Normalization of Hematologic Markers and Fatigue in Patients with Paroxysmal Nocturnal Hemoglobinuria Treated with Pegcetacoplan and Baseline Hemoglobin at or Above 10 g/dL

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OBJECTIVE

The aim of this post hoc analysis was to determine normalization rates for hemoglobin (Hb), lactate dehydrogenase (LDH), absolute reticulocyte count (ARC), and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue and safety in a subgroup of patients with PNH and baseline Hb levels ≥10.0 g/dL treated with pegcetacoplan from the PEGASUS (NCT03500549), PADDOCK (NCT02588833), and PRINCE (NCT04085601) studies.

CONCLUSIONS

- In most patients with PNH who had less severe anemia, elevated markers of hemolysis (ARC and LDH) were normalized after pegcetacoplan treatment, regardless of prior complement inhibitor treatment
- Pegcetacoplan treatment resulted in clinically improved fatigue score
- The safety profile of pegcetacoplan was consistent with previously reported results[3,6,7,8]

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Disclosures: MY reports current employment and equity holder in publicly-traded company with Apellis. JP reports consultancy, honoraria, membership on an entity's Board of Directors or advisory committees with Blueprint Medicines, MSD, Grunenthal, Bristol Myers Squibb, Apellis, and F. Hoffmann-La Roche Ltd; consultancy, membership on an entity's Board of Directors or advisory committees with Amgen; speakers bureau with Chugai and Pfizer; and membership on an entity's Board of Directors or advisory committees, speakers bureau with Novartis, Alexion, and Boehringer Ingelheim. ND and SO "nothing to declare". RPL reports consultancy, honoraria, research funding with Novartis, Pfizer, and Alexion; research funding with Amgen; and consultancy and honoraria with Apellis and Swedish Orphan Biovitrum AB. PS reports membership on an entity's Board of Directors or advisory committees with Blueprint Medicines and Swedish Orphan Biovitrum AB; Honoraria, Membership on an entity's Board of Directors or advisory committees and Speakers Bureau with Alexion and Bristol Myers Squibb; Honoraria and Membership on an entity's Board of Directors or advisory committees with MSD and Novartis. NS reports membership of advisory committee with Alexion. MA-A reports current employment with Apellis. TA reports current employment and equity holder in publicly-traded company with Apellis. EP reports employment at Swedish Orphan Biovitrum AB. RSW reports consultancy, honoraria, research funding, and speakers bureau with Alexion and F. Hoffmann-La Roche Ltd. and research funding and speakers bureau with Apellis.

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CONTEXT

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, life-threatening disease characterized by chronic complement-mediated hemolysis and thrombosis[1,2]
- Patients with PNH experience anemia, fatigue, and dyspnea, and may require blood transfusions that can negatively impact quality of life[3]
- Pegcetacoplan (PEG) provides comprehensive hemolysis control and is the first approved C3 inhibitor for US adults with PNH[4] and EU adults with PNH who remain anemic despite stable C5 inhibitor treatment (ie, eculizumab [ECU] or ravulizumab) for ≥3 months[5]

METHODS

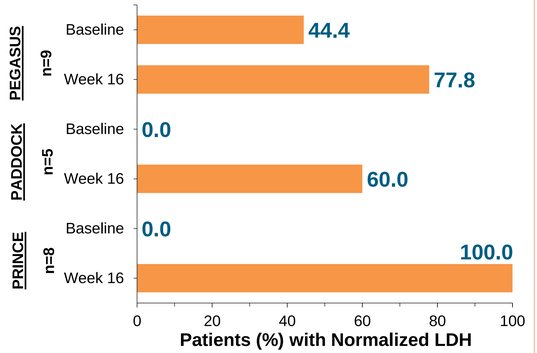
- Enrolled patients had PNH and anemia (hemoglobin [Hb] <10.5 g/dL) despite ≥3 months ECU treatment (PEGASUS)[6] or were naïve to complement inhibitor therapy and received supportive care only (blood transfusions, corticosteroids, anticoagulants, and supplements [iron, folate, B12] in countries where complement inhibitors were not approved or widely available; PADDOCK[7] and PRINCE[8])
- This post hoc analysis included adults with PNH, baseline Hb levels ≥10.0 g/dL, and no transfusions within 14 days of baseline
- Normalization of hematologic and fatigue endpoints were evaluated after 16 weeks of PEG monotherapy
- Normalization was defined as follows: Hb ≥ the lower limit of normal range (female: 12.0 g/dL, male 13.6 g/dL), lactate dehydrogenase (LDH) ≤ the upper limit of normal (226.0 U/L), absolute reticulocyte count (ARC) ≤ the upper limit of normal (120.0x10^9 cells/L), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue ≥ the general population norm (43.6)[9]
- Patients who received transfusions (PRINCE only), withdrew from the study, escaped from control (supportive care only) to PEG, or were missing data at the specified time point were considered not normalized

