Biosimilars Report

LYMPHOMA CANADA

Survey Results of Canadian Patients and Prescribers on Knowledge and Use of Biosimilars in Lymphoma and CLL

Oncology biosimilars have just begun to enter the Canadian market for breast and colorectal cancers, and hematological and other cancers, and will be widely available in the near future. Between 2019-2020, Lymphoma Canada conducted surveys to assess the current level of knowledge, understanding and comfort of use of biosimilars among lymphoma patients and Canadian prescribers specialized in hematology and oncology. The surveys assessed information regarding responders' use and basic knowledge of biosimilars, understanding of biosimilar development and level of comfort with extrapolation, interchangeability and switching. A 19-question and 17-question survey were developed and administered to patients and hematologists and oncologists respectively. Data collection occurred between June and December 2019 and included online and paper responses.

Patient Results

SUMMARY OF RESULTS

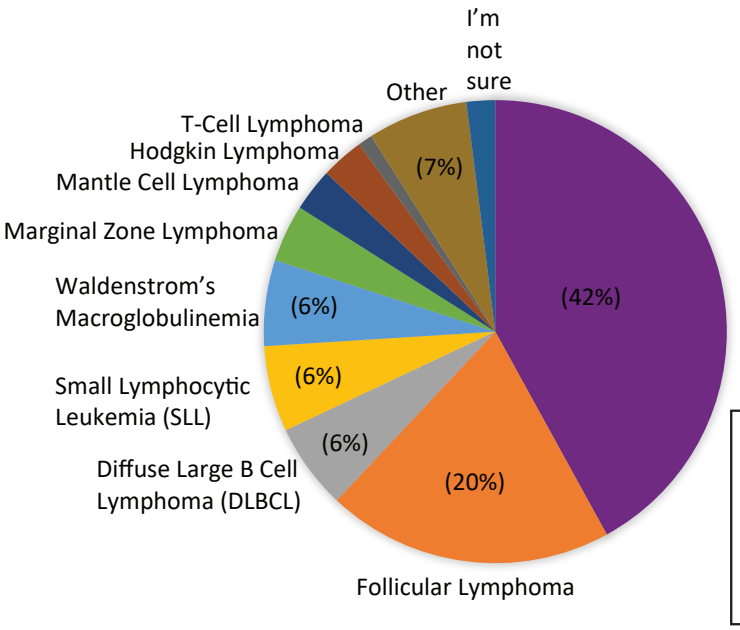
Overall, 436 Canadian patients who had been diagnosed with lymphoma or CLL responded to the patient survey. With more than half of respondents treated or currently being treated with Rituximab (Rituxan), a type of immunotherapy (antibody therapy) treatment for lymphoma patients, the majority of respondents were not knowledgeable about biosimilars, including a number of Rituximab biosimilars currently approved by Health Canada. Of those who were familiar with biosimilars, most had learned about them from a general website or a patient organization. For patients who had some understanding of biosimilars they were either not comfortable with them or had additional concerns. There was concern among the majority of respondents about the safety, efficacy and tolerability of biosimilars, and most wanted to have all information about a rituximab biosimilar before it was prescribed. Further, many respondents were confident that their clinician would provide them with the treatment option best suited for their lymphoma. In such cases, patients would fully accept the biosimilar treatment or switch to a biosimilar from the reference biologic if recommended by their physician.

