# Post Hoc Analysis of the Effect of Pegcetacoplan Treatment of Patients with Paroxysmal Nocturnal Hemoglobinuria and Baseline Hemoglobin Levels Greater Than 10 Grams per Deciliter

Abstract #2194

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## CONCLUSIONS

- ✓ Patients with paroxysmal nocturnal hemoglobinuria (PNH) and baseline hemoglobin levels ≥10.0 g/dL achieved further improvements in hematologic and clinical outcomes with pegcetacoplan treatment
- ✓ These findings demonstrate that pegcetacoplan is effective in this subgroup of patients with less severe anemia and contributes to a decline in overall hemolytic activity
- ✓ Therefore, the utility of pegcetacoplan may not be restricted to patients with PNH and low baseline hemoglobin levels, and pegcetacoplan may be efficacious in patients with less severe anemia and baseline hemoglobin levels of ≥10.0 g/dL

## INTRODUCTION

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare and acquired disease that involves complement-mediated hemolysis, thrombophilia, and various degrees of bone marrow failure[1]
- Pegcetacoplan is the first therapy for PNH that targets the C3 complement protein and was approved by the U.S. FDA for treatment of adults with PNH on May 14, 2021
- The efficacy and safety of pegcetacoplan has been demonstrated in patients with PNH and screening hemoglobin levels <10.5 g/dL who:
  - Remained anemic despite stable eculizumab (C5-inhibitor) treatment for ≥3 months (PEGASUS Phase 3 study)[2]
  - Were naïve to treatment with complement-inhibitors (PADDOCK[3] Phase 1b and PRINCE[4] Phase 3 studies)

## AIMS

This post hoc analysis evaluated effect of 16 weeks of pegcetacoplan treatment on hematologic and clinical parameters among patients with PNH and baseline hemoglobin levels ≥10.0 g/dL as a population representative of patients with less severe anemia

## METHODS

### Post Hoc Analysis Cohorts

Adult patients with PNH from the PADDOCK, PEGASUS, and PRINCE studies with baseline screening hemoglobin levels ≥10.0 g/dL and no transfusions ≤14 days prior to measurement

**Table 1.** Patient Characteristics and Post Hoc Analysis Endpoints

| Study | Patient Population | Analysis Cohorts (Total N) | Post Hoc N | Subcutaneous PEG Dose |
|---|---|---|---|---|
| **PADDOCK** NCT02588833 **Phase 1b** | Complement-inhibitor[a] naïve patients | PEG treatment (N=20) | 6[b] | 270-360 mg/day |
| **PRINCE** NCT04085601 **Phase 3** | Patients were complement-inhibitor[a] naive within 3 months prior to screening | PEG treatment (N=35) | 8[b] | 1080 mg twice/week |
| **PEGASUS** NCT03500549 **Phase 3** | Patients were anemic despite stable eculizumab treatment for ≥3 months (average >4 years) | PEG treatment during the RCP (N=41) | 6[b] | 1080 mg twice/week |
| | | Switched from eculizumab to PEG during the OLP (N=39) | 3[c] | |

**Endpoints Analyzed After 16 Weeks of Pegcetacoplan Monotherapy for All Cohorts**

- Change from baseline in Hb levels, ARC, LDH levels, and FACIT-Fatigue scores
- Number and percentage of patients who:
  - Had a Hb response (≥1.0 g/dL Hb increase from baseline without transfusion[d])
  - Achieved Hb levels ≥12.0 g/dL in the absence of transfusion[d]

Abbreviations: ARC, absolute reticulocyte count; FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; LDH, lactate dehydrogenase; OLP, open-label period; PEG, pegcetacoplan; RCP, randomized controlled period

[a] Complement inhibitors: i.e., eculizumab, ravulizumab

[b] The post hoc analysis endpoint for the PADDOCK, PRINCE, and PEGASUS RCP subgroups was Week 16

[c] The post hoc analysis endpoint for the PEGASUS subgroup that switched to pegcetacoplan during the OLP was Week 32 (16 weeks of pegcetacoplan treatment)

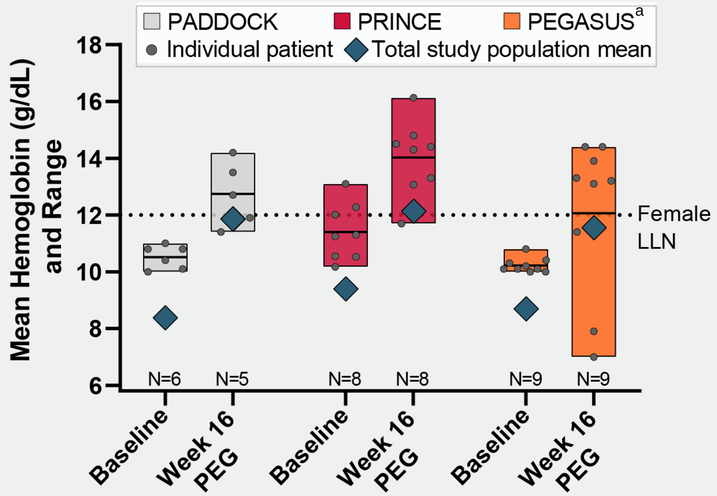
[d] Includes any transfusion during the 16-week analysis period

## RESULTS

### Hemoglobin Levels Following 16 Weeks of Pegcetacoplan Treatment

- Patients from the PADDOCK, PRINCE, and PEGASUS studies with baseline hemoglobin levels ≥10.0 g/dL achieved further improvements in hemoglobin levels after 16 weeks of pegcetacoplan treatment (**Fig. 1**)

