Benefit of pegcetacoplan in patients with paroxysmal nocturnal hemoglobinuria irrespective of baseline transfusion status

Britta Höchsmann,[1,2] Ana Boban,[3,4] Marta Morado,[5] Peter Hillmen,[6] Sheena Patel,[7] Johan Szamosi,[7] Elena Surova,[7] Jens Panse[8,9]

[1]Institute of Transfusion Medicine, University of Ulm, Ulm, Germany; [2]Institute of Clinical Transfusion Medicine and Immunogenetics, German Red Cross Blood Transfusion Service, Baden-Württemberg-Hessen and University Hospital of Ulm, Ulm, Germany; [3]Division of Haematology, Department of Internal Medicine, University Hospital Center Zagreb, Zagreb, Croatia; [4]School of Medicine, University of Zagreb, Zagreb, Croatia; [5]Department of Hematology, Hospital Universitario La Paz, Madrid, Spain; [6]Apellis Pharmaceuticals, Inc., Waltham, MA, USA; [7]Swedish Orphan Biovitrum AB, Stwasockholm, Sweden; [8]Department of Oncology, Hematology, Hemostaseology and Stem Cell Transplantation, University Hospital RWTH Aachen, Aachen, Germany; [9]Centre for Integrated Oncology (CIO), Aachen Bonn Cologne Düsseldorf (ABCD), Aachen, Germany.

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CONCLUSIONS

- **Key efficacy parameters** were **achieved and maintained long-term for up to 192 weeks irrespective of baseline transfusion status** across C5i-experienced and -naïve patients.
- The results **highlight the benefit of initiating pegcetacoplan in C5i-experienced or -naïve patients**, regardless of transfusion burden, a conventional marker of PNH severity.

INTRODUCTION

PNH is characterized by **complement-mediated hemolysis**, resulting in **increased thrombosis risk** and **substantial symptom burden**.[1]

There is an **ongoing need to further understand relevance of baseline characteristics**, as predictors of treatment response, to guide treatment decision making.

Pegcetacoplan is a **complement C3/C3b inhibitor approved in Europe, the US and other countries for the treatment of adult patients with PNH**, providing **efficient control of intravascular and extravascular hemolysis**.[2-5]

In **Phase 3 trials**, **pegcetacoplan demonstrated significant and sustained improvements in hematologic and clinical parameters** in complement 5 inhibitor (C5i)-experienced (PEGASUS) and -naïve (PRINCE) adult patients with PNH.[6-8] Pegcetacoplan's efficacy and safety is further **supported by long-term and real-world data**.[9-15]

AIM

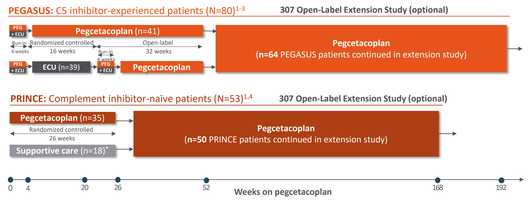
Evaluate the effect of baseline transfusion status on key hematological and clinical responses to pegcetacoplan treatment in C5i-experienced and -naïve patients with paroxysmal nocturnal hemoglobinuria (PNH) over long-term follow-up.

METHODS

This *post-hoc* analysis assessed **long-term efficacy and safety of pegcetacoplan in 2 subpopulations, PNH patients with </≥4 red blood cell (RBC) concentrates in the 12 months prior to study enrollment**, as part of an integrated analysis of the pivotal Phase 3 trials (PEGASUS [NCT03500549], PRINCE [NCT04085601]) and the subsequent ongoing open-label extension (OLE) study (NCT03531255) (**Figure 1**).

Time-aligned outcomes, including **hemoglobin (Hb), lactate dehydrogenase (LDH), absolute reticulocyte count (ARC), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue, and number of annualized RBC concentrates on pegcetacoplan treatment** were assessed for **up to 192 weeks**.

Figure 1. Integrated analysis data set[7]



* Patients in the PRINCE supportive care arm could escape to the pegcetacoplan arm before the end of the 26 weeks if they experienced a qualifying event of hemoglobin decrease by ≥2 g/dL or thrombosis.
ECU, eculizumab; PEG, pegcetacoplan.

