

Idelalisib and rituximab for chronic lymphocytic leukaemia



Final results of a study of rituximab with idelalisib or placebo in patients with relapsed chronic lymphocytic leukaemia have shown that idelalisib was efficacious in the long term and had an expected safety profile.

In the randomised, phase 3 study, 220 patients were assigned (1:1) to receive intravenous rituximab at 375 mg/m² on day 1 of week 0 and at 500 mg/m² on day 1 of weeks 2, 4, 6, 8, 16, and 20, and either 150 mg oral idelalisib twice a day (n=110) or a placebo (n=110) between May, 2012, and August, 2013. 75 patients who had received at least one dose of idelalisib were enrolled in the extension study and continued to receive 150 mg idelalisib twice a day. The primary endpoint was progression-free survival, and secondary endpoints included overall response, overall survival, and safety.

After a median follow-up time of 18 months (range 0.3–67.6), patients

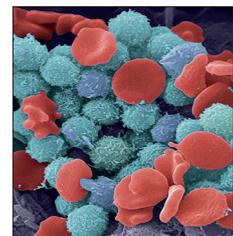
who received idelalisib in both the primary study and the extension study had a median progression-free survival of 20.3 months (95% CI 17.3–26.3). 94 (85%) of 110 patients achieved an overall response (including one complete response). Median overall survival was 40.6 months (95% CI 28.5–57.3) in the idelalisib and rituximab group and 34.6 months (16.0 to not reached) in the placebo and rituximab group. Prolonged exposure to idelalisib increased all grade (51 [46%] of 110) and grade 3 or worse (18 [16%]) diarrhoea, all grade (12 [11%]) and grade 3 or worse colitis (nine [8%]), and all grade (11 [10%]) and grade 3 (seven [6%]) pneumonitis.

Study author Jeff Sharman (Willamette Valley Cancer Institute and Research Center, Eugene, OR, USA) said, "Elderly patients with chronic lymphocytic leukaemia and

comorbid conditions which precluded administration of traditional cytotoxic therapy did very poorly on rituximab monotherapy. Addition of idelalisib yielded clinically meaningful improvements in overall response, progression free survival, and overall survival with an acceptable safety profile." He added: "Future studies will evaluate novel PI3K inhibitors and combination studies with other novel agents."

Matthew Davids (Dana-Farber Cancer Institute, Boston, MA, USA) said, "An important aspect of this paper is that survival was equivalent irrespective of *TP53* status. This distinguishes idelalisib from other novel agents approved in chronic lymphocytic leukaemia, which typically show shorter survival for patients with this high-risk disease marker."

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