Patient Demographics

436 Patients

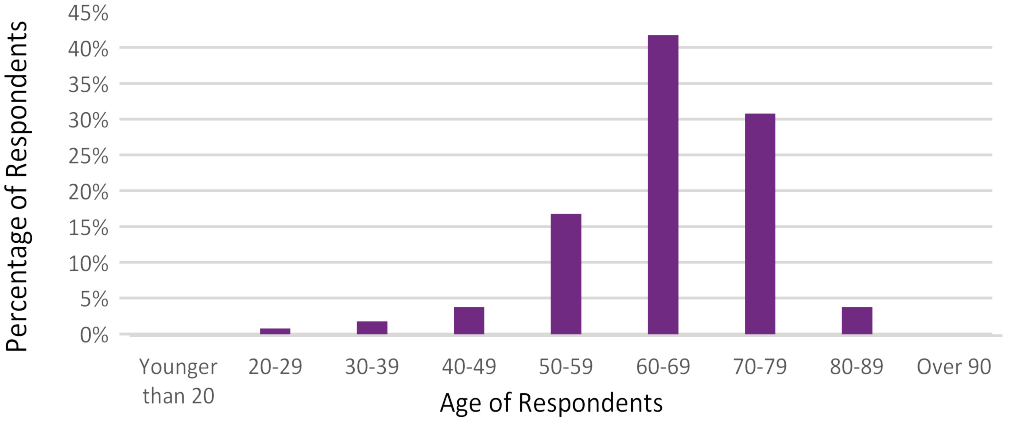
43% Male	57% Female

Survey respondents by Lymphoma Subtype



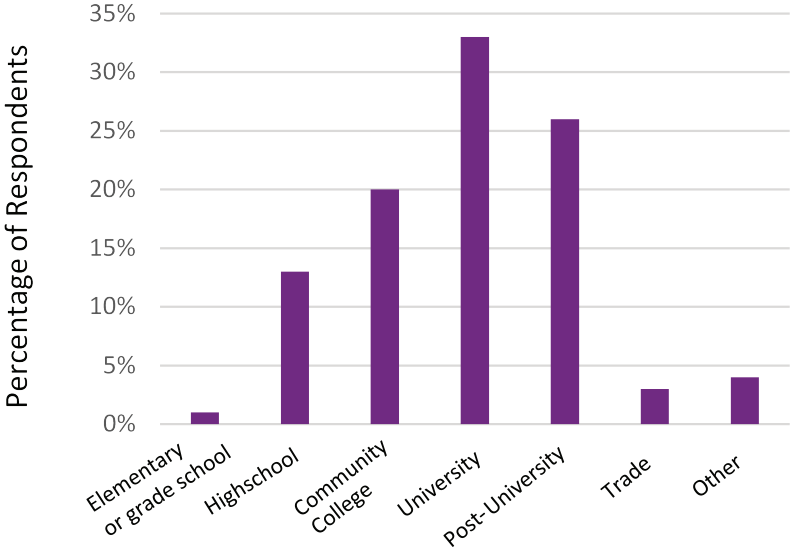
The top respondents were from the CLL (42%) & Follicular Lymphoma (20%) patient population.

Survey respondents by Age Range

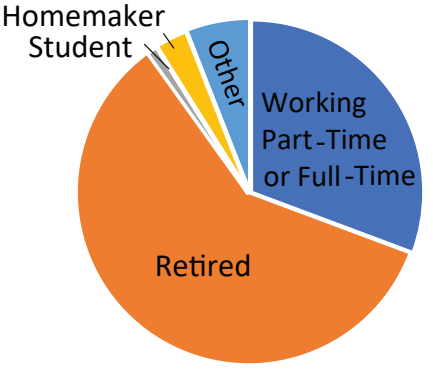


The majority of respondents were between the ages of 50-79 years.

Survey respondents by Education Level



Survey respondents by Work Status



The majority of respondents had an education level above and beyond that of high school, and the majority of patients (60%) are currently retired.

Summary of Major Findings

1 Treatment Experience with Rituximab

Respondents were asked what treatment phase they were in at the time of the survey. More than one-quarter (28%) were in the 'watch & wait' phase and had not received any treatment for their lymphoma or CLL. More than half (51%) were in remission following one or more lines of therapy and 20% were in treatment for the first time or after one or more relapses. More than half of respondents (60%) were being treated, or had been treated in the past, with rituximab.

