Fixed-duration ibrutinib plus venetoclax may benefit patients with high-risk chronic lymphocytic leukemia

June 7 2023

Credit: CC0 Public Domain
First-line ibrutinib (Imbruvica) plus venetoclax (Venclexta) led to high response and survival rates in patients with chronic lymphocytic leukemia (CLL) whether or not their cancer harbored high-risk genetic features typically associated with poor outcomes, according to results recently published in *Clinical Cancer Research*.

Patients with high-risk CLL, defined by deletion of 17p, mutated TP53, and/or unmutated immunoglobulin heavy chain (IGHV), historically have had a greater risk of disease progression and death than patients whose CLL does not contain these features. For many years, patients with high-risk CLL had limited treatment options due to a lack of response to chemoimmunotherapy, the former standard of care for CLL.

Recently, the standard of care for CLL has moved away from chemoimmunotherapy to first-line targeted therapy regimens, such as those involving inhibitors of Bruton's tyrosine kinase (BTK) or BCL-2 with or without CD20-directed antibody therapy, explained John Allan, MD, an associate professor of clinical medicine at Weill Cornell Medicine.

Allan and colleagues previously reported results from the phase II CAPTIVATE trial, which showed that patients with CLL experienced durable responses to fixed-duration first-line treatment with the BTK inhibitor ibrutinib in combination with venetoclax. As opposed to continuous treatment, fixed-duration treatment is administered for a limited amount of time to reduce the risk of toxicities or treatment resistance.

While the trial results suggested that fixed-duration ibrutinib plus venetoclax may be a beneficial first-line treatment for CLL, the benefit of this regimen for patients with high-risk CLL remained unclear.
"Since high-risk genetic features inform treatment selection, understanding the efficacy of fixed-duration ibrutinib plus venetoclax in patients with high-risk CLL is important to determine how this regimen fits in the first-line treatment algorithm for the disease," Allan explained.

The latest publication reports outcomes of a subgroup of patients in the CAPTIVATE trial who were treated with fixed-duration ibrutinib plus venetoclax and whose baseline genetic risk features were known. Of the 195 patients included in this subgroup, 129 had high-risk CLL and 66 had low-risk CLL.

Over 95% of these patients had responses to the combination therapy, regardless of whether their CLL harbored high-risk genetic features, and 61% and 53% of patients with and without high-risk disease, respectively, had complete responses.

Eighty-eight percent of patients with high-risk CLL and 92% of patients without high-risk CLL experienced PFS of at least 36 months. Moreover, more than 95% of patients with and without high-risk CLL were alive 36 months after beginning treatment.

"Previously reported results from the CAPTIVATE study demonstrated deep and durable responses with sustained PFS after fixed-duration therapy with ibrutinib plus venetoclax for first-line treatment of CLL," said Allan. "The current analysis builds upon those results by demonstrating that these clinical outcomes are maintained at these early time points in patients with CLL harboring high-risk genomic features. While further follow-up is required to understand longer term outcomes, these results support fixed-duration ibrutinib plus venetoclax as a treatment approach for this patient population."

Allan noted that the results observed in this study compared favorably to
historical data with other targeted therapy approaches, but he cautioned that differences in patient population and study design preclude direct comparison.

Fixed-duration ibrutinib and venetoclax led to similar adverse events regardless of the presence of high-risk genetic features, Allan added. The most common adverse events were diarrhea, neutropenia, nausea, and arthralgia in both groups. Serious adverse events were observed in 22% and 21% of patients with and without high-risk CLL, respectively.

A limitation of the study is that it was exploratory in nature and not powered to perform statistical comparisons between patients with and without high-risk CLL features.


Provided by American Association for Cancer Research

Citation: Fixed-duration ibrutinib plus venetoclax may benefit patients with high-risk chronic lymphocytic leukemia (2023, June 7) retrieved 12 June 2023 from https://medicalxpress.com/news/2023-06-fixed-duration-ibrutinib-venetoclax-benefit-patients.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.