

Promising new combination therapy for non-GCB DLBCL

Ibrutinib plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) improves event-free survival, progression-free survival, and overall survival compared with R-CHOP alone in patients younger than 60 years with untreated non-germinal centre B-cell (non-GCB) diffuse large B-cell lymphoma (DLBCL), according to a recent study.

In a randomised, multicentre, phase 3 trial, Anas Younes (Memorial Sloan Kettering Cancer Center, New York, NY, USA) and colleagues randomly assigned patients with previously untreated non-GCB DLBCL to receive 560 mg ibrutinib per day plus R-CHOP (n=419) or placebo plus R-CHOP (n=419) in six or eight 21-day cycles. The primary endpoint was event-free survival in the intent-to-treat population and the activated B-cell (ABC) DLBCL subgroup. Secondary endpoints included

progression-free survival, overall survival, and safety.

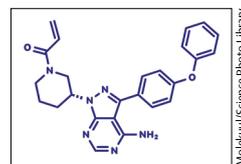
Median follow-up was 34.8 months. ABC subtype disease was confirmed in 567 (76%) of 747 evaluable patients, balanced between the two treatment groups. Ibrutinib plus R-CHOP did not improve event-free survival compared with placebo plus R-CHOP in either the intention-to-treat (hazard ratio [HR] 0.934; 95% CI 0.726–1.200, p=0.5906) or the ABC population (HR 0.949; 95% CI 0.704–1.279, p=0.7311). However, results from preplanned subgroup analyses showed that given ibrutinib plus R-CHOP, those in patients younger than 60 years had improved event-free survival (HR 0.579; 95% CI 0.380–0.881), progression-free survival (HR 0.556; 95% CI 0.359–0.860), and overall survival (HR 0.330; 95% CI 0.162–0.673) compared with older patients. Older patients also had an increased risk of serious adverse

events with ibrutinib plus R-CHOP vs R-CHOP alone (166 [63.4%] of 262 vs 89 [38.2%] of 233).

“These data provide hope that therapeutic interruption of the B-cell receptor signalling pathway can add value to standard R-CHOP chemotherapy in patients with ABC/non-GCB diffuse large B-cell lymphoma,” explained Younes.

“ABC DLBCLs are a subgroup of lymphomas with poor prognosis,” commented Fabrice Jardin (Centre Henri-Becquerel, Rouen, France). “Although the primary endpoint of this study was not met, event-free survival, progression-free survival, and overall survival were improved in patients less than 60 years of age. Further investigation is warranted to propose ibrutinib plus R-CHOP as a new standard of care in younger patients.”

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Published Online
March 28, 2019
[http://dx.doi.org/10.1016/S1470-2045\(19\)30212-8](http://dx.doi.org/10.1016/S1470-2045(19)30212-8)

For the study by Younes and colleagues see *J Clin Oncol* 2019; published online March 22.
DOI:10.1200/JCO.18.02403