P829 A PHASE III RANDOMIZED CLINICAL TRIAL COMPARING SB12 (PROPOSED ECUILIZUMAB BIOSIMILAR) WITH REFERENCE ECUILIZUMAB IN PATIENTS WITH PAROXYSMAL NOCTURNAL HEMOglobinuria

Topic: Bone marrow failure syndromes incl. PNH - Clinical

Jun Ho Jang1, Roberta Demichelis Gomez2, Horia Bumbea3, Larysa Nogaieva4, Lily Lee Lee Wong5, Soo Min Lim6, Jihye Park7, Younsoo Kim8, Sanghyun Cho7

1 Hematology-Oncology, Samsung Medical Center, Seoul, Korea, Republic Of; 2 Hematology, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico; 3 Hematology, Bucharest Emergency University Hospital, Bucharest, Romania; 4 Regional Treatment-Diagnostic Hematology Center, Communal Nonprofit Enterprise Cherkasy Regional Oncology Dispensary of Cherkasy Oblast Council, Cherkasy, Ukraine; 5 Hematology Unit, Hospital Queen Elizabeth, Kota Kinabalu, Malaysia; 6 Department of Medicine, Hospital Sultanah Aminah, Johor Bahru, Malaysia; 7 Clinical Development, Samsung Bioepis, Incheon, Korea, Republic Of; 8 Biometrics, Samsung Bioepis, Incheon, Korea, Republic Of

Background:
SB12, a proposed eculizumab biosimilar, is a humanized monoclonal antibody that blocks complement C5 cleavage, thereby inhibits terminal complement-mediated intravascular hemolysis.

Aims:
The randomized, double-blind, multicenter, cross-over study was aimed to demonstrate comparable clinical efficacy by evaluating the lactate dehydrogenase (LDH), safety, pharmacokinetics (PK), pharmacodynamics (PD), and immunogenicity of SB12 and reference eculizumab (ECU) in paroxysmal nocturnal hemoglobinuria (PNH) patients (NCT04058158).

Methods:
A total of 50 patients aged ≥ 18 years with a confirmed diagnosis of PNH and ≥ 1.5 upper limit of normal range (ULN) of LDH without previous exposure to a complement inhibitor were included. 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). Patient received 600 mg of SB12 (TS1) or ECU (TS2) 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). The treatment was switched to ECU (TS1) or SB12 (TS2) at Week 26, and switched treatment was provided until Week 50.

Primary endpoints were 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 × ULN, 1.2 × ULN] = [−337.2, 337.2], where ULN = 281 U/L. 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 were LDH profile over time and number of units of packed red blood cells (pRBCs) transfused throughout the study period, safety, PK, PD, and immunogenicity.

Results:
Of the 50 randomized patients, 49 patients received the study treatment and 46 patients completed the study. Baseline demographic and disease characteristic were comparable between the two treatment sequences. The 95% CI of mean difference in LDH level at Week 26 between SB12 and ECU (SB12 – ECU: 34.48, 95% CI [−47.66, 116.62]).
lied within the pre-defined equivalence margin. The 90% CI of ratio of time-adjusted AUEC of LDH between SB12 and ECU (SB12/ECU: 1.08, 90% CI [0.95, 1.23]) lied within the pre-defined equivalence margin. The overall LDH profile during the study period was also comparable. The mean number of units of pRBCs transfused during Period 1 (TS1: 1.1 U; TS2: 0.9 U, respectively) and Period 2 (TS1: 1.1 U; TS2: 1.0 U, respectively) was comparable.

Treatment-emergent adverse events (TEAEs) was reported in 72.3% for SB12 and 68.1% in ECU. Three patients in SB12 and 2 patients in ECU had serious TEAEs. None of three serious TEAEs reported in SB12 were related to the treatment. Two of three TEAEs (cellulitis; infusion site hypersensitivity) reported in ECU were treatment-related, and 1 death due to major adverse vascular event (portal vein thrombosis) not related to the treatment was reported in ECU. The mean eculizumab serum trough concentrations and the mean terminal complement activities in both treatment sequences were comparable. No patient developed anti-drug antibodies during the study period.

Image:

Summary/Conclusion:

SB12 showed clinical equivalence to ECU measured by LDH. SB12 and ECU were comparable in terms of safety, PK, PD, and immunogenicity.