Pegcetacoplan for adolescents and adults with C3 glomerulopathy or primary immune-complex membranoproliferative glomerulonephritis: Enrollment status of the VALE extension

INFO15-TH

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CONCLUSIONS

- **The ongoing VALE extension study assesses long-term efficacy and safety of pegcetacoplan in a broad population of patients ≥12 years old with C3G or primary IC-MPGN**

OBJECTIVE

To describe the study design and enrollment status of VALE (NCT05809531), a phase 3 extension study to evaluate long-term efficacy and safety of pegcetacoplan in C3G and primary IC-MPGN

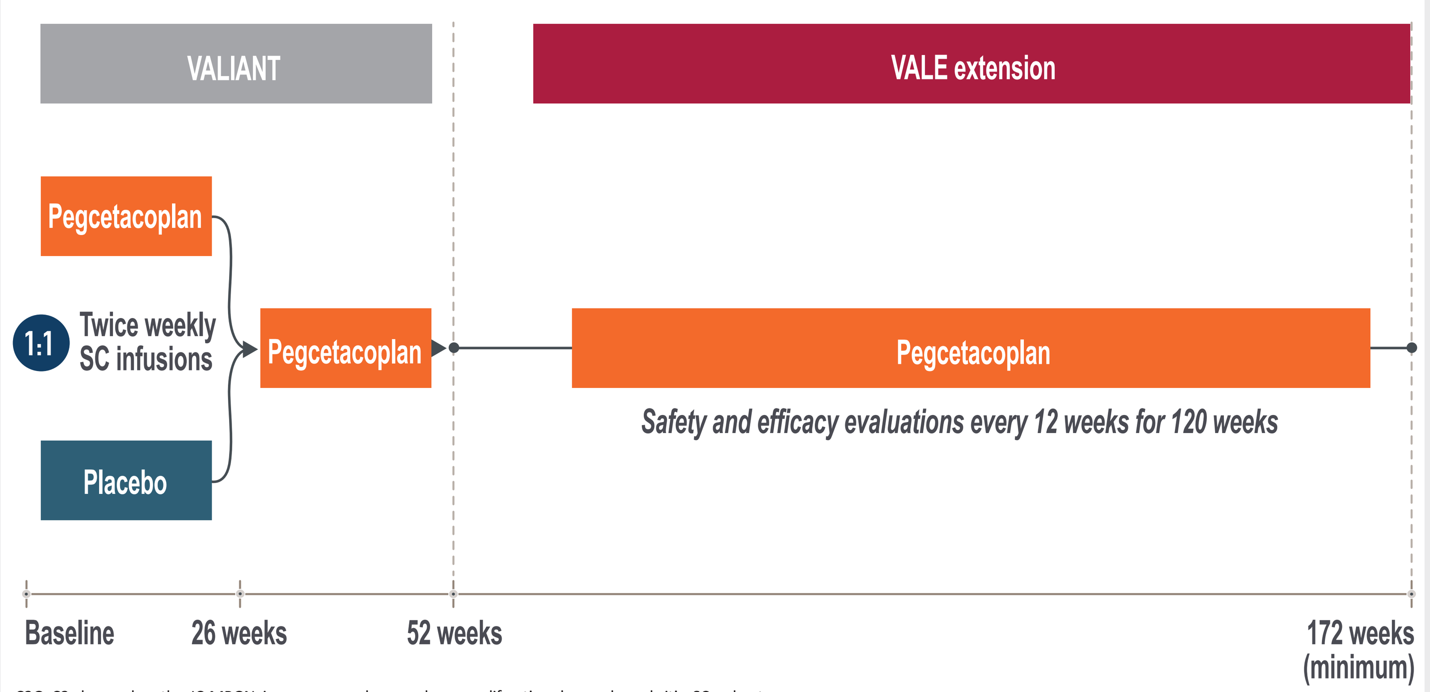
INTRODUCTION

- C3G and primary (idiopathic) IC-MPGN are rare diseases caused by C3 dysregulation that results in abnormal deposition of C3 breakdown products in the kidney, causing inflammation, kidney damage, and kidney failure[1–5]
- Pegcetacoplan blocks overactivation of alternative, classical, and lectin complement pathways by binding to C3 and C3b to regulate C3 cleavage and downstream activation[5,6]
- In the phase 3 VALIANT (NCT05067127) trial in patients with C3G or primary IC-MPGN, pegcetacoplan reduced proteinuria by 68.1% (vs placebo), reduced C3 staining to 0 in 71.4% of patients, and stabilized eGFR at week 26[7]
 - Improvements were maintained at week 52
- Pegcetacoplan has recently been approved in the United States for treatment of adult and pediatric patients aged 12 years and older with C3G or primary IC-MPGN, to reduce protienuria[8]
- VALE (NCT05809531), a phase 3 extension of the VALIANT trial, was initiated to assess long-term efficacy and safety of pegcetacoplan in patients with C3G or primary IC-MPGN[9]

