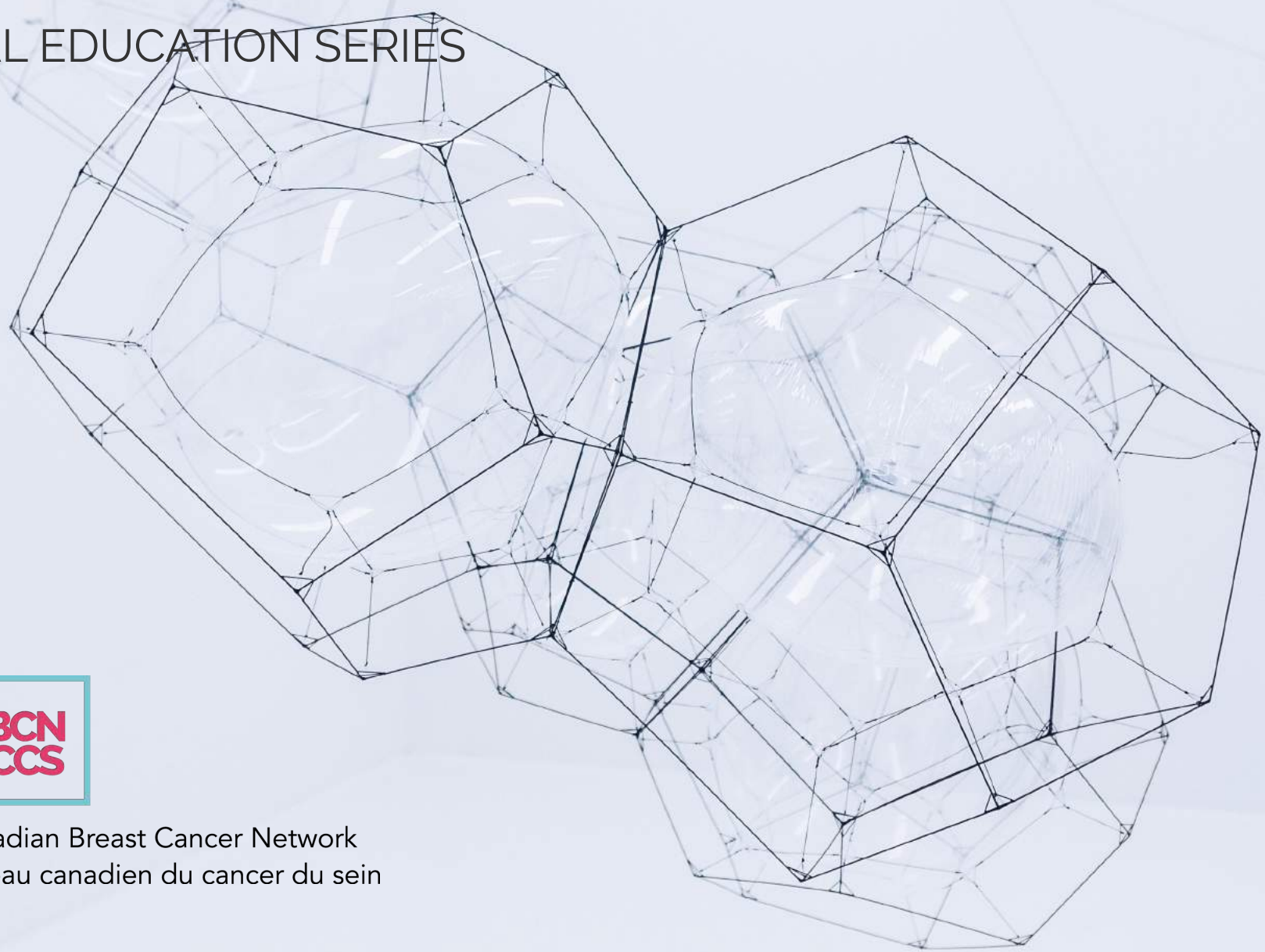
# BIOSIMILARS

## AND BREAST CANCER

A DIGITAL EDUCATION SERIES



CBCN
RCCS

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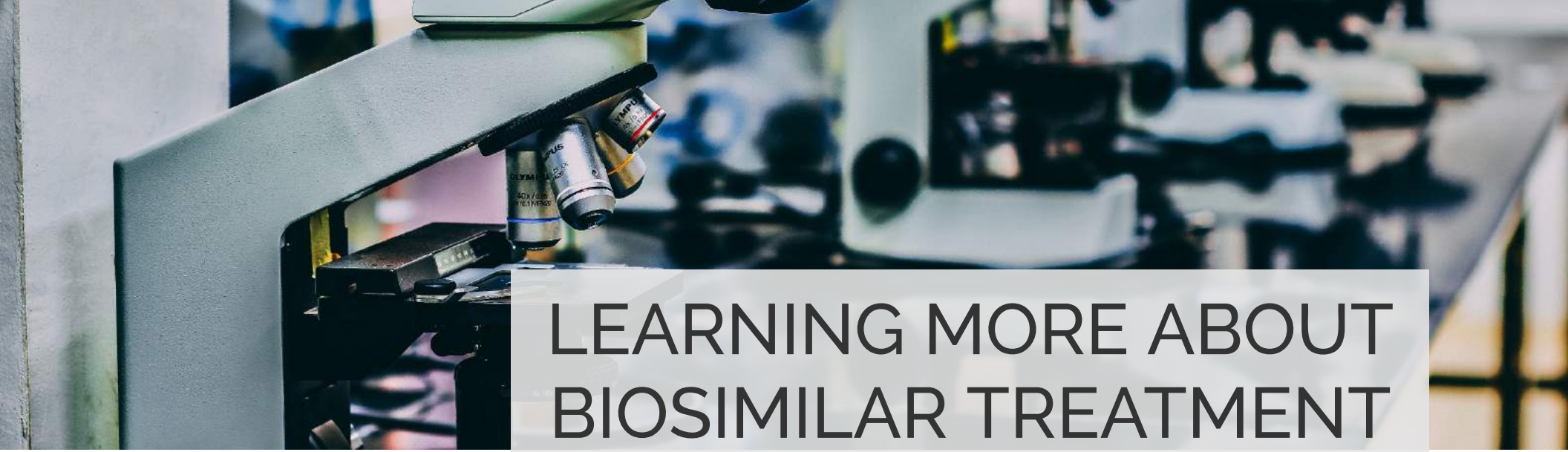


# LEARNING MORE ABOUT BIOSIMILAR TREATMENT OPTIONS

Biosimilar drugs will soon be entering the breast cancer treatment landscape and are already available for support medications. With these emerging treatment options, it's important to know more about them so you can make informed decisions about your treatment plan.

## What is a biosimilar?

In short, a biosimilar is a drug manufactured to imitate a biologic drug. Biologics are very complex drugs that use living cells or tissues from humans, plants or microorganisms[1]. They are one of the leading innovative medicines and have changed the landscape for cancer treatment today.

Typically, when a new drug is manufactured and approved for use, a patent is issued. This means that no other manufacturer can replicate the drug. When the patent expires, other manufacturers can reproduce the same drugs at a lesser cost. These are called generic drugs. Generic drugs use the exact same formula as the original product. Biosimilars, like generic drugs, are also produced after a patent expires and they are also produced as a less costly alternative to a biologic drug. The difference is, biosimilars cannot be an exact replica of a biologic because the living cells used to create the drug cannot be exactly replicated.

Instead, biosimilar manufacturers recreate a similar environment to produce the same results as the original biologic. Therefore, the makeup of each drug will be comparable but not identical.

Right now, biosimilars have not yet entered into the Canadian market for treating cancer and the United States FDA has only just recently approved two biosimilars for cancer treatment, including one for breast cancer. This will soon change, however, as biologic drug patents for cancer begin to expire. The breast cancer treatment landscape has advanced considerably over the past 20 years with the development of targeted therapies. Many of these new therapies are biologic drugs that will soon be coming off patent, opening the door for many new biosimilar alternatives.

## Efficacy of a biosimilar

It's imperative for a biosimilar to be as effective as its biologic counterpart. Health Canada has specific standards for biosimilar manufactures when proving the drug's effectiveness. First, a biosimilar manufacturer must compare its drug to that of a reference biologic drug and prove that the active medical ingredients (the living cells or tissues used) are similar. Furthermore, the biosimilar must use the same dosage, format, and strength as the reference biologic and demonstrate comparable safety, efficacy, and effectiveness through testing and trials. Health Canada uses a rigorous approval process to ensure patient safety and drug efficacy.

