PO119

Injection Site Reactions in Adults With Paroxysmal Nocturnal Haemoglobinuria Receiving Subcutaneous Pegcetacoplan for Up to 3 Years

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CONCLUSIONS

- **Most injection site reactions (ISRs) were mild and none led to treatment discontinuation.**
- **Over time, ISR rates may have decreased as patients gained confidence with self-administrating pegcetacoplan (PEG).**
- **High adherence and improved FACIT-Fatigue scores suggest ISRs are not a barrier to PEG treatment.**

INTRODUCTION

- Paroxysmal nocturnal haemoglobinuria (PNH) is a rare, acquired, haematologic disease characterised by complement activation leading to haemolysis, anaemia, fatigue, haemoglobinuria and life-threatening thrombosis.[1]
- Complement inhibition is the standard of care for PNH treatment.[2–4] However, complement 5 inhibitors (C5i) may not provide full disease control in some patients due to residual intravascular and emergent extravascular haemolysis.
- Pegcetacoplan (PEG) is the first approved C3-targeted therapy for PNH and has demonstrated improvements in haematological outcomes for patients with PNH in two phase 3 trials: **PEGASUS** (NCT03500549) in C5i-experienced patients and **PRINCE** (NCT04085601) in C5i-naive patients.[5,6]
- The long-term safety and efficacy of PEG in patients with PNH from **PEGASUS**, **PRINCE** and other phase 1b–3 trials of PEG is being evaluated in the 307 open-label extension (OLE) study (307 OLE; NCT03531255).[7]
- An integrated analysis of **PEGASUS**, **PRINCE** and the 307 OLE showed maintained efficacy and safety of PEG for up to 3 years.[8]
- PEG is administered subcutaneously by the patient, potentially lowering treatment burden compared to intravenous therapies for PNH.[9] However, subcutaneous treatments can sometimes lead to injection site reactions (ISRs).

AIM

- Assess ISR treatment-emergent adverse events (TEAEs) in an integrated analysis of patients treated with PEG from **PEGASUS**, **PRINCE** and the 307 OLE for up to 3 years.

METHODS

- Patients received PEG 1,080 mg subcutaenously twice weekly, with dosage escalations allowed as follows:
  - In patients with a lactate dehydrogenase concentration of >2× the upper limit of normal (226 U/L), dosing frequency could be increased to every 3 days (with the option to increase to 3 times weekly in the 307 OLE).
- Adherence was defined as the total number of doses received from initiation until data cut (31 January 2023) divided by expected doses.
- TEAEs, including ISR TEAEs, were recorded from initiation of PEG monotherapy through 3 years (**PEGASUS**) or 2.5 years (**PRINCE**).
  - ISR TEAE severity was defined as mild, moderate or severe.
- Quality of life was assessed by mean Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scores from PEG initiation through 3 years (**PEGASUS**) or 2.5 years (**PRINCE**) of treatment.

RESULTS

Patients and dosing

- Overall, 114 patients from **PEGASUS** (n=64) and **PRINCE** (n=50) enrolled in the 307 OLE.
- PEG dosing increased from twice weekly to every 3 days in 13/80 **PEGASUS** (16.3%) and 9/52 **PRINCE** patients (17.3%), and from twice weekly to 3 times weekly in 7/80 **PEGASUS** (8.8%) and 4/52 **PRINCE** patients (7.7%) during the 307 OLE.
- More than 92% of patients had adherence of ≥95%.

Treatment-emergent adverse events

- TEAE results are described in **Figure 1**.
- Overall, 35.6% of patients experienced ISR TEAEs across **PEGASUS** and **PRINCE** populations for up to 3 and 2.5 years, respectively (**Table 1**).
  - ISR rates decreased from 38.8% (Year 0 to 1) to 9.1% (Year 2 to 3) in **PEGASUS** patients and from 17.3% (Year 0 to 1) to 9.1% (Year 2 to 2.5) in **PRINCE** patients (**Table 1**).
- Most ISRs in **PEGASUS** and **PRINCE** were of mild severity (**Figure 2**).
- No ISRs were serious or led to treatment discontinuation.

Quality of life

- FACIT-Fatigue scores improved from below the population norm at baseline to close to or at the normal range after 3 years of treatment (**Figure 3**).

