

Long Term Findings of ASPEN Study: Clinical Outcomes

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The phase III ASPEN study demonstrated the comparable efficacy and improved safety of zanubrutinib versus ibrutinib in patients with Waldenström macroglobulinemia (WM). Here, we report long-term follow-up outcomes from ASPEN trial. The primary end point was the sum of very good partial response (VGPR) + complete response (CR) rates. At 44.4-month median follow-up, VGPR + CR rates were 36.3% with zanubrutinib versus 25.3% with ibrutinib in cohort 1 and 30.8% with one CR in cohort 2. In patients with CXC motif chemokine receptor 4 mutation, VGPR + CR rates were 21.2% with zanubrutinib versus 10.0% with ibrutinib (cohort 1). Median progression-free survival and overall survival were not reached. Fewer progression-free survival (PFS; hazard ratio [HR], 0.63 [95% CI, 0.36 to 1.12]) and overall survival (OS; HR, 0.75 [95% CI, 0.36 to 1.59]) events were observed on zanubrutinib (cohort 1). In patients with *CXCR4*^{MUT} WM on ibrutinib, the median PFS was 39.8 months. Any-grade adverse events (AEs) of diarrhea (34.7% v 22.8%), muscle spasms (28.6% v 11.9%), hypertension (25.5% v 14.9%), atrial fibrillation/flutter (23.5% v 7.9%), and pneumonia (18.4% v 5.0%) were more common with ibrutinib versus zanubrutinib; neutropenia (20.4% v 34.7%) was less common with ibrutinib versus zanubrutinib (cohort 1). Zanubrutinib was associated with lower risk of AE-related treatment discontinuation. Overall, these findings confirm the long-term response quality and tolerability associated with zanubrutinib.