CADTH

CADTH COMMON DRUG REVIEW

Patient Input

LETERMOVIR (PREVYMIS)

(Merck Canada Inc.)

Indication: Text Indicated for the prophylaxis of cytomegalovirus (CMV) infection or disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).

CADTH received patient input for this review from:

Myeloma Canada and Lymphoma Canada

December 22, 2017

Patient Group	Myeloma Canada and Lymphoma Canada

1. About Your Patient Group

www.Myeloma.ca

www.lymphoma.ca

2. Information Gathering

The data presented in this patient submission reflects the collaboration between two patient groups; Lymphoma Canada and Myeloma Canada. The survey was developed to address common experiences with respect to an allogeneic stem cell transplant undergone by patients with blood, plasma cell and lymphoid cancers, alike. This survey was sent to Myeloma Canada and Lymphoma Canada patient memberships; it was also promoted via social media channels by the Leukemia & Lymphoma Society of Canada and BMT InfoNet. Individuals had the opportunity to respond to the survey between December 13th and December 18th 2017.

The survey was designed to understand the impact of an allogeneic stem cell transplant and its effect on the patient's quality of life and on the theoretical impact of preventing complications from this treatment on patients. The survey included specific questions directed to patients who have had this procedure as well as questions about complications associated with a stem cell transplant. No questions regarding the impact of Prevymis™ (letermovir), an anti-viral medication that is given post-transplant to prevent infection from a virus called cytomegalovirus (CMV), were included in the survey as both organizations had no ability to identify patients who had received this medication through a clinical trial. Moreover, the real benefit of this medication for patients is in preventing a CMV infection, hence patients would be hard pressed to provide feedback on something that may not have occurred based on taking this medication. The clinical benefits and side effect profile of letermovir are best described by the manufacturer and CADTH, through the CDR, is best equipped to evaluate the clinical benefit of letermovir in preventing a medical complication. We focused on what it was like for patients to live with the consequences of an allogenic stem cell transplant and what it would be like to minimize the complications and side effects associated with this treatment. We believe our approach highlight to CADTH the impact of this procedure for patients and how a medication designed to prevent an infection can reduce the burden of a stem cell transplant for a patient.

A total of 135 responded to the patient survey. Among these respondents, a total of 103 were eligible to be included in this survey as they had experienced an allogeneic stem cell transplant. Of these, 69 were from Canada (representing mostly Ontario and British Columbia), 25 were from the US and the reminder from Europe and Australia.

Note: In all open-ended questions, the responses have been grouped into categories and the percentage of responses for each category given. In all cases, the total is greater than 100% because some of the responses fell into more than one category.

The majority of respondents were older than 50 years of age: 32% were between 61-70 years of age and 32% were between 50 – 61 years of age. A few (10%) were between 19 and 40 years old. A little over half (51.5%) were female and 48.5% were male.

3. Disease Experience

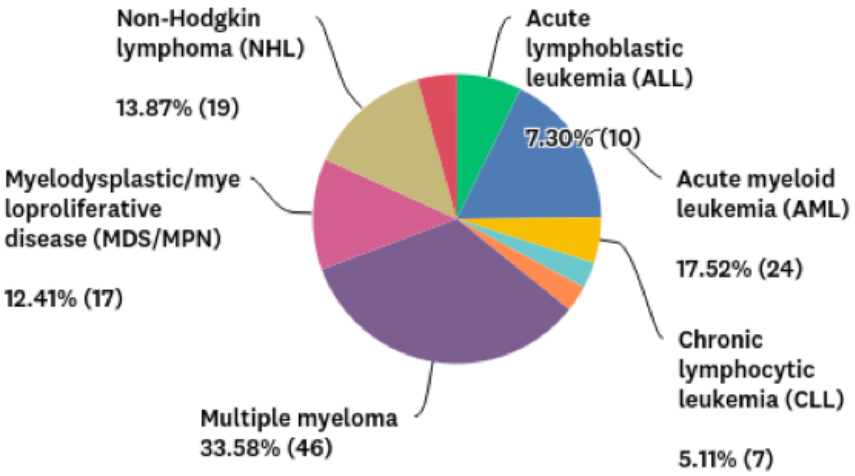
Autologous transplant in patients under 65 is the standard of care for patients with newly-diagnosed myeloma; however allogeneic transplant can be an option. Few patients are good candidates for an allogeneic transplant because it is difficult to find good donor matches (even with siblings) and the procedure has a greater risk of complications such as infections, graft-versus-host disease (GvHD) and death.