RESULTS

In the 12 months prior to study enrollment, **64 patients had received <4 RBC concentrates** (PEGASUS+OLE, n=36; PRINCE+OLE, n=28) and **68 patients had received ≥4 RBC concentrates** (PEGASUS+OLE, n=44; PRINCE+OLE, n=24).

At baseline, mean (standard deviation [SD]) **age was 46.2 (16.0) years and 47.9 (14.8) in the <4 and ≥4 RBC concentrates group, respectively**; **50% (n=32) and 60% (n=41) of patients** were **female.** As expected, there was a **higher proportion of patients with concomitant aplastic anemia** in the **group with higher baseline transfusion status** (**Table 1**).

Table 1. Patient baseline characteristics

n (%)	<4 RBC concentrates* (N=64)	≥4 RBC concentrates* (N=68)
Age, years, mean (SD)	46.2 (16.0)	47.9 (14.8)
<65 years	53 (83)	56 (82)
≥65 years	11 (17)	12 (18)
Sex, n (%)		
Female	32 (50)	41 (60)
Male	32 (50)	27 (40)
History of aplastic anemia, n(%)	9 (14)	21 (31)

* RBC concentrates 12 months prior study enrollment.
RBC, red blood cell; SD, standard deviation.

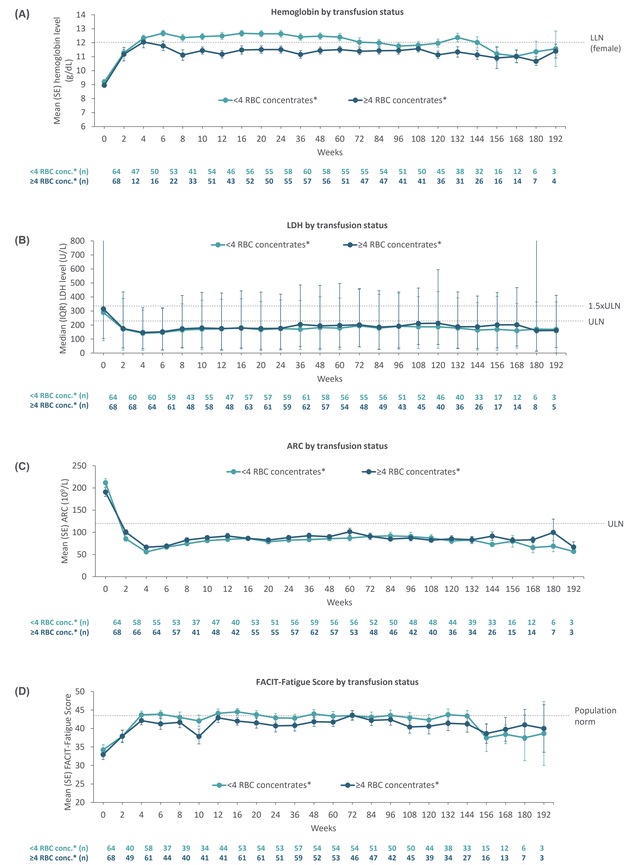
Efficacy

Overall, **trends in improvements with pegcetacoplan in mean Hb, LDH, ARC and FACIT-Fatigue over time were consistent** between transfusion status groups (</≥4 RBC concentrates).

- By Week 4 after pegcetacoplan initiation, **mean (standard error) Hb levels increased from 9.2 (0.2) g/dL and 9.0 (0.1) g/dL at baseline to 12.3 (0.2) g/dL and 12.1 (0.4) g/dL in the <4 and ≥4 RBC concentrates group**, respectively. Improvements were **sustained for up to 192 weeks**
- **Median LDH decreased** to **below the upper limit of normal** (ULN) by **Week 4** and remained mostly **stable up to 192 weeks**
- **Initial reductions in mean ARC were sustained below the ULN**
- Improvements in hematological parameters translated into rapid increases in **mean FACIT-Fatigue scores and improvements were largely maintained long-term** (**Figure 2**)

Annualized transfusion burden was **reduced** in both groups **regardless of baseline transfusion status**, which supports the improvements seen across other hematological parameters (**Table 2**).

