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Decreasing rates of injection site reactions over time: Long-term outcomes across multiple indications support pegcetacoplan for C3G/primary IC-MPGN

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CONCLUSIONS

- Results show consistently positive experience across studies in C3G/primary IC-MPGN and PNH, with **mostly mild injection site reactions**, **rates decreasing over time** and **high treatment compliance overall**
- Findings suggest a positive **patient improvement with self-administration over time**, with **injection site reactions not becoming a treatment barrier**

INTRODUCTION

- C3 glomerulopathy (C3G) and primary (idiopathic) immune-complex membranoproliferative glomerulonephritis (IC-MPGN) are rare diseases driven by uncontrolled C3 activation, excessive glomerular deposition of C3 breakdown products, and progressive kidney failure[1,2]
- Pegcetacoplan offers targeted treatment by selectively binding C3/C3b. Based on the Phase 3 VALIANT study[3], pegcetacoplan was EMA- and FDA-approved for treatment of adults and paediatric patients (≥12 years) with C3G and primary IC-MPGN, and has also been approved since 2021 for treatment of adults with paroxysmal nocturnal haemoglobinuria (PNH), a rare haematological disease, based on Phase 3 PEGASUS and PRINCE studies[4,5]
- Pegcetacoplan is administered by subcutaneous (SC) infusion. A single-use, on-body injector **(FIGURE 1)** is available in the US[6], Brazil, Saudia Arabia, and South Korea, and will soon be available in other regions to simplify patient experience. Injection site reactions (ISRs) are a common adverse event (AE) with SC therapies[7], which may influence compliance, patient experience, and long-term treatment success[8]

AIM

Characterise ISRs across indications in VALIANT for C3G/IC-MPGN patients and in PEGASUS, PRINCE and their long-term extension (LTE) study for PNH patients

FIGURE 1. enFuse injector

METHODS

- Patients receiving ≥1 dose of pegcetacoplan in VALIANT, PEGASUS, and PRINCE were included. All adults received 1,080 mg via 20 mL SC infusion twice weekly, with dose adjustments permitted in PNH studies. Adolescents (≤49 kg) with C3G/primary IC-MPGN received a body weight-matched regimen
- ISR included a set of preferred term treatment-emergent AEs (TEAEs; see Figure 2 for preferred terms included in ISRs). ISR TEAE incidence, severity and temporal trends were analysed from pegcetacoplan initiation through 52 weeks in VALIANT, 2.5 years in PRINCE plus LTE study, and 3 years in PEGASUS plus LTE study. Treatment compliance and potential ISR-related discontinuations were also evaluated

RESULTS

- 120 patients from VALIANT were included. Overall, 29 (24.2%) experienced ≥1 ISR while on pegcetacoplan
- The rate of ISRs decreased from the initial 26-week randomised controlled period (RCP) to the subsequent 26-week open-label period (OLP) in patients who received pegcetacoplan for both treatment periods, The decrease was observed in adults and adolescents **(TABLE 1)** and overall **(FIGURE 2)**, suggesting that tolerability improved with patient experience
- There were no severe ISRs and most ISRs were mild. Pegcetacoplan discontinuation due to ISR occurred in 1 patient (short duration of non-severe cutaneous reaction that resolved). Overall, compliance was high (≥90–≤100%) for the RCP (63 patients [100%]) and OLP (114 patients [96.6%])

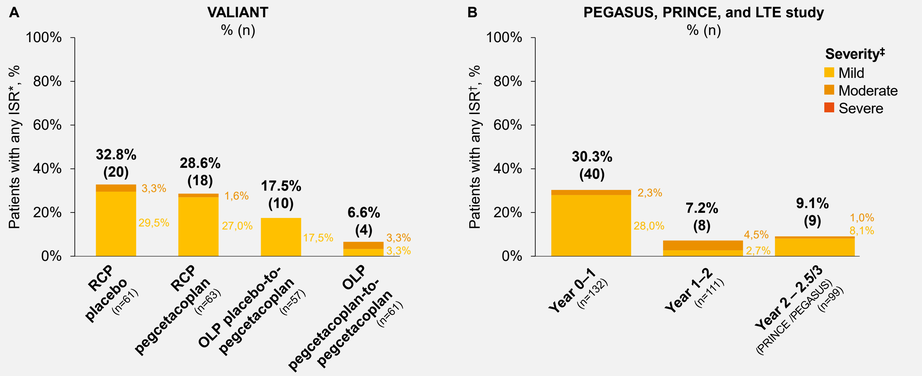
TABLE 1. ISR in VALIANT by study period and age group

