Interim analysis of the ongoing COMPLETE study on the real-world effectiveness of pegcetacoplan in patients with paroxysmal nocturnal hemoglobinuria (PNH)

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CONCLUSIONS

- The COMPLETE study includes a diverse patient population, reflecting real-world treatment with pegcetacoplan in patients with paroxysmal nocturnal hemoglobinuria (PNH).
- After 6 months on pegcetacoplan treatment, improvements in hematologic parameters were detected, with a median hemoglobin (Hb) increase of 2.3 g/dL, which was sustained at 12 months. This was consistent with the benefits observed in clinical trials.
- Consistent reduction in lactate dehydrogenase (LDH), absolute reticulocyte count (ARC), and total bilirubin along with mostly maintained levels of ferritin through the study period showed beneficial effects of pegcetacoplan for treatment of PNH.
- Hematologic improvements were accompanied by decreased need for red blood cell transfusions (RBCT) on pegcetacoplan treatment, maintained over the study period.
- Future data from the COMPLETE study will broaden our understanding of the real-world effectiveness and safety of pegcetacoplan in patients with PNH.

INTRODUCTION

- PNH is characterized by complement-mediated hemolysis, increasing thrombosis risk, and significant symptom burden.[1]
- Complement 5 inhibitors (C5i) decrease intravascular hemolysis; however, in many patients, residual intravascular and emerging extravascular hemolysis with persistent anemia may be seen, leading to transfusion dependence and impaired quality of life.[2–12]
- Pegcetacoplan is the first complement C3 and C3b inhibitor approved in Europe, the US, and other countries for the treatment of adult patients with PNH, targeting both intravascular and extravascular hemolysis.[13–14]
- In Phase 3 trials, pegcetacoplan significantly improved Hb levels and other clinical outcomes in C5i-experienced (PEGASUS NCT03500549) and -naïve (PRINCE NCT04085601) adult patients with PNH.[15–17] Away from the clinical trial setting, there is a need to understand the effectiveness and real-world usage of pegcetacoplan in routine clinical practice.

AIM

- To report the updated interim data (as of January 12, 2025) on the real-world effectiveness of pegcetacoplan in adult patients with PNH from the ongoing COMPLETE study.

METHODS

Study design

- COMPLETE (NCT05776472) is an ongoing Phase 4, multicenter, observational study aiming to recruit 200 patients from 80 sites in Europe, the Middle East, Canada, and Australia.[18,19]
- A prospective observation period of 24 months constitutes the main part of the study, supplemented by retrospective data for up to 12 months before pegcetacoplan starts.

Study population

- Eligibility criteria include adult (age ≥18 years) patients with a documented diagnosis of PNH who either initiated routine pegcetacoplan treatment before enrollment or were newly prescribed pegcetacoplan at enrollment. Patients are excluded if they had participated in an interventional clinical study within 3 months of enrollment or had initiated pegcetacoplan treatment as part of such a study.

Primary endpoints

- Change in Hb from pegcetacoplan initiation to 6 months.

Secondary endpoints

- Changes in LDH, ARC, total bilirubin, and ferritin, as well as Hb improvement (achieving Hb ≥12 g/dL or an Hb increase of ≥2 g/dL), are assessed from treatment start and every 6 months until study end.
- Annualized number and units of RBCT.
- Adverse events (AEs).

Data analysis

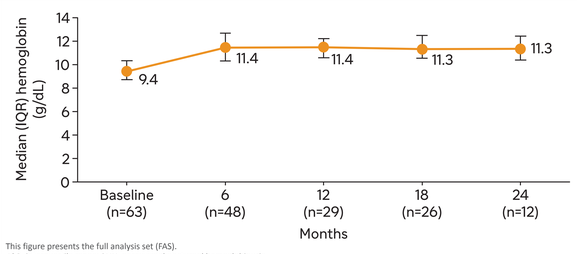
- Descriptive statistics were used to summarize patient data and to assess the primary and secondary endpoints.
- Baseline was defined as the initiation of pegcetacoplan treatment.
- Reported AEs were classified using the Medical Dictionary for Regulatory Authorities (MedDRA).

Table 1: Patient characteristics at baseline (pegcetacoplan initiation)

