Normalization of Hemoglobin, Lactate Dehydrogenase, and Fatigue in Patients with Paroxysmal Nocturnal Hemoglobinuria Treated with Pegcetacoplan

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OBJECTIVE

We aimed to determine normalization rates for hemoglobin, lactate dehydrogenase (LDH), and fatigue in patients with paroxysmal nocturnal hemoglobinuria (PNH) from phase 3 trials PEGASUS (NCT03500549) and PRINCE (NCT04085601).

CONCLUSIONS

- Overall, pegcetacoplan treatment rapidly increased hemoglobin, normalized LDH, and improved fatigue scores in patients with PNH compared with eculizumab and control (supportive care) treatment
- These data corroborate findings in pegcetacoplan studies in PNH that showed rapidly improved clinical and fatigue parameters, and a favorable safety profile[5,6,8,9]

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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]
- Pegcetacoplan (PEG) provides comprehensive hemolysis control and is the first approved C3 inhibitor for US adults with PNH[3] and EU adults with PNH who remain anemic despite stable C5 inhibitor treatment (ie, eculizumab or ravulizumab) for ≥3 months[4]

METHODS

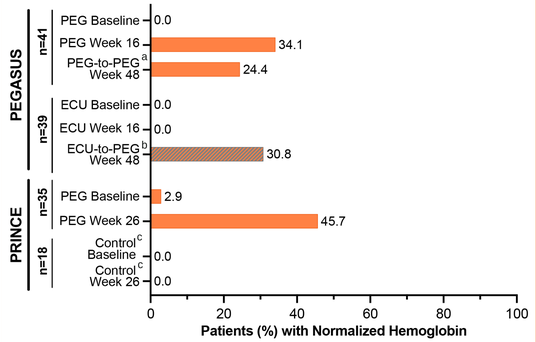
- Enrolled patients had PNH and anemia (hemoglobin <10.5 g/dL) despite ≥3 months eculizumab (ECU) treatment (PEGASUS)[5] or were naïve to complement inhibitor therapy and received supportive care only (blood transfusions, corticosteroids, anticoagulants, and supplements [iron, folate, B12] in countries where complement inhibitors were not approved or widely available; PRINCE)[6]
- Normalization of hematologic and fatigue endpoints were assessed for PEGASUS at baseline, Week 16 (RCP; PEG and ECU) and Week 48 (OLP; PEG-to-PEG and ECU-to-PEG groups) and for PRINCE at baseline and Week 26 (PEG and control) and defined as follows:
  - Hemoglobin ≥ the lower limit of the gender-specific normal range (female: 12 g/dL, male 13.6 g/dL)
  - Lactate dehydrogenase (LDH) ≤226 U/L, the upper limit of normal
  - Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue ≥ 43.6, the general population norm[7]
- Patients who received a transfusion (hemoglobin/LDH endpoints only), withdrew from the study, were lost to follow-up, or escaped from control (supportive care only) to pegcetacoplan, were considered not normalized

RESULTS

Baseline Population & Characteristics

- Population size:
  - PEGASUS: N=80 (PEG, n=41; ECU, n=39)
  - PRINCE: N=53 (PEG, n=35; CTRL, n=18)
- Overall age in years, mean (range), was similar across treatment groups:
  - PEGASUS: PEG, 50.2 (19–81) and ECU, 47.3 (23–78)
  - PRINCE: PEG, 42.2 (22–67) and CTRL, 49.1 (20–74)
- The proportion of female patients was similar across treatment groups, n (%):
  - PEGASUS: PEG, 27 (66.0) and ECU, 22 (56.0)
  - PRINCE: PEG, 16 (45.7) and CTRL, 8 (44.4)
- Years since PNH diagnosis, median (range):
  - PEGASUS: PEG, 6.0 (1–31) and ECU, 9.7 (1–38)
  - PRINCE: PEG, 3.4 (0.1–27.1) and CTRL, 4.7 (0.1–15.1)