Those with lymphoma and chronic or acute leukemias typically receive one or more lines of chemotherapy and/or targeted therapy after diagnosis. If these treatments fail, patients may then be considered for an autologous or allogeneic stem cell transplant, depending on the nature of their disease and eligibility. Those who relapse after an autologous transplant may subsequently receive an allogeneic transplant.

In this survey, patients were asked what type of cancer they had been diagnosed with. Approximately 30% were diagnosed with a type of leukemia, 33% with myeloma, 14% with lymphoma and the rest with MDS or MPN.

What was your initial diagnosis?

Answered: 137 Skipped: -1

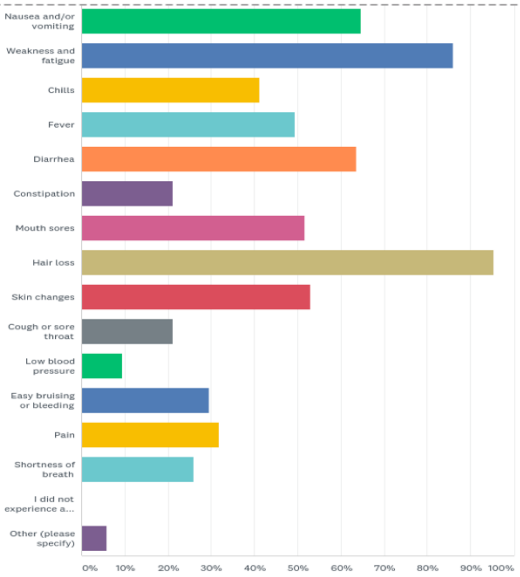


Of the 135 respondents who answered the survey, 82 had one allogeneic stem cell transplant (ASCT) and 3 had a double ASCT. The rest of this report analyses the responses of these patients only, unless otherwise specified. Only 9 of these patients had their ASCT more than 10 years ago. 47% stayed in the hospital for less than one month, post-transplant, while 48% stayed 1-3 months. Four remained hospitalized for 3-9 months.

The conditioning phase of the ASCT, and the transplant itself did result in significant symptoms and/or side effects for patients. Fatigue, weakness, hair loss and diarrhea where the most common.

Did you experience any of the following side effects from your conditioning treatments (high-dose chemotherapy and/or total body radiation received before transplant) or your transplant? (Select all that apply)

