Investigational targeted drug induces responses in aggressive lymphomas

April 3 2012

(Medical Xpress) -- Preliminary results from clinical trials in a subtype of lymphoma show that for a number of patients whose disease was not cured by other treatments, the drug ibrutinib can provide significant anti-cancer responses with modest side effects.These results were presented as part of the opening plenary session at the American Association of Cancer Research (AACR) Annual Meeting 2012 on April 1 by researchers at the National Cancer Institute (NCI), part of the National Institutes of Health, and colleagues.

Lymphomas are the fifth most common form of cancer. They are caused by an abnormal proliferation of white blood cells, can occur at any age, and are often marked by lymph nodes that are larger than normal, fever, and weight loss. Diffuse large B-cell lymphomas (DLBCL), which were studied in this trial, are aggressive cancers that grow rapidly and represent 30 percent to 40 percent of newly diagnosed lymphomas. DLBCL originates from B cells, which play a crucial role in the body's immune response.

There have been no major advances in the treatment of DLBCL in more than a decade. However, important advances have been made in understanding that this disease is comprised of at least three molecular subtypes, each derived from B cells at unique stages in their development. The activated B-cell (ABC) subtype of DLBCL accounts for approximately 40 percent of cases and has the poorest clinical outcome with current therapy.

Recent genetic studies have revealed that chronic activity of receptors that sit on the surface of B cells play an important role in the progression of ABC lymphomas. In normal B cells, these B-cell receptors help the cells recognize infections. In malignant B cells of ABC lymphomas, these receptors provide crucial signals that promote tumor cell survival. Over one-fifth of ABC tumors have mutations that alter the activity of the B-cell receptor. Based on these findings, researchers looked for ways to target B-cell receptor signaling therapeutically. This research identified the enzyme Bruton's tyrosine kinase (BTK) as a key element in the B-cell receptor pathway that is required to maintain the survival of ABC lymphoma cells.

“Our trial is a prime example of precision medicine,” said Louis Staudt, M.D., Ph.D., deputy chief, Metabolism Branch at NCI. “A better understanding of the changes in cancer cells is leading us to what we hope will be more effective treatment strategies tailored to the genetic profile of each patient’s cancer.”

Based on this molecular research, investigators chose to use the drug ibrutinib (formerly PCI-32765), a potent inhibitor of BTK, in their clinical trials. Ibrutinib is an oral, highly specific and irreversible inhibitor of the BTK enzyme. Pharmacyclics Inc., Sunnyvale, Calif., and Janssen Research and Development, L.L.C., Horsham, Pa., are developing the drug to target B-cell malignancies, including various forms of leukemia, lymphoma and multiple myeloma.

In studies led by Staudt and his NCI colleague, Wyndham Wilson, M.D., ibrutinib was first evaluated in a pilot trial at NCI in ABC DLBCL, and is now being evaluated in an ongoing multicenter study in DLBCL. Results from the pilot trial and individual cases from the ongoing trial indicate that the use of the single agent pill form of ibrutinib can elicit major anti-lymphoma effects with minimal side effects.

Participants in these studies were given ibrutinib as a pill at a fixed dose of 560 milligrams daily until the disease progresses. Ibrutinib induced multiple responses including some complete remissions in ABC lymphomas. Remissions were also observed in patients with non-ABC DLBCL, suggesting a broader role for the B-cell receptor pathway in this type of lymphoma. A final analysis will provide additional insights into the safety and efficacy of ibrutinib in the treatment of DLBCL.

“These results illustrate how an understanding of the molecular machinery inside a cancer cell can lead to new therapies which can kill tumor cells while sparing normal cells, thus greatly reducing toxicities for patients,” said Staudt.

More information: To read details about this trial (identifier # NCT01325701), please go to clinicaltrials.gov/ct2/show/NC … cond=lymphoma&rank=5

Provided by National Institutes of Health

Citation: Investigational targeted drug induces responses in aggressive lymphomas (2012, April 3) retrieved 19 April 2024 from https://medicalxpress.com/news/2012-04-drug-responses-aggressive-lymphomas.html