British Columbia Cancer Agency

Centre for Lymphoid Cancer *Newsletter*

Lymphoma ◆ Leukemia ◆ Myeloma

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Lymphoid Cancer Education Day 11 May 2018

Our annual BCCA-CLC Lymphoid Cancer Education Day will be held at the Jewish Community Center at the 41st and Oak (950 West 41st Ave) on Friday May 11, 2018. Presentations by researchers from the BC Cancer Agency and the BC Cancer Research Center will address the basic biology, causes and new treatments for lymphoid cancers and related patient advocacy for research and health care funding. Disease-specific breakout sessions are planned and participants are encouraged to ask questions and participate in an informal open discussion.

Details about Lymphoid Cancer Education Day: ***http://www.bccancer.bc.ca/about/events/lymphoid-cancer-education-forum.*** Seating is limited and the event usually fills up so be sure to register online by April 28, 2018: ***www.bccancerfoundation.com/lymphoidforum***

2017 Education Day Summary Lymphoma 101 Session: Dr. Diego Villa

Lymphoid cancers are the 5th most common cancers in Canada. The majority of these types of cancers in Western countries are of **B-cell origin**, and T-cell cancers make up only about 10% of all lymphomas. Although the incidence has risen in the past three decades, mortality rates have declined due to advanced classification/diagnosis and improved clinical management of the diseases.

Lymphoid malignancies arise from lymphocytes, the cells of the immune system. The immune system ordinarily functions to detect and destroy invading microorganisms and cancerous cells. This natural defense system comprises many types of immune cells such as B-cells, T-cells and other white blood cells. The main function of B cells is to produce antibodies, which are immunoglobulin molecules whose job is to recognize invading pathogens for destruction by macrophages, cytotoxic T cells and natural killer cells. Antibodies are made of light and heavy chains and recognize foreign invaders by binding to antigens in a "lock and key" fashion. As this is a very specific response, each antibody has to be able to bind a specific antigen of an invading pathogen to induce a proper immune response. To create the antibody diversity that covers millions of antigens one would encounter in a lifetime, B cells randomly rearrange gene segments, known as variable (V), diversity (D), and joining (J) genes, which encode the heavy chain (similar event occurs for the light chain). This event takes place in the bone marrow. Similarly, there are other molecular events during B cell development that give rise to the antibody diversity: somatic hypermutation which introduces point mutations, deletions or duplications in the V region and class switch which results in gene exchange between different isotypes of immunoglobulin (antibodies). These routine events take place in the germinal centre of lymph nodes. During the course of B cell development, random "mistakes" in these molecular processes may occur, which could lead to development of B cell lymphomas.

Lymphoid cancers or lymphoma can be generally categorized in two clinical types: indolent and aggressive lymphomas. The most common indolent lymphoid cancers are follicular lymphoma and chronic lymphocytic leukemia, which progress slowly over years and can sometimes be managed without medical treatment. They are generally considered incurable. Diffuse large B-cell lymphoma, on the other hand, represents an aggressive type of

lymphoma, which requires treatment at the time of diagnosis. Despite the aggressive nature of this type of lymphoid disease, it can be cured with therapeutic intervention. The therapies currently available for these lymphoid cancers are standard chemotherapy, radiotherapy and emerging targeted therapies, which include inhibitors of B-cell receptor signaling and immune checkpoints.

Novel Therapies for Lymphoma Session: Dr. Kerry Savage

Rituximab is one of the first monocloncal antibody-based therapies that were approved by Health Canada. It was approved to treat lymphoma in 1997and specifically targets a B-cell surface marker called CD20 and kills B-cells directly and indirectly (by activating other immune cells). Rituximab is also known to provide synergistic effects with chemotherapy. Due to its high response rate observed in diffuse large B-cell lymphoma (DLBCL) in earlier studies, Rituximab-combination chemotherapy became the new standard therapy to treat this aggressive lymphoid cancer in BC since 2001.

In 2014, Health Canada approved the next generation of anti-CD20 monoclonal antibodies, called **obinutuzumab**, which has an enhanced ability to target and kill B-cells. Combination therapy with chlorambucil (a chemotherapy) is now used to treat older or frail patients with chronic leukocytic lymphoma (CLL). Furthermore, obinutuzumab can be combined with bendamustine to treat refractory cases of follicular lymphoma (FL).

Another monoclonal antibody called **brentuximab vedotin** is conjugated with a chemotherapy drug and targets a different cell surface marker, CD30. Brentuximab vedotin was approved for use to treat relapsed Hodgkin lymphoma (HL) and anaplastic T-cell lymphoma in 2013.

As described in the previous issue of the newsletter, there are a number of drugs that have been developed to target specific molecules in the B-cell receptor signaling pathway. For example, **ibrutinib**, a drug that inhibits an enzyme called Bruton's tyrosine kinase that mediates B-cell receptor signaling for survival has shown a high response rate and long remission in CLL patients. In addition to CLL, ibrutinib was recently approved to treat mantle cell lymphoma and lymphoplasmacytic lymphoma (Waldenstrom's macroglobulinemia) by Health Canada, and its access is still limited for these diseases.

Other targeted therapies that are currently tested or waiting for approval include **BCL2 inhibitors**, which sequester an overexpressed protein in lymphoma, allowing cell death and **checkpoint inhibitors**, which target molecules involved in immune escape. Of particular interest, the latter show promising results with potential for highly effective management of lymphoid cancers in the near future. We will cover the details of checkpoint inhibitors in a following issue of our newsletter.

BioCancer Initiatives: Update

Last year, the Centre for Lymphoid Cancer was joined by breast and prostate tumor groups to develop **BioCancer Initiatives**. The purpose of these initiatives is to create a province-wide translational research platform for all tumor types to collect and store biospecimens, which include mainly blood and tumor tissues (left over biopsy materials), and associated clinical data for research purposes.

Using the biomaterials and clinical information that is collected, researchers can conduct translational research, the results of which will facilitate development of more effective diagnostic and therapeutic intervention.

Currently, centres in Vancouver, Abbotsford, Vancouver Island, Prince George, Fraser Valley and Southern Interior are fully enrolling newly diagnosed patients for all three cancer programs.

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