Biosimilars

AND THEIR ROLE IN CANCER TREATMENT

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Biosimilars and Their Role in Cancer Treatment

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Biosimilars introduce competition into the drug development process, which can lead to cost savings for patients and spur the development of new treatments.

Overview of Biosimilars

When chemical-based drugs are approved by the U.S. Food and Drug Administration (FDA), the company that developed the drug is given a patent—the exclusive right to produce and market the specific drug for a set number of years. After the patent expires and after FDA approval, other companies are allowed to produce and market drugs with the same chemical make-up. In all important ways, these drugs—called generics—are the same as the original.

Other medications called biologics are derived from a living system, such as a microorganism, plant or animal. Most biologics are very large and complex mixtures of molecules that are not easily identified or characterized, and are produced using cutting-edge technologies.

Biologics are also approved by the FDA and given a patent, and other companies are allowed to compete once that patent expires. However, those competing products (called biosimilars) have allowable differences because they are made from a living organism.

Although they are not an exact copy, biosimilars are expected to produce the same clinical result as the original product, and have no clinically meaningful differences in terms of safety, purity and potency.

Biologics include a wide range of products such as blood and blood components, vaccines, hormones and allergens (anti-allergy medications). Monoclonal antibodies are an especially important biologic; they are used in the treatment of many conditions, including breast cancer, lymphoma, rheumatoid arthritis, psoriasis, ulcerative colitis and Crohn's disease.

The first biosimilar, filgrastim-sndz (Zarxio), was approved by the FDA in 2015. Both filgrastim-sndz and the original product, filgrastim (Neupogen) are bone marrow stimulants, which can help the body make white blood cells after cancer treatments.

The era of biosimilars has just begun, as the patents of many biologics are set to expire in the coming years.

The Approval Process for Biosimilars

The Biologics Price Competition and Innovation Act of 2009 (BPCI Act) was signed into law in March 2010 as part of the Affordable Care Act. The BPCI Act created an abbreviated approval process for biosimilars, the goal of which is to demonstrate the biosimilarity between the proposed product and the original product, not to independently establish the safety and effectiveness of the proposed product.

A "totality of the evidence" approach is taken by the FDA in evaluating biosimilars for approval. The results from clinical trials are important, but findings from research conducted prior to clinical trials is also considered.

Once a biosimilar is approved for use by the FDA, it can be approved for additional indications (conditions) based on a concept called "extrapolation of data." If the data collected on the biosimilar in preclinical work shows the same clinical result as the original product (the biologic), additional clinical trials do not have to be conducted.

For instance, the clinical trial for the biosimilar filgrastim-sndz studied its effectiveness and safety in a clinical trial whose participants were being treated for breast cancer. When approval was granted by the FDA for filgrastim-sndz, it was as a bone marrow stimulant for the same five indications approved for the original product, filgrastim:

- Patients with cancer receiving myelosuppressive chemotherapy (treatment that stops or slows the growth of blood-forming cells in the bone marrow)
- Patients with acute myeloid leukemia receiving chemotherapy
- Patients with cancer undergoing bone marrow transplantation
- Patients undergoing autologous peripheral blood progenitor cell collection and therapy (a method of replacing blood-forming stem cells destroyed by cancer treatment)
- Patients with severe chronic neutropenia (abnormally low count of a type of white blood cell)

Biosimilars Used in the Treatment of Cancer

Including filgrastim-sndz, there are currently sixteen biosimilars approved by the FDA for use in the treatment of cancer.

2017

- **Bevacizumab-awwb (Mvasi),** a biosimilar to bevacizumab (Avastin), for the treatment of five types of cancer:
  - Non-squamous non-small cell lung cancer (NSCLC)
  - Metastatic colorectal cancer (mCRC)
  - Glioblastoma
  - Metastatic renal cell carcinoma
  - Persistent, recurrent or metastatic carcinoma of the cervix
- **Trastuzumab-dkst (Ogivri)** for the treatment of HER2-positive breast cancer or HER2-positive gastric cancer. It is a biosimilar to trastuzumab (Herceptin).

