Transcript Details

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CLL17 Trial Insights: Fixed-Duration vs Continuous Therapy in Frontline CLL

Ryan Quigley:
You're listening to *Project Oncology* on ReachMD, and this is an *AudioAbstract.* I'm Ryan Quigley, and today, we'll be taking a look at new results from the phase three CLL17 trial, which directly compared fixed-duration and continuous targeted therapy in patients with previously untreated chronic lymphocytic leukemia, or CLL. These data were presented at the 2025 American Society of Hematology Annual Meeting.

For frontline CLL, clinicians and patients have two different treatment paradigms: continuous BTK inhibition, commonly with ibrutinib, or fixed-duration regimens with venetoclax given over one year. Until now, these approaches had never been studied head-to-head in a randomized trial. CLL17 directly compared these strategies, examining whether fixed-duration regimens can deliver outcomes that are non-inferior to continuous BTK inhibitor therapy.

In this phase three, international trial, 909 patients with untreated CLL were randomized to one of three treatment arms:

- Continuous ibrutinib monotherapy,
- Fixed-duration venetoclax plus obinutuzumab,
- Or fixed-duration venetoclax plus ibrutinib.

The primary endpoint was progression-free survival at three years. Both fixed-duration approaches were evaluated for non-inferiority to continuous therapy.

At a median follow-up of just under three years, progression-free survival was similar across all arms:

- 81.1 percent for venetoclax-obinutuzumab,
- 79.4 percent for venetoclax-ibrutinib,
- And 81.0 percent for ibrutinib alone.

In each comparison, the adjusted confidence interval stayed below the non-inferiority margin.

But progression-free survival is only part of the picture. Complete responses were more common in the venetoclax-based arms, and undetectable minimal residual disease, or uMRD, in peripheral blood followed a similar pattern. 73 percent of patients with venetoclax-obinutuzumab and 47 percent of those with venetoclax-ibrutinib achieved uMRD, but none of the patients receiving continuous ibrutinib did. And in bone marrow, this difference persisted. Keep in mind that the trial didn't assess the clinical implications of uMRD, so these findings should be viewed as descriptive rather than definitive.

Looking at overall survival, three-year rates were above 90 percent in all groups with no meaningful differences, which is what we'd expect at this early follow-up point in frontline CLL.

Subgroup results across IGHV status and other risk features generally tracked with the primary findings. And because only a small number of patients had *TP53* mutations or 17p deletions, any numerical differences in that subset really need to be interpreted with caution.

Safety findings also followed the known profiles of these regimens, with the most common adverse events being infections, gastrointestinal issues, and hematologic toxicities. In the ibrutinib arm, cardiac disorders and second cancers were reported more often. Now, the study wasn't powered for safety comparisons, so these patterns should be interpreted cautiously. But they do add to the body

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of evidence that time-limited treatment may reduce cumulative exposure to BTK inhibitor-related toxicities.

Looking ahead, several questions remain important: how best to manage relapse after fixed-duration therapy, how sequencing might evolve with newer BTK inhibitors, and whether MRD could eventually help individualize treatment duration. For many patients, fixed-duration approaches appear comparable to continuous ibrutinib over the first three years, offering another evidence-based option in frontline care.

This has been an *AudioAbstract* for *Project Oncology,* and I'm Ryan Quigley. To access this and other episodes in our series, visit ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

Reference

Al-Sawaf O, Stumpf J, Zhang C, et al. Fixed-duration versus continuous targeted treatment for previously untreated chronic lymphocytic leukemia: results from the randomized CLL17 trial. Abstract presented at: 2025 American Society of Hematology Annual Meeting; Nov 1-4, 2025; San Diego, CA.

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