

Brukinsa Beats Imbruvica for Chronic Lymphocytic Leukemia

The newer targeted therapy zanubrutinib works better and has fewer side effects than the older ibrutinib.

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Next-Generation Targeted Therapy Zanubrutinib Found Superior to Ibrutinib for CLL and SLL

The targeted drug [zanubrutinib \[Brukinsa\]](#) showed superior efficacy with fewer side effects than [ibrutinib \[Imbruvica\]](#) in the first head-to-head comparison between the two drugs among people with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL), according to data presented at the [64th American Society of Hematology Annual Meeting and Exposition](#). The findings were simultaneously published in [The New England Journal of Medicine](#).

CLL and SLL are cancers affecting lymphocytes, a type of white blood cell. While they are generally slow-growing cancers, they often recur after initial treatment, underscoring the continuing need for more effective therapies.

At two years, 79% of patients taking zanubrutinib and 67% of those taking ibrutinib were still alive without evidence of their cancer returning. The study was conducted in patients whose CLL or SLL had not responded to an initial course of therapy or came back after an initial response. The results revealed a particularly dramatic difference in people whose CLL has del(17p) and/or TP53 mutations, mutations present in about one-quarter of relapsed CLL and SLL tumors that are associated with a poorer prognosis.

“Zanubrutinib not only improves the response rate, it also improves progression-free survival compared to ibrutinib, including in our highest risk patients,” said Jennifer R. Brown, MD, PhD, of Dana-Farber Cancer Institute and Harvard University. “Progression-free survival is pretty much our gold standard for efficacy, so our data suggest that zanubrutinib should really become the standard of care in this setting.”

Zanubrutinib is a Bruton tyrosine kinase (BTK) inhibitor that has received Food and Drug Administration (FDA) approval for treating several other types of cancer. Ibrutinib, currently a standard therapy for CLL and SLL, was the first BTK inhibitor to gain FDA approval but can cause significant side effects, including heart rhythm disorders. BTK inhibitors are given orally and work by interfering with a key signaling pathway in cancer cells.

“The BTK inhibitor drug class has been transformative for CLL therapy, but the first-in-class drug ibrutinib has been somewhat hard to tolerate for many patients, with cardiac side effects being one of the biggest problems,” said Dr. Brown. “We found that zanubrutinib caused fewer adverse events, and in particular much less cardiac toxicity.”

The Phase III ALPINE trial enrolled 652 patients with relapsed or refractory CLL or SLL in 15 countries. Half of the participants received zanubrutinib and half received ibrutinib; patients continued taking their assigned treatment until their cancer grew worse or they experienced unacceptable side effects.

At a median follow-up of about 2.5 years, patients taking zanubrutinib had a significantly higher overall response rate and superior progression-free survival, a finding that held across all major predefined subgroups. Participants taking zanubrutinib also experienced fewer adverse events that led to drug discontinuation, dose reduction, or dose interruption. Fatal cardiac events occurred in six of the patients taking ibrutinib and none of those taking zanubrutinib.

The researchers will continue to track outcomes and analyze trends among patient subgroups, including those with del(17p), TP53, complex karyotype and other mutations. Additional studies are planned to assess the use of zanubrutinib in combination with other therapies.

Abstract LBA-6: Zanubrutinib Demonstrates Superior Progression-Free Survival (PFS) Compared with Ibrutinib for Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma (R/R CLL/SLL): Results from Final Analysis of ALPINE Randomized Phase 3 Study

This [news release](#) was published by the American Society of Hematology on December 13, 2022.

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