Sustained long-term real-world effectiveness and safety of pegcetacoplan in patients with PNH: Ongoing COMPLETE Phase 4 study

PS1794

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CONCLUSIONS

- Treatment with pegcetacoplan resulted in considerable improvements in markers of haemolytic anaemia (Hb, LDH, and ARC) and a reduced need for annualised RBCTs and RBC units.
  - These benefits were observed as early as 6 months after treatment initiation and were maintained for up to 3 years.
- No new safety signals were observed, supporting the long-term use of pegcetacoplan.
- The COMPLETE study includes a broad and representative population of adult patients with PNH, mirroring real-world clinical practice; the study findings confirm the clinically meaningful benefits of pegcetacoplan in treating adults with PNH, and demonstrate its effectiveness in an international real-world patient population.

INTRODUCTION

- PNH is an acquired, rare, and potentially life-threatening haematological disease that is characterised by complement-mediated IVH. Patients with PNH have a substantial symptom burden and multiple clinical manifestations including anaemia, fatigue, and thrombosis.[1,2]
- C5is control IVH. However, many patients may experience residual IVH and/or emerging EVH with persistent anaemia (via C3 deposition in RBCs), potentially leading to transfusion dependence and a compromised quality of life.[2–8]
- Pegcetacoplan is a C3/C3b inhibitor approved for the treatment of adults with PNH, providing a broad control of haemolysis by addressing IVH and EVH.[9,10]
- Pivotal Phase 3 trials in C5i-experienced (PEGASUS; NCT03500549) and complement inhibitor-naïve (PRINCE; NCT04085601) patients with PNH showed that pegcetacoplan was superior in improving haematological and other clinical outcomes versus eculizumab and supportive care, respectively.[11,12]
- There is a growing body of real-world evidence on the use of pegcetacoplan to treat adults with PNH,[13,14] supporting the efficacy and safety outcomes observed in clinical trials.

OBJECTIVE

- To present interim analysis results from the ongoing Phase 4 COMPLETE study (NCT05776472) to characterise the long-term real-world effectiveness of pegcetacoplan for the treatment of adults with PNH.[15]

METHODS

Study design

- COMPLETE is a long-term, ongoing, observational Phase 4 study enrolling adult patients across Europe, the Middle East, Canada, and Australia.
- The main part of the study involves a prospective observational period of ~36 months; in total, retrospective and prospective data will be collected for 36–72 months, including a ≤12-month retrospective period prior to pegcetacoplan treatment initiation.
- The interim analysis presented here is based on a data cut-off of 5 January 2026.

Study population

- Eligible patients include adults (≥18 years) with a documented diagnosis of PNH who have initiated routine pegcetacoplan treatment either before or at enrolment.
- Patients are excluded if they have participated in an interventional clinical study within 3 months of study enrolment.

Study endpoints

- The primary endpoint is the change in Hb levels at 6 months after pegcetacoplan initiation (i.e., change from baseline).
- Secondary endpoints include:
  - improvement in Hb (defined as achieving Hb ≥12 g/dl or a ≥2 g/dl increase) assessed every 6 months from pegcetacoplan initiation to study end
  - change from baseline in LDH, ARC, bilirubin, and ferritin assessed every 6 months from pegcetacoplan initiation to study end
  - absolute levels of Hb, LDH, ARC, bilirubin, and ferritin assessed at pegcetacoplan initiation and every 6 months until study end
  - transfusion support requirements, evaluated by recording the annual number of RBCTs and units of RBCs
  - adverse events.

Data analysis

- Datasets included: 1) the FAS, defined as all consenting patients who met all eligibility criteria at enrolment; 2) the FAS-6, defined as a subset of the FAS with available Hb data at the 6-month timepoint. This analysis focuses on the FAS-6 for the primary endpoint and the FAS for all other analyses, unless stated otherwise.
- Descriptive statistics were used to summarise patient data and to analyse the primary and secondary endpoints.
- Reported adverse events were classified using the Medical Dictionary for Regulatory Activities.

RESULTS

Baseline characteristics

- As of 5 January 2026, 125 eligible patients were enrolled across 14 countries; 125 patients were included in the FAS and 107 patients in the FAS-6.
- **Table 1** presents the baseline characteristics for the FAS and FAS-6. In the FAS, median (IQR) age was 53.0 (37.0, 66.0) years and 51.2% of patients were female; the corresponding values for the FAS-6 were 51.0 (36.0, 66.0) years and 51.4% of patients, respectively.