RESULTS

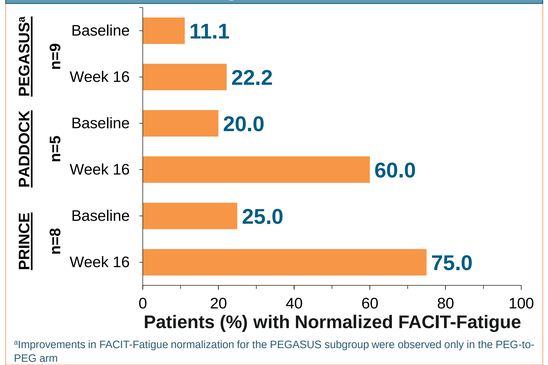
Baseline Population & Characteristics

- Overall, 23 patients had Hb levels ≥10.0 g/dL at baseline:
  - PEGASUS: n=9 (PEG-to-PEG n=6, ECU-to-PEG n=3)
  - PADDOCK: n=6 (1 patient in PADDOCK that stopped dosing at Day 29 and left the study due to physician decision is not included in the normalization analysis)
  - PRINCE: n=8
- Mean age (range) in years was similar across studies: PEGASUS, 49.0 (34.0–72.0); PADDOCK, 41.3 (22.0–67.0); PRINCE, 44.0 (30.0–63.0)
- Proportion of female patients, n (%): PEGASUS, 5 (55.6); PADDOCK, 3 (50.0); PRINCE, 2 (25.0)
- Median years (range) since PNH diagnosis: PEGASUS, 6.0 (3.4–24.1); PADDOCK, 6.4 (1.8–16.4); PRINCE, 1.5 (0.4–14.0)

LDH Normalization

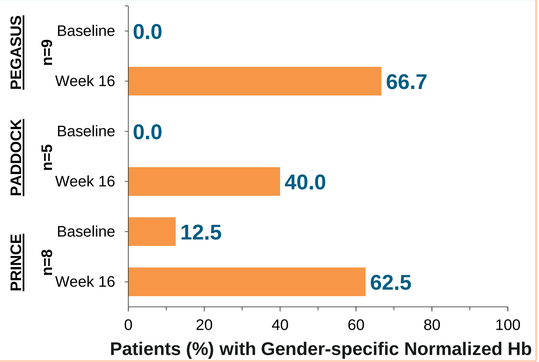


FACIT-Fatigue Normalization

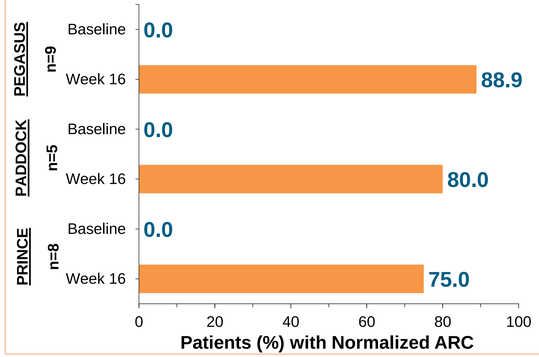


[a]Improvements in FACIT-Fatigue normalization for the PEGASUS subgroup were observed only in the PEG-to-PEG arm

Hemoglobin Normalization



ARC Normalization



Safety

	PEGASUS n=9	PADDOCK n=6[a]	PRINCE n=8
Any AEs, n (%)	7 (77.8)	4 (66.7)	7 (87.5)
Serious AEs, n (%)	1 (11.1)[b]	0	0
Injection Site Reactions, n (%)	3 (33.3)	0	1 (12.5)
Infections and Infestations[c], n (%)	3 (33.3)	1 (16.7)	1 (12.5)
Thrombotic Events, n (%)	0	0	0

[a] One PADDOCK patient who discontinued the study at Day 29 (physician decision) was excluded from normalization analyses, but included in this safety analysis
[b] The serious adverse event was documented as breakthrough hemolysis and considered unrelated to pegcetacoplan; this event did not lead to study discontinuation
[c] Observed infections included nasopharyngitis, urinary tract infection, viral infection, gastrointestinal infection, tonsillitis, vulvovaginal mycotic infection

Abbreviations: AE(s), adverse event(s); ARC, absolute reticulocyte count; ECU, eculizumab; ECU-to-PEG, eculizumab treatment for 16 weeks then switched to pegcetacoplan through Week 48; FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; LDH, Lactate dehydrogenase; PEG, pegcetacoplan; PEG-to-PEG: pegcetacoplan treatment for 16 weeks, then continued through Week 48; PNH, paroxysmal nocturnal hemoglobinuria. Control treatment was supportive care only (eg, transfusions, corticosteroids, anticoagulants, supplements [iron, folate, B12] in countries where complement inhibitors were not approved or widely available