2018

- **Pegfilgrastim-jmdb (Fulphila) and pegfilgrastim-cbqv (Udenyca)** to reduce risk of infection during cancer treatment. Biosimilars to pegfilgrastim (Neulasta), both drugs are bone marrow stimulants that can help the body make white blood cells.
- **Filgrastim-aafi (Nivestym)** is a bone marrow stimulant to help the body make white blood cells after receiving cancer medications. It is a biosimilar to filgrastim (Neupogen).
- **Rituximab-abbs (Truxima),** a biosimilar to rituximab (Rituxan) for the treatment of non-Hodgkin lymphoma.
- **Trastuzumab-pkrb (Herzuma),** a biosimilar to trastuzumab (Herceptin) for the treatment of HER2-positive breast cancer.

2019

- **Trastuzumab-dttb (Ontruzant), trastuzumab-qyyp (Trazimera) and trastuzumab-anns (Kanjinti)** for the treatment of HER2-positive breast cancer, HER2-positive gastric cancer or gastroesophageal junction adenocarcinoma. They are biosimilars to trastuzumab (Herceptin).
- **Bevacizumab-bvzr (Zirabev),** a biosimilar to bevacizumab (Avastin) for the treatment of six types of cancer:
  - Non-squamous non-small cell lung cancer (NSCLC)
  - Metastatic colorectal cancer (mCRC)
  - Glioblastoma
  - Metastatic renal cell carcinoma
  - Persistent, recurrent or metastatic carcinoma of the cervix
  - Ovarian cancer
- **Rituximab-pvvr (Ruxience),** a biosimilar to rituximab (Rituxan) for the treatment of non-Hodgkin lymphoma.
- **Pegfilgrastim-bmez (Ziextenzo),** a biosimilar to pegfilgrastim (Neulasta) to reduce risk of infection during cancer treatment.

2020

- **Pegfilgrastim-apgf (Nyvepria),** a biosimilar to pegfilgrastim (Neulasta) to reduce risk of infection during cancer treatment.
- **Rituximab-arrx (Riabni),** a biosimilar to rituximab (Rituxan) for the treatment of non-Hodgkin lymphoma.

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

The Role of Pharmacists in Your Cancer Treatment Journey

Pharmacists are highly accessible members of the health care community. While pharmacists are often employed by independent or chain drug stores, they also work in clinics, hospitals and specialty pharmacies (organizations which manage the dispensing, reimbursement, case management and other services specific to medications for complex or chronic conditions).

Regardless of the type of medicine that a doctor prescribes, pharmacists help people by:

- **Explaining how the medication works.** Your doctor or another member of your health care team may have reviewed the ins-and-outs of the medication when you received your prescription, but hearing the information more than once is helpful—especially at what can be a stressful time.
- **Reinforcing how the medication is to be taken.** For example, some medications should be taken with meals; others should be taken on an empty stomach. If the medication is self-administered via an injection, the pharmacist can explain the proper injection technique.
- **Reviewing what side effects might occur.** This information is provided in the Package Insert (PI) that accompanies the medication, but it can be valuable to hear it explained in everyday language. The pharmacist can also monitor any side effects you may experience and offer guidance (in collaboration with your health care team) on possible ways to relieve the symptoms these side effects may cause.

- **Explaining what your insurance covers.** An insurer may require that a generic (or biosimilar) version of the drug be dispensed, if one exists. When possible, contact your insurance company prior to your doctor visit and print out the preferred drug list. Your physician can then prescribe the version of the medication that is covered, or start the prior authorization process immediately. Your pharmacist can help explain any differences between the original drug and the covered drug, including any out-of-pocket cost implications.
- **Ensuring patients take their medication as prescribed.** Pharmacists can provide tips to help you take your medication as prescribed, such as using a pill sorter to stay organized, and signing up for automated refill reminder calls or text messages from the pharmacy. They may also suggest that you download a medication reminder app for use on your smart phone or tablet. Many of these apps are available for free or at a small cost.
- **Recommending financial resources.** There are a number of financial aid organizations and patient assistance programs available to help patients with their out-of-pocket expenses. Your pharmacist can be a good source of information about these resources.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan.

There are certain side effects that may occur across different treatment approaches. Following are tips and guidance for managing these side effects.

Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, contact a member of your health care team.
- Choose foods that contain soluble fiber, like beans, oat cereals and flaxseed, and high-pectin foods such as peaches, apples, oranges, bananas and apricots.
- Avoid foods high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Be as physically active as you can. Taking a short walk an hour or so before meals can help you feel hungry.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.

There are also prescription medications that may help, such as modafinil. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

Managing Pain

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication to determine if they are safe and to make sure they will not interfere with your treatments. Many pain medications can lead to constipation, which may make your pain worse. Your doctor can prescribe medications that help to avoid constipation.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.

Bone Loss

Some therapies can cause bone loss, which increases the risk for osteoporosis (a condition in which bones become weak and brittle, leading to a higher risk of fracture). Talk with your health care team about how exercise and changes in your diet may help keep your bones healthy. It's also important to talk to your doctor about the medications available for bone health:

- Bisphosphonates such as zoledronic acid (Zometa and others) slow the process by which bone wears away and breaks down. These medications belong to a class of drugs called osteoclast inhibitors.
- RANK ligand inhibitors block a factor in bone development known as RANK ligand, which stimulates cells that break bone down. By blocking RANK ligand, these drugs increase bone density and strength. So far, the only drug approved in this class is denosumab (Xgeva, Prolia). Like bisphosphonates, RANK ligand inhibitors are a type of osteoclast inhibitor.

Communicating With Your Health Care Team

As you manage your cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurses, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with symptoms related to your illness or treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, you should ask your most important questions first.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person who accompanies you can serve as a second set of ears. They may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, ask if you can use it to take notes. Writing notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your oncologist and oncology nurse are essential members of your health care team, but there are other health care professionals who can help you manage your care:

- Your primary care physician should be kept updated about your cancer treatment and any test results.
- Make sure your oncologist knows of any other medical conditions you have, or any pain you are experiencing, so that they can consult with your primary care physician or your specialist if needed.
- Your local pharmacist is a great source of knowledge about the medications you are taking; have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions. (See the section "The Role of Pharmacists in Your Cancer Treatment Journey" for additional information.)

Remember, there is no such thing as over-communication. Your health care team wants to know about how you're feeling overall, which includes your level of pain, your energy level, your appetite, and your mood and spirits.

Cancer*Care's* Free Support Services and Programs

It can be very difficult to receive a diagnosis of cancer, and adjusting to the necessary changes in your life can be challenging.

Cancer*Care* can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and provide information on support groups and other resources.

To learn more about how Cancer*Care* helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network, composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q: What is bioequivalence and how does it relate to the FDA's approval of generics and biosimilars?

A: Bioequivalence is the primary factor in the FDA's approval of generic (chemical-based) drugs. It means that the generic drug delivers the same amount of active ingredient(s) to the targeted cancer cells as does the original brand-name drug. Although the approval process of biosimilars differs from that of generics, clinical trials must prove bioequivalence—that the biosimilar has no clinically meaningful difference when compared to the original biologic drug.

Q: Does Medicare cover biosimilars?

A: Medicare Part D (prescription drug coverage) has its own list of covered drugs, which is called a formulary. If the original drug (the biologic) is covered under the formulary of the drug plan, the biosimilar will also typically be covered. This is because the biosimilar has been approved by the FDA for the sameindication(s) as the biologic. Additionally, a biosimilar is generally less expensive than the biologic.

Q: Are the side effects for biosimilars the same as for the original biologic?

A: As biologics and biosimilars are bioequivalent, sharing the same efficacy (effectiveness) and safety profile, the potential side effects are the same or very similar.

Q: I am being treated with a biologic therapy. If a biosimilar becomes available, will I be automatically placed on it?

A: Standard medical practice is for your doctor to discuss the potential move from any biologic drug to its biosimilar; there would not be an automatic change. However, a change should be strongly considered, as biosimilars are as effective as the original biologic drug, have the same safety profile and may be considerably less expensive.

Resources

CancerCare®
800-813-HOPE (800-813-4673)
www.cancercare.org

American Cancer Society
800-227-2345
www.cancer.org

Cancer.Net
Patient information from the American Society of Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute
800-422-6237
www.cancer.gov

Cancer Support Community
888-793-9355
www.cancersupportcommunity.org

National Coalition for Cancer Survivorship
877-622-7937
www.canceradvocacy.org

CLINICAL TRIALS WEBSITES

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