2 Knowledge of Biosimilars

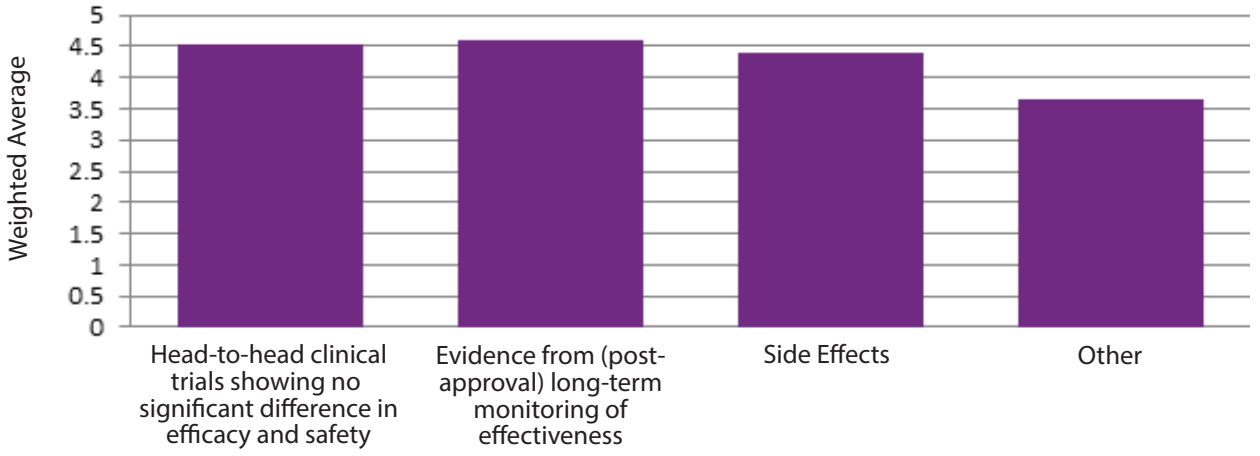
When patients were asked how familiar they were with biosimilars, 75% responded "not at all familiar", while 22% were "somewhat familiar" and 3% were "very familiar". For those who were somewhat or very familiar with biosimilars, they reported obtaining information about biosimilars from multiple sources, most often seeking information online or through a patient organization:

Source of Information about biosimilars	Respondents (%)
Healthcare provider	10%
Patient organization	24%
Government or not-for-profit organization	5%
Pharmaceutical industry	6%
General website	36%
Other	19%

Respondents were also asked whether they were aware of any rituximab biosimilars that could be used to treat lymphoma or CLL. Most (61%) were not aware that rituximab biosimilars existed.

Respondents were asked that if a biosimilar is considered to be effective and safe by Health Canada, how important certain factors would be in their decision to start treament with a biosimilar rather than the reference biologic drug. Patients rated these factors on a scale from 1 (not at all important) to 5 (very important). Head-to-head clinical trials and evidence from long-term monitoring of effectiveness were rated most important by respondents.

Survey respondents Rate the Importance of Factors
Affecting their Decision to Start Treatment with a Biosimilar



3 Perceptions About Being Treated with a Rituximab Biosimilar

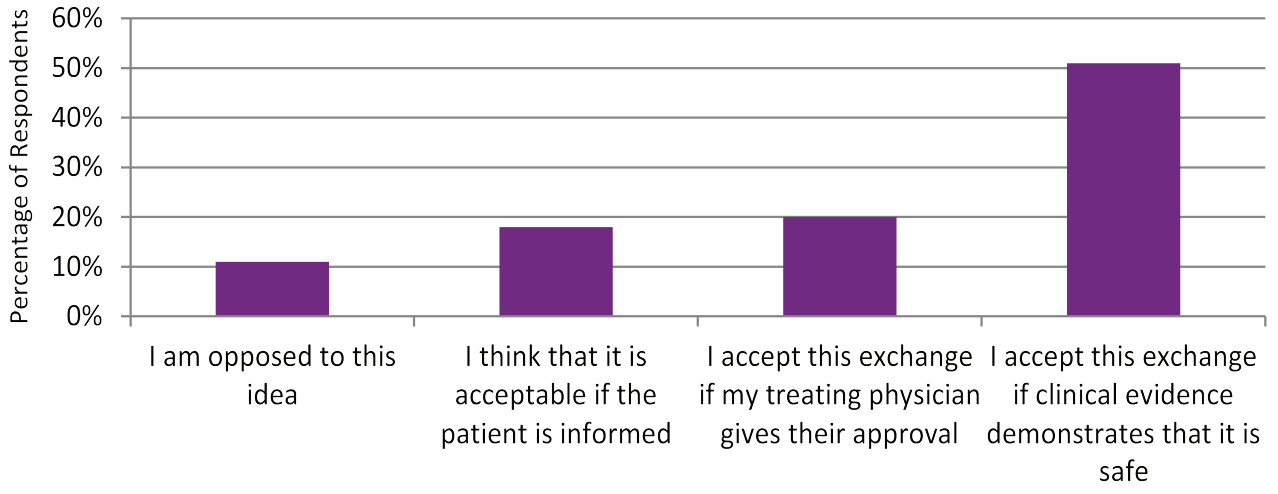
Patients were asked if they had any concerns about being prescribed a rituximab biosimilar. Overall, most respondents did have concerns about the efficacy, safety and tolerability of a rituximab biosimilar.

