LymphomaHub

CLL/SLL

Venetoclax potential for relapsed CLL patients who progressed after BCRi therapies

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B-cell receptor pathway inhibitors (BCRi) such as ibrutinib and idelalisib are used to treat chronic lymphocytic leukemia (CLL). However, if patients become refractory to these therapies or develop resistance it can lead to poorer outcomes. Venetoclax, a BCL-2 inhibitor, is a proposed alternative option following relapse in these patients, as it is independent of the BCR pathway.

An interim analysis of a phase II trial conducted by Jeffrey Jones, from the Ohio State University, and colleagues, demonstrated that venetoclax had good clinical activity with high response rates in patients with R/R CLL after prior BCRi exposure. Another phase II study was conducted to evaluate venetoclax treatment efficacy and safety in patients with relapsed/refractory (R/R) CLL after progression with idelalisib treatment. The study, conducted by Steven Coutre, from the Stanford Cancer Center, Stanford University of Medicine, and colleagues, was published in Blood on the 5 January 2017 (NCT02141282).

Study Overview

- 36 eligible patients were included in the study; this included a diagnosis of R/R CLL who had also received idelalisib as the last BCRi treatment before trial enrolment
- Study participants were assigned to either the main cohort (n=21) or the expansion cohort for patients who received idelalisib or ibrutinib as prior therapy (n=15)
- Patients received 20mg of venetoclax once daily for one week, then dose escalation until 400mg once daily
- Patients were closely monitored due to the possible risk of tumor lysis syndrome (TLS) by increasing the dose
- Primary endpoints were overall response rate (ORR) and safety and secondary endpoints included duration of response (DOR), time to progression (TTP), progression-free survival (PFS) and overall survival (OS)

Key Findings

- Median time on venetoclax treatment = 14 months
- Median time to first response = 2.5 months (1.6–8.1)
- ORR (investigator-assessed) for all patients was 67%, which was similar for both cohorts
- Median PFS, DOR and OS have not yet been reached but investigators have estimated a 12-month PFS rate of 79% (95% CI; 62%–90%) and a 12-month OS rate of 94% (95% CI; 78%–99%)
- Week 24 MRD rates for 20 patients were undetectable in peripheral blood (40%)
- Adverse events that were grade ≥3 included: neutropenia (50%), thrombocytopenia (25%), anemia (17%) and hypokalemia (11%)

The authors concluded that venetoclax monotherapy for patients who progressed after idelalisib treatment could be a viable option in terms of both safety and efficacy. They recommended that idelalisib treatment is discontinued no more than 3 days before commencing treatment with venetoclax, in order to prevent the risk of TLS.

References

1. Coutre S. et al. Venetoclax for patients with chronic lymphocytic leukemia who progressed during or after idelalisib therapy. Blood. 2018 Jan 5. PII: blood-2017-06-788133. DOI: 10.1182/blood-2017-06-788133. [Epub ahead of print]