Figure 1. Summary of recorded TEAEs

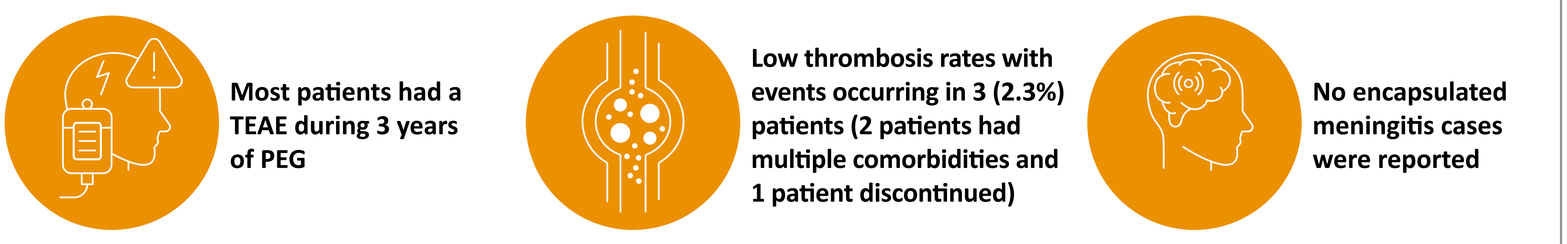
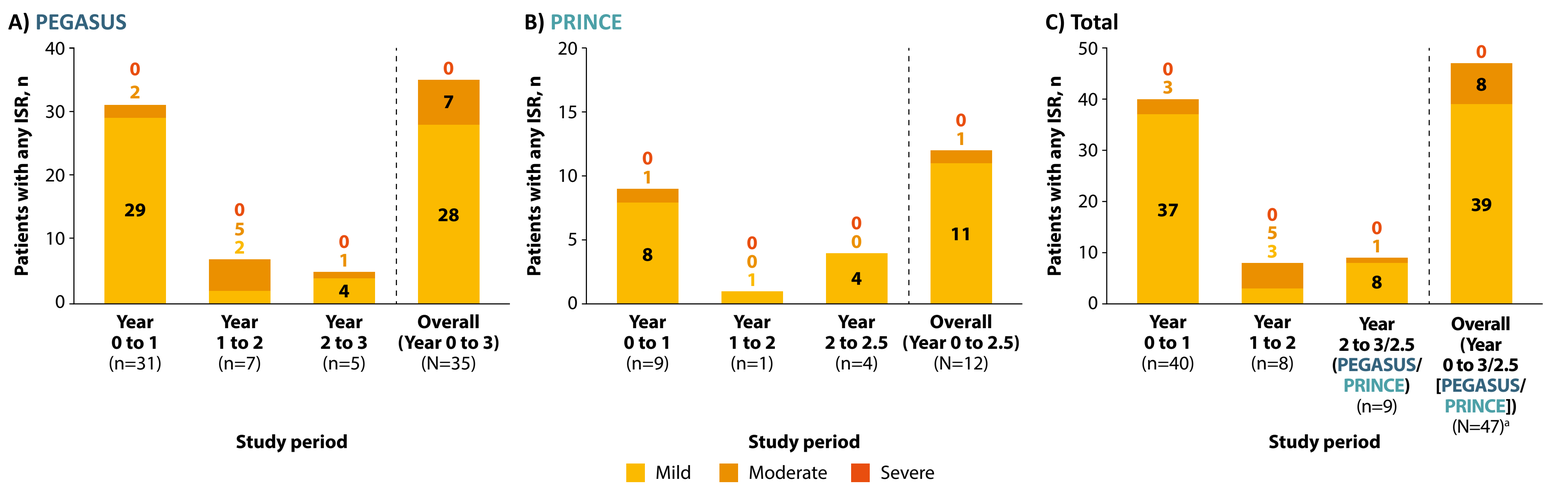


Table 1. Rates of ISRs[a] over time in C5i-experienced (PEGASUS), C5i-naive (PRINCE) and the combined (total) population of patients with PNH receiving PEG monotherapy

	Study Period			
	Year 0 to 1	Year 1 to 2	Year 2 to 3 (PEGASUS)/ Year 2 to 2.5 (PRINCE)	Overall (Year 0 to 3 [PEGASUS]/ Year 0 to 2.5 [PRINCE])[b]
PEGASUS population	n=80	n=62	n=55	N=80
Any ISR TEAE, n (%)	31 (38.8)	7 (11.3)	5 (9.1)	35 (43.8)
PRINCE population	n=52	n=49	n=44	N=52
Any ISR TEAE, n (%)	9 (17.3)	1 (2.0)	4 (9.1)	12 (23.1)
Total population	n=132	n=111	n=99	N=132
Any ISR TEAE, n (%)	40 (30.3)	8 (7.2)	9 (9.1)	47 (35.6)