Answered: 85 Skipped: 0

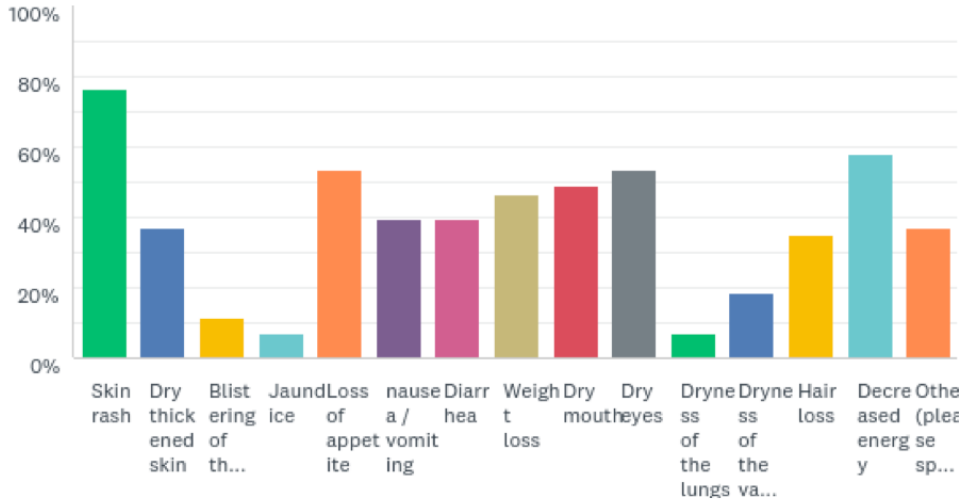


When asked which side effects they found the most difficult to tolerate, 62 patients responded and found the most difficult to tolerate were: mouth sores / dryness 23%, nausea 16%, fatigue 16%, and pain 11%.

55% (47) of patients experienced graft-versus-host disease (GVHD) after their transplant. The symptoms of GVHD patients experienced are listed below (only 43 patients answered).

Which symptoms of GVHD did you experience?

Answered: 43 Skipped: 42



Because of GVHD, 63% patients required additional visits to the transplant centre to monitor and/or treat the GVHD. 14 (32.5%) were readmitted to the transplant unit after going home, 13% had to stay longer in the hospital, 30% had to visit the Emergency Department and 23% had no other visit requirement.

4. Experiences with Currently Available Treatments

When patients were asked to describe the impact of GVHD on your quality of life and your ability to participate in your normal daily activities one can conclude that GVHD has a significant impact on the patient's quality of life and this experience has a profound impact on them. Use of medication to control GVHD generated significant side effects, like bloating, immune system weakness, extreme fatigue and inability to return to work.

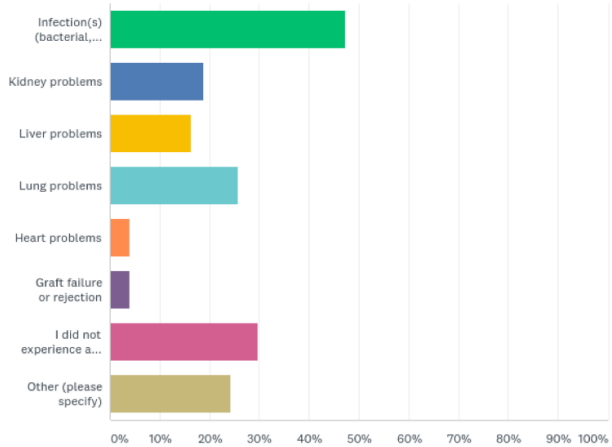
Comments included:

- "I was unable to return to work until 2 years after my transplant due to GVHD. I had severe fatigue for those 2 years which made daily activities difficult to manage."
- "GVHD caused a lot of problems for me but after about a year most of the bad symptoms were gone"
- "Throughout my acute GVHD I was in the hospital or on daily visits so they were able to manage it with pain meds and other drugs. While suffering acute I was not able to participate in daily activities by myself. The only Chronic symptoms that I have are with my eyes. They get red/itchy very easily and hinder me from reading, studying, and using the computer for extending bouts of time."
- "Unable to live a normal life, I'm just surviving at this point."
- "No more normal. New normal was slow, painful and frustrating."
- "Generally controlled as long as avoid trigger irritants - eg perfumed soaps"
- "Well it ended my work career, but I have learned to live with what I now am. They put a monster inside you as a cure, and it takes a bit to learn how to coexist. But on the bright side, you are a chimera! How cool is that!"

