



Recent findings mean renewed hope for people with soft tissue and bone sarcomas, and a major impact on the treatment of GIST.

Bone, Soft Tissue, and Gastrointestinal Stromal Tumors

A Report on the Latest Research and Treatments from ASCO—the American Society of Clinical Oncology

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Gastrointestinal Stromal Tumor (GIST)

For people with rare cancers of the upper intestinal tract called **gastrointestinal stromal tumors (GISTs)**, treatment options used to be limited. Chemotherapy rarely worked against the cancer, and radiation was not very effective either. It usually came down to surgical removal of the cancer.

However, in 2002, researchers reported that a drug called imatinib (Gleevec) shrank tumors in about 50 percent of patients with GIST. Moreover, the tumors continued to grow in only about 15 percent of patients who used imatinib. The drug works by preventing substances called **receptors** from sending signals to cancer cells to grow and multiply.

The findings on imatinib had a tremendous impact on GIST treatment. The research was among the first and most important demonstrations of a new class of drugs that target cancer cells primarily, while sparing healthy tissues and causing few side effects. The discovery energized the entire field of cancer research.

But although imatinib slows or stops cancer growth when people first take it, after about two years more than half the patients become resistant to the drug. Researchers suspect that once cancer cells are exposed to the drug for a period of time, cancer cells are able to adapt (that is, become resistant to it), and continue growing. During the past several years, researchers have been looking at different ways to treat imatinib-resistant GIST.

SURGERY AND GIST

In a German study, more than 100 people underwent surgery to remove GIST tumors. All of the patients had been treated with imatinib for at least three months. Their tumors were either shrinking in response to the drug, or growing despite it.

A year after the surgery, a significant number of patients had survived, with no growth of the cancer. In addition, the surgery proved to be relatively safe.

In a separate study, French researchers compared two groups of people with advanced GIST that had **metastasized**—that is, spread from the initial tumor to another part of the body. One group received imatinib alone, while the other group underwent surgical removal of the **metastases** (new, distant tumors) followed by treatment with imatinib.



After about two years, a slightly greater percentage of patients treated with imatinib alone had survived, compared with those treated with surgery and the drug. Most of the people treated with surgery had GIST tumors in the area of the intestine called the small bowel. More research is needed to see whether the study's results hold true among patients with tumors affecting different areas of the intestinal tract.

SUNITINIB (SUTENT) AND GIST

Researchers have identified a new drug called sunitinib (Sutent), which appears to work on GIST cancer cells that have become resistant to the drug imatinib. Sunitinib attacks several mechanisms in cancer cells, cutting off their blood supply and blocking their ability to grow.

According to recent study of nearly 100 people with advanced GIST who had used imatinib, those with certain genetic mutations were most likely to benefit from treatment with sunitinib. After sunitinib treatment, patients with the genetic mutations survived more than a year longer than those who

What's New, What's Important

- In a German study, surgery proved relatively safe and effective in the treatment of people with gastrointestinal stromal tumors (GIST) that resist treatment with the drug imatinib (Gleevec).
- The new drug sunitinib (Sutent) appears to work on GIST cancer cells that have become resistant to imatinib. Tailoring treatment with the drug to a person's genetic profile may increase its effectiveness.
- A unique new chemotherapy called trabectedin (Yondelis) benefitted a small group of people with myxoid liposarcomas—the most common form of cancers arising from fat tissue.
- An experimental drug called AP23573 holds promise as a treatment for sarcomas—forms of cancer that arise in the bones and soft tissues, such as fat and muscle.

did not have the mutations. The findings suggest that tailoring treatment to a person's genetic profile may increase the treatment's effectiveness.

Trabectedin (Yondelis) and Myxoid Liposarcomas

A unique new chemotherapy made from a marine substance benefitted a small group of people with **myxoid liposarcomas**—the most common form of cancers arising from fat tissue. The drug, which is called trabectedin (Yondelis), binds to cancer cells' **DNA**—the genetic material inside the cell. This can either destroy the cell or interfere with its ability to multiply.

For the clinical trial, researchers examined the records of 44 people with advanced myxoid liposarcomas who were treated with trabectedin every three to four weeks. This study showed

that after about 14 months, approximately 85 percent of patients' tumors had disappeared, shrunk, or stopped growing.

Research with the promising new drug is ongoing in people with liposarcomas and other types of cancer.

On the Horizon: AP23573 for Bone and Soft Tissue Cancers

An experimental drug holds promise as a treatment for **sarcomas**—forms of cancer that arise from the bones and soft tissues, such as fat and muscle. Called AP23573, the drug blocks the actions of **mTOR**—a substance that acts like a master switch, turning on a number of different reactions in cells that promote cancer growth.

In a clinical trial, the new drug was given to more than 200 people with various types of sarcomas that had continued growing despite extensive treatment. The drug benefitted 25 percent of the patients, either shrinking the cancer or halting its spread. What's more, only a small percentage of people who took the drug experienced severe side effects.

Participants with soft tissue tumors did not experience any cancer growth for 15 months, overall. This effect was striking, given that in previous studies testing other drugs, soft tissue sarcomas have resumed growing within seven or eight months, on average.

The findings offer renewed hope for people with soft tissue and bone sarcomas—cancers for which few new drugs have been introduced during the past 15 to 20 years. Research with AP23573 is ongoing.