Table 1. Baseline characteristics

	FAS (n=125)	FAS-6 (n=107)
Median (IQR) age, years	53.0 (37.0, 66.0)	51.0 (36.0, 66.0)
Female, n (%)	64 (51.2)	55 (51.4)
History of aplastic anaemia, n (%)	42 (33.6)	36 (33.6)
Prior C5i, n (%)	100 (80.0)	91 (85.0)
Eculizumab	73 (58.4)	67 (62.6)
Ravulizumab	42 (33.6)	38 (35.5)
Crovalimab	6 (4.8)	6 (5.6)
Hb <10.5 g/dl, n (%)	85[a] (72.0)	76[b] (74.5)
Median (IQR) time from PNH diagnosis to pegcetacoplan initiation, months	49.5[c] (19.5, 98.2)	51.1[d] (19.8, 104.2)

[a]Data missing for seven patients; n=85/118. [b]Data missing for five patients; n=76/102. [c]Data missing for eight patients; n=117. [d]Data missing for six patients; n=101.
C5i, complement 5 inhibitor; FAS, full analysis set; FAS-6, 6-month full analysis set; Hb, haemoglobin; IQR, interquartile range; PNH, paroxysmal nocturnal haemoglobinuria.

Efficacy

- The median (IQR) duration of pegcetacoplan treatment was 21.8 (13.0, 29.6) months for the FAS and 22.5 (13.3, 30.5) months for the FAS-6.

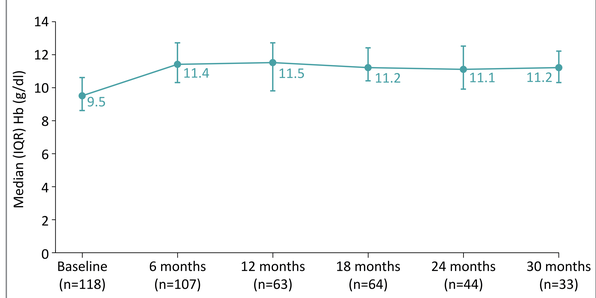
Primary endpoint

- In the FAS-6 (n=102; data missing: n=5), Hb levels increased from baseline to 6 months; the median (IQR) absolute change in Hb was 2.2 (0.8, 3.4) g/dl and the corresponding median (IQR) relative change was 24.1% (8.0, 39.5).

Secondary endpoints

- Median (IQR) Hb levels increased from 9.5 (8.6, 10.6) g/dl at baseline to 11.4 (10.3, 12.7) g/dl at 6 months after pegcetacoplan initiation; Hb levels stayed consistent over the next 24 months of treatment, with a median (IQR) Hb level of 11.2 (10.3, 12.2) g/dl at 30 months (**Figure 1**).

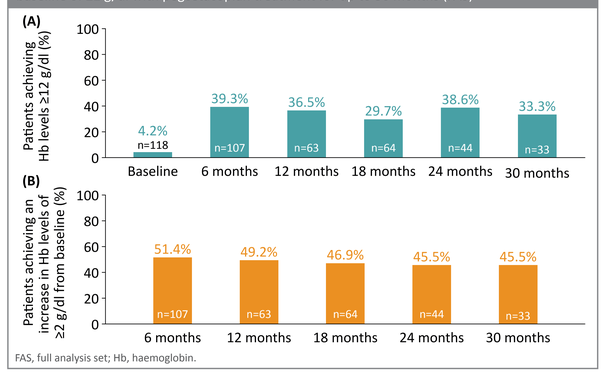
Figure 1. Hb levels with pegcetacoplan treatment for up to 30 months (FAS)



FAS, full analysis set; Hb, haemoglobin; IQR, interquartile range.

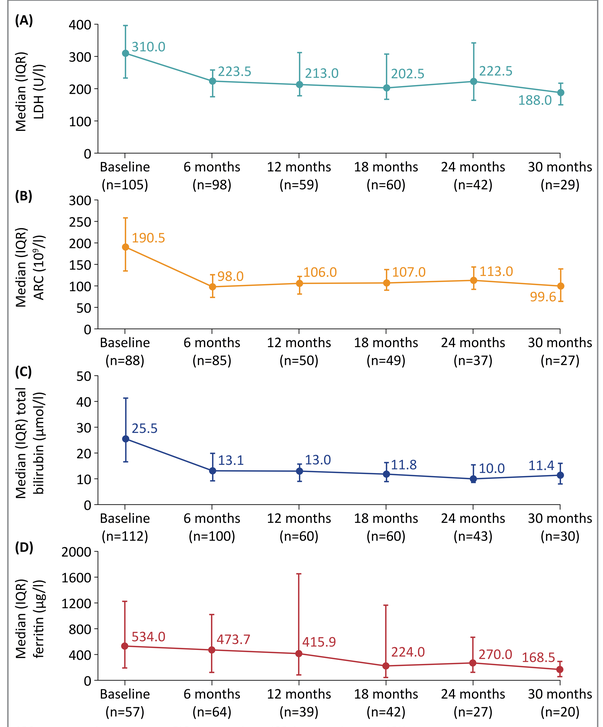
- At baseline, 4.2% of patients had Hb levels ≥12 g/dl; the proportion of patients achieving these levels increased considerably following pegcetacoplan initiation (6 months: 39.3% of patients; 30 months: 33.3% of patients [**Figure 2A**]).
- The percentage of patients who achieved an increase in Hb levels of ≥2 g/dl following pegcetacoplan treatment initiation was 51.4% at 6 months, and remained stable up to 30 months (45.5%; **Figure 2B**).

