Session: Novel hemophilia treatments, pre-clinical

OC 21.5 - An Open-label,Dose-Escalation,Multicenter Phase I Study to Evaluate the Safety,Immunogenicity,and Pharmacokinetics/pharmacodynamics（PK/PD）of Single Dose SS109 in Hemophilia A/B patients with Inhibitor

Sunday, June 23, 2024 15:45 – 16:00 ICT Room: Ballroom B1

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Background: Bleeding episodes (BEs) in hemophilia patients with inhibitors require the administration of bypassing agents such as activated recombinant human factor VII (rhFVIIa). SS109 is a long-acting rhFVIIa-Fc fusion protein. Nonclinical studies showed that the hemostasis of SS109 is better than that of NovoSeven® in same dose, and half-life is 2.5 times longer than that of NovoSeven® in cynomolgus monkeys.

Aims: To evaluate the safety, immunogenicity, and PK/PD characteristics of single-dose SS109 in hemophilia (FVIII activity ≤1% or FIX activity ≤2%) patients with inhibitors.

Methods: In this first-in-human, open-label, dose-escalation, multi-center study, 27 male patients aged 18-65 years were enrolled. Five doses of SS109 (30, 60, 120, 240, and 360 μg/kg) were examined, and the safety, immunogenicity, and PK/PD were evaluated. This study received approval by each site's IEC/IRB and written informed consents were obtained from all patients.

Results: Single dose of SS109 at all 5 doses was well-tolerated. Two adverse events occurred in 2 patients (7.4%) were possibly related to SS109. No hypersensitivity or allergic reactions occurred. Table 1 summarizes the baseline-corrected FVII activity PK parameters of SS109. Both the Cmax and the AUC were dose dependent across 5-dose level, with linear dose proportionality being observed within the dose range from 120 to 360μg/kg (Figure 1). The mean half-life ranged from 9.5 hours to14.5 hours, 3 to 7-fold longer than that of NovoSeven®. The aPTT and PT in patients were immediately shortened but returned to the baseline level around 24h and between 48h and 72h, respectively. The maximum reduction (ΔEmax) of PT and aPTT after SS109 administration are shown in Table1.

Conclusion(s): This study demonstrated that SS109, a long-acting rhFVIIa-Fc, was well-tolerated and had dose-dependent PK/PD characteristics that support further assessment of its potential hemostasis efficacy in BEs in hemophilia patients with inhibitors.