After a biosimilar has been given a Notice of Compliance (NOC) by Health Canada, the manufacturer can begin marketing the drug for use in Canada. Like all drugs on the market, biosimilars continue to be closely monitored for safety after its NOC. Manufacturers are required to monitor all side effects that are reported to them and notify Health Canada about any serious side effects[2]. Health Canada investigates all complaints and reports related to drug safety.

## Being prescribed a biosimilar

Since the drug makeup is not exact, a pharmacist *cannot* automatically interchange a biosimilar for a biologic like they can for non-biologic drugs. Being prescribed a biosimilar is a decision between you and your oncologist. If you are already on a reference biologic, switching to a biosimilar is dependent on your unique preferences and situation. Considerations to change your treatment plan should always be discussed with you in advance.

Cost is a large contributing factor in prescribing biosimilars. Because they are less costly than brand name biologics, they provide less of a burden on the healthcare system. But cost can be a factor for individual patients as well. Ontario and several east coast provinces do not cover the cost of oral treatments so a more affordable option might be appealing to you.

Biosimilars may or may not be right for you. But you can benefit from knowing your treatment options and understanding what is available. For more information about biosimilar drugs, read Health Canada's Factsheet on the subject here.

# WHAT ARE THE DOCTORS SAYING?

Now that you've learned about biosimilar treatment options, it may also be of interest to learn what the physician perspective is. We connected with Dr. Sandeep Sehdev, a medical oncologist at the Ottawa Hospital, to get his perspective on biosimilars and what he thinks is important for patients to understand about them.

## What do you think is important for your patients to understand about biosimilars?

***They are safe:*** By the time biosimilars reach the patient they will have been thoroughly vetted by Health Canada for their chemical and biological similarity to the original drug. Health Canada reviews the biosimilar for any suggestion of potential safety concerns before it can be marketed.

***They aren't new:*** Biosimilars have been used in Canada and other countries throughout Europe for some time now in other disease areas.

***They cost less:*** While they are not the same as "generic" chemical drugs, the concept is the same in that they are another version made by another company to lower costs. Similarly, to generic drugs, those savings will be expected to be put towards funding the costs of ever-increasing new advances in cancer treatments.

***You will always be monitored:*** Finally, as we do for all cancer drugs, clinicians and health authorities will be continually monitoring how you are doing on the medication and how the medication is doing overall for any concerns about effectiveness or safety.

## What are some of the opportunities that you see with biosimilars?

***More options equal better costs:*** An increased number of "brands" should increase competition and decrease the cost of treatment—something even our patients are overwhelmed by.

***Savings can fund newer treatments:*** The savings will, of necessity, be redirected to other newer very costly advances in cancer treatment. New therapies require extensive research into the science underlying cancer biology and the development of complex biological agents, often used in combinations. The same patients offered biosimilars today would almost certainly benefit from these new therapies in the future.

## What are some things patients should consider if they are going to be using a biosimilar?

***Don't be afraid to ask questions:*** Patients should know that they may feel free to ask their doctors or pharmacists any questions about they may have.

***The more you know:*** As we, the medical field, feel strongly that they are functionally similar, there should be no particular considerations to be had, aside from a sense of reassurance gained by a better understanding of biosimilars and how they will be used in Canada.

# UNDERSTANDING BIOSIMILAR DRUG DEVELOPMENT

*To understand how biosimilar therapies are developed, it's helpful first to learn more about how traditional biologics are manufactured and assessed for safety and efficacy.*

## Step 1: Analytical characterization

A biologic drug's structure and functional activity are assessed carefully to provide insights on how compatible the drug is with the human body, whether the drug should be moved forward in the development process, and for quality control purposes.

## Step 2: Non-Clinical studies

These involve living organisms or cells to determine a drug's toxicity profile and ensure safe human exposure to a treatment.

