MEDICAL INNOVATION: FLUOROURACIL (PHARMACEUTICAL: SMALL MOLECULE)

Physician: Dr. Charles Heidelberger
Industry: Hoffmann- La Roche

Situation

One of the leading causes of cancer-related deaths

Cancer of the colon, otherwise known as colorectal cancer, is the third most commonly diagnosed cancer in the world. Over a million new cases of colorectal cancer are diagnosed each year globally, and over half a million people die from the disease annually. According to the American Cancer Society, colorectal cancer is one of the leading causes of cancer-related deaths in the United States.

There is no single cause of colon cancer. Almost all colon cancer starts in glands in the lining of the colon, and most begin as noncancerous (benign) polyps, which slowly develop into cancer over time. Today, however, early diagnosis can often lead to a complete cure, through a combination of surgery, drug regimens (chemotherapy) and radiation treatment.

Physician-Industry Collaboration

Fighting the growth of tumors through drug innovation

In the early 1950s colon cancer patients had few options but invasive surgery to try to remove cancerous tumors, and often the surgery failed to prevent a spread or recurrence of the disease in the near- and medium-term. A young researcher at the University of Wisconsin's McArdle Laboratory, Charles Heidelberger, set to work to change that.

Heidelberger had a keen interest in the biosynthesis of nucleic acids in tumors, and the development of drugs that could prevent the spread of cancers as part of chemotherapy treatments. In a series of experiments with mice, he reasoned that introducing a fluorine atom into the structure of a pyrimidine known as uracil could prevent the growth of certain tumors by interfering with the synthesis of DNA and RNA.

Following his discovery, Heidelberger enlisted the cooperation of Robert Duschinsky at the drug company Hoffman-LaRoche to perfect the synthesis of the new substance known as 5-fluorouracil so that tests on its therapeutic effects on tumors could be expanded. The clinical trials, conducted at the McArdle Laboratory, demonstrated the clear promise of the new drug, and fluorouracil was approved for chemotherapeutic treatment of several human malignancies, particularly cancer of the colon.

As a result, over the next half century, fluorouracil quickly became an important weapon in fighting cancer, particularly pre- and post-surgery for colon cancer, as well as in other cancers, including breast and certain head and neck cancers.

Innovation Benefits

Helping cure colon cancer altogether

For several decades, post-surgery chemotherapy regimens based on fluorouracil have been a standard part of the treatment for high-risk mid- to late-stage colon cancer. Many clinical trials have shown that fluorouracil regimens not only improve overall survival; they also reduce the high risk of recurrence within the first two years after surgery.

Fluorouracil can even help cure patients of the disease altogether. A 2009 study showed that, five years after treatment with fluorouracil-based adjuvant chemotherapy, the risk of tumor recurrence dropped to 1.5 percent, and dropped again to 0.5 percent by eight years after treatment. Instead of delaying recurrence, "[Fluoroutracil]-based chemotherapy truly eradicates the disease and results in long-term cure in some patients," explained Dr. Daniel Sargent, professor of biostatistics and oncology at the Mayo Clinic and lead author of the study.

Patient Benefits

Beating her cancer back

As she described to the Cancer Information Center, After years of suffering from persistent gastrointestinal problems and flu-like symptoms, 45-year-old Jeannie T. decided to see her general practitioner about the condition. Despite being in good general health, a CT scan revealed she suffered from mid-stage colon cancer that threatened to spread quickly to other areas of her body.

After consulting a surgeon who was well-known for this type of procedure, she had a colon resection, followed by a six-month course of chemotherapy with fluorouracil.

Now, 16-months from her last chemotherapy treatment, Jeannie appears to have beat her cancer back; there are no signs of a recurrence.

"I am healthier and feel better than I have in 10-15 years, which leads me to wonder how long the cancer had been lying dormant yet still dragging my system down," she said. "I am extremely lucky to have caught my tumor in time…I recommend that anyone feeling the same way I did get checked out as soon as possible so they can get treated before it's too late!"