METHODS

- In the open-label, nonrandomized VALE extension study, participants ≥12 years old who completed VALIANT through week 52 and had clinical benefit will continue twice-weekly doses of pegcetacoplan for a minimum of approximately 2.5 years (**Figure 1**)

Figure 1. Design of the VALIANT phase 3 trial and subsequent VALE extension trial of pegcetacoplan treatment for participants with C3G or primary IC-MPGN


VALIANT
VALE extension
Pegcetacoplan
1:1
Twice weekly SC infusions
Pegcetacoplan
Placebo
Pegcetacoplan
Safety and efficacy evaluations every 12 weeks for 120 weeks
Baseline
26 weeks
52 weeks
172 weeks (minimum)

C3G, C3 glomerulopathy; IC-MPGN, immune-complex membranoproliferative glomerulonephritis; SC, subcutaneous.

- Key VALIANT inclusion and exclusion criteria and additional inclusion criteria for VALE participants are shown in **Table 1**

METHODS *(cont.)*

Table 1. Key inclusion and exclusion criteria for VALIANT and key inclusion criteria for VALE

VALIANT Key inclusion criteria	VALIANT Key exclusion criteria
▪ Adolescents (12-17 y) weighing ≥30 kg or adults (≥18 y) ▪ Diagnosis of primary C3G or IC-MPGN (with or without previous renal transplant) ▪ Evidence of active renal disease ▪ Willingness and ability to self-administer pegcetacoplan or have a specified caregiver available to administer pegcetacoplan ▪ Vaccination against *Streptococcus pneumoniae*, *Neisseria meningitidis* (types A, C, W, Y, and B), and *Haemophilus influenzae* (type B) were required to be initiated ≥14 days prior to randomization; it was recommended for all series to be completed with coadministration of prophylactic antibiotics while receiving pegcetacoplan per the ACIP immunization schedule for complement deficiencies	▪ Previous exposure to pegcetacoplan ▪ Evidence of improving kidney disease in the 8 weeks prior to screening or during the screening period ▪ C3G or IC-MPGN secondary to another condition in the opinion of the investigator ▪ Inability or unwillingness to follow the study protocol ▪ Evidence of ongoing drug or alcohol abuse or dependence, per investigator opinion ▪ Presence of a condition that creates an undue risk for the participant or will confound interpretation of the study, per investigator opinion

VALE Key inclusion criteria
▪ Completed the VALIANT trial through week 52 ▪ Experienced clinical benefit from pegcetacoplan in the VALIANT trial, per investigator opinion ▪ Must remain on a stable regimen for treatment according to the requirements of the VALIANT trial ▪ Vaccinated per VALIANT requirements and agreed to receive additional vaccinations recommended by ACIP or other similar local applicable guidelines for adults or children with complement deficiencies and/or immunocompromising conditions

ACIP, Advisory Committee on Immunization Practices; C3G, C3 glomerulopathy; IC-MPGN, immune-complex membranoproliferative glomerulonephritis.

- Pegcetacoplan dosages were determined based on participant age, with adjustments for body weight in adolescents (ie, pediatric patients 12–17 years of age) (**Table 2**)

Table 2. Pegcetacoplan SC dosage regimen for participants in the VALE extension trial

Age, body weight	Pegcetacoplan dosage
Adults (18 years of age and older)	
▪ All weights	▪ 1080 mg twice weekly
Adolescent patients 12–17 years of age[a]	
▪ ≥50 kg	▪ 1080 mg twice weekly
▪ 35 to <50 kg	▪ 810 mg twice weekly
▪ 30 to <35 kg	▪ 648 mg twice weekly

SC, subcutaneous.
[a]Dosing will be adjusted as appropriate for adolescents/pediatric participants who enter adulthood or who have weight changes during the study.

