HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH WALDENSTRÖM MACROGLOBULINEMIA (WM) TREATED WITH ZANUBRUTINIB VS IBRUTINIB IN THE PHASE 3 ASPEN TRIAL

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ABSTRACT BODY:

INTRODUCTION: The open-label, multicenter, randomized, phase 3 ASPEN trial (NCT03053440) compared the next-generation BTK-inhibitor zanubrutinib (ZANU) with ibrutinib (IBR) in adult patients (pts) with WM. Treatment with ZANU yielded deep, early, and durable responses and improved long-term safety/tolerability vs IBR.

OBJECTIVE: To evaluate health-related quality of life (HRQoL) outcomes in Cohort 1 (pts with activating mutations in *MYD88*) in both the intention-to-treat (ITT) population and pts achieving a complete response (CR) or very good partial response (VGPR) by Cycle 25.

MATERIALS AND METHODS: Patient-reported outcome (PRO) data were collected using the EORTC QLQ-C30 and EQ-5D-5L VAS at baseline (Cycle 1, Day 1), every 3 cycles up to Cycle 13, and every 6 cycles thereafter; 1 cycle constituted 28 days. A linear mixed model for repeated measures analysis assessed differences between arms for key PRO endpoints of global health status (GHS)/QoL, physical and role functioning, and symptoms of fatigue, diarrhea, and nausea/vomiting (N/V) at 4 key clinical cycles (Cycles 4, 7, 13, and 25). Clinically meaningful treatment difference was defined as ≥5 points difference from baseline.

RESULTS: Cohort 1 included 201 pts (102 ZANU; 99 IBR). Compliance rates for PRO instruments were high (ZANU: 92% [min], 96% [max]; IBR: 84% [min], 95% [max]). In the ITT population, diarrhea and N/V symptom scores were stable from baseline through all key clinical cycles in the ZANU arm; pts on IBR

experienced initial worsening of diarrhea and N/V from baseline. In other key PRO endpoints, both arms experienced improvements and differences between arms were not statistically significant (Table). There was no CR in either arm. The VGPR rate was higher among pts receiving ZANU than IBR (38.2% vs 25.3%; *P*=0.0374). In general, the pts on ZANU who achieved VGPR experienced greater functional and symptomatic improvements than the pts with VGPR on IBR; treatment differences for diarrhea (-19.83) and N/V (-10.98) were clinically meaningful by Cycle 4, whereas differences for physical functioning and fatigue were clinically meaningful at Cycle 7 (10.42 and -11.76) and again at Cycle 25 (10.45 and -13.53).

CONCLUSION: In the ASPEN study of pts with *MYD88*-mutated WM, treatment with ZANU was associated with greater improvements in HRQoL vs IBR. These results support the use of ZANU as an effective option for BTK-inhibitor therapy in pts with WM.

Table: Treatment difference in key PRO endpoints (ITT population)

PRO	Estimated mean treatment difference between ZANU and IBR arms (95% CI)			
	Cycle 4	**Cycle 7**	**Cycle 13**	**Cycle 25**
GHS/QoL	-2.35 (-8.53, 3.84)	-0.65 (-6.10, 4.80)	-2.37 (-7.58, 2.84)	-1.07 (-7.11, 4.97)
Physical functioning	-0.18 (-5.37, 5.00)	1.76 (-3.59, 7.11)	-2.80 (-8.09, 2.48)	0.53 (-4.23, 5.29)
Role functioning	-2.85 (-10.36, 4.67)	-1.81 (-9.27, 5.65)	1.53 (-5.80, 8.86)	3.05 (-3.73, 9.83)
Diarrhea	**-7.26 (-12.62, -1.90)[a]**	-4.90 (-10.63, 0.84)	-3.37 (-8.67, 1.93)	0.57 (-4.76, 5.91)
Fatigue	-1.76 (-8.14, 4.62)	0.34 (-5.52, 6.20)	1.10 (-4.81, 7.01)	-0.05 (-6.34, 6.24)
Nausea/vomiting	**-5.57 (-9.49, -1.66)[b]**	0.80 (-1.62, 3.21)	-1.52 (-3.85, 0.81)	-0.33 (-3.13, 2.47)

[a]*P*=0.0082. [b]*P*=0.0055. Based on a linear mixed model for repeated measures. The model included repeated measurements of PRO endpoints up to Cycle 25 as the dependent variable, with the baseline PRO score and treatment arm by timepoint interaction as covariates. An unstructured covariance matrix was used. Clinically meaningful differences are in **bold**.