**Figure 1.** Hemoglobin Levels at Baseline and Week 16 of Pegcetacoplan Treatment




Abbreviations: LLN, lower limit of normal; PEG, pegcetacoplan;

[a] This analysis was performed using the original baseline for ECU patients; a second analysis using Week 16 as the baseline for ECU patients revealed similar results (data not shown)

### Additional Hemoglobin Outcomes

- The majority of patients with baseline hemoglobin levels ≥10.0 g/dL demonstrated a hemoglobin response and hemoglobin levels ≥12 g/dL in the absence of transfusions at Week 16 after pegcetacoplan treatment initiation in all three trials (**Table 2**)
- These results suggest that pegcetacoplan can further improve hemoglobin levels in patients with less severe anemia and baseline hemoglobin levels of ≥10.0 g/dL

**Table 2**. Hemoglobin Response and Patients with Hemoglobin Levels ≥12 g/dL at Week 16

| Additional Hemoglobin Outcomes at Week 16 of Pegcetacoplan Treatment | PADDOCK (N=5)[a] | PRINCE (N=8) | PEGASUS (N=9)[b] |
|---|---|---|---|
| Patients with ≥1.0 g/dL improvement in hemoglobin levels in the absence of transfusions, n (%) | 5 (100.0) | 8 (100.0) | 7 (77.8) |
| Percentage of patients with hemoglobin ≥12.0 g/dL in the absence of transfusions, n (%) | 3 (60.0) | 7 (87.5) | 6 (66.7) |
| Mean change from baseline to Week 16 in hemoglobin levels, g/dL (SD) | 2.3 (1.1) | 2.6 (0.8) | 1.8 (2.7) |

Abbreviations: SD, standard deviation

[a] One PADDOCK patient was excluded from the hemoglobin response, hemoglobin ≥12.0 g/dL, and change from baseline analyses because they stopped pegcetacoplan treatment at Day 29 (prior to the Week 16 endpoint) and left the study due to physician decision

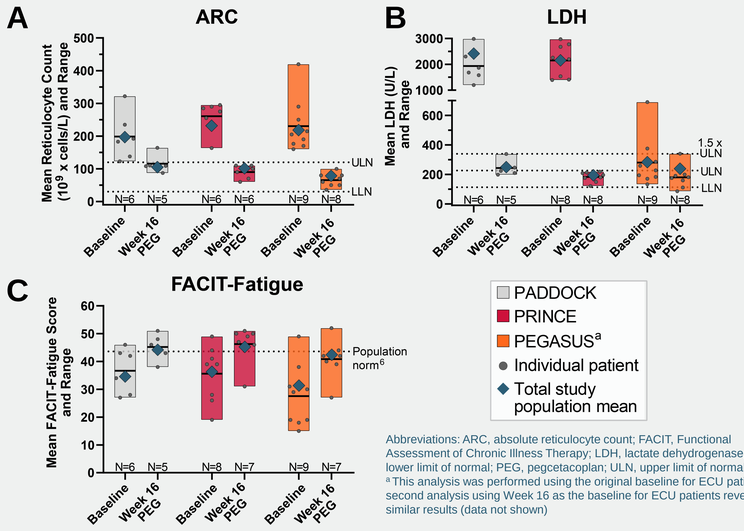
[b] This analysis was performed using the original baseline for patients who switched from eculizumab to pegcetacoplan during the open-label period at Week 17; a second analysis using Week 16 as the baseline for eculizumab patients revealed similar results (data not shown)

## RESULTS, continued

### ARC, LDH Levels and FACIT-Fatigue Scores following 16 Weeks of Pegcetacoplan Treatment

- Elevated baseline ARC suggest ongoing hemolysis in these patients despite having hemoglobin levels ≥10.0 g/dL (**Fig. 2A**)
- Patients from all three trials demonstrated improvements in ARC, LDH Levels, and clinically significant increases in FACIT-Fatigue scores (≥3-point increase[5]) following 16 weeks of pegcetacoplan treatment (**Fig. 2A-C**)

**Figure 2.** ARC, LDH, & FACIT-Fatigue at Baseline and Week 16 of Pegcetacoplan Treatment




Abbreviations: ARC, absolute reticulocyte count; FACIT, Functional Assessment of Chronic Illness Therapy; LDH, lactate dehydrogenase; LLN, lower limit of normal; PEG, pegcetacoplan; ULN, upper limit of normal;

[a] This analysis was performed using the original baseline for ECU patients; a second analysis using Week 16 as the baseline for ECU patients revealed similar results (data not shown)

### Safety and Adverse Events

- No deaths occurred in the ≥10.0 g/dL baseline subgroup in any of the three trials
- One PEGASUS patient (4.2%) in this subgroup who was treated with pegcetacoplan during the randomized controlled period experienced a serious adverse event classified as breakthrough hemolysis that was deemed not related to pegcetacoplan and did not lead to study discontinuation (**Table 3**)
- Adverse events of interest (such as injection site reactions and some infections and/or infestations) occurred at similar rates between the subgroups in all three trials (**Table 3**)
  - However, no encapsulated bacterial infections were observed
- No thrombotic events occurred in the subgroups from the three trials (**Table 3**)

**Table 3**. Adverse Events

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

[a] One PADDOCK patient stopped pegcetacoplan treatment at Day 29 and left the study due to physician decision; but was included in this safety analysis

[b] The serious adverse event was documented as breakthrough hemolysis - deemed not related to pegcetacoplan and did not lead to study discontinuation

[c] Observed infections included: nasopharyngitis, urinary tract infection, viral infection, gastrointestinal infection, tonsillitis, vulvovaginal mycotic infection

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