Baseline characteristics	FAS (N=70)	6MAS* (N=48)
Median age (IQR) at pegcetacoplan initiation, years	50.6 (35.2, 65.5)	53.0 (40.4, 65.9)
Female, n (%)	37 (54.4)	22 (45.8)
History of aplastic anemia before pegcetacoplan initiation, n (%)	24 (35.8)	15 (31.9)
Median time from PNH diagnosis to pegcetacoplan initiation (IQR), months	56.5 (25.9, 108.7)	55.8 (24.4, 105.4)
Complement inhibitor transition from†, n (%)		
Eculizumab	42 (60.0)	34 (70.8)
Ravulizumab	27 (38.6)	18 (37.5)
Crovalimab	4 (5.7)	3 (6.3)
Iptacopan	1 (1.4)	1 (2.1)
Median Hb (IQR), g/dL	9.4 (8.7, 10.3)	9.2 (8.7, 10.1)
Hb <10.5 g/dL, n (%)	50 (80.6)	39 (84.8)
Median LDH (IQR), U/L	303 (243, 367)	326 (244, 368)
Median total bilirubin (IQR), µmol/L	27.5 (20, 46)	27.4 (21.7, 46)
Median ARC (IQR), 10^9 cells/L	208.4 (158.4, 253.8)	199 (152.9, 252.5)
Median ferritin (IQR), µg/L	533 (190.5, 1070)	516 (249, 1137)
Median duration of pegcetacoplan treatment (IQR), months	15.9 (8.5, 22.3)	15.9 (9.6, 22.2)

*Patients without Hb data for 6-months timepoint excluded. †More than one C5i could be reported; therefore, the sum can exceed 100%.
ARC, absolute reticulocyte count; C5i complement 5 inhibitor; FAS, full analysis set; Hb, hemoglobin; IQR, interquartile range; LDH, lactate dehydrogenase; 6MAS, 6-month analysis set.

Figure 1: Hemoglobin levels (g/dL) over 24 months



This figure presents the full analysis set (FAS).
IQR, interquartile range; PNH, paroxysmal nocturnal hemoglobinuria.

RESULTS

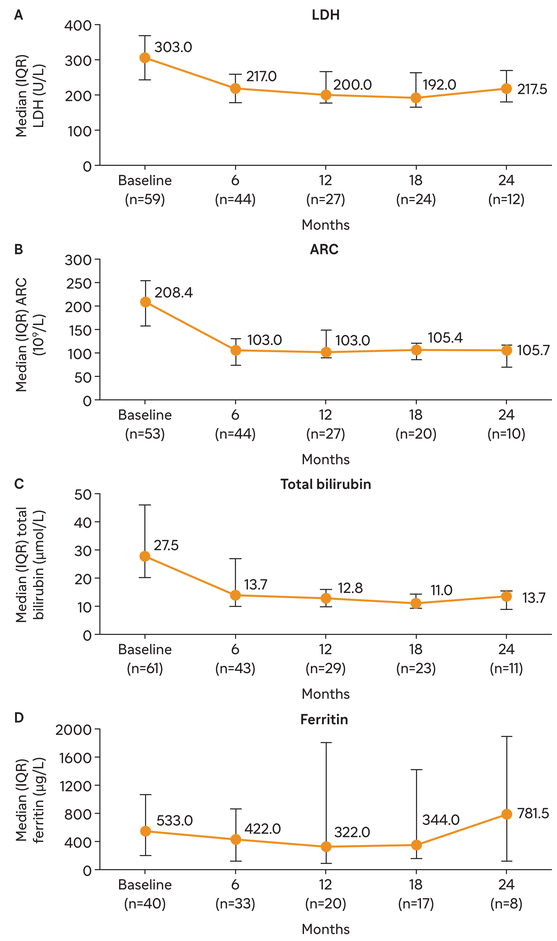
Baseline characteristics

- As of January 12, 2025, 70 eligible patients were enrolled from 38 sites in 11 countries; 70 patients were included in the full analysis set (FAS), with 48 patients contributing to the 6-month analysis set (6MAS).
- Six patients discontinued the study (switched to another treatment, n=5; other, n=1).
- **Table 1** summarizes the baseline characteristics of the FAS and 6MAS cohorts.

Efficacy

- From baseline to 6 months, the median Hb increase (n=46) was 2.3 g/dL (IQR 0.8, 3.3), corresponding to a median (IQR) percentage increase in Hb of 23.3% (7.8–39.5%).
- Median Hb was increased from 9.4 g/dL at baseline to 11.4 g/dL at both 6 months (n=48) and 12 months (n=29) with sustained treatment effectiveness through 24 months (**Figure 1**).
- Among evaluable patients at 6 months:
  - 54.3% (25/46) showed at least a ≥2 g/dL increase in Hb from baseline to 6 months.
  - 41.7% (20/48) achieved Hb ≥12 g/dL.
- The LDH, ARC, and total bilirubin levels decreased within the first 6 months of treatment; the median levels below the upper limit of normal were achieved and maintained for these parameters (**Figures 2A, 2B and 2C**). Ferritin levels showed a modest or no decline during the first 18 months of pegcetacoplan treatment (**Figure 2D**); few patients were included in the 24-month measurement, making the evaluation at this timepoint uncertain.
  - At 6 months, median (IQR) changes from baseline in hematologic parameters were as follows: LDH (n=40), –88.0 U/L (–28.5, –176.5); total bilirubin (n=41), –15.4 µmol/L (–6.9, –30.0); ARC (n=37), –104×10^9/L (–56, –135); and ferritin (n=23), –71 µg/L (+83, –250).