Concern regarding biosimilar use	Respondents (%)
That the molecular basis of the biosimilar is different from that of the reference drug (the original drug)	30%
The safety of the biosimilar	60%
The tolerability of the biosimilar	61%
That the biosimilar could be less effective than the reference drug	70%
You have no specific concerns about biosimilars	6%

When asked how much information they would like to receive about a rituximab biosimilar before being prescribed one to treat their lymphoma or CLL, most respondents (62%) wished to receive all the necessary information available.

Information needs before receiving treatment with a rituximab biosimilar	Respondents (%)
You don't need to know which drug you are receiving as long as the biosimilar has the same efficacy and safety profile as the reference drug	1%
You would like to be informed about it, but you trust the pharmacist or your treating physician if they prescribe/deliver it	20%
You wish to know if you receive the biosimilar or the reference drug	17%
You wish to have all the necessary information before the drug is administered and obtain written information to be used for future care	62%

When asked about a patient's opinion in switching from their reference biologic drug to its biosimilar (also known as interchangeability) most respondents accepted that biosimilars could be interchangeable with the reference drug if there is clinical evidence showing that it is safe:



When patients were asked about their confidence in being switched from a rituximab biologic to its biosimilar during the course of their treatment with their clinician's guidance, most respondents (59%) would accept the switch:

Respondents' confidence about switching from the rituximab reference drug to a biosimilar	Respondents (%)
I would be fully confident	26%
I would be worried but would accept the switch	33%
I would probably not accept the switch	10%
I would ask for a second opinion	21%
I don't know	10%

Respondents were asked how confident they would be taking a rituximab biosimilar if their physician prescribed it. Most respondents would be fully confident or would accept the biosimilar therapy, even if they were worried about the treatment:

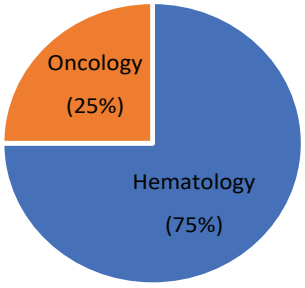
Respondents' confidence about receiving treatment with a rituximab biosimilar	Respondents (%)
I would be fully confident	36%
I would be worried but would accept the treatment	27%
I would probably not accept it	5%
I would ask for a second opinion	21%
I don't know	11%

