eBulletin

November 2021

CLL Canada UPDATE - ISSUE 24

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1. A word from the CLL Canada Board Chair

This summer marked a turning point for many of us, as we realized that COVID vaccines will not enable us to turn a corner and leave the pandemic behind. And this despite the significant benefits of vaccination. An analysis published in the New England Journal of Medicine concludes that "We need to learn to live with this illness, just as we have learned to live with influenza."

So where does this leave CLL patients and other immune compromised people? As we report in this issue of the CLL Canada eBulletin, they can obtain a third dose of the vaccine. Another article describes a treatment that can prevent hospitalization which is coming to Canada, albeit slowly due to Canada having a more cautious approach than our neighbour to the south and the need to administer the treatment by infusion in a hospital or clinic, among other reasons. We also report on a study that found vaccines do have a protective effect in blood cancer patients.

As encouraging as this news might be, it still leaves us with very little guidance on whether to resume activities that may expose us to COVID, a situation we explored in our August eBulletin, available on our website.

This month, CLL Canada will be participating in a meeting of patient groups worldwide who will discuss the problems faced by patients and what we as patient groups could do to ameliorate the situation. The pandemic has shown us that we really need to work together to have an impact.

We hope that you will find our eBulletin a useful benefit from membership in a club none of us really wanted to join. Send your comments and suggestions to cllcanada.org@gmail.com

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2. Monoclonal antibody therapy is slowly coming to Canada

Ontario and Saskatchewan have started programs of monoclonal antibody therapy for Covid-19 patients to prevent severely immunosuppressed people from being hospitalized.

St. Joseph's hospital in Hamilton launched Ontario's first COVID-19 monoclonal antibody therapy clinic, a treatment shown in early studies to reduce hospitalization by 71 per cent, and death by 70 per cent in high-risk COVID-positive patients. The treatment is a mix of drugs casirivimab and imdevimab called Regen-COV, authorized by Health Canada last June and used in the US, the UK and Australia.

Monoclonal antibodies work best when given early in the COVID-19 illness, within 10 days after symptoms appear. The therapy has proven beneficial for high-risk people, such as CLL patients who are the immune compromised.

So, what are monoclonal antibodies? They are antibodies created (cloned) in a laboratory to target a specific virus. They can fight COVID-19 well before the body produces its own antibodies, thereby helping to reduce the severity of the disease and lower hospitalization and death rates. Monoclonal antibodies are administered by infusion, so they must be given to patients in a clinic or hospital

Please let us know if you have information on the use of monoclonal antibodies in your province, so we can share the information with CLL Canada members. Write us a cllcanada.org@gmail.com .

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3. Study Finds COVID Vaccines Offer Some Protection to Blood Cancer Patients

A recently published study has found a significant reduction in the mortality rate of blood cancer patients (including CLL) who catch COVID despite being fully vaccinated. This would suggest that vaccines have a protective effect in CLL

patients, even if they provide less protection than they do to the general population.

As one of the study's authors put it "With these preliminary data, we show that vaccination is not able to completely protect, but surely it has a strong role in reducing the mortality of COVID-19 for people with blood cancers."

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4. Third dose of COVID Vaccines for CLL Patients

A third dose of COVID vaccine is now available in most provinces for people 70 or older as well as the immunocompromised, which includes CLL patients. Lymphoma Canada has published useful report with web links to information for each province in its COVID Information Hub. You can access the report directly here.

While the national guidelines specify that patients should be under "active treatment," we have heard reports that CLL patients on watch and wait or in remission have been able to receive a third dose. It is recommended you speak with your CLL doctor if for some reason you are refused a third dose.

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5. The role of Immunoglobulin in the progression of CLL

It's always interesting when researchers tackle the same subject from opposite angles but come to the same conclusions. Whereas one researcher found that CLL patients with lower overall immunoglobulin levels tended to have more aggressive CLL, the other one finds that the higher a patient's immunoglobulins, the slower his or her CLL will progress.

A study of prognostic factors in CLL found that CLL patients with lower immunoglobulin levels tend to have more advanced disease (Binet/Rai stage) and worse CLL prognostic factors (e.g. del(17/)/TP53 mutations and trisomy 12). Although these patients progressed faster to treatment, their overall survival was no different than those with higher immunoglobulin levels.

A 2018 study on blood IgG demonstrated that immunoglobulins (IgG) block cell mechanisms essential to the survival of cancerous B-cells, thereby slowing the progression of CLL. So, the immunoglobulin replacement therapy (IgRT) that many CLL patients take to prevent infections may also reduce the progression of the CLL itself! As such, CLLers may wish to discuss their immunoglobulin levels with their physicians to decide if IgG replacement therapy is right for them.

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6. Global Leukemia Patient Experience Survey 2021

We invite you to participate in an international survey about the diagnosis, care, and treatment of your leukemia or that of a person to whom you are a caregiver.

The survey has been created to build a global picture of the experience of people with leukemia as well as to identify their key issues and unmet needs. Organizations representing patients from around the world, including CLL Canada, will use this information to better serve patients and to carry their voices to decision makers.

The survey is run by the Acute Leukemia Advocates Network (ALAN) in partnership with the CLL Advocates Network (CLLAN) and the CML Advocates Network (CMLAN).

Please follow this link before December 1 to complete the survey:

https://www.oc-meridian.com/IQVIAIF/completion/custom/default.aspx?slid=164&did=

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7. Treatment News

This month we follow up on two items covered in the May 2021 edition of the CLL Canada eBulletin.

Earlier this fall, the manufacturers of both Acalabrutinib and Venetoclax reached a pricing agreement with the pan-Canadian Pharmaceutical Alliance (pCPA), representing governments. Now it is up to each province to decide whether it will pay for these treatments. So far, we have heard that Quebec has listed Venetoclax first line on it's formulary (it was already there for relapsed patients).