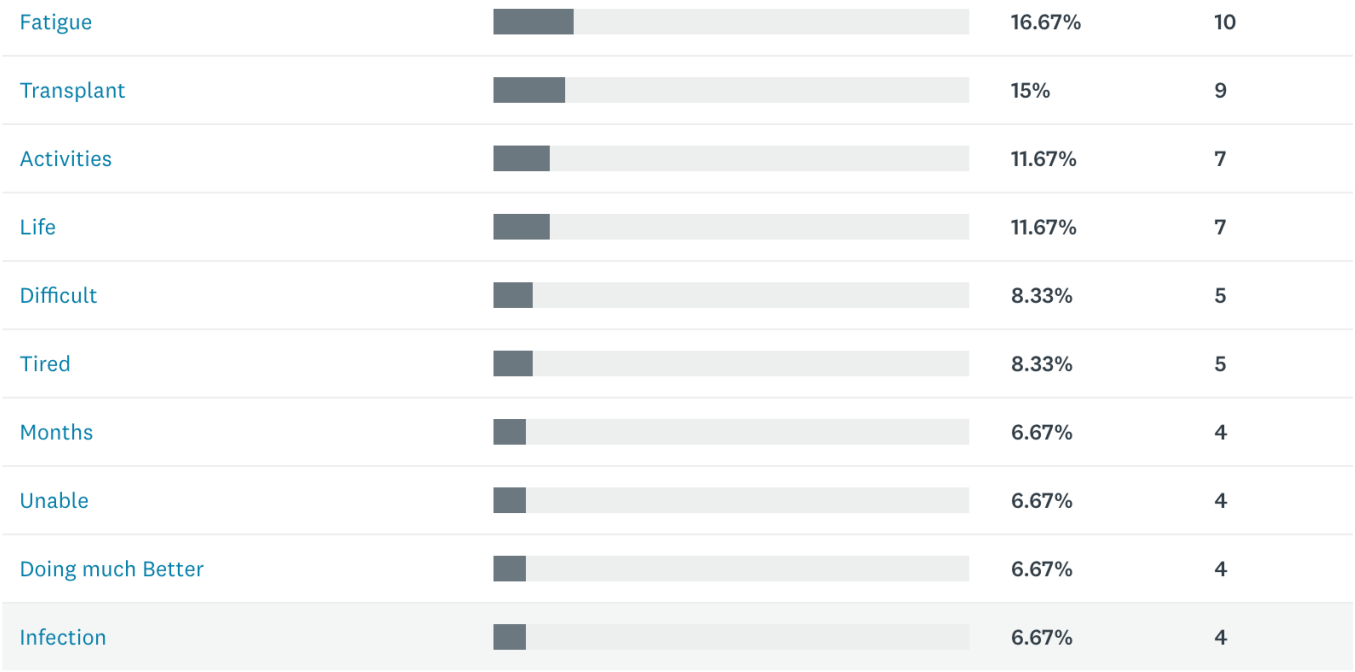
Patients experienced a number of complications after their transplant. Of most significance, 35/74 (47%) patients experienced infections (bacterial, viral or fungal). Other complications included lung, kidney and liver problems more often.

Did you experience any of the following complications after transplant?

Answered: 74 Skipped: 11



To deal with these complications patients used antibiotics (76% of patients), antivirals (77% of patients), antifungals (70% of patients), corticosteroids (62% of patients) and blood transfusions (49% of patients). When asked to described the impact of transplant complications on their quality of life and the ability to participate in normal daily activities, patients shared over 60 comments and descriptions. Of most importance are:



Fatigue	16.67%	10
Transplant	15%	9
Activities	11.67%	7
Life	11.67%	7
Difficult	8.33%	5
Tired	8.33%	5
Months	6.67%	4
Unable	6.67%	4
Doing much Better	6.67%	4
Infection	6.67%	4

An important consideration for patients is the need to leave their community for their transplant; this was the case for 42% of patients. The major reason is that a transplant facility is not available in their community. This lack of access represents an added negative impact on patients and their loved ones tasked with looking after them. Of these patients, 14 had to be away from home over 3-6 months, 3 for 6-9 months and others for a shorter period of time (4 up to one month, 10 for 1-3 months).

