

UPDATED RESULTS OF THE ASPEN TRIAL FROM A COHORT OF PATIENTS WITH WILD-TYPE *MYD88* (*MYD88*^{WT}) WALDENSTRÖM MACROGLOBULINEMIA

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Introduction: Inhibitors of Bruton tyrosine kinase (BTK) have shown significant activity in patients with Waldenström macroglobulinemia (WM) harboring a mutation in the *MYD88* gene. However, lower response rates and shorter progression-free survival have been reported in patients with WM who lack such mutations. The ASPEN trial (NCT03053440) evaluated zanubrutinib, a potent and selective BTK inhibitor, in patients with WM.

Methods: In the ASPEN trial, *MYD88* gene mutations were assessed at study entry by a central laboratory (NeoGenomics). Based on these results, patients were assigned to cohort 1 (*MYD88*^{mut+}) or cohort 2 (*MYD88*^{WT} or unknown mutation status). Patients received zanubrutinib 160 mg twice daily until disease progression. This abstract presents the safety and efficacy of zanubrutinib in patients with *MYD88*^{WT} WM.

Results: In total, 28 patients with WM were enrolled in cohort 2; of which, 26 had *MYD88*^{WT}. The median age of patients in cohort 2 was 72 years; five patients were treatment-naïve and

23 patients had relapsed/refractory (≥ 1 prior therapy) WM. Most patients had intermediate- (39.3%) or high-risk (42.9%) disease (defined by the International Prognostic Scoring System for WM). At a median follow-up of 17.9 months, two patients discontinued zanubrutinib due to adverse events and six experienced disease progression; there were no cases of disease transformation. In patients with confirmed *MYD88^{WT}*, overall response rate by independent review committee was 80.8%, with a major response rate of 50.0% including a very good partial response rate of 26.9% (**Table**). Progression-free survival event-free rate at 12 months was 72.4%. The most frequently reported adverse events were diarrhea, anemia, contusion, pyrexia, and upper respiratory tract infection. Major hemorrhage was reported in two patients, and atrial fibrillation was reported in one patient. There were no fatal adverse events.

Conclusions: Zanubrutinib showed clinically meaningful antitumor activity, including achieving major responses and durability of responses, and was considered well tolerated with a low discontinuation rate due to adverse events, in patients with *MYD88^{WT}* WM.

Table. Best Overall Response by Independent Central Review in Patients With *MYD88^{WT}* WM

	Treatment-naïve WM (n=5)	Relapsed/refractory WM (n=21)	Overall (N=26)
Median follow-up, months	19.3	17.1	17.9
Best overall response by IRC, n (%)			
Complete response	0	0	0
Very good partial response	1 (20.0)	6 (28.6)	7 (26.9)
Partial response	1 (20.0)	5 (23.8)	6 (23.1)
Minor response	2 (40.0)	6 (28.6)	8 (30.8)
Stable disease	1 (20.0)	3 (14.3)	4 (15.4)
Progressive disease	0	1 (4.8)	1 (3.8)

IRC, independent review committee; WM, Waldenström macroglobulinemia.