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POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Efficacy of SB12 (Eculizumab Biosimilar) in Asian and Non-Asian Patients with Paroxysmal Nocturnal Hemoglobinuria: Subgroup Analysis of a Global Phase III Randomized Controlled Trial

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Background SB12 is a humanized monoclonal antibody biosimilar to reference eculizumab (ECU) which received marketing authorization in Europe in May 2023 after a comprehensive biosimilarity demonstration including non-clinical and clinical assessments. The pivotal SB12 Phase III study demonstrated equivalent clinical efficacy by evaluating lactate dehydrogenase (LDH) and comparable safety, pharmacokinetics, pharmacodynamics, and immunogenicity between SB12 and ECU in patients with paroxysmal nocturnal hemoglobinuria (PNH) (Jun Ho Jang et al., eJHaem 2022).
Objective To analyze the efficacy of SB12 in Asian and non-Asian patients with PNH from the pivotal phase III study.
Methods A total of 50 adult patients with a confirmed diagnosis of PNH and ≥ 1.5 upper limit of normal range (ULN) of LDH without previous exposure to a complement inhibitor (naïve) were randomized. All patients provided written informed consents and were randomized (1:1) to treatment sequence I (TS1: SB12 to ECU, n=25) or II (TS2: ECU to SB12, n=25), to receive 600 mg of SB12 or ECU intravenously every week for first 4 weeks (initial phase) and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter (maintenance phase). Patients were switched to ECU or SB12 at Week 26, and switched treatment was provided until Week 50. The primary endpoints included LDH level at Week 26 and time-adjusted area of under the effect curve (AUEC) of LDH from Week 14 to Week 26 and Week 40 to Week 52. Equivalence was declared for LDH level at Week 26 if the two-sided 95% confidence interval (CI) of the mean difference in between SB12 and ECU lied within the pre-defined equivalence margin of $[-1.2 \times ULN, 1.2 \times ULN] = [-337.2, 337.2]$, where ULN = 281 U/L. In addition, equivalence was declared for time-adjusted AUEC of LDH if the two-sided 90% CI of the ratio of geometric means between SB12 and ECU lied within the pre-defined equivalence margin of [0.77, 1.29]. Secondary endpoints included the LDH profile over time. Overall, post-hoc analysis in Asian and Non-Asian (based on race) patients who received either ECU or SB12 during the study period was conducted for the aforementioned efficacy endpoints.
Results Asian patients were 27 (54.0%) of total 50. Overall, 15 (60%) Asian patients and 10 (40%) Non-Asian patients were randomized to TS1 and 12 (48%) Asian patients and 13 (52%) Non-Asian patients were randomized to TS2. Baseline demographic and disease characteristic were comparable between the two treatment sequences, with no significant differences between the treatment sequences by race between Asian and Non-Asian patients. The 95% CI of mean difference in LDH level at Week 26 between SB12 and ECU in Asian (SB12 − ECU: -12.02, 95% CI [−126.87, 102.83]) and Non-Asian patients (SB12 − ECU: 76.12, 95% CI [−56.75, 208.99]) lied within the pre-defined equivalence margins (Table). The 90% CI of ratio of time-adjusted AUEC of LDH between SB12 and ECU in Asian patients (SB12/ECU: 1.01, 90% CI [0.92, 1.10]) lied within the pre-defined equivalence margin and was also comparable in Non-Asian patients (SB12/ECU: 1.15, 90% CI [0.90, 1.46]). The overall LDH profile during the study period was also comparable between Asian and Non-Asian patients. No patient developed anti-drug antibodies during the study period and no patient discontinued due to lack of efficacy. While the limited

sample size suggests for caution, the comparable efficacy results by Asian and Non-Asian subgroups are also comparable to previously published results in the overall population (Jun Ho Jang et al., eJHaem 2022), with no significant differences identified.

Conclusion SB12 showed comparable efficacy to ECU in complement-inhibitor naïve PNH patients in both Asian and Non-Asian subgroups. No patient developed anti-drug antibodies nor discontinued due to lack of efficacy during the study period.

Disclosures Park: *Samsung Bioepis:* Current Employment. **Kim:** *Samsung Bioepis:* Current Employment. **Jung:** *Samsung Bioepis:* Current Employment. **Russo:** *Samsung Bioepis:* Current Employment.

Table. Subgroup Analysis of Primary Endpoints (Lactate Dehydrogenase -LDH- at Week 26 and Time-adjusted AUEC of LDH) by Asian vs Non-Asian, Study SB12-3003) (*Post-hoc* analysis)

Lactate Dehydrogenase (U/L) at Week 26[a]						
	SB12		ECU		Mean difference (SB12 – ECU)	
Subgroup	n	LSM	n	LSM	Estimate	(95% CI)
Race						
Asian	13	269.71	10	281.73	-12.02	(-126.87, 102.83)
Non-Asian	10	309.84	13	233.72	76.12	(-56.75, 208.99)
Time-adjusted AUEC (U/L) of LDH[b]						
	SB12		ECU		Ratio (SB12/ECU)	
Subgroup	n	Geometric LSM	n	Geometric LSM	Estimate	(90% CI)
Race						
Asian	18	280.58	18	278.52	1.01	(0.92, 1.10)
Non-Asian	20	286.74	20	249.87	1.15	(0.90, 1.46)

AUEC = area under the effect curve; CI = confidence interval; ECU = reference eculizumab; LSM = least squares mean; n = number of patients in each subgroup.
[a]Per-protocol Set-LDH at a Single Timepoint. Least squares mean (LSM) difference and its 95% CI in original scale were obtained by applying delta method to the LSM ratio estimated from a linear model with natural log-transformed LDH at Week 26 as dependent variable, and treatment and gender as fixed effects.
[b]Per-Protocol Set for AUEC of LDH. Geometric Means Ratio and 90% CI was obtained by performing back transformation of least squares mean difference and its 90% CI from the linear mixed model with natural log-transformed time-adjusted AUEC of LDH as dependent variable, and treatment and gender as fixed effects.

Figure 1

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