Promising Results for Novel Triplet Therapy in High-Risk Chronic Lymphocytic Leukemia

Treatment with Calquence, Venclexta and Gazyva, guided by measurable residual disease, showed positive results for CLL.

December 8, 2024 By Dana-Farber Cancer Institute

Researchers at Dana-Farber Cancer Institute are presenting a promising advance in the treatment of chronic lymphocytic leukemia (CLL), particularly for patients with the high-risk TP53 aberration. This is one of the first studies demonstrating efficacy of time-limited triplet therapy in high-risk CLL.

In this Phase 2 trial, a time-limited regimen of acalabrutinib [Calquence], venetoclax [Venclexta], and obinutuzumab [Gazyva](AVO), guided by measurable residual disease (MRD), showed positive results. The AVO triplet achieved high rates of durable response across a broad population of patients with CLL, and in particular also demonstrated favorable outcomes for high-risk patients with TP53 aberrations.

These findings were presented by Matthew Davids, MD, MMSC, Clinical Research Director in the Division of Lymphoma at Dana-Farber, at the 66th American Society for Hematology (ASH) Annual Meeting and Exposition on December 7 in San Diego, CA, and published concurrently in the Journal of Clinical Oncology.

This study marks an important shift in how CLL patients with high-risk genetics might be treated in the future.

“Our data in patients with CLL with high-risk TP53 aberration complement the data in the AVO arm of the phase 3 AMPLIFY study in patients with standard-risk CLL and suggest that this regimen can be considered as a new standard of care option for a broad population of patients with CLL,” said Davids.

The study evaluated the efficacy and safety of the AVO regimen in 72 patients, including 45 with TP53 aberrant CLL, a group that has traditionally faced limited treatment options. The results demonstrate that 42% of patients achieved complete remission with undetectable MRD in the bone marrow by the 16th treatment cycle, with equivalent results in patients regardless of TP53

status. The study achieved an overall response rate of 98.6%, with most patients experiencing lasting remissions even after completing therapy.

The time-limited AVO regimen provided durable remission in patients with TP53 aberrations, with four-year progression-free survival and overall survival rates of 70% and 88%, respectively. The treatment was well-tolerated, with low rates of cardiovascular toxicity and bleeding complications.

“The AVO triplet was well-tolerated for most patients, suggesting that the regimen can be considered as an option even in older patients and those with co-morbidities who desire a highly effective time-limited treatment with the potential to achieve deep responses leading to durable remissions after completing therapy,” said Davids.

This study fills in a gap in the data from the AVO arm of the Phase 3 AMPLIFY trial (which focused exclusively on patients without TP53 aberrations), extending its applicability to patients with high-risk TP53 aberrations, a group that has shorter remissions after currently approved time-limited targeted therapies for CLL. The durable remissions observed with AVO, coupled with the favorable safety profile, suggest that this regimen represents a promising new treatment option for this challenging patient population. These findings lay the groundwork for future randomized trials to further evaluate the potential of AVO relative to other approved regimens for this population.

This news release was published by Dana-Farber Cancer Institute on December 7, 2024.

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