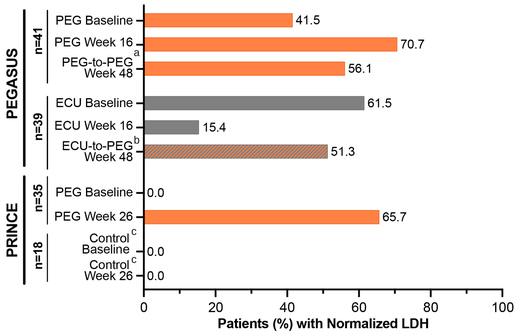
Hemoglobin Normalization Rates



Hemoglobin normalization was observed as early as Week 2 in a substantial proportion of the pegcetacoplan-treated population

- PEGASUS: 43.9%
- PRINCE: 22.9%

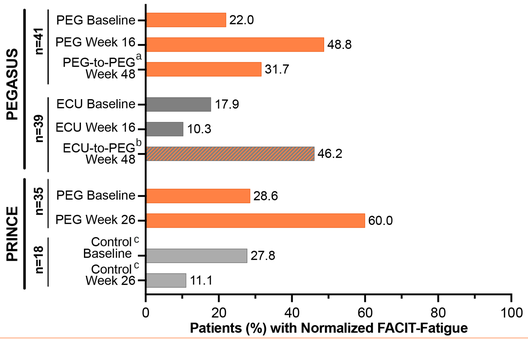
LDH Normalization Rates



Normalization of LDH was observed as early as Week 2 in a substantial proportion of the pegcetacoplan-treated population

- PEGASUS: 87.8%
- PRINCE: 51.4%

FACIT-Fatigue Normalization Rates



Safety

PEGASUS	RCP PEG n=41	RCP ECU n=39	Total OLP PEG n=77
Any AE, n (%)	36 (87.8)	36 (92.3)	71 (92.2)
PEG-related	14 (34.1)	--	34 (44.2)
Serious AEs, n%	7 (17.1)	5 (12.8)	18 (23.4)
PEG-related	1 (2.4)	--	4 (5.2)
TEAEs leading to PEG discontinuation, n (%)	2 (4.9)	--	4 (5.2)
Special interest AEs, n (%)			
Injection site reactions	15 (36.6)	1 (2.6)	20 (26.0)
Infections	12 (29.3)	11 (28.2)	43 (55.8)
Sepsis	0	0	3 (3.9)
Hypersensitivity	5 (12.2)	2 (5.1)	14 (18.2)
Hemolytic disorders	5 (12.2)	14 (35.9)	18 (23.4)
Thrombosis	0	0	2 (2.6)

PRINCE	Overall PEG* n=46	Control n=18
Any AE, n (%)	33 (71.7)	12 (66.7)
PEG-related	13 (28.3)	--
Serious AEs, n%	4 (8.7)	3 (16.7)
PEG-related	0	--
TEAEs leading to PEG discontinuation, n (%)	0	--
Special interest AEs, n (%)		
Injection site reactions	14 (30.4)	--
Infections	9 (19.6)	5 (27.8)
Sepsis	0	0
Hypersensitivity	9 (19.6)	1 (5.6)
Hemolytic disorders	0	0
Thrombosis	0	0

* Includes patients randomized to the control arm who were offered escape to PEG if they demonstrated hemoglobin levels ≥2 g/dL below baseline measurement or presented with a qualifying thromboembolic event secondary to PNH

Footnotes: [a] PEG-to-PEG, pegcetacoplan treatment for 16 weeks during the RCP then continued on pegcetacoplan through Week 48 of the OLP; [b] ECU-to-PEG, eculizumab treatment for 16 weeks during the RCP then switched to pegcetacoplan through Week 48 of the OLP; [c] Control, supportive care only (eg, transfusions, corticosteroids, anticoagulants, supplements [iron, folate, B12] in countries where complement inhibitors were not approved or widely available

Abbreviations: AE(s), adverse event(s); CTRL, control; ECU, eculizumab; FACIT, Functional Assessment of Chronic Illness Therapy; LDH, Lactate dehydrogenase; OLP, open-label period; PEG, pegcetacoplan; PNH, paroxysmal nocturnal hemoglobinuria; RCP, randomized controlled period; TEAE, treatment emergent adverse event