Hematologist/Oncologist Results

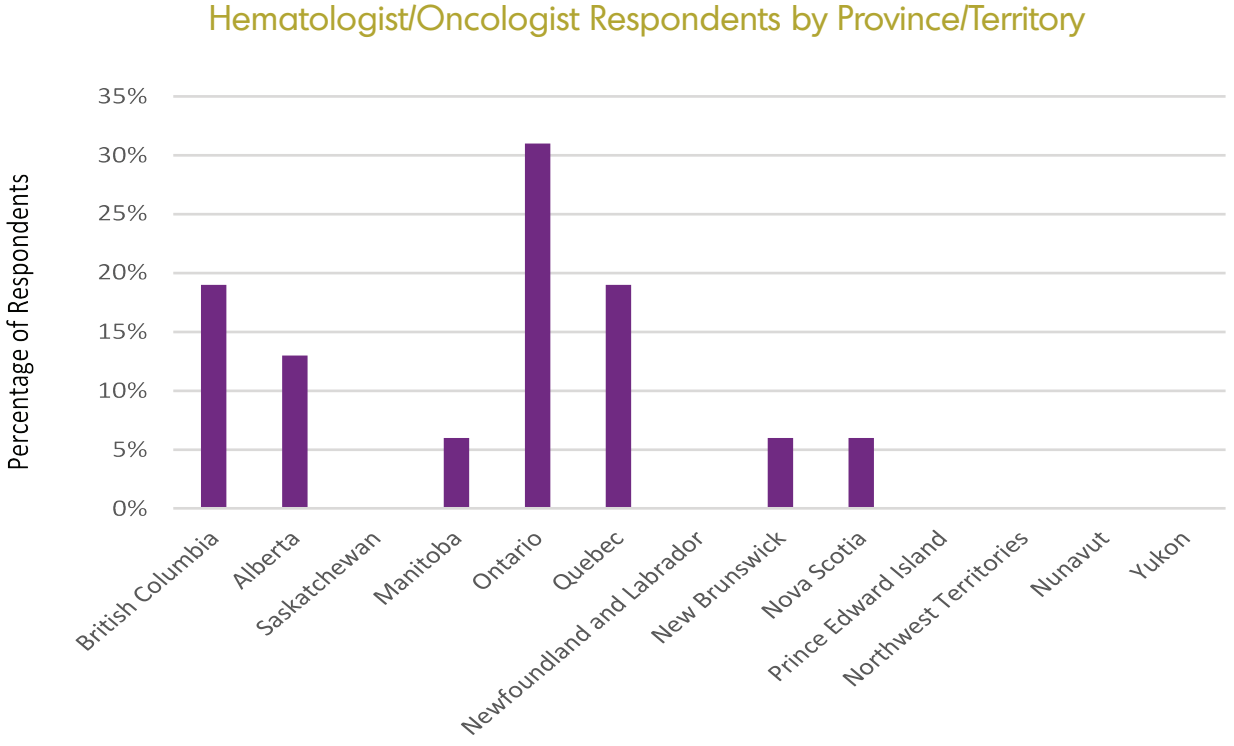
SUMMARY OF RESULTS

Overall, 16 hematologists and oncologists responded to the physician survey. Low levels of prescriber use, but high levels of general knowledge among prescribers were found. Most prescribers had not prescribed treatment with a biosimilar because the biosimilar(s) were not yet approved for use or reimbursed within their jurisdiction. Most respondents rated their general knowledge of biosimilars as average to high. Some gaps in knowledge included biosimilar development, clinical trial design and endpoint selection, and requirements for extrapolation. However, the majority of respondents had in-depth knowledge on biosimilars and their interchangeability with the reference biologic, and did not anticipate switching to cause significant effects to patients.

Prescriber Demographics



All respondents identified themselves as hematology or oncology prescribers. The majority of respondents specialized in hematology (75%) and the remainder were in an oncology specialty.



