Experimental drug may boost leukemia survival, without chemo

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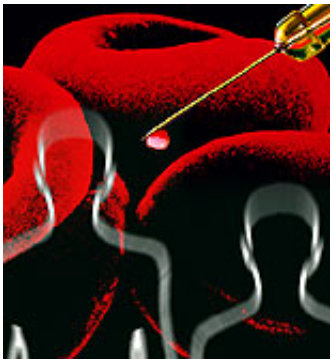

Idelalisib is being fast-tracked for FDA approval for use in patients with chronic lymphocytic leukemia.

(HealthDay)—An experimental drug may extend the lives of people with certain hard-to-treat forms of leukemia and lymphoma—without the need for traditional chemotherapy, according to two studies released Wednesday.

The drug, called idelalisib, targets a specific enzyme on white blood cells known as B cells. Researchers found that for people with certain forms of recurrent blood cancers, the drug substantially extended the time that patients lived with no tumor progression.

One of the trials, of patients with chronic lymphocytic leukemia (CLL), was stopped early because the benefits of idelalisib over standard

treatment became so clear. The drug is now up for expedited review by the U.S. Food and Drug Administration (FDA), for possible approval.

A cancer researcher not involved in either trial called the CLL results "fantastic."

If idelalisib is approved, "I think patients stand to see a tremendous extension in healthy survival," said David Fruman, a professor of molecular biology and biochemistry at the University of California, Irvine.

Fruman co-wrote an editorial published with the studies in the March 13 issue of the *New England Journal of Medicine.*

In one trial, researchers recruited 220 patients with recurrent CLL who could not have conventional chemotherapy for various reasons. Some had other serious health conditions that made chemo too risky and others had suffered too many toxic effects on the immune system from prior chemo rounds.

All of the patients received the standard option for cases like theirs: an IV drug called rituximab, which is less toxic than chemo but only moderately effective at keeping the cancer at bay. Half of the patients also received idelalisib, a pill taken twice a day.

Overall, 81 percent of idelalisib patients saw their cancer regress, compared with only 13 percent of those on standard treatment.

After six months, 93 percent of idelalisib patients were progression-free, versus 46 percent in the comparison group. At one year, 92 percent and 80 percent, respectively, were still alive.

The trial was stopped early last October at the recommendation of an

independent monitoring board, so all of the study patients could start on the drug. The FDA has granted idelalisib "breakthrough therapy" status for CLL, which means the agency will give it a faster-than-normal review for possible approval.

To Dr. Richard Furman, the lead researcher on the CLL study, the big advance is that the treatment requires no chemotherapy—which typically means a drug that affects the body in a systemic way.

"This isn't like chemotherapy," said Furman, an oncologist at NewYork-Presbyterian/Weill Cornell Medical Center in New York City. "This is an effective agent that doesn't damage the rest of the body."

That doesn't mean there are no side effects. So far, diarrhea and skin rash seem to be the main problems, Furman said.

In this study, 40 percent of the patients on idelalisib had what was considered a serious adverse effect, such as fever or pneumonia. But so did 35 percent of patients in the comparison group. Furman said that suggests the problems are largely due to the rituximab or the cancer itself.

CLL is a usually slow-growing cancer of the white blood cells that mainly affects older adults. In the United States, about 15,700 people are diagnosed with CLL each year, and about 4,600 die of the disease, according to the American Cancer Society.

Chemotherapy is the standard treatment for CLL. It often works at first, but most people eventually relapse. Their cancer may become resistant to various chemotherapy drugs, or the toxic effects of those medications may become too much.

Idelalisib is among a new class of drugs called tyrosine kinase inhibitors.

It targets a specific enzyme that helps fuel the growth of cancerous B cells, the type of white blood cell that usually goes wrong in CLL.

That specificity helps explain its effectiveness and relative lack of toxic effects versus chemo, said Fruman, the editorialist.

In the second study, a separate research group tested idelalisib in 125 patients with "indolent" non-Hodgkin lymphoma—another slow-growing form of blood cancer. The patients had all relapsed or not responded to standard treatment, including rituximab in combination with chemotherapy.

The researchers started the whole study group on idelalisib, and 57 percent saw their tumors shrink. Typically, the patients went a year before their cancer began to progress again.

That study was an earlier-stage one, and there was no comparison group. But the results were similar to or better than other treatments for relapsed non-Hodgkin lymphoma, Fruman said.

Gilead, the company developing idelalisib, funded both trials. The company recently submitted an application to the FDA to win approval for indolent non-Hodgkin lymphoma as well. It was granted a standard—not expedited—review.

If the drug is approved for either cancer, Fruman predicted that doctors won't limit it to patients with more advanced disease who cannot have chemo.

"I think doctors will prescribe it earlier in the course of the disease, to avoid chemotherapy," he said.

There are, however, still many unknowns—including the long-term

effectiveness and safety of idelalisib. As far as safety, severe diarrhea could become an issue in the long run, since that's usually a "late-onset" complication, Furman said.

As of now, patients seem to need the drug indefinitely. "The expectation is that it will be a lifelong therapy," Furman said.

No one knows how much the drug will cost. But there is another tyrosine kinase inhibitor, called ibrutinib, that the FDA approved just last month for certain CLL cases. It's priced at more than $90 per pill.

Furman acknowledged that cost could be an obstacle to giving idelalisib earlier on to CLL patients who could have standard chemo. But he argued that if the new tyrosine kinase inhibitors could turn CLL into a "manageable, chronic disease like high blood pressure," it would be worth it.

More information: The Leukemia and Lymphoma Society has more information on blood cancers.