July 5. 2021

Dear Mr. Moneo

Thank you for your response to our letter about CAR T-cell therapy treatment in British Columbia. We agree that British Columbia works hard to address patient concerns and provide care for its patients. However, the lack in providing local standard of care therapy for Diffuse Large B-cell Lymphoma [DLBCL] adult patients and Acute Lymphoblastic Leukemia [ALL] pediatric patients means that not all British Columbians within the province are receiving the best care that the province is known for. It also means that the world renowned lymphoma and leukemia clinical experts in BC are unable to treat their patients locally with this innovative therapy.

While we acknowledge the data that you provided in your letter, there is more recent long-term data that supports both the safety and clinical effectiveness, as well as the cost-effectiveness of CAR T-cell therapy. In fact, studies are now evaluating CAR-T in earlier lines of therapy and in combination with other interventions to further increase the clinical effectiveness of CAR T-cell therapy.

CAR T-cell therapies have produced remarkable clinical responses in clinical trials and in the real world setting for both the adult and pediatric populations. Patients that receive CAR T-cell therapy have relapse or refractory disease and have exhausted all other curative options, often two or three previous lines of therapy. CAR T-cell therapy is often a last effort at survival for these individuals. Particularly in the DLBCL patient population, there is no standard of care [SOC] treatment following stem-cell transplantation relapse. Options for patients include palliative approaches or clinical trials. However, with the advancement and responses observed with CAR-T therapy, clinicians with access to this treatment now use it as SOC in this setting. CAR T-cell therapy addresses an unmet need in the patient population, providing durable responses and tolerable safety profiles.

There are a number of published studies that address the concerns you listed in your letter regarding the lack of clinical efficacy and cost-effectiveness and need for CAR T-cell therapy including;

- A study presented at the American Society for Clinical Oncology [ASCO] in 2020 reported the longest follow-up of patients in remission following CAR T-cell therapy, with 51% of patients achieving more than three years duration of response [DOR].[1]
- A study published in November 2021 in the Journal of Clinical Oncology presented long-term data on children and young adults [CAYA] with B-cell ALL treated with CD19 CAR T-cell therapy. This study looked at the role of sequential therapy with allogeneic hematopoietic stem-cell transplant [alloHSCT]. Of the 50 CAYA patients treated, 31 [62%] achieved complete remission [CR].[2]

[1] Long-Term Follow-Up of Anti-CD19 Chimeric Antigen Receptor T-Cell Therapy

[2] Long-Term Follow-Up of CD19-CAR T-Cell Therapy in Children and Young Adults With B-ALL

- A study published in the Journal of Clinical Oncology in December 2019 found that modest delays to accessing CAR-T could significantly reduce the effectiveness of the therapy with a wait time of just one to nine months increasing predicted mortality from 36.1% to 76.3%.[3]
- Another study published in 2019 in the American Journal of Managed Care suggests that the social value of CAR T-cell therapy is significantly limited by treatment delays.[4] As you can see there is considerable evidence pointing to the benefit of this therapy and its significant impact on patients quality of life.
- A study presented at American Society for Hematology in 2019 suggested that CAR-T was found to be cost-effective by reducing other healthcare expenses related to the disease: treatment with CAR-T was associated with fewer hospitalizations, fewer emergency room [ER] visits and lower total healthcare costs.[5]
- Another study published in the Journal of Comparative Effectiveness Research in February 2020 found that CAR-T provided more incremental quality adjusted life years than the average pharmaceutical intervention and more than the average non-pharmaceutical intervention, while retaining similar cost effectiveness.[6]

Since CAR-T became available in Canada, BC patients have not been able to access treatment locally, requiring out-of-province and out-of-country travel. Travel across borders is particularly dangerous for immunocompromised patients, as are DLBCL and ALL patients, especially in the setting of the COVID-19 pandemic where there are increased travel risks. Further barriers include being away from family and support networks for extended time periods, significant out-of-pocket costs related to travel and accommodation, and continued travel delays and difficulties caused by the COVID-19 pandemic. In particular, patients who must travel out-of-country to receive care have substantial out of pocket costs and do not have access to manufacturer patient support programs.

For patients eligible to receive CAR-T who cannot access it within British Columbia, this comes at a high cost physically, emotionally and financially.

We are aware of the implementation issues that existed with the introduction of CAR T-cell therapy in Canada, however well-established pathways have now been integrated across the Canadian landscape. Provinces like Quebec, Ontario and Alberta, have worked hard and quickly to ensure local access for their patients, thereby limiting travel, delays in access, and cost to the patient. We invite you to communicate

[3] Impact of Increasing Wait Times on Overall Mortality of Chimeric Antigen Receptor T-Cell Therapy in Large B-Cell Lymphoma: A Discrete Event Simulation Model

4 The Potential Impact of CAR T-Cell Treatment Delays on Society

[5] Medicare Patients Receiving Chimeric Antigen Receptor T-Cell Therapy for Non-Hodgkin Lymphoma: A First Real-World Look at Patient Characteristics, Healthcare Utilization and Costs

[6] CAR-T therapy and historical trends in effectiveness and cost–effectiveness of oncology treatments

with counterparts across the country who have created access for their patients, either through the establishment of CAR-T centres in-province or through interprovincial agreements.

With an increasing number of CAR T-cell therapies being developed and approved for new indications, and thus an increasing volume of patients who will be eligible to receive CAR T-cell therapy currently and in the future, the government of British Columbia must overcome the ongoing access delays to not only implement appropriate healthcare infrastructure now, but prepare for greater CAR-T use for new indications.

We invite you to read the white paper on chimeric antigen receptor therapy produced by the cancer collaborative in 2019 which evaluates many of the implementation barriers you have outlined in your letter dated May 25. 2021. The white paper can be accessed here. We also invite you to peruse highlights from ASCO 2020 here [highlights from ASCO 2021 will be available shortly]. The Canadian Association for Provincial Cancer Agencies [CAPCA] has also recently included CAR-T as a strategic priority through their supporting innovation pillar which outlines the need to enhance evidence-based implementation of new and emerging technologies.[7] While we have no affiliation, Dr. Kim Chi, as head of BC Cancer, is aware of the work that is being done through CAPCA and can certainly help the Ministry of Health in BC navigate the uncertainties associated with CAR T-cell therapy - as other provinces have already undertaken.

British Columbians can no longer wait to have access to this proven therapy in-province. The clinicians in BC are ready, the patients are ready, and the BC government must respond to this need. We request an urgent meeting to discuss with you the dire needs of patients in BC before the close for the summer holidays. We also ask that funding be allocated to centres that are currently ready to deliver this innovative therapy to patients.

We prefer to discuss directly with you and the office of the ministry of health of British Columbia rather than through a media directed campaign.

Sincerely,

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[7] CAPCA - our work

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CC.
The Honorable John Horgan, Premier British Columbia
The Honorable Adrian Dix, BC Ministry of Health
Stephen Brown, Deputy Minister, BC Ministry of Health
Dr. Kim Chi, Vice President and Chief Medical Officer, BC Cancer Agency