New drug may be best treatment for leukemia yet

TIME

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June 20, 2013 -- Updated 1437 GMT (2237 HKT)

Ibrutinib, seen here, is being considered a breakthrough drug that might one day replace chemotherapy.

STORY HIGHLIGHTS

- The new drug ibrutinib is being called a potential breakthrough in leukemia treatment
- It's currently being tested on tumors that target the body's immune system
- If approved, it could eventually replace chemotherapy

(TIME.com) -- It's called ibrutinib, and it's a potential breakthrough in treating chronic lymphocytic leukemia (CLL) that could leave patients with fewer side effects than chemotherapy.

In research published in the New England Journal of Medicine (NEJM), scientists report that the experimental drug, which differs from broadly acting chemotherapy agents by specifically targeting certain cancer-causing processes, significantly prolongs the life of patients.

Ibrutinib is currently being tested on tumors that target the body's immune system, such as CLL

and mantle cell lymphoma (MCL).

CLL is the second most common form of leukemia among adults in the U.S., and about 15,000 Americans, most of whom are elderly, are diagnosed with the blood and bone marrow cancer every year.


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The drug is the first to bind to and block the activity of a protein known as Bruton's tyrosine kinase (BTK), which plays an important role in helping immune cell tumors, which develop from abnormally growing blood stem cells, to grow.

Once ibrutinib binds to the immune system's B-cells, it prevents tumors growing in these cells

from signaling for the nutrients they need to grow and divide. According to the study, the drug doesn't seem to affect the body's T-cells, as chemotherapy agents do, so patients experience fewer side effects.

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Early work on animals showed that the experimental drug effectively shut down tumor cell division, so the researchers tested the compound on 85 CLL patients who had all tried and failed to respond to at least two other anti-cancer treatments. Some even harbored genetic mutations associated with particularly aggressive forms of CLL that typically lead to death within two years of diagnosis.

The patients were randomized to take one of two different doses of an ibrutinib pill a day. After nearly two years of treatment, 71% of this hard-to-treat group had responded with slower tumor growth, and at 26 months, 75% showed no additional progression of their cancer. At the end of the study period, 83% of the participants were still alive, and most of the patients only complained of diarrhea and fatigue.

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"This is truly a breakthrough drug for CLL. I have been a CLL specialist since 1997, and we have not had a drug like this come into the field yet," says study author Dr. John C. Byrd, the director of the division of hematology at The Ohio State University Comprehensive Cancer Center.

"The most common thing I have heard patients say is that it brings their disease under control and makes them feel how they did before their cancer. I've heard that at least a dozen times."

The scientists and patients were most encouraged by the fact that the the drug helped them to enjoy a longer period of time, on average, in which their tumors remained stable and didn't progress, than they they had while using chemotherapy agents.

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The MCL patients showed similarly positive results. MCL is an aggressive form of non-Hodgkin lymphoma that generally doesn't respond to existing chemotherpay, immune-based treatment or stem cell transplants.

But in a separate study also appearing in NEJM involving 111 advanced MCL patients, about 68% of the participants responded to ibrutinib and 58% were alive after 18 months on the therapy. The response rate was encouraging since the last agent to treat MCL was approved by the Food and Drug Administration (FDA) with a 30% response rate.

That efficacy data, combined with the experimental drug's favorable side effect profile, has some doctors hoping that ibrutinib might one day replace the harsher chemotherapy agents that are currently the standard of care for these cancers.

"With chemotherapy, you get it for a specific period of time because patients cannot tolerate the side effects long term. This is an oral medicine that targets something the leukemia cells are dependent on but the rest of the body isn't," says Byrd.

"People can take a pill once a day and generally they tolerate it well. The side effects are much

less than the chemo or other therapies that would be used in this setting."

Ibutrinib is the first agent to specifically target the BTK pathway, but it's part of a wave of new anti-cancer agents that have been developed to act as more precise, smart bomb medications that destroy just cancer cells while leaving healthy cells intact. That allows them to minimize the often intolerable side effects of harsher drugs like chemotherapy agents, which tend to wipe out both healthy and cancerous cells at once.

"In some situations there have been some medications we have tested where patients have said they would rather not be treated and pass (away) from their leukemia than go through the side effects of their medicine that is not going to cure them," says Byrd.

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Both of the clinical trials, which were sponsored by ibrutinib's developer, Pharmacyclics, involved older adults, who are most often affected by these cancers, so the researchers believe the results should be applicable to most patients diagnosed with these diseases.

The studies also suggest that patients may benefit from longer progression-free survival if they start therapy earlier in the course of their disease.

"Right now, after this drug gets approved, it will likely be used in the setting of relapse initially, but there are ongoing studies that are looking at it for initial therapy. It is something that is especially (beneficial) for elderly patients who do not tolerate chemotherapy well. This will likely replace chemotherapy," says Bryd.

The fact that even patients with the most aggressive types of CLL, which are driven by genetic mutations, responded to ibrutinib also hints that the experimental drug may become an important part of treating these cancers in coming years.

The FDA designated it as breakthrough therapy, and Pharmacyclics and Janssen, who are jointly developing the drug, plan to file a New Drug Application (NDA) with the FDA for the use of ibrutinib to treat B-cell malignancies by 2014.

This article intially published on TIME.com.