PHARMACEUTICALS

MEDICAL INNOVATION: GLEEVEC (PHARMACEUTICAL: SMALL MOLECULE)

Physician: Dr. Brian Druker
Industry: Novartis, Dr. Nicholas Lydon, Dr. Elisabeth Buchdunger and Dr. Juerg Zimmerman

Situation

No good options for treating a deadly cancer

Chronic myelogenous leukemia (CML) is a type of cancer diagnosed in about 4,500 Americans each year. It usually occurs in people who are middle-aged or older, although it can also occur in children. CML causes too many white blood cells to be made in the bone marrow, the spongy tissue inside the large bones in the body that makes red and white blood cells and platelets, each of which perform specific and important functions in the body.

Normally bone marrow cells called blasts mature into these three types of blood cells. In the early phase of CML, the body accumulates too many white blood cells, but these cells mature and function properly, and symptoms are not serious. Without treatment, however, the disease advances over a period of several years to a point of "blast crisis," in which many immature blood and bone marrow cells accumulate – a condition that rapidly causes death.

As recently as a decade ago, CML patients had no good options to treat their disease – either a highly risky bone marrow transplant for which few patients qualified, or chemotherapy treatment that prolongs survival only by an average of two years, with debilitating side effects.

Physician-Industry Collaboration

A passion for finding a cure

In the early 1980s, a young oncology fellow named Dr. Brian Druker began looking for a better alternative to treating CML. He zeroed in on a family of enzymes called tyrosine kinases, and for five years studied their effect on cancer in animals. Through his expertise in the enzymes, Druker was introduced to Dr. Nicholas Lydon at Novartis who was interested in developing inhibitors of the enzymes, and was already working with two of his Novartis colleagues, Dr. Elisabeth Buchdunger and Dr. Juerg Zimmerman, on the project. Druker suggested to Lyndon and his team that CML might be the first disease where an approach targeting these enzymes could be validated. Novartis initially had other enzymes in mind, but at Druker's suggestion, Lydon added tyrosine kinases to the company's research program, and Druker began working with Lydon full-time on the link between CML and the enzymes.

STI571 was one of the specific enzyme inhibitors that Lyndon arranged for Druker to work on, and Druker discovered that the compound killed CML cells while sparing normal cells. For the next four years, Lydon and Druker worked to keep STI571 on the development track at Novartis and in 1998, the first clinical trial of the drug – now known as Gleevec (imatinib) – was launched. As doctors gradually increased doses of the drug in CML patients who no longer responded to chemotherapy, they noticed dramatic responses. Gleevec restored normal blood counts in 53 out of 54 of the patients, a response rate rarely seen in cancer with a single agent.

After one year on the medicine, 51 of the 53 were still doing well and most reported few side effects.

Innovation Benefits

Targeting the cancer and leaving healthy cells alone

In the decade since Gleevec received FDA approval in 2001, the drug has dramatically brightened the outlook for patients with CML. Most patients treated with the drug achieve full remission of their disease, and the five-year survival rate of patients on the drug is close to 90 percent. Unlike traditional chemotherapy, Gleevec targets the genetic abnormality that causes the cancer and leaves healthy cells alone, thereby causing far fewer side effects. And the drug is very easy to administer -- just a simple pill daily, with no need for infusions or injections.

Several clinical trials with Gleevec are already under way to find other tumors that might respond to the drug, and it has shown to be an effective therapy for patients with gastrointestinal stromal tumor (GIST) and hypereosinophilic syndrome (HES). And, given the success of Gleevec and the recent explosion of powerful molecular technology now available in cancer research, scientists are searching intensively to discover correct targets in other cancers as well.

Patient Benefits

"My whole life in front of me"

As described by PhRMA's Innovation.org, after being diagnosed with CML in 1998, Suzan M. began her battle against the disease with a combination chemotherapy of hydroxyurea and interferon. She began to experience debilitating side effects, including depression, weight loss, hair loss, and fatigue so severe she had to stop working.

Suzan had heard about a clinical trial involving a new drug called Gleevec, but, at that time, the supply was only adequate for the limited number of patients enrolled in a Phase I Study. Knowing what a difference the drug might make for her and others, Suzan circulated a petition to members of an Internet support group, collecting some 4,000 signatures and sent the petition, along with a letter, to the Chief Executive Officer of Novartis. In the letter, she explained how encouraged CML patients were about the data generated by the trials and asked that the studies be expanded so that more patients could participate.

In fact, the company had already assigned the highest priority to the development of Gleevec and was already expanding the larger clinical trials to test the drug. Suzan and thousands of other CML patients gained access to Gleevec through the trials.

Suzan's cancer is now in remission and she is now studying to be a molecular biologist. "One minute I was looking at death," she said. "The next, I was looking at my whole life in front of me!"