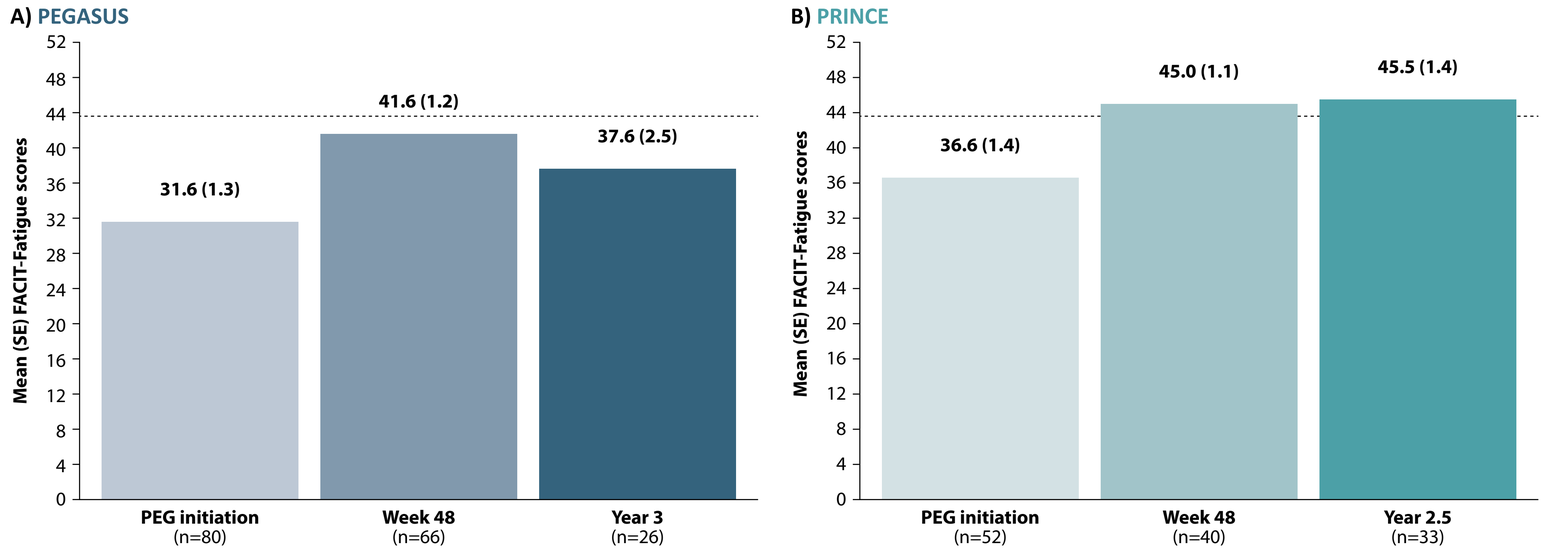
[a] Events of ISRs included the following preferred terms: injection site erythema, induration, reaction, haemorrhage, pain, pruritis, swelling, bruising, scar, discolouration, extravasation, haematoma, oedema and rash, infusion site swelling, infusion-related reaction and vaccination site pain; [b] Patients with events in multiple subperiods (e.g. an event in Year 0 to 1 and an event in Year 1 to 2) were counted once in the overall period.

Figure 2. Rates of ISRs[a] by severity over time in PEGASUS, PRINCE and the combined (total) population of patients with PNH receiving PEG through up to 3 years



ISR severity, as reported by investigators, was defined as mild (mild/passing discomfort that did not limit activities; no treatment required), moderate (discomfort limiting daily activities; may have required treatment), or severe (significant symptoms preventing activities; may have required hospitalisation/invasive intervention). [a] Patients with events in multiple subperiods (e.g. an event in Year 0 to 1 and an event in Year 1 to 2) were counted once in the overall period.

Figure 3. Mean (SE) FACIT-Fatigue scores in PEGASUS and PRINCE patients receiving PEG monotherapy through up to 3 years



FACIT-Fatigue scores range from 0 to 52; higher scores indicate less fatigue and greater quality of life. Mean (SD) FACIT-Fatigue score obtained from the general population norm was 43.6 (9.4).[10]

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Disclosures

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Abbreviations

C3: complement 3; **C5i:** complement 5 inhibitors; **FACIT:** Functional Assessment of Chronic Illness Therapy; **ISR:** injection site reaction; **OLE:** open-label extension; **PNH:** paroxysmal nocturnal haemoglobinuria; **PEG:** pegcetacoplan; **SE:** standard error; **TEAE:** treatment-emergent adverse event.

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