Long-term follow-up of a pivotal phase II trial of ibrutinib for relapsed Waldenström's Macroglobulinemia

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BACKGROUND:
We have previously shown that ibrutinib is highly active in patients with Waldenström's macroglobulinemia (WM). MYD88(L265P) and CXCR4(WHIM) mutations are frequent in WM, with MYD88 (L265P) being present in nearly all cases of WM and CXCR4(WHIM) in about a third. We have shown that the presence of these mutations affects responses to ibrutinib. Here we present long-term follow-up data on the pivotal trial.

METHODS:
Sixty-three patients with WM who had received at least one prior therapy were treated with ibrutinib at the dose of 420 mg daily. A total of forty 28-days cycles were planned. At the end of the planned 40 cycles, responding patients could continue on commercial ibrutinib.

RESULTS:
As of July 2016, the median follow-up for the 63 patients was 37 months. At 37 months, the estimated rate of progression-free survival was 82.0% (95% CI, 69.1 to 89.9), the estimated rate of event-free survival was 68.1% (95% CI, 55.1 to 78.1), and the estimated rate of overall survival was 90.0% (95% CI, 77.4 to 95.8). Twenty five of the 63 patients enrolled were taken off study, 10 of those due to progression of disease. Patients with both wild type CXCR4 and wild type MYD88 had significant worse outcome, and longer time to first response. The incidence of grade 2 or higher treatment-related adverse events was similar to the initial report and included neutropenia, thrombocytopenia, procedure-associated bleeding and arrhythmia. No new or unexpected adverse events were associated with longer treatment.

CONCLUSIONS:
Long term follow-up of patients on single agent ibrutinib for relapsed WM confirmed that the ibrutinib is associated with durable responses and that the great majority of patients who achieve a response early on are able to safely continue on treatment with ongoing responses. We confirmed that MYD88 and CXCR4 mutational status is an important biomarker for predicting depth of response.

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