

PHARMACEUTICALS

MEDICAL INNOVATION: NEUPOGEN (PHARMACEUTICAL: BIOLOGICALS)

Physicians: Janice Gabilove, Jeffrey Crawford

Industry: Amgen (George Rathmann, Dan Vapnek, Philip Whitcome)

Situation

A dangerous form of cancer treatment

Cancer is a disease in which cells grow abnormally and often uncontrollably in various organs and areas of the body. It is caused by a range of internal and external factors that are difficult to identify. According to the American Cancer Society, the disease is the second-leading cause of death in the U.S. each year, after heart disease, killing over half a million Americans of all ages. More than 1.5 million new cases of cancer are diagnosed annually in the country, and the disease costs over \$100 million in direct medical expenditures each year.

Chemotherapy represents one of the main forms of treatments for many types of cancer. It involves the use of various drugs and chemical agents to stop cancerous cells from growing in the body. Unfortunately, in addition to attacking cancerous cells, chemotherapy also kills healthy cells and lowers a patient's white blood cell count, thereby weakening the body's immune system and increasing the risk of dangerous infections. For this reason, many patients who are good candidates for early-stage treatment of their cancer often decided that the promise of chemotherapy is not worth the risk and side effects.

Physician-Industry Collaboration

Cracking the code of white blood cell production

In the early 1980s, a small biotechnology in southern California, Amgen, was hard at work on a number of promising cancer treatments. Scientists at the company studied the production of neutrophils, which are the most common type of white blood cells in the body and critical to the body's immune system. Chemotherapy patients often suffer from neutropenia, or a dramatic lowering of these types of cells in the blood.

After several years of research led by a strategic team including George Rathmann, Dan Vapnek and Philip Whitcome, the Amgen team became the first to decode the chemical characteristics of so-called human granulocyte colony-stimulating factor, or G-CSF, a type of protein critical to the production of neutrophils. With the chemical formula in place, Amgen was soon able to reproduce G-CSF synthetically and begin testing of the compound in animals.

Once the compound was shown to be safe in animal testing, G-CSF then underwent critical human testing in clinical trials, including at the hands of Janice Gabilove of Memorial Sloan-Kettering Cancer Center and Jeffrey Crawford of Duke University Medical Center. Their research demonstrated that administering G-CSF to patients prior to and following chemotherapy and bone marrow transplants allowed them to maintain much higher white blood cell counts and made them much less susceptible to infections and complications through acute neutropenia. Amgen received approval from the U.S. Food and Drug Administration (FDA) for G-CSF, known as Neupogen (Filgrastim) for use in cancer patients in 1991.

Innovation Benefits

A revolution in chemotherapy and bone-marrow treatment

Since that time, Neupogen has revolutionized the way cancer patients are treated with chemotherapy and bone marrow transplants, making both far less risky and well-tolerated. Patients who use Neupogen are also able to undergo more aggressive and heavier chemotherapy treatments, since their white blood cell levels remain sufficiently elevated by the drug.

Amgen has since produced a second-generation form of Neupogen known as Neulasta that is able to remain in the body for much longer and only requires one dose per cycle of chemotherapy, instead of daily injections. Both drugs have made a difference to millions of cancer patients worldwide, and they are also used in stem cell treatments and for people exposed to high amounts of radiation because of their ability to stimulate the growth of white blood cells.

Patient Benefits

'The drug helped save my life'

Anthony Herrera was a famous actor who played the character James Stenbeck on CBS's *As the World Turns* for a span of close to thirty years. In 2005, Herrera described his courageous battle with a form of cancer known as a lymphoma during [testimony](#) at a U.S. Senate hearing on research into stem cell treatments:

In January 1997 at New York Hospital, I was diagnosed with mantle cell lymphoma and was told, "This disease will kill you. There is nothing we can do. You are going to die." That night I debated whether to put my .38 Smith & Wesson to my temple and pull the trigger, or saddle up. I pondered each option.

I then went to Sloan Kettering where I was told, "We are going to work hard and hope for the best." They had a new protocol for mantle cell treatment developed with a hospital in Paris. I was the fifth patient in the United States to undergo this regimen, massive amounts of chemotherapy and total body irradiation to kill lymphoma cells and take my immune system to zero."

On August 1, 1997, I received an autologous stem cell transplant; I injected myself with a drug called Neupogen every day. My mouth was full of sores. My skin was gray. I had no hair, no fingernails, no toenails, but I was found to be in remission. One year later, August 15, 2000, a CT-scan showed that I had relapsed. The disease was back. I was told [that] without treatment [I would] die in less than 12 months and that another donor lymphocyte infusion could kill [me]. There was a small amount of disease, so I had time to think.

Six weeks later, I saddled up and requested a CT-scan. At this juncture, medical history was made. This scan showed less disease than six weeks before, which meant that my new immune system had started fighting the lymphoma without chemotherapy, without drugs, without radiation. My new immune system was taking out the cancer, my new immune system and my bone marrow created by donor stem cells [produced with the aid of Neupogen.] The drug...helped save my life.