Ibrutinib and rituximab for chronic lymphocytic leukaemia

Results of a phase 3 trial have shown that treatment with ibrutinib and rituximab improved progression-free survival compared with standard chemoimmunotherapy in patients with chronic lymphocytic leukaemia.

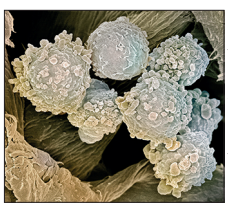
529 patients with previously untreated chronic lymphocytic leukaemia were randomly assigned (2:1) to receive either 420 mg ibrutimab and rituximab (50 mg/m^2 on day 1, cycle 2; 325 mg/m^2 on day 2, cycle 2; 500 mg/m^2 on day 1, cycles 3–7), or chemoimmunotherapy with fludarabine, cyclophosphamide, and rituximab. The ibrutinib–rituximab group received 6 cycles of treatment after an initial cycle of ibrutinib alone, followed by ibrutinib alone until disease progression, and the chemoimmunotherapy group received 6 cycles of treatment. Progression-free survival was the primary endpoint and overall survival was a secondary endpoint.

At a median follow-up of 33·6 months, 3-year progression-free survival in the ibrutinib–rituximab group was 89·4% (95% CI 86·0–93·0) and 72·9% (65·3–81·3) in the chemoimmunotherapy group (hazard ratio [HR] 0·35, 95% CI 0·22–0·56; p<0·001). 3-year overall survival in the ibrutinib–rituximab group was 98·8% (95% CI 97·6–100) and 91·5% (86·2–97·0) in the chemoimmunotherapy group (HR 0·17, 95% CI 0·05–0·54; p<0·001). Frequencies of grade 3 or worse adverse events were similar between groups: 282 (80·1%) of 352 patients in the ibrutinib–rituximab group and 126 (79·7%) of 158 patients in the chemoimmunotherapy group.

Study author Tait Shanafelt (Stanford University School of Medicine, Stanford, CA, USA) said, "The primary challenge is that this approach requires patients to take daily therapy continuously. Future trials are evaluating whether combining ibrutinib with other novel targeted treatments can lead to deeper remissions and eliminate the need for patients to take therapy indefinitely."

Stephan Stilgenbauer (Ulm University, Ulm, Germany) commented that it was impressive that the intervention was compared with the standard of care, "but it is unfortunate that ibrutinib–rituximab was chosen as the experimental arm rather than ibrutinib alone, as other trials have shown that the addition of rituximab does not increase efficacy." He added that the study, together with results from other trials, is clearly practice-changing, as ibrutinib-based therapy is now the standard of care in the front-line treatment of this patient group.

Robert Stirrups



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For the **study by Shanafelt and colleagues** see *N Engl J Med* 2019; **381:** 432–43