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HEADLINE: Drug Progress on Hard-to-Treat Cancers Is Cited

BYLINE: By Robert Langreth and Michael Waldholz, Staff Reporters of The Wall Street Journal

BODY:

Cancer researchers presented promising early test results of several drugs that exploit new insights into the biology of cancer cells to attack some of the hardest-to-treat cancers.

At a scientific meeting in Washington yesterday, researchers presented early-stage human-trials results of a new gene-based cancer drug from AstraZeneca PLC of Britain.

The drug is one of several in development designed to block a protein called EGF receptor that is overabundant in many cancers of the lung, breast, head and neck, and prostate. The test results indicated the drug may stabilize difficult-to-control tumors, and, in some cases, shrink them significantly.

"We were able to show that a laboratory concept has relevance to the care of patients," said Mark Kris, a lung-cancer specialist at Memorial Sloan-Kettering Cancer Center in New York who helped conduct the trial.

The drug, brand-named Iressa, inhibits the activity of EGF receptor, a protein that sits on the surface of cancer cells and receives messages from growth hormones telling a cell to divide. In some cancers, the tumor cells overproduce copies of EGF receptor, which helps lead to the aberrant and relentless growth seen in cancer cells.

At the science meeting, researchers at Memorial Sloan-Kettering reported that, in a test of 64 patients with advanced stages of cancer, the drug was able to stabilize or reduce tumor size in 15 test subjects. In four patients with lung cancer, one of the most difficult of all cancers to treat, the drug caused major tumor shrinkage. All four patients are still responding to the drug after several months, the researchers said. This number of responses is considered significant, given the extremely low response rate to most treatments for advanced lung cancer.

Researchers at AstraZeneca hope the drug will have an even more powerful effect when combined with standard chemotherapy drugs or radiation. The researchers said Iressa doesn't appear to cause the kind of severe nausea and other toxic effects often produced by standard chemotherapy; its side effects are an acne-like facial rash and diarrhea.

George Blackledge, medical director of oncology for AstraZeneca, said that largescale human tests will begin early next year.

AstraZeneca is competing with several other companies working on EGF receptor blockers, including Pfizer Inc. and ImClone Systems Inc., a small New York biotechnology company.

Last May, researchers at M.D. Anderson Cancer Center in Houston reported that an injectable protein against EGF receptor made by ImClone also produced an effect in difficult-to-treat head and neck cancers, when combined with a widely used chemotherapy drug. Imclone is now conducting a large trial of the drug, C225. Pfizer said yesterday at an analyst meeting in New York that its experimental EGF receptor-blocking drug, CP358,774, was in the second stage of human testing for ovarian, lung and head and neck cancer.

At the science meeting in Washington yesterday, the first of its type to be jointly sponsored by the American Association of Cancer Research, the U.S. National Cancer Institute and the European Organization for Research and Treatment of Cancer, researchers also presented promising reports on other cancer-attacking approaches. Several companies are targeting cancer-growth factors, such as tyrosine kinase.

Researchers from the Parker Hughes Cancer Center in St. Paul, Minn. reported results from a small, preliminary test showing that a experimental drug, B43Genistein, was active in treating patients with acute lymphoblastic leukemia, or ALL, that hadn't responded to standard cancer therapy. The researchers said their early study was the first to show that blocking so-called tyrosine kinase enzymes, which are part of the same cellgrowth signaling pathway as EGF receptor, was useful in treating a leukemia cancer.

A separate report by researchers in Germany working with American Home Products Corp.'s Wyeth-Ayerst Research unit, showed that an experimental agent, CCI-779, was well-tolerated. Of 12 patients treated, the drug was able to reduce tumor size in three patients with kidney cancers that hadn't responded to previous therapy. The drug blocks the action of an enzyme mTOR, that regulates the synthesis of proteins that promote cell division, the researchers said.

Researchers from Symphar SA, a closely held Swiss drug maker, reported that its experimental drug Apomine appears to block tumor growth by inhibiting the action of still another newly found cell-growth protein called FXR. The company is co-developing the drug with publicly traded Ilex Oncology Inc., San Antonio.

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