Figure 2. Patients achieving (A) Hb levels ≥12 g/dl and (B) an increase in Hb levels from baseline of ≥2 g/dl with pegcetacoplan treatment for up to 30 months (FAS)



FAS, full analysis set; Hb, haemoglobin.

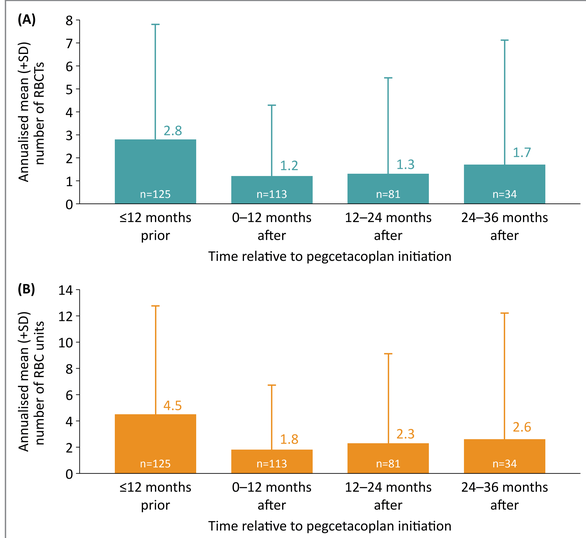
Figure 3. (A) LDH, (B) ARC, (C) total bilirubin, and (D) ferritin levels with pegcetacoplan treatment for up to 30 months (FAS)



ARC, absolute reticulocyte count; FAS, full analysis set; IQR, interquartile range; LDH, lactate dehydrogenase.

- Median LDH and ARC levels decreased between baseline and 6 months of pegcetacoplan treatment (LDH by 28% to 223.5 U/l; ARC by 49% to 98.0 × 10^9/l) and remained decreased throughout the 30 months (LDH ranging 188.0–222.5 U/l; ARC ranging 99.6–113 × 10^9/l [**Figure 3A, 3B**]).
- Median bilirubin and ferritin levels decreased from baseline (when levels were elevated) to 6 months after treatment initiation and decreased levels were maintained through to 30 months of treatment (**Figure 3C, 3D**).
- The mean number of annualised RBCTs and RBC units decreased from before pegcetacoplan initiation to 0–12 months after initiation and remained low up to 24–36 months after initiation (**Figure 4**).
- Haemolytic events requiring additional intervention occurred in 11.5–12.5% of patients per 6-month study interval between 6 and 30 months after pegcetacoplan initiation.

Figure 4. Annualised number of (A) RBCTs and (B) RBC units before and during pegcetacoplan treatment for up to 36 months (FAS)



The whiskers represent the mean + 1 SD.
FAS, full analysis set; RBC, red blood cell; RBCT, red blood cell transfusion; SD, standard deviation.

Safety

- Up to the data cut-off on 5 January 2026, adverse events occurred in 48.8% (n=61/125) of patients; 10.4% (n=13/125) of patients had at least one adverse event classified as related to study treatment.
- SAEs occurred in 24.0% (n=30/125) of patients; 1.6% (n=2/125) of patients had an SAE classified as related to study treatment.
- Adverse events leading to treatment discontinuation were reported for 0.8% (n=1/125; headache) of patients.

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Abbreviations: ARC, absolute reticulocyte count; C3, complement 3 protein; C5i, complement 5 inhibitor; EVH, extravascular haemolysis; FAS, full analysis set; FAS-6, 6-month full analysis set; Hb, haemoglobin; IQR, interquartile range; IVH, intravascular haemolysis; LDH, lactate dehydrogenase; PNH, paroxysmal nocturnal haemoglobinuria; RBC, red blood cell; RBCT, red blood cell transfusion; SAE, serious adverse event.

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