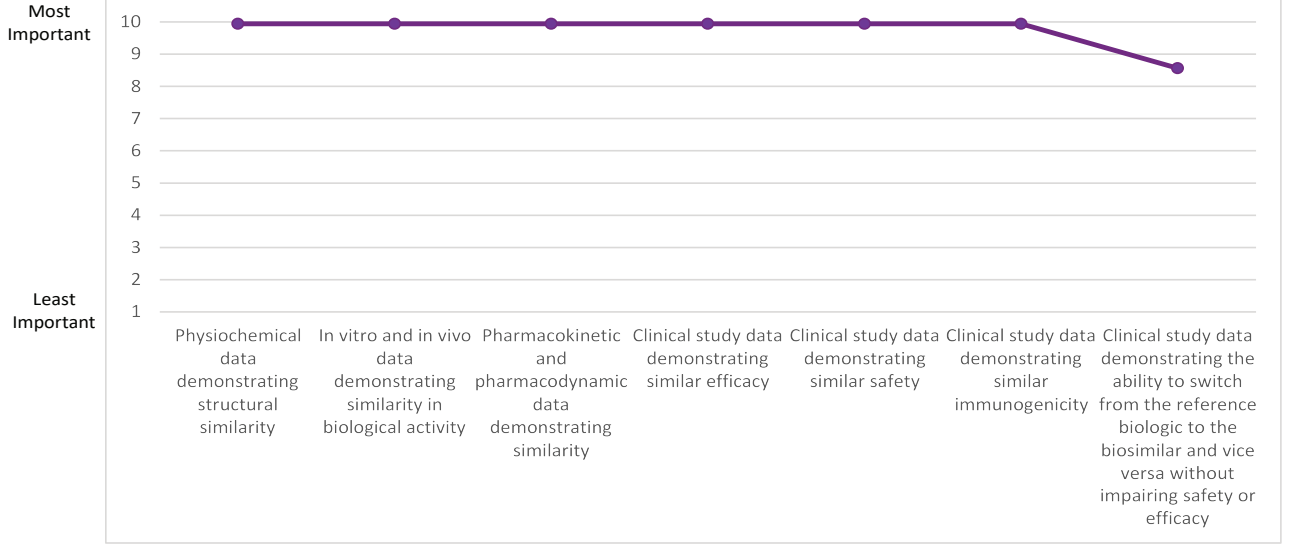
1 Knowledge of Biosimilars

When asked to rate their overall knowledge of biosimilars, the most commonly selected option on a scale of 1 (very low knowledge) to 5 (very high knowledge) was option 3 (56%). Options 3, 4, and 5 were selected by 100% of prescribers, indicating that all respondents consider themselves to have an average to very high level of knowledge on biosimilars. In total, 100% of prescribers were also able to identify the most accurate definition of a 'biosimilar' which is "highly similar to an approved biological medicine, with no clinically meaningful differences in safety and efficacy profile". Overall, none of the respondents use biosimilars in routine practice, with 75% indicating this was because biosimilars were not approved or reimbursed yet within their jurisdiction.

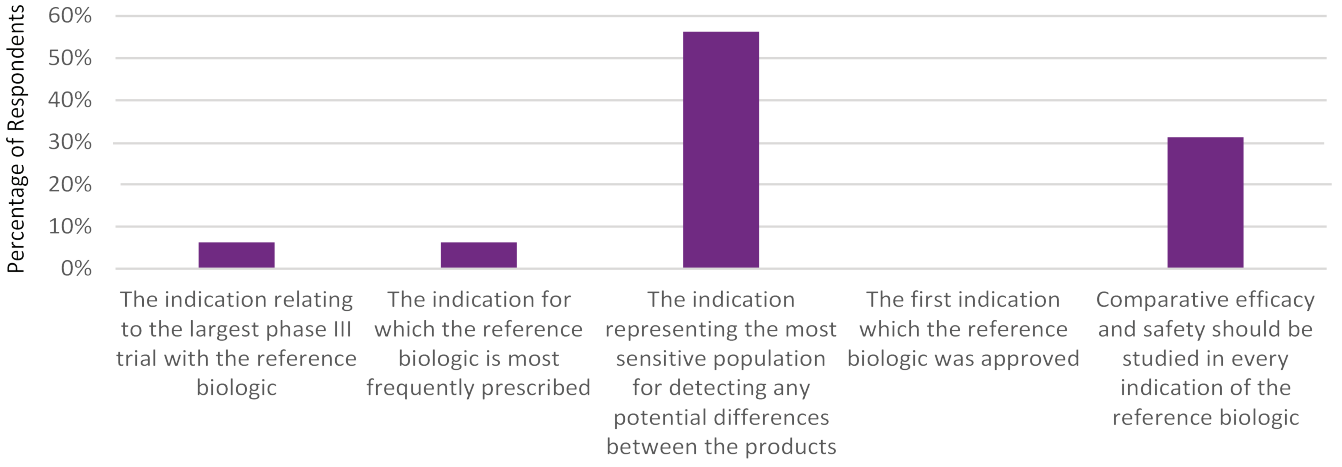
On a scale assessing comfort level in using a Health Canada approved biosimilar to treat a patient that is suitable to receive the reference biologic, prescribers rated their level of comfort from 1 (not at all comfortable) to 5 (very comfortable). Options 4 and 5 were chosen by the majority of prescribers.

2 Biosimilar Development

Most prescribers feel they have an average to moderate level of knowledge of the biosimilar development process and the threshold of clinical evidence required for approval of a biosimilar. When asked to rate their level of knowledge on a scale of 1 (very low knowledge) to 5 (very high knowledge), 64% selected option 3 and 19% selected option 4. With respect to data considered the most important in determining the suitability of a biosimilar for use, prescribers rated all types of data to be very important, with a lower importance rating for data demonstrating ability to switch from the reference biologic to the biosimilar:



On a knowledge rating scale, with 1 being very low knowledge and 5 being very high knowledge, responses suggest that most prescribers feel they have an average level of knowledge regarding clinical trial design and endpoint selection for biosimilar studies, with 75% selecting options 3 and 4. Most prescribers (56%) chose 'the endpoint representing the most sensitive population for detecting any potential differences between the biosimilar and reference biologic, and least influenced by patient or disease-related factors' as the most important factor to assess in studies comparing the clinical efficacy of a biosimilar with its reference biologic:



