Abstract: P816

Title: LONG-TERM OUTCOMES OF PEGCETACOPLAN TREATMENT IN PATIENTS WITH PAROXYSMAL NOCTURNAL HEMOGLOBINURIA AND BASELINE HEMOGLOBIN LEVELS GREATER THAN 10 GRAMS PER DECILITER

Abstract Type: Poster Presentation

Topic: Bone marrow failure syndromes incl. PNH - Clinical

Background:

Paroxysmal nocturnal hemoglobinuria (PNH) is characterized by complement-mediated hemolysis and increased risk of thrombosis. Complement C5 inhibitors (C5i) reduce intravascular hemolysis (IVH); however, extravascular hemolysis (EVH) can become evident, resulting in persistent anemia.

Pegcetacoplan (PEG) is the first complement C3 inhibitor (C3i) approved by the EMA/FDA for the treatment of adults with PNH and targets IVH and EVH.

In Phase 3 trials, PEG significantly increased hemoglobin (Hb) levels and improved other hematologic/clinical parameters in C5i-experienced (PEGASUS NCT03500549) and -naïve (PRINCE NCT04085601) adult patients (pts) with PNH. Mean Hb at baseline for both studies was <10 g/dL (mean Hb: 8.7 g/dL [PEGASUS], 9.1 g/dL [PRINCE]). Long-term efficacy and safety of PEG specifically in PNH pts with baseline Hb ≥10 g/dL have not been assessed.

Aims:

Evaluate long-term efficacy and safety of PEG in pts with PNH and baseline Hb ≥10.0 g/dL as part of an integrated analysis of the pivotal Phase 3 trials (PEGASUS, PRINCE) and the subsequent ongoing open-label extension study (NCT03531255) for up to 3 years.

Methods:

For this integrated analysis, baseline was defined as time of PEG initiation, regardless of when this occurred in the Phase 3 trials. Adult PNH pts with baseline Hb ≥10.0 g/dL at study entry or last assessment before switching to PEG from eculizumab (PEGASUS) / non-complement inhibitor supportive care (PRINCE) were included.

Pts initially received PEG 1080 mg subcutaneously twice weekly but dose escalations to once every 3 days or 3 times weekly were permitted if a patient's LDH level was greater than 2× upper limit of normal (ULN).

Long-term analyses were performed from baseline up to Weeks 132 (2.5 years, PRINCE) and 156 (3 years, PEGASUS). Efficacy endpoints included changes from baseline in Hb, absolute reticulocyte count (ARC), lactate dehydrogenase level (LDH), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F). Safety was assessed from PEG monotherapy initiation for up to 3 years.

Results:

At defined baseline (data cutoff: 31/01/2023), 33 pts (n=16 PEGASUS, n=17 PRINCE) had Hb ≥10.0 g/dL. Mean (standard deviation [SD]) age was 47.0 (13.1) years and 51.5% (17) of pts were female.

At Week 2 after PEG initiation, mean (SD) Hb levels increased to 12.3 (1.8) g/dL in PRINCE and 12.8 (1.1) g/dL in PEGASUS, and levels remained stable through 2.5 (PRINCE) and 3 years (PEGASUS) (**Figure**). Median LDH stabilized below 1.5× ULN (**Figure**) and there were sustained reductions in ARC.

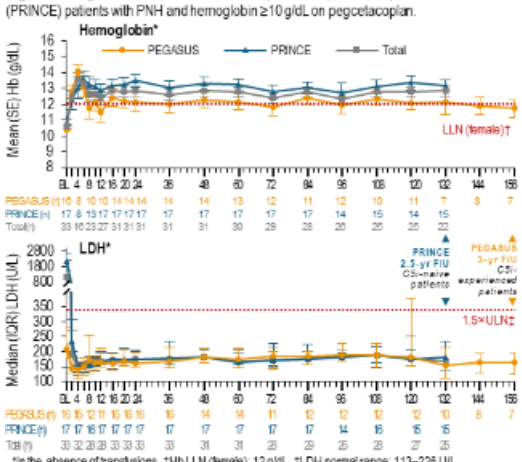
Improvements in hematologic parameters translated into rapid increases in mean FACIT-F scores, approaching the general population norm by Week 4, and the improved quality of life (QoL) was largely maintained long-term.

In the 3-year follow-up, serious adverse events (SAEs) were reported in 42.4% (14) of pts, none were PEG-related. Serious treatment-emergent infections occurred in 24.2% (8) of pts, none of which were PEG-related. There was 1 case of deep vein thrombosis. Two adverse events (AEs) led to PEG discontinuation and there were no AEs leading to death. There were no new safety signals.

Conclusion:

The analysis demonstrated sustained efficacy of PEG in both C5i-experienced and -naïve pts with PNH and mild anemia at baseline. Safety profile was consistent with reports in shorter treatment periods. Pts with Hb ≥10 g/dL experienced swift and sustained improvements in hematologic parameters and enhanced QoL with PEG, showing these pts can also benefit from switching to PEG and underlining its significance as the sole C3i with substantial Phase 3 data in this patient group.

Figure. Hemoglobin* and LDH* levels in C5i-experienced (PEGASUS) and -naïve (PRINCE) patients with PNH and hemoglobin ≥10 g/dL on pegcetacoplan.



*In the absence of transfusions. †Hb LLN (female): 12 g/dL. ‡LDH normal range: 113–226 U/L
BL, baseline; C5i, complement C5 inhibitor; F/U, follow-up; Hb, hemoglobin; IQR, interquartile range; LDH, lactate dehydrogenase; LLN, lower limit of normal; SE, standard error; ULN, upper limit of normal.

Keywords: Anemia, Paroxysmal nocturnal hemoglobinuria (PNH), Complement