## Step 3: Clinical Studies

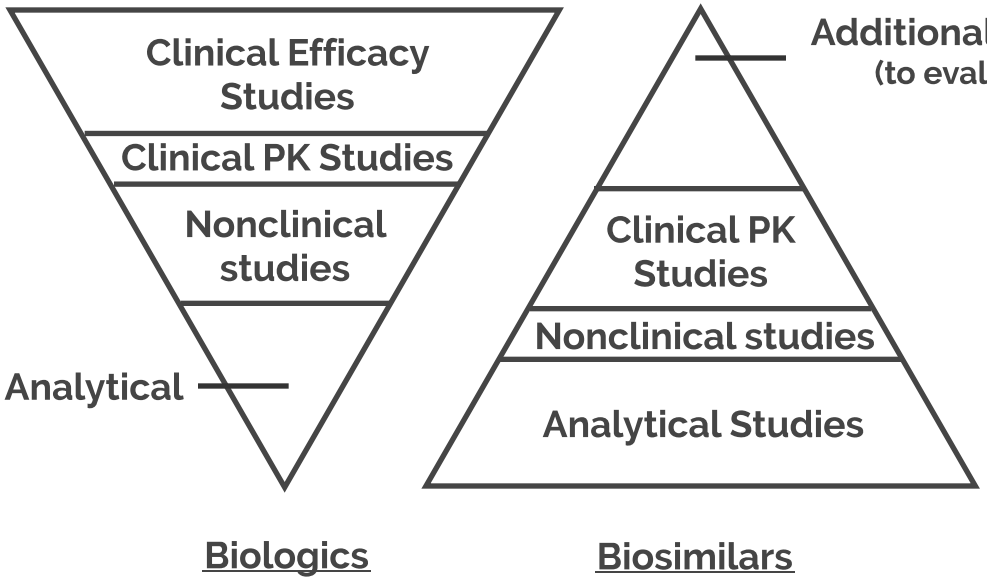
### *Clinical Pharmacology:*

Explore the pharmacodynamics (PD) and pharmacokinetics (PK) of a drug.

Pharmacodynamics research explores the biochemical and physiological impact of the drug on the body. Pharmacokinetic studies, on the other hand, show how the drug moves through the body. Used together, these studies can inform decisions around dosing, clinical benefits and adverse effects of a treatment.

### *Clinical Efficacy:*

Conducted to assess the drug's performance in human beings. These include clinical trial studies, which examine the safety and efficacy of a new drug in patients. These involve studies comparing the new treatment to standard therapies that are already available, to a placebo that contains no active ingredients, or to no interventions at all. The studies measure specific outcomes in participants to ensure that the treatment is meeting intended targets and to highlight the clinical benefits of the new drug.




*Biosimilar drug development involves many of the same steps but with a different focus. The primary objective of the entire biosimilar development process is to demonstrate the similarity of the biosimilar to the original biologic in terms of quality, safety and efficacy.*

*Regulators, like Health Canada, use the nonclinical and clinical data comparing the biosimilar and the reference product to make approval decisions. They review the data on a case-by-case basis and make their final decision based on the entirety of the data.*

### Analytical Studies:

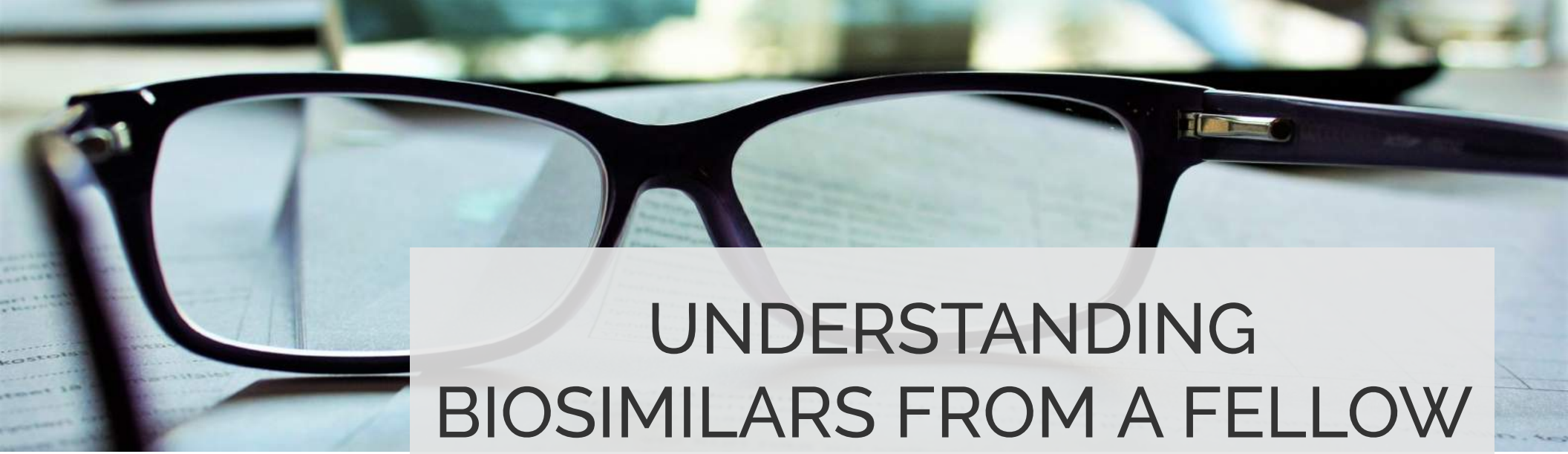
In biosimilar development the analytical characterization stage has the largest focus, as manufacturers work to demonstrate that the structure and function of the biosimilar therapy is similar to the original biologic drug. This is in contrast to new biologic therapies where the majority of the effort and focus is spent on clinical efficacy studies.