Patients were asked to rate the impact of various aspects of their transplant and follow-up care:

As it relates to your transplant and follow-up care, please rate the following:

Answered: 63 Skipped: 22

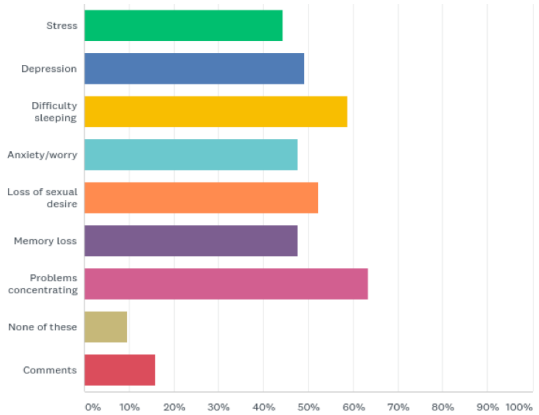
	LITTLE IMPACT ON MY LIFE 1	2	3	4	SIGNIFICANT IMPACT ON MY LIFE 5	N/A	TOTAL	WEIGHTED AVERAGE
Number of clinic visits	7.94% 5	11.11% 7	15.87% 10	12.70% 8	52.38% 33	0.00% 0	63	3.90
Length of stay in the transplant centre	6.35% 4	7.94% 5	12.70% 8	12.70% 8	58.73% 37	1.59% 1	63	4.11
Treatment toleration	7.94% 5	9.52% 6	31.75% 20	14.29% 9	36.51% 23	0.00% 0	63	3.62
Post-transplant medication schedule	4.76% 3	15.87% 10	20.63% 13	25.40% 16	28.57% 18	4.76% 3	63	3.60
Post-transplant medication side effects	9.52% 6	14.29% 9	19.05% 12	25.40% 16	25.40% 16	6.35% 4	63	3.46
Number or frequency of infections	30.16% 19	20.63% 13	19.05% 12	7.94% 5	17.46% 11	4.76% 3	63	2.60
Graft-versus-host disease (GVHD)	20.63% 13	12.70% 8	11.11% 7	15.87% 10	22.22% 14	17.46% 11	63	3.08
Fatigue	4.76% 3	11.11% 7	15.87% 10	23.81% 15	44.44% 28	0.00% 0	63	3.92

5. Improved Outcomes

Having to undergo an ASCT has a significant impact on patients' lives; problems concentrating, stress, difficulty sleeping, depression, and lack of sexual desire were sited amongst the most common psychological or emotional effects.

Please indicate if any of the following affected your quality of life after your transplant? Check all that apply.

