Phase 3 study strengthens support of ibrutinib as second-line therapy for CLL

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In a head-to-head comparison of two Food and Drug Administration-approved drugs for the treatment of relapsed chronic lymphocytic leukemia (CLL), ibrutinib significantly outperformed ofatumumab as a second-line therapy, according to a multicenter interim study published in the OnLine First edition of the *New England Journal of Medicine*. Ibrutinib (Imbruvica) is the first drug designed to target Bruton's tyrosine kinase (BTK), a protein essential for CLL-cell survival and proliferation.

CLL, the most common form of leukemia, causes a gradual increase in white blood cells called B lymphocytes, or B cells. The National Cancer Institute estimates that 15,680 Americans were diagnosed with CLL and 4,580 died from the disease in 2013.

In the current phase 3 trial, patients were randomized to receive once-a-day oral ibrutinib or the anti-CD20 antibody ofatumumab, a drug considered part of the current standard of care for CLL.

Of the 391 patients enrolled to the phase 3 study, 195 were randomized to ibrutinib and 196 to ofatumumab. Median follow-up was 9.4 months and showed that ibrutinib significantly lengthened progression-free survival as a second-line therapy for CLL before anything else is used.

"At median follow-up, 86 percent of patients on ibrutinib had durable response and were continuing treatment with minimal side effects. This is remarkable, especially considering that standard CLL therapies typically produce a 35-40 percent response rate," says John C. Byrd, MD, principal investigator of the study and hematology division director at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James.)

At six months, 83 percent of patients treated with ibrutinib experienced progression-free survival compared to 49 percent of patients on ofatumumab.

"Ibrutinib significantly prolonged progression-free survival, resulting in a 78 percent reduction in the risk of disease progression or death in patients treated with ibrutinib compared with ofatumumab," adds Byrd. "We observed similar progression-free survival results regardless of age, clinical stage or unique factors such as genetic mutation status."

In 2013, Byrd and his team reported findings from a phase 1b/2 study of 85 patients with relapsed CLL patients on ibrutinib in the *New England Journal of Medicine*. Based on positive early response rates, the Data Monitoring Committee recommended patients be given option to switch to the ibrutinib arm of the study. At that time, 29 percent of patients with confirmed disease progression on ofatumumab crossed over to the ibrutinib arm of the study.

At 12 months, the overall survival rate among patients treated with ibrutinib was 90 percent compared to 81 percent in ofatumumab arm. Additionally, 43 percent of patients on ibrutinib achieved partial response to treatment compared with just 4 percent of patients receiving ofatumumab.

"There is no question that ibrutinib far outperforms existing therapies we have for CLL, and we're excited to see this drug improving the outcome for patients who were once considered incurable," says Byrd.

Provided by Ohio State University Medical Center