### Nonclinical Studies:

The non-clinical steps are less extensive for biosimilars. The goal for these studies is to ensure that any differences observed in quality do not end up impacting on the safety and efficacy of the biosimilar as compared to the reference drug.

### Clinical studies:

Also less comprehensive for biosimilars. Clinical studies compare the safety, effectiveness, pharmacokinetics, and the ability of the drug to produce an immune response in a patient, of the biosimilar to the reference treatment using the same dosage and method of administration. Biosimilar manufacturers also conduct clinical trials in the most sensitive patient populations and measure the most sensitive clinical endpoints to identify any differences between the biosimilar and the reference biologic.



# UNDERSTANDING BIOSIMILARS FROM A FELLOW BREAST CANCER PATIENT

**By: Diana Ermel**

*First of all, I recommend having a look at our biosimilars fact sheet to help you understand the difference between biologics and biosimilars.*

As a breast cancer survivor and board member of CBCN, I am very interested in how biosimilars will be used in breast cancer treatment in Canada. While not commonly understood today, biosimilars will soon be a household discussion among breast cancer patients. As patients, it is important for us to know how biosimilars will be used to treat cancer, especially if they are going to be used as effective alternatives to brand name treatments. Here are some of the points that I think are important for us, as patients, to consider.

**Safety and Efficacy:** A key priority for all patients is knowing that their treatments are going to be safe and effective—it is no different with biosimilars. The most frequently asked question is if these drugs are as effective as the originator drugs they replicate. Health Canada has a rigorous approval process in place when it comes to biosimilars, as well as guidelines for their use. I think we can be reassured by that stewardship. Biosimilars are already being used to treat a number of chronic diseases in Canada and have been in use to treat patients with cancer in Europe for a number of years. However, it's not yet certain how they will be used as part of a full and comprehensive cancer treatment plan. It's clear that patients need more information to understand how biosimilars will be regulated so that we can build our trust and comfort in being treated with these therapies.

## Informed decision-making:

Treatment outcomes are another concern for patients. If your current treatment plan is working well you may feel that switching could jeopardize it. But, if it's not working as expected, biosimilars could improve access and options. It's important that patients are able to make informed decisions when it comes to the use of biosimilars to treat their cancer. In order to do that, we need to have open conversations with our health care providers about which treatment is right for us.

## Access:

Another consideration patients should be aware of is the cost of the biosimilar compared to brand name drugs. For injectable treatments, the cost isn't the first consideration a patient has when making treatment decisions. This is because our provincial health body pays for the treatment. For oral treatments, however, there are several provinces that lag behind the rest of Canada. These provinces require patients to pay out of pocket or through private insurance for oral drugs. Having a treatment that is less costly on the system and on your own pocketbook is seen as a win by many people. Since it is already so complicated for patients to have to navigate affording and accessing cancer treatments, biosimilar therapies need to be used by the health care system in a way that will help expand patients' treatment options and access to cancer therapies.

