Abstract: S187

Title: KP104, A BIFUNCTIONAL C5 MAB-FACTOR H FUSION PROTEIN, EFFECTIVELY CONTROLS INTRAVASCULAR AND EXTRAVASCULAR HEMOLYSIS IN COMPLEMENT INHIBITOR-NAÏVE PNH PATIENTS: LONG-TERM RESULTS FROM A PHASE 2 STUDY

Abstract Type: Oral Presentation

Session Title: Clinical and translational in bone marrow failure syndromes and PNH

Background:

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare and life-threatening hematologic disease characterized by intravascular and extravascular hemolysis (IVH and EVH) mediated by effectors of the complement terminal and alternative pathways (TP and AP), respectively. KP104 is a novel bifunctional recombinant fusion protein composed of a humanized anti-C5 mAb and the N-terminal functional domain of complement regulator factor H, enabling simultaneous inhibition of TP and AP. In an interim analysis of a Phase II study (NCT05476887) in complement inhibitor-naïve PNH patients (n=18), KP104 has demonstrated a favorable safety profile and effective control of both IVH and EVH at week 24/25, including a rapid and sustained normalization of lactate dehydrogenase (LDH), substantial improvement in hemoglobin (Hgb), complete blood transfusion avoidance, and clinically meaningful improvement in FACIT-Fatigue scores (Zhang, ASH 2023).

Aims:

We report the updated long-term data of the Phase II study of KP104. As of the data cutoff date of January 4, 2024, patients had received 33-58 weeks of treatment, of which at least 16 weeks were under the optimal biological dose (OBD) regimen.

Methods:

Eighteen complement inhibitor-naïve PNH patients were enrolled in three dose-ascending cohorts, with 6 patients per cohort. After completing 12/13 weeks of primary treatment phase, all patients entered a long-term extension phase, during which they transitioned from the starting dose to a weight-tiered OBD: 1,920 mg SC Q2W for 45-79kg and 2,400 mg SC Q2W for 80-120kg.

Results:

Clinical improvements observed at week 24/25 were sustained and/or further enhanced in all patients, except for one patient in Cohort 3 with co-existing myeloproliferative neoplasms (MPN) (Figure 1). As of the data cutoff, 100% (18/18) of patients sustained an Hgb increase of ≥2 g/dL from baseline, with mean (SD) Hgb levels increasing by 7.0 (2.1) g/dL over baseline, and 88.9% (16/18) patients achieving Hgb normalization (≥12 g/dL). LDH <1.5xULN was achieved by 94.4% (17/18) patients (except for the MPN patient), with a mean (SD) % LDH reduction of 84.3 (8.7) % from baseline. Additionally, 100% (18/18) and 94.4% (17/18) of patients remained free from RBC transfusion and breakthrough hemolysis (BTH), respectively.

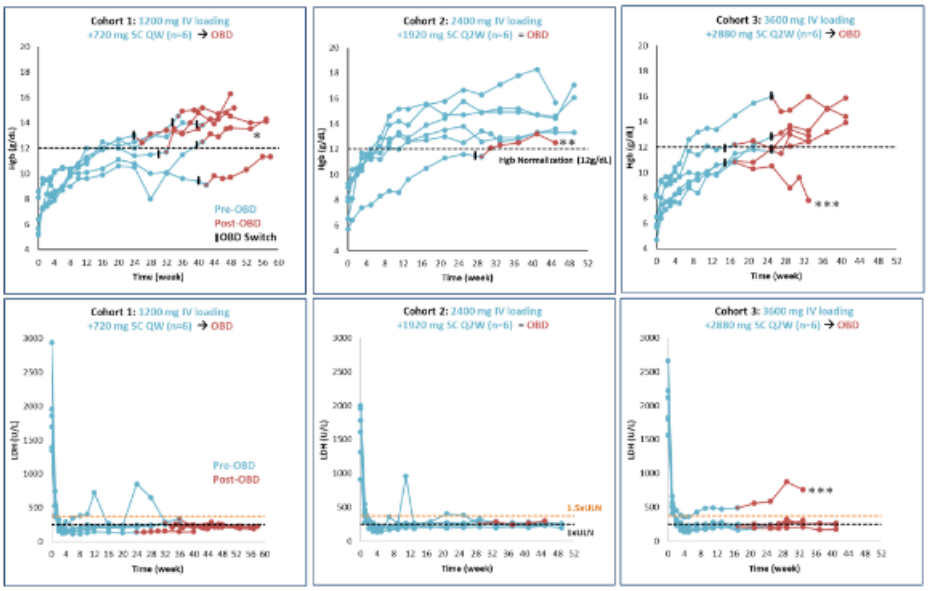
KP104 continued to be well-tolerated, with no occurrences of serious adverse events or treatment-emergent adverse events (TEAEs) leading to drug discontinuation or study withdrawal. All 18 patients remained free from major adverse vascular events, and no severe adverse events were reported. The most frequently reported TEAEs were COVID-19 (38.9%), injection site induration (27.8%), hyperuricemia (16.7%), headache (11.1%), nasopharyngitis (11.1%), and influenza-like illness (11.1%). One patient in the lowest dose cohort experienced a temporary BTH due to an episode of gastroenteritis before the OBD switch. The issue was promptly resolved after an additional dose, and this patient remained free of BTH after switching to OBD.

Summary/Conclusion:

The long-term results of KP104 treatment in this Phase II study demonstrate consistent safety and improved

clinical response over those observed at week 24/25, affirming KP104's durable efficacy in controlling both IVH and EVH in complement inhibitor-naïve PNH patients. The data provide compelling clinical evidence that KP104, a potent first-in-class bifunctional complement inhibitor, may represent a novel first-line monotherapy option for PNH with desired efficacy and safety (Notaro, NEJM 2022).

Figure 1. Sustained Improvement in Hgb and LDH Levels Following OBD Switch



* Patient with BTH and body-weight adjusted OBD
** Patient with body-weight adjusted OBD
***Patient with co-existing myeloproliferative neoplasms

Keywords: Hemolysis, Bone marrow failure, Complement, Paroxysmal nocturnal hemoglobinuria (PNH)