3 Extrapolation of Indications

Most prescribers (75%) were able to identify the most appropriate definition of 'extrapolation of indications' which is "authorization of a biosimilar in indications of the reference biologic in the absence of specific clinical trial/data for the biosimilar in those indications". Despite the high proportion of prescribers being able to select the appropriate definition, most consider their understanding of extrapolation to be below average or average, with 75% selecting options 2 and 3 on a scale of 1 (very low understanding) to 5 (very high understanding):

1 = very low	2	3	4	5 = very high	Weighted average
0%	13%	62%	19%	6%	3.2

However, the majority of prescribers would feel comfortable using a biosimilar in an extrapolated indication with 69% of prescriber's selecting ratings 4 or 5 on a comfort level scale, with 1 being not at all comfortable and 5 being very comfortable.

4 Interchangeability and Switching

There was a high level of agreement among prescribers regarding switching a patient from a biosimilar to the reference biologic or vice versa, with prescribers agreeing that there is minimal impact on efficacy and safety (rated on a scale of 1 = strongly disagree to 5 = strongly agree):

Prescribers' confidence about switching from the rituximab reference drug to a biosimilar	Weighted Average
I DO NOT anticipate that switching will have a significant effect on the treatment benefit the patient receives from the product	3.9
I DO NOT anticipate that switching will lead to emergence of additional adverse effects	3.9
I DO NOT anticipate that switching will lead to harmful immunogenicity	3.4

Among prescribers, there was a low level of concern for reduced clinical efficacy, adverse event and increased risk of immune reactions when switching a patient's treatment from a reference biologic to a biosimilar (rated on a scale of 1 = not at all concerned to 5 = very concerned):

Prescribers' concern about switching from the rituximab reference drug to a biosimilar	Weighted Average
Potential loss of clinical efficacy	2.1
Potential for adverse events	2.1
Potential for increased risk of immune reactions	2.2

Summary

Biosimilar medicines present an opportunity to provide patients with cutting-edge therapy, while improving cost-efficiency on the healthcare system. A biosimilar drug is a highly similar copy of a reference biologic drug. Oncology biosimilars have just begun to enter the Canadian market for hematological and other cancers, and will become more accessible and available in the near future. Currently Rituximab and Filgrastim biosimilars are on the market for lymphoma and CLL. To understand Canadian patient and prescriber perspectives on biosimilar therapies, Lymphoma Canada conducted two surveys between 2019 and 2020. These surveys provided detailed information regarding responders' use and basic knowledge of biosimilars, understanding of biosimilar development, and level of comfort with extrapolation and interchangeability.

PATIENT SUMMARY

Canadian lymphoma patients were generally not very familiar with biosimilars or aware of them as a treatment option, even with the majority of patients being treated with rituximab, a drug with biosimilar options available in Canada. For the low percentage of Canadian patients that were somewhat to very familiar with a biosimilar therapy, sources of information included online searches and speaking with patient organizations. Only a small portion of individuals reported receiving this information from their healthcare providers. As a patient's healthcare team is their first source of valuable and relevant information, this data indicates a gap in knowledge translation between patients and their healthcare provider(s) regarding biosimilar treatment options. With the results of this survey showing that patients have full trust in their physician's decision on using a biosimilar therapy or switching from the standard reference biologic drug to a biosimilar equivalent, it is important that patients are informed on available biosimilar therapies and confident in their treatment decision.

PRESCRIBER SUMMARY

Canadian healthcare prescribers indicated that they have an average to high level knowledge of biosimilars and would be comfortable providing this as a treatment option for eligible patients. However, a gap in prescriber knowledge was identified on clinical data demonstrating the safety and efficacy in switching from the reference biologic to its biosimilar. On the other hand, prescribers have been able to gain valuable information from clinical studies that detect differences between the biologic and biosimilar in the most sensitive patient population, while also assessing safety and efficacy. Another gap included prescriber's understanding of extrapolation (i.e. authorization of biosimilar use in the absence of clinical trial data for a particular indication). Some barriers to biosimilar use in Canada as indicated by prescriber's include delayed approvals and/or reimbursement within their region. With this information on prescriber knowledge and comfort with biosimilar use, there are still opportunities to continue provide relevant clinical and educational resources to healthcare providers on biosimilars, especially as biosimilars become more accessible and available for use in Canada.