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Challenge Your Thinking

Safety and low incidence of meningococcal infections with pegcetacoplan in C3G/primary IC-MPGN and PNH

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CONCLUSIONS

- **>3,500 patient-years (py) of experience over 10 years** across clinical trials and routine practice continues to demonstrate a **favourable risk-benefit profile** for pegcetacoplan
- **Overall encapsulated bacterial infection rates** (0.17/100 py) are **consistent with or lower than** meningococcal infection rates reported for C5 inhibitors eculizumab (0.28/100 py in clinical trials and 0.25/100 py in real-world) and ravulizumab (0.18/100 py in clinical trials and 0.10/100 py in real-world)[10]
- **No encapsulated meningococcal infections** observed, reflecting **effective mitigation**

INTRODUCTION

- C3 glomerulopathy (C3G) and primary (idiopathic) immune-complex membrano-proliferative glomerulonephritis (IC-MPGN) are rare diseases driven by uncontrolled C3 activation, excessive glomerular deposition of C3 breakdown products, and progressive kidney failure[1,2]
- Current treatment relies on non-specific immunosuppression, which does not target the underlying pathophysiology[2] and has a broad adverse effect profile[3]
- Pegcetacoplan offers targeted treatment by selectively binding C3/C3b. Based on the Phase 3 VALIANT study, where pegcetacoplan led to a 68.1% relative proteinuria reduction vs placebo, glomerular C3 clearance in 71% of patients and stabilisation of eGFR compared to placebo (+6.3 mL/min/1.73 m^2) at 26 weeks[4], pegcetacoplan was EMA- and FDA-approved for treatment of adults and paediatric patients (≥12 years) with C3G and primary IC-MPGN[5,6]
- Pegcetacoplan 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[5-8]
- Pegcetacoplan showed a favourable safety profile in Phase 3 studies, despite the class-related infection risk associated with complement inhibition

AIM

To review pegcetacoplan safety across indications including clinical trials and post-marketing, with a focus on infections

METHOD

- Adults received pegcetacoplan 1,080 mg via subcutaneous infusion twice weekly. Dose adjustments were permitted in PNH patients. Adolescents ≤49 kg received a body weight-matched regimen
- Cumulative exposure was the sum of total treatment duration in patients who received ≥1 dose of systemically administered pegcetacoplan across clinical trials and post-marketing estimates
- Patients were up to date with or received mandatory vaccinations per study protocol or in accordance with post-marketing risk minimisation measures (i.e. vaccinations against *S. pneumoniae*, *N. meningitidis*, and *H. influenzae*; prophylactic antibiotics were not required in patients up to date with vaccination). Encapsulated bacterial infection adverse events (AEs) that occurred despite patients having received relevant vaccinations were based on safety reporting from all systemic pegcetacoplan trials and real-world settings and used to estimate infection rates. Treatment discontinuations and deaths due to AEs were assessed from clinical trials

RESULTS

- As of 13 February 2026, there were in total 3,530 py of systemically administered pegcetacoplan across clinical trials and the post-marketing setting **(FIGURE 1)**
- Across 319 py of glomerular disease trial data, 5 confirmed encapsulated bacterial infections were reported:
  - 4 cases of *S. pneumoniae*: 2 severe and 2 moderate in severity (in all cases, pegcetacoplan treatment was interrupted/temporarily withheld during the events and treatment resumed once the infections were resolved)
  - 1 case of *H. influenzae* pneumonia: moderate in severity (pegcetacoplan treatment continued during the event and the infection resolved)
- Across 600 py of PNH trial data, no cases of encapsulated bacteria infections occurred
- No pegcetacoplan-related deaths were reported across clinical trials
- Real-world safety data (2,360 py) are consistent with those from clinical trials

FIGURE 1. Pegcetacoplan exposure and safety overview

3,530 patient-years of cumulative exposure over >10 years of experience

	2,360 py Real-world settings Includes all experiences outside of trial settings, including post-marketing data*	600 py† PNH clinical trials	319 py† Glomerular disease clinical trials	251 py† Other clinical trials
Infections, n				
Infections with non-encapsulated *N. meningitidis*	1‡	0	0	0
Infections with encapsulated bacteria for which patients had received vaccinations	1§	0	5	0
Serious	1	0	4	0
Non-serious	0	0	1	0
Treatment discontinuation due to any TEAEs, n (%)	NR‖	20 (12.2)¶	5 (3.3)#	NC
Graft loss related to pegcetacoplan, n	0	NA	0	NA
Death related to pegcetacoplan, n	NR	0	0	0**

* Post-marketing exposure is an estimation based on sales data/distribution.
† Sum of total treatment duration in all patients who received ≥1 dose of systemically administered pegcetacoplan in respective clinical trials (glomerular disease trials: NCT03453619, NOBLE [NCT04572854], VALIANT [NCT05067127], VALE [NCT05809531]; PNH trials: NCT02264639, NCT03593200, NCT02588833, NCT04901936, PEGASUS [NCT03500549], PRINCE [NCT04085601], NCT03531255; other clinical trials: NCT04579666 [ALS], NCT03226678 [AIHA, CAD], NCT05096403 [CAD], NCT05148299 [TA-TMA]).
‡ 1 case of serious non-encapsulated meningococcal sepsis in a complex PNH patient (pegcetacoplan treatment continued during event and infection resolved)[9].
§ 1 case of serious *S. pneumoniae* infection.
‖ Treatment discontinuations are not collected in the post-marketing setting.
¶ Includes 164 pegcetacoplan-treated patients across NCT02264639, NCT03593200, NCT02588833, PEGASUS (up to 3 years), and PRINCE (up to 2.5 years).
# Includes 151 pegcetacoplan-treated patients across NCT03453619, NOBLE, and VALIANT.
** There was one case of death due to aspiration pneumonia judged possibly related by the investigator, however assessed as not related by the sponsor.
AIHA, autoimmune haemolytic anaemia; ALS, amyotrophic lateral sclerosis; C3G/primary IC-MPGN, C3 glomerulopathy/primary (idiopathic) immune complex membranoproliferative glomerulonephritis; CAD, cold agglutinin disease; NA, not applicable; NC, not calculated; NR, not reported; PNH, paroxysmal nocturnal haemoglobinuria; py, patient year; TA-TMA, transplant-associated thrombotic microangiopathy; TEAE, treatment-emergent adverse event.

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