Figure 2. Hematological and clinical outcomes over time by baseline transfusion status; (A) Hb, (B) LDH, (C) ARC, (D) FACIT-Fatigue



* RBC concentrates 12 months prior study enrollment. ARC, absolute reticulocyte count; conc., concentrates; FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; IQR, interquartile range; LDH, lactate dehydrogenase; LLN, lower limit of normal; RBC, red blood cell; SE, standard error; ULN, upper limit of normal.

Table 2. Annualized transfusion burden prior to and during pegcetacoplan treatment

Median (range)	<4 RBC concentrates* (N=64)	≥4 RBC concentrates* (N=68)
Number of RBC concentrates within 12 months prior to pegcetacoplan	1 (0; 3)	8 (2; 30)
Number of annualized RBC concentrates on pegcetacoplan treatment†	0 (0; 9.8)‡	0 (0; 41.1)‡

* RBC concentrates 12 months prior study enrollment. † Annualized transfusions were calculated based on in-study transfusions and follow-up time available. ‡ Of the 14 patients who had in-study transfusions, 4 patients had <12 months follow up. ‡ Of the 26 patients who had in-study transfusions, 10 patients had <12 months follow up.
RBC, red blood cell.

Safety

Table 3 summarizes adverse events (AEs) in PNH patients treated with pegcetacoplan by transfusion status. **In the up to 192 weeks of follow-up** pegcetacoplan **safety profile was comparable between the groups** with **no new safety signals.** 35 (55%) and 38 (56%) patients with <4 and ≥4 RBC concentrates, respectively, experienced serious AEs, deemed pegcetacoplan-related in 2 and 4 patients. 6 (9%) and 11 (16%) patients discontinued pegcetacoplan due to an AE. No *Neisseria meningitides* infections were observed.

Table 3. Summary of adverse events in PNH patients by transfusion status

n (%)	<4 RBC concentrates* (N=64)	≥4 RBC concentrates* (N=68)
Any AE	63 (98.4)	66 (97.1)
AEs related to PEG	26 (40.6)	35 (51.5)
SAEs	35 (54.7)	38 (55.9)
SAEs related to PEG	2 (3.1)	4 (5.9)
AEs leading to study drug discontinuation	6 (9.4)	11 (16.2)
AEs leading to death†	2 (3.1)	3 (4.4)
AEs of special interest		
AEs related to infusion reaction	26 (40.6)	28 (41.2)
SAEs related to infusion reaction	0	0
Treatment emergent infections	51 (79.7)	50 (73.5)
Serious treatment emergent infections related to PEG	0	2 (2.9)

* RBC concentrates 12 months prior study enrollment.
† None were deemed related to pegcetacoplan.
AE, adverse event; PEG, pegcetacoplan; RBC, red blood cell; SAE, serious adverse event.

REFERENCES

1. Hill A et al. Nat Rev Dis Primers 2017;3:17028;
2. EMPAVELI (pegcetacoplan) US Prescribing Information. 2021;
3. ASPAVELI (pegcetacoplan) EMA SmPC 2024;
4. Aspaveli® (pegcetacoplan) SwissPAR 2023;
5. Empaveli™ (Pegcetacoplan) Canada Product Monograph 2022;
6. Hillmen P et al. N Engl J Med 2021;384:1028-37;
7. Peffault de Latour R et al. Lancet Haematol 2022:9:e648-59;
8. Wong RSM et al. Blood Adv 2023;7:2468-78;
9. de Castro C et al. ASH 2023; Abstract 574;
10. Griffin M et al. Am J Hematol 2024;99:816-23;
11. Vallejo C et al. EHA 2024; Abstract P1917;
12. Panse J et al. ASH 2024; Abstract 5085;
13. Mulherin et al. Hematol Rep 2024;
14. Wilson K et al. Eur J Haematol 2024;112(4):516-529;
15. Metafuni E et al. Br J Haematol 2025;206:1246-9.

CONTACT INFORMATION

Britta Höchsmann | b.hoechsmann@blutspende.de

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ABBREVIATIONS: AE, adverse event; ARC, absolute reticulocyte count; C5i, complement C5 inhibitor; conc., concentrates; FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; IQR, interquartile range; LDH, lactate dehydrogenase; LLN, lower limit of normal; OLE, open-label extension; PEG, pegcetacoplan; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell; SD, standard deviation; SE, standard error; ULN, upper limit of normal.

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