In May, we had speculated that Zanubrutinib might come to Canada for CLL patients. Readers will recall that this drug is a Btk inhibitor, as are Ibrutinib and Acalabrutinib. Recently one of our members informed us that he had been prescribed Zanubrutinib by his hematologist.

Should you wish to be treated with Zanubrutinib, BeiGene, the manufacturer, has a support program that can assist patients in obtaining the treatment and paying for it. Your doctor can find out more at this web site https://www.brukinsa.ca/en/ . Patients can get information by contacting Innomar Strategies at 1-833-234-4366, Monday through Friday from 8 a.m. to 5 p.m. Eastern Time (ET).

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8. The BTK Inhibitor Story

By Spencer B. Gibson, Ph.D., Kipnes Endowed Chair in Lymphatic Disorders, Professor, Department of Oncology, University of Alberta

The arrival of Ibrutinib a decade ago was a major event in the CLL world. Here at last was a treatment targeting cancer cells instead of damaging all rapidly growing cells, cancerous or not, the way chemotherapy does. The result is a better control of CLL with fewer side effects. Ibrutinib, along with Acalabrutinib and Zanubrutinib

which work in a similar fashion, are called BTK inhibitors because they target the Bruton Tyrosine Kinase.

So, who is this Bruton and why is a CLL treatment named after him?

Our story begins with Dr. Ogden Bruton, who in the 1950's discovered that children suffering from recurring infections could be brought back to health by injections of an antibody called immunoglobulin. It was later discovered that the cause of this disease, called agammaglobulinemia, was a mutation in a protein which controls the creation of immunoglobulins in a cell. This protein belonged to a family of proteins called Tyrosine Kinases, and was named the Bruton Tyrosine Kinase, or BTK for short, in honour of Dr. Bruton.

What does this have to do with CLL? Quite a lot, as it turns out. Tyrosine kinases act as signals that cause cells to grow, to move or to release proteins that affect other cells. The function of the BTK is to signal our white blood cells to produce immunoglobulins.

As it turns out, researchers discovered that CLL hijacks the BTK signal to allow cancerous cells to grow, survive and accumulate in lymph nodes and bone marrow. They then observed that blocking the BTK signal causes CLL cells to leave lymph nodes and bone marrow for the bloodstream, where they die like normal cells. Over the course of 20 years and much research the first molecule to effectively block BTK was developed and approved, the BTK inhibitor Ibrutinib.

Now we can see why BTK inhibitors need to be taken indefinitely. The BTK signal must be blocked on a continuing basis, lest it be once again used by the CLL to ensure the growth and survival of cancerous cells.

Unfortunately, some patients become resistant to BTK inhibitors. BTK is not the only signal in cancerous cells to be hijacked in order to promote CLL growth and survival. This emphasizes the need to better understand how proteins are changed in CLL, so to come up with more effective targeted treatments. Nevertheless, Dr. Bruton would be amazed that his discovery of a treatment for a childhood disease would lead to an effective treatment for an adult leukemia.

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9. CLL Canada Board member Eric Pitters' CLL Journey

You can imagine the shock. During my annual physical, my GP told me he was referring me to an oncologist because I most likely had leukemia.

It was like a bullet through my head. "What is a leukemia"? What do I tell my wife and adult kids? On that lovely spring day of April 2005, I suddenly felt I had lost control of my life!

Once home, I told my wife point-blank that I had been diagnosed with leukemia. She told me to stop joking. I insisted I wasn't. She then got up out of her chair,

banged my chest sobbing that it couldn't be true. We hugged each other for a long time.

The diagnosis was confirmed in July. I asked about immediate treatment but was told that it wouldn't likely start for another year or 2. So, I had to live with the fact that this cancer was growing in me all the time. This "Watch, Wait and Worry" took some getting used to.

After 2 years, it was suggested I enter a clinical trial at Princess Margaret Hospital. A clinical trial? Isn't that for people on their last legs! The hematologist at PMH won my trust by taking the time to answer all my questions. With her guidance I entered the 3-year trial with Revlimid (Lenalidomide) taken orally and continued on the drug for another 4 years before relapsing.

I wanted to know everything about this disease, I had to be in control! I consulted various internet sites, but what made the difference was my hematologist's invitation to doctors' conferences on leukemia. The more I learn more about CLL and its treatments, the less I am worried!

Upon relapsing on Revlimid, I had four treatments of FCR (Fludarabine, Cyclophosphamide and Rituximab) which gave me an 18-month remission. I then entered a new clinical trial with Acalabrutinib on one side and Idelalisib and Rituximab (IR) on the other. After six cycles of IR I became intolerant of the regimen. I was then switched to the Acalibrutinib side, which I continue to do well on. The staff at Princess Margaret Hospital have treated me exceptionally well.

There are many advantages to participating in clinical trials. It is one way to get the latest treatments (drugs) well before they become widely available. You are frequently monitored and have access to the best labs in the US for blood and bone marrow testing.

My prognosis is good. Infections are held at bay through monthly IVIG infusions and precancerous skin lesions are looked after by my dermatologist. Should I relapse on this trial, I would not hesitate to participate in another one.

Aside from my belief in education, how do I emotionally get through all of this? My highly supportive wife, Rhonda.

Keep learning and movin' on…

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10. CLL Canada has Openings on its Board of Directors

We have some openings on our board of directors for CLL patients and caregivers from across Canada. We are an all-volunteer organization, so board members play an active role in our activities. You can find information about CLL Canada and the role of the board on our website, here.

Should you be interested or want more information before deciding to apply, send us an email cllcanada.org@gmail.com

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