	Study period			
	Week 0–26		Week 27–52	
≥1 ISR*, n/N (%)	RCP placebo	RCP pegcetacoplan	OLP placebo-to-pegcetacoplan	OLP pegcetacoplan-to-pegcetacoplan
Adolescents (12–17 years)	11/27 (40.7)	9/28 (32.1)	6/25 (24.0)	1/27 (3.7)
Adults (≥18 years)	9/34 (26.5)	9/35 (25.7)	4/32 (12.5)	3/34 (8.8)

*See Figure 2 for preferred terms included in ISRs. ISR, injection site reaction; OLP, open-label period; RCP, randomised controlled period; TEAE, treatment-emergent adverse event.

- 132 patients from PEGASUS, PRINCE and the LTE study were included. Overall, 47 (35.6%) experienced ≥1 ISR over up to 2.5–3 years. ISR rates decreased over time from 40 patients (30.3%, year 0–1) to 9 patients (9.1%, year 2–2.5/3) **(FIGURE 2)**
- ISRs were mild in 39/47 patients (83.0%). No ISRs were serious or led to treatment discontinuation. Overall, >92% of patients had adherence of ≥95% over 2.5–3 years of treatment

FIGURE 2. ISRs over time in patients with C3G/primary IC-MPGN in VALIANT (A) and patients with PNH in PEGASUS, PRINCE, the LTE study (B)



*Events of ISRs included the following terms: Injection site swelling, erythema, pruritus, pain, reaction, induration, irritation, bruising, hypoesthesia, infusion site erythema, swelling, pain, pruritus, bruising, discomfort, haematoma, haemorrhage, induration, oedema, rash, reaction, discolouration; application site pain; administration site pain; chills; oedema; pain; peripheral swelling; puncture site pain. †Events of ISRs included the following preferred terms: Injection site erythema, induration, reaction, haemorrhage, pain, pruritus, swelling, bruising, scar, discolouration, extravasation, haematoma, oedema and rash; infusion site swelling; infusion-related reaction; vaccination site pain. ‡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). C3G/primary IC-MPGN, C3 glomerulopathy/primary (idiopathic) immune complex membranoproliferative glomerulonephritis; ISR, injection site reaction; LTE, long-term extension; OLP, open-label period; PNH, paroxysmal nocturnal haemoglobinuria; RCP, randomised controlled period.

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DISCLOSURES

NM has nothing to disclose. **AM** has received consultant and speaker fees from Sobi. **DZ** has received consulting fees from Sobi, Apellis, and Novartis. **ASG** has received consultant fees from Aurinia, Chinook, GSK, Horizon, Kaneka, Novartis, Travere, ValenzaBio, and Vera, research funding from Amgen, Aurinia, Chinook, Travere, ValenzaBio, and Vera, and honoraria from Aurinia, Calliditas, and Kaneka. **CMN** has received consultant fees from Alexion Pharmaceuticals, Apellis, Biocryst Pharmaceuticals, Novartis, and Vertex, DSMB fees from Silence Therapeutics and clinical trial support from Apellis, Biocryst Pharmaceuticals, Novartis, and Travere. **SP** is an employee of Swedish Orphan Biovitrum AB. **LF** is an employee of Swedish Orphan Biovitrum AB and may hold stock or stock options. **AC** is an employee of Apellis Pharmaceuticals and may hold stock or stock options. **CdC** reports consultancy at Apellis, data safety monitoring board at Regeneron, advisory board at Omeros, honoraria from Novartis, Alexion, BioCryst, and Apellis, and research funding from Alexion and Apellis. **DPG** is supported by the St Peter's Trust for Kidney, Bladder and Prostate research and has consulted or presented for Alexion, Alnylam, Novartis, Bayer, GSK, Britannia, Sobi, Vifor, Sanofi, Otsuka, Calliditas, Vera and Apellis. **RJK** has received research funding from Novartis and Sobi, is a consultant at or received speaker fees from Sobi, AstraZeneca, Alexion, Novartis, Florio, Omeros and Otsuka, is a member of advisory boards at Alexion, AstraZeneca, Novartis, Sobi, Roche and Amgen.

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