Ibrutinib Monotherapy Moderately Effective in Relapsing or Refractory Follicular Lymphoma (FL)

Ibrutinib, a Bruton tyrosine kinase (BTK) inhibitor, showed modest efficacy in relapsing or rituximab-refractory follicular lymphoma (FL).

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January 18, 2018- Patients with rituximab-sensitive FL showed significantly higher response rates to ibrutinib when compared with patients with rituximab resistant disease, a phase 2 consortium trial showed.

Nancy L. Bartlett, MD, with the Division of Oncology and Siteman Cancer Center in the Washington University School of Medicine in St. Louis, Missouri, and colleagues reported their findings in the January 11, 2018 issue of *Blood*.

The B-cell receptor (BCR) pathway plays an important role in the differentiation and functioning of normal B cells. The Bruton tyrosine kinase (BTK) enzyme stimulates the BCR pathway and consequently the proliferation of B cells. B-cell lymphomas are characterized by a dysregulation of the BCR pathway and enhanced BCR activation.

Ibrutinib is an irreversible BTK inhibitor approved in the treatment of B-cell lymphomas, and has shown promising activity in phase 1 studies in patients with FL. Based on these results, the authors evaluated ibrutinib in a phase 2 trial in relapsing or rituximab-resistant FL.

A total of forty patients with FL were enrolled and received 560 mg/day of ibrutinib for continuous 28-day cycles until disease progression or intolerance. Enrollment criteria included lack of response or relapse after 6-month treatment with rituximab in a prior treatment (50%), and resistance to the latest chemotherapy regimen (35%).

The primary endpoint of the study was the overall response rate (ORR), and secondary end points were safety, overall survival (OS), time to response, duration of response (DOR), progression free survival (PFS), and time to treatment failure (TTF).

This trial showed an ORR of 37.5% with 5 patients (12.5%) achieving a complete response and 10 patients (25%) scoring a partial response. The median PFS was 14 months and the 2-year PFS was 20.4%. Patients who had previously responded to rituximab had significantly higher ORR (52.6%) than rituximab-resistant patients (16.7%) ($p=0.04$).

The presence of a *CARD*-11 mutation in FL patients positively correlated with a poor response to ibrutinib, except for the wild type mutation. “These findings suggest that somatic mutations present in a lymphoma before treatment may have an impact on the response to a targeted therapy such as ibrutinib and could potentially be used to inform clinical decisions,” investigators noted.

The most common side effects were neutropenia (10%), lymphopenia (7.5%), anemia (7.5%) and infection (7. 5%). The dose of ibrutinib was reduced in 5 patients after neutropenia developed, and the drug was discontinued in 3 patients.

“Response rates to ibrutinib in relapsed FL do not seem to be as encouraging as those seen in other B-cell lymphomas and CLL. Higher response rates in patients with rituximab-sensitive disease may support assessment of the drug in earlier lines of therapy,” the authors concluded.

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