Figure 2: LDH (A), ARC (B), total bilirubin (C), and ferritin (D) levels over 24 months in patients with PNH treated with pegcetacoplan



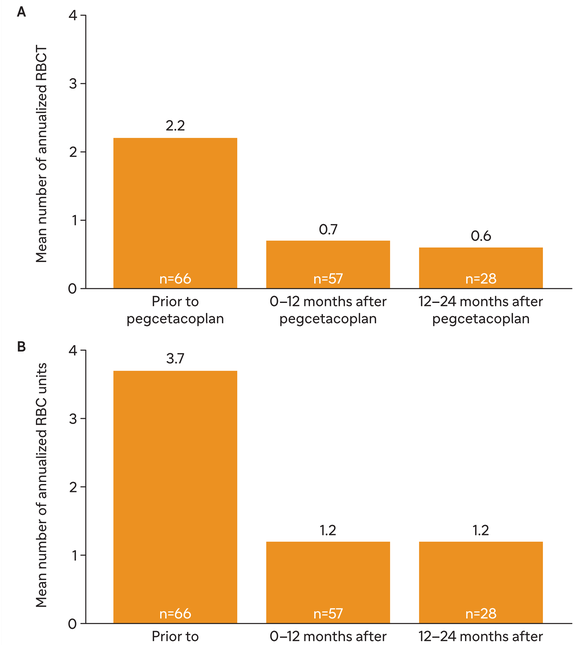
ARC, absolute reticulocyte count; IQR, interquartile range; LDH, lactate dehydrogenase; PNH, paroxysmal nocturnal hemoglobinuria.

- The annualized number of required RBCT events and units decreased on pegcetacoplan treatment and were maintained over the study period.
  - Prior to pegcetacoplan initiation, the mean (SD) annualized RBCT was 2.2 (4.74) in 66 patients (20 patients had at least one RBCT). This rate decreased to 0.7 (1.98) during the first 12 months following pegcetacoplan treatment (n=12 patients had at least one RBCT) and remained stable through 24 months (**Figure 3A**).
  - A similar trend was observed in the annualized number of red blood cell (RBC) units required over the 24-month treatment period (**Figure 3B**).
- Acute hemolytic events requiring additional intervention occurred in 6/60 pts (10%) during the period from 4 to 9 months.

Safety

- 22 patients experienced AEs, the majority of which were mild or moderate in severity (**Table 2**).
- 11 patients experienced an AE related to study treatment, and one patient experienced an SAE related to study treatment (**Table 2**).
- There were no infections with encapsulated bacteria or any other serious infections.

Figure 3: Annualized number of (A) RBCT and (B) RBC units before and during pegcetacoplan treatment in patients with PNH through 24 months



PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell; RBCT, red blood cell transfusion; SD, standard deviation.

Table 2: Patients experiencing at least one AE

Category	Total (N=70)	
	n (%) *	Events
Any adverse event	22 (31.4)	60
Mild	10 (14.3)	26
Moderate	8 (11.4)	12
Severe	10 (14.3)	22
Patients with at least 1 SAE	6 (8.6)	7
Patients with at least 1 AE related to study treatment	11 (15.7)	13
Patients with at least 1 SAE related to study treatment	1 (1.4)	1

*Percentages are calculated using the number of patients from FAS as the denominator.
AE, adverse event; SAE, serious adverse event.

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Abbreviations: 6MAS, 6-month analysis set; AE, adverse event; ARC, absolute reticulocyte count; C5i, complement 5 inhibitors; FAS, full analysis set; Hb, hemoglobin; IQR, interquartile range; LDH, lactate dehydrogenase; MedDRA, Medical Dictionary for Regulatory Authorities; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell; RBCT, red blood cell transfusion; SAE, serious adverse event; SD, standard deviation.

Acknowledgements: The study was funded by Swedish Orphan Biovitrum AB. Medical writing support was provided by Vivek Khanna, PhD, The Salve Healthcare Communications, funded by Swedish Orphan Biovitrum AB.

Disclosures: RPdL: Apellis: Consultancy, Honoraria; Alexion: Consultancy, Honoraria, Research Funding; Novartis: Consultancy, Honoraria, Research Funding; Pfizer: Consultancy, Honoraria, Research Funding; Swedish Orphan Biovitrum AB: Consultancy, Honoraria. **LM:** no disclosures. **CGG:** Swedish Orphan Biovitrum AB, Samsung and Novartis. **RT:** Alexion AstraZeneca Rare Disease: Honoraria, Membership on an entity's Board of Directors or advisory committees; Novartis: Honoraria, Membership on an entity's Board of Directors or advisory committees; Swedish Orphan Biovitrum AB: Honoraria, Membership on an entity's Board of Directors or advisory committees. **HM:** Swedish Orphan Biovitrum AB: Current Employment, Current holder of stock options in a privately held company. **SL:** Swedish Orphan Biovitrum AB: Current Employment.

Presented at the 30th EHA Congress, Milan, June 12–15, 2025.