As biosimilar therapies for cancer come to Canada, there will be more and more questions about how they will be regulated and used by the health care system. As breast cancer patients, we need to be equipped with adequate information to make informed decisions about our treatment. Going forward, it's clear that ensuring that these treatments are used in a safe, effective, and transparent way that increases overall access to essential cancer medications will be the most important priority for patients and organizations like CBCN.


# A CLINICAL PERSPECTIVE

**By: Dr. Jawaid Younus, Medical Oncologist/Hematologist at London Health Sciences Centre**

We are all familiar with generics. The exact copy of the known chemical formula used in the original medicine is what constitutes the generic form of any medicine. There are multiple reasons why generics are able to be mass produced at a lower cost. An important step includes manufacturers of generics having to provide proof that their version is an exact copy of the chemical formula of the original medicine and that when used in healthy individuals, the metabolism remains very similar to the original compound. This shortened pathway of getting approved from Health Canada or a similar regulatory agency ensures less economic burden to manufacturers and provides the obvious advantage of a significantly lower price, as well as improved accessibility for patients.

Medicines that are derived from a biologic system (cells, bacteria, etc.) are called biologics. Such medicines are in common use in oncology, rheumatology, and other fields of medicine. A copy of the original biologic medicine is called a biosimilar. Biologics have a highly complex structure and therefore biosimilars may not be an exact copy of the original molecule. Health Canada evaluates the applications of biosimilars as a new drug under the Food and Drug Act/Regulations. Health Canada has the Biologics and Genetics Therapies Directorate along with the Marketed Health Product Directorate to evaluate and process the applications for a new biosimilar product. A biosimilar has a similar structure to the original molecule; however, its immunogenicity, which means its ability to induce an immune response, and often one or more efficacy parameters are tested in actual patients in the form of a clinical trial. The complex manufacturing steps and the clinical trial evaluation adds significantly to the cost incurred by the manufacturers. Thus it is expected that biosimilars are not going to be as inexpensive as generics.

There are more questions than answers in the emerging field of biosimilars. The mere introduction of the biosimilar as a "new" entity in the list of therapeutic options presents a learning curve for the clinicians. Should we be replacing the original molecules with biosimilars, similar to generics? Should a patient on treatment with an antibody be switched to the biosimilar instead? There are no standardized recommendations or even a guideline that exists to direct the decision making and thus this presents as a challenge for the treating physicians. In addition, should we be discussing the switch or the use of a biosimilar with our patients? In the oncology world, the intent of treatment is extremely important, and the approach to adjuvant therapy is different than for the advanced disease. One could hypothesize that the introduction of biosimilars will be relatively easier in the advanced setting of the disease as the intent of the therapy is to control the disease, improve disease-related symptoms and prolong the disease-free and overall survival. This approach may provide enough experience and familiarity to the clinicians and pave the path for the introduction of biosimilars in the adjuvant setting where the intent is prevention of the disease/cure.

Our experience with generics has been different. Despite some variability with generics compared to the original compound, we do not discuss the use of generics in any setting of the disease with our patients. We are using generic chemotherapy and anti-estrogen drugs routinely in the adjuvant and in the advanced disease setting. Then why should we be concerned about the use of biosimilars in these clinical settings? This concern stems from the fact that biosimilars are regarded as a "new" drug and tested within trials to confirm relevant characteristics like efficacy and safety. Should one trial in a particular setting be considered as providing enough evidence to start using the biosimilar for that stage of the cancer? The issue also remains that if the biosimilar is tested in the advanced setting, then should we feel comfortable in using it in other clinical stages like adjuvant or neo-adjuvant? Let us consider another scenario; a biosimilar had been tested in a trial involving advanced breast cancer patients and was approved. Are we able to use the same biosimilar in patients with cancer of esophagus or stomach? The original biologic product had to undergo multiple clinical trials in every stage of the disease and a similar set of trials for each of the cancers to get specific indications for its use.

The post-marketing surveillance by Health Canada may give us some answers from the safety perspective for biosimilars. However, the efficacy parameters are complicated and hard to follow. It will be extremely difficult for an individual clinician or even a cancer centre to accurately collect the efficacy data on biosimilars on a longitudinal basis.

