		
Daiichi-Sankyo	x			
Kite	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Mary Lynn Savoie
Position: Clinical Associate Professor, University of Calgary, Division of Hematologic Malignancies Arthur EJ Child Comprehensive Cancer Centre; and Secretary, CLSG

Date: 16.12.24

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis			X	
BMS/Celgene	X			
Amgen			X	
Servier	X			
Jazz	X			

Declaration for Clinician 4

Name: Joseph Brandwein
Position: Staff Hematologist and Professor, University of Alberta, Edmonton, AB; and Board Member, CLSG
Date: 16.12.24

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Amgen	X			
Astellas	X			
BMS	X			
Pfizer	X			
Abbvie	X			
Daiichi Sankyo	X			
Servier	X			
Jazz	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: David Sanford
Position: Hematologist, Leukemia/Bone Marrow Transplant Program of BC; and Board Member, CLSG
Date: 16.12.24

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Table 3: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Astellas	X			
Abbvie	X			
Pfizer	X			
Bristol Myers Squibb	X			
Jazz	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 6

Name: Waleed Sabry
Position: Hematologist, Saskatoon Cancer Center. Professor Hemato-Oncology, University of Saskatchewan; and Board Member, CLSG
Date: 16.12.24

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Table 3: Conflict of Interest Declaration for Clinician 6

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Incyte	X			
GSK	X			
Novartis	X			
Janssen	X			
JAZZ		X		
Beigene		X		

* Place an X in the appropriate dollar range cells for each company.

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Declaration for Clinician 7

Name: Brian Leber
Position: Professor of Medicine (Hematology) , McMaster University; Hematologist, Juravinskl Hospital/Cancer Centre of Hamilton Health Sciences; and Treasurer, CLSG
Date: 16.12.24

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Table 3: Conflict of Interest Declaration for Clinician 7

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Pfizer		x		
Abbvie		x		
Novartis		x		
BMS/Celgene		x		
Servier		x		
AMGEN		x		
Jazz		x		
Astellas		x		
Astex	x			
Paladin	x			
Alexion/GSK		x		
Roche	x			
SOBI		x		
Janssen	x			
Otsuka	x			
Treadwell	x			
Takeda	x			
Taiho	x			

Declaration for Clinician 8

Name: Lalit Saini
Position: Physician, London Health Sciences; and Board Member, CLSG
Date: 16.12.24

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 8

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie	X			
Servier		X		
BMS	X			
AMGEN	X			
Novartis	X			
Daiichi	X			
GSK	X			
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 9

Name: Kristjan Paulson
Position: Hematologist, Associate Professor, University of Manitoba; and Board Member, CLSG
Date: 16.12.24

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Table 3: Conflict of Interest Declaration for Clinician 9

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Amgen	X			
Astellas	X			
Novartis	X			
Jazz	X			
Pfizer	X			
Sanofi	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 10

Name: John Storring
Position: Physician, McGill University Health Centre; and Board Member, CLSG
Date: 15-12-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 10

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbive				X
Amgen		X		
Astellas			X	
BMS/Celgene				X
Daiichi-Sankyo	X			
Jazz			X	
Janssen		X		
Novartis				X
Paladin			X	
Pfizer		X		
Taiho		X		
Teva		X		

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 11

Name: Imran Ahmad, MD
Position: Division Head, Hematology-Medical Oncology-Cellular Therapy, Hôpital Maisonneuve-Rosemont, Montreal; and Board Member, CTTC
Date: 17-12-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 11

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis		X		
Medexus Pharma	X			
AbbVie	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 12

Name: Kylie Lepic
Position: Medical Director, Cellular Therapy and Transplant Program, Hamilton Health Sciences; and President CTTG
Date: 18-12-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 12

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Sanofi	X			
Novartis	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 13

Name: Jonas Mattsson
Position: Medical Director, Messner Allogeneic Transplant Program, Princess Margaret Cancer Centre, University Health Network; and Director-at-Large, Research, CTTC
Date: 19-12-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 13

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Takeda Canada Inc.		X		
Jazz Pharmaceuticals Canada Inc.	X			
Medexus Pharmaceuticals Inc.	X			
TFF Pharmaceuticals Inc.	X			
Anocca AB	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 14

Name: Dennis Kim
Position: Head, Malignant Hematology Program, Princess Margaret Cancer Centre
Date: 19-12-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Daichi-Sankyo	X			
Astellas	X			

* Place an X in the appropriate dollar range cells for each company.