Answered: 63 Skipped: 22

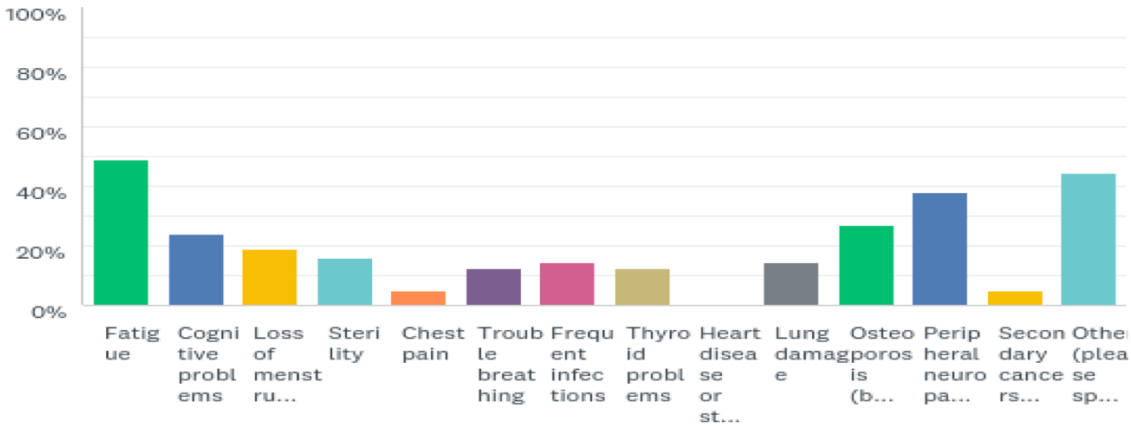


Patients were asked to explain how their transplant(s) has impacted their day-to-day life and quality of life? (For example, if it affected their ability to manage their family obligations? Work? Exercise? Volunteer? Etc.). This question generated 52 comments from patients and the responses were quite revealing as they shared the impact on many aspects of life that most healthy individuals take for granted. The best way to summarize these comments is best described by the following word cloud:

Patients were asked if they had experienced any of the following late or long-term treatment side effects (side effects that lasted longer than 2 years, or appeared two years or later after the end of treatment). Answers demonstrate that ASCT does have a lingering impact on the quality of life of patients.

Have you experienced any of the following late or long-term treatment side effects? (side effects that lasted longer than 2 years, or appeared two years or later after the end of treatment) Please check all that apply.

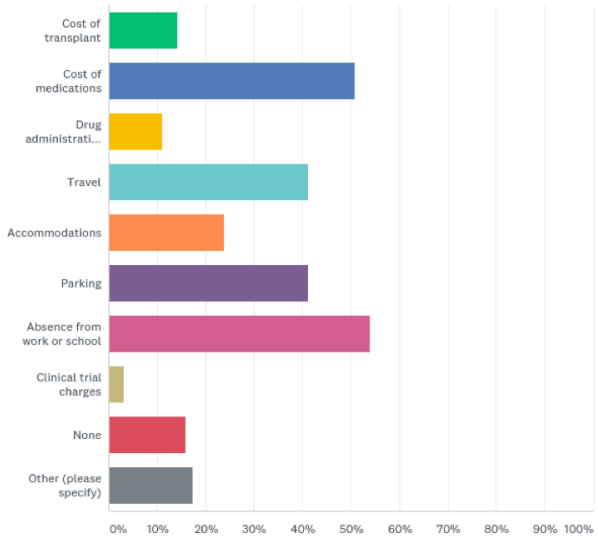
Answered: 63 Skipped: 22



Patients also experienced financial impacts as a consequence of their transplant. The following chart describes these in more detail:

What are the financial implications of transplant for you? Check all that apply.

Answered: 63 Skipped: 22



6. Experience with Drug Under Review

As mentioned earlier, we did not seek input from patients with experience with letermovir as this was not an option for the patient groups.

7. Anything Else?

This survey demonstrates that patients experience significant complications and negative consequences of a ASCT. Therefore, the ability to limit or to remove these issues—like reducing the risk of an infection—represent a significant benefit to the patient's quality of life and can likely reduce the stress associated with managing the complications of the transplant. Given the overall clinical significance on disease free survival and overall survival rates on lymphoma, leukemia and myeloma patient outcomes, the benefits of ASCT outweigh the possible negative complications. However, patients experience significant changes in their quality of life, hence any treatment that can minimize this impact represents a positive outcome.

Appendix 1: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, 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.
   - Myeloma Canada: NO
   - Lymphoma Canada: 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.
   - Collaboration between Myeloma Canada and Lymphoma Canada.

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.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Janssen – Myeloma Canada and Lymphoma Canada				X
Amgen – Myeloma Canada				X
Takeda – Myeloma Canada				X
Celgene – Myeloma Canada				X
Merck – Myeloma Canada and Lymphoma Canada			X	
Lundbeck – Lymphoma Canada				X
Abbvie – Lymphoma Canada				X
AstraZeneca – Lymphoma Canada			X	
Seattle Genetics – Lymphoma 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: Martine Elias
Position: Director Access, Advocacy and Community Relations
Patient Group: Myeloma Canada
Date: Dec 19 2017

Name: Robin Markowitz
Position: CEO
Patient Group: Lymphoma Canada
Date: Dec 19 2017