There is another angle to watch in the unfolding biosimilar story. In future, there will be many manufacturers producing biosimilars. This will present a challenge to reimbursement authorities as ideally all approved biosimilars should be available as an treatment option. Will the decision to prefer one biosimilar over the other rest on physicians or pharmacists? In Ontario, clinicians and pharmacists are forced to use only one granulocyte colony stimulating factor (GCSF) biosimilar under the limited use code. In this way, the ministry of health, under reimbursement heading, may hold all the power to use a particular biosimilar.

The bottom line with biosimilars remains the same as with generics. We would like to have cheaper and easier access to these complex biologic molecules for every eligible patient. Within this context, we would like to ensure safety and efficacy as well as freedom of choice to select the best-suited product for our patients. We hope that with further experience and exposure to the biosimilars, we may get better answers and solutions for clinicians, pharmacists, and for the regulatory institutions.

# WHAT'S COMING DOWN THE PIPELINE?

Biosimilar therapies have already been in use in Canada for a few years, mostly in the chronic disease and supportive care settings. But soon they will be used for treating cancer as well. There isn't a lot of information about these new oncology biosimilars, and it's important that breast cancer patients are aware of how their treatment plans may be impacted by these new therapies. We explore some of the emerging biosimilar therapies that will be used to treat cancer patients soon.

In the supportive care setting, many cancer patients are already receiving biosimilar treatment. Filgrastim (Neupogen) and pegfilgrastim (Neulasta) are commonly prescribed to reduce infection from febrile neutropenia in cancer patients. In recent years, a number of manufacturers have developed biosimilars for these two treatments. These include the treatments Grastofil, a biosimilar for filgastrim, and Lapelga, a biosimilar for pegfilgrastim.  Biosimilar therapies for treating febrile neutropenia are currently being used in many cancer centres across the country.

In oncology, biosimilar products are currently being developed for potential use in routine cancer treatment. This year, Health Canada approved Mvasi, a biosimilar for bevacizumab (Avastin). This treatment has been approved for the indications of metastatic colorectal cancer and locally advanced, metastatic or recurrent non-small cell lung cancer and is the first biosimilar treatment approved for the treatment of cancer in Canada.

Other biosimilars in development include those for the treatment of chronic lymphocytic leukaemia (CLL) and some types of non-Hodgkin lymphoma. Biosimilars for rituximab (Rituxan) are currently being developed by various manufacturers, although none have been approved by Health Canada at this time.

In breast cancer specifically, biosimilars are currently being developed for the treatment trastuzumab (Herceptin). These include Ogivri, developed by Mylan pharmaceuticals, Herzuma, developed by Celltrion in partnership with Teva, Trazimera developed by Pfizer, and Kanjinti, developed by Amgen. These biosimilars will be seeking approval for both early-stage and locally advanced or metastatic breast cancer.

Biosimilar development for cancer is ramping up. In addition to the treatments listed here, numerous other manufacturers are exploring bringing new biosimilar treatments to Canada. These new therapies have the potential to dramatically shift the cancer treatment landscape and will have a major impact on how cancer patients will be able to access treatments.

You may want to discuss biosimilar treatments with your healthcare provider. We've shared three questions below that can help you get the conversation started.

**1. Am I being prescribed a biosimilar? If so, why?**

**2. Are biosimilars effective for my condition?**

**3. How will the biosimilar fit into my treatment plan?**

# Who We Are & How We Help

CBCN exists to ensure that patients are supported through information, education and advocacy. Our aim is to ensure that all Canadians diagnosed with breast cancer have access to the best care, regardless of where they live in Canada.

***Information & Education:*** We provide breast cancer patients & families with credible, easy to understand information

- Newly Diagnosed Metastatic Breast Cancer Guide
- Never Too Young: Young Women's Psychosocial Support Handbook
- Digital Navigation Tools
- CBCN.ca

***Giving Patients a Voice:*** We advocate on a variety of issues identified by patients to ensure that decision makers understand & consider the patient perspective

- Digital campaigns on priority issues
- Comprehensive reports that highlight the lived experience of patients

***Connection:*** We connect patients and families with resources, research, breast cancer related events, and each other

- A blog that shares the latest research, patient stories and information for a better quality of life
- E-newsletter to keep up on the latest CBCN resources
- Social media campaigns that encourage dialogue and engagement
- In-person events that provide face-to-face connection

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