People With Chronic Lymphocytic Leukemia May Not Need Continuous Treatment

Targeted therapy combinations taken for a year matched an indefinite course of Imbruvica for first-line treatment.

December 11, 2025 By Liz Highleyman

Combination regimens taken for a fixed duration can work as well as a continuous course of a single drug for initial treatment of chronic lymphocytic leukemia (CLL), according to research presented at the American Society of Hematology Annual Meeting and Exposition (ASH 2025) and published in The New England Journal of Medicine.

Study participants treated with Venclexta (venetoclax) and Imbruvica (ibrutinib) or Venclexta and Gazyva (obinutuzumab) for a year had progress-free survival rates comparable to those of people who received an indefinite course of Imbruvica alone. Venclexta is a BCL-2 inhibitor and Imbruvica is a BTK inhibitor, both taken as once-daily pills, while Gazyva is a CD-20 directed monoclonal antibody administered by IV infusion.

The aim of fixed-duration therapy is to allow patients to have extended treatment-free intervals while remaining in remission, said lead investigator Othman Al-Sawaf, MD, PhD, of the University of Cologne in Germany. “In terms of practical implications, when I return from ASH to the clinic, I will be much more confident in using fixed-duration treatments for most patients,” he said.

CLL, the most common type of adult leukemia, involves overproduction of abnormal white blood cells, usually antibody-producing B cells. These malignant lymphocytes can crowd out normal blood cells, leading to low blood cell counts, increased susceptibility to infections and other complications. Chemotherapy and targeted therapies can put CLL into remission, but relapse is common.

The Phase III CLL17 trial (NCT04608318) enrolled 909 previously untreated CLL patients. About 68% were men and the median age was 66 years. They were randomly assigned to one of the three regimens. Patients assigned to Venclexta plus Imbruvica received a lead-in of three 28-day cycles of Imbruvica followed by 12 cycles of both medications. Those assigned to Venclexta plus Gazyva received both drugs for six cycles followed by six additional cycles of Venclexta alone. Those assigned to Imbruvica monotherapy were treated until they experienced disease

progression or intolerable side effects.

In a planned interim analysis, three-year progression-free survival rates were 79% with Venclexta plus Imbruvica, 81% with Venclexta plus Gazyva and 81% with continuous Imbruvica monotherapy, showing that the two fixed-duration combinations were noninferior to indefinite treatment with Imbruvica alone. Three-year overall survival rates were 96%, 92% and 96%, respectively.

Minimal residual disease (MRD)—a measure of remaining malignant cells after treatment—was undetectable in peripheral blood in 47% of people in the Venclexta plus Imbruvica group and 73% of those in the Venclexta plus Gazyva group, but none of those treated with Imbruvica alone. Undetectable MRD rates in bone marrow were 40%, 62% and 0%.

Results were more variable for people with certain high-risk mutations such as TP53 alterations (8% of the study population). For these patients, continuous therapy may still be a better approach, Al-Sawaf acknowledged. The Venclexta plus Gazyva regimen appeared to work best for less fit elderly patients, who may have more trouble tolerating Imbruvica.

All regimens were generally safe. The most common adverse effects across the regimens were infections, gastrointestinal symptoms and low blood cell counts, consistent with prior studies of CLL treatment. Infections were most common in the group treated with Gazyva, and blood and lymphatic disorders were more common among those treated with either combination regimen, while the rate of cardiac adverse events was higher with continuous Imbruvica.

Based on these results, fixed-duration treatment with Venclexta plus Imbruvica or Venclexta plus Gazyva "may therefore represent the preferred treatment option for patients with previously untreated CLL," the researchers concluded.

Al-Sawaf suggested that the findings may also apply to newer and better tolerated BTK inhibitors like Calquence (acalabrutinib) and Brukinsa (zanubrutinib). "The rationale behind this study was really a comparison of treatment paradigms," he said. "I think, generally, this is the first signal of the paradigm of fixed-duration treatments for frontline CLL."

Click here for more news about chronic lymphocytic leukemia.
Click here for more reports from ASH 2025.
