Risk of hypertension in patients with CLL/SLL who participated in ALPINE: a post hoc analysis

Dulce Ramirez,[1] Lipeng Chen,[2] Jun Zhang,[1] Wassim Aldairy,[1] William B. White[3]

[1]BeiGene USA, Inc, San Mateo, CA, USA [2]BeiGene, Ltd, Beijing, China; [3]Cardiology Center, University of Connecticut Health Center, Canton, CT, USA

Background: Bruton tyrosine kinase (BTK) inhibitors are an important therapeutic option for patients with CLL/SLL. The first-generation BTK inhibitor, ibrutinib, is associated with an increased risk of hypertension. Zanubrutinib is a next-generation BTK inhibitor designed to maximize BTK occupancy and minimize toxicity with fewer off-target effects.

Aims: Evaluate the risk of developing hypertension based on initiation of antihypertensives (anti-HTN) in a post hoc analysis of ALPINE (NCT03734016).

Methods: Anti-HTN use in the zanubrutinib (n=324) and ibrutinib (n=324) treatment arms was assessed. The definition of anti-HTN was based on Standardized Drug Grouping; concomitant anti-HTN were adjudicated by an independent hypertension specialist blinded to BTK inhibitor assignment. Time to initiating new anti-HTN and time to adding a new class of anti-HTN were assessed using the Kaplan-Meier method. Comparisons of time-to-onset endpoints were analyzed based on the log-rank test.

Results: At baseline, patient characteristics were generally balanced between the zanubrutinib and ibrutinib arms (median age, 66.7 vs 67.1 years; male, 65.1% vs 71.4%; history of hypertension, 50.9% vs 50.0%; type 2 diabetes mellitus, 10.1% vs 8.9%). Among patients not on anti-HTN at baseline, 20.7% (n=35/169) of zanubrutinib- and 28.7% (n=51/178) of ibrutinib-treated patients initiated anti-HTN during the study. Among all patients, fewer patients in the zanubrutinib arm initiated new anti-HTN (28.4% [n=92/324] vs 32.4% [n=105/324]) and the anti-HTN were initiated later (hazard ratio [HR], 0.77; P-value=.071). Additionally, statistically fewer patients in the zanubrutinib arm compared with the ibrutinib arm started anti-HTN in a new class (24.1% [n=78/324] vs 29.3% [n=95/324]) and the anti-HTN were started later (HR, 0.72; P-value=.034). The event rates for initiation of new anti-HTN or a new class of anti-HTN were consistently lower in the zanubrutinib vs ibrutinib arm at each timepoint (**Table**).

Summary/Conclusion: In ALPINE, initiation of new anti-HTN or a new class of anti-HTN occurred less frequently in the zanubrutinib arm vs the ibrutinib arm in patients with CLL/SLL. Adoption of anti-HTN occurred sooner with ibrutinib than zanubrutinib. These findings should be considered when initiating BTK inhibitor therapy in patients with CLL/SLL who have an elevated cardiovascular risk.

	Initiation of new anti-HTN				Initiation of new class of anti-HTN			
	Zanubrutinib		Ibrutinib		Zanubrutinib		Ibrutinib	
	No. at risk	Cumulative event rate, %	No. at risk	Cumulative event rate, %	No. at risk	Cumulative event rate, %	No. at risk	Cumulative event rate, %
3 mo	289	8.4	271	11.0	295	6.5	277	9.1
6 mo	268	12.9	238	19.0	276	10.4	246	16.4
12 mo	238	19.5	208	24.6	252	14.7	216	22.0
18 mo	214	23.7	169	30.7	225	19.5	179	27.0
24 mo	149	28.0	115	33.8	157	23.5	127	29.2
30 mo	106	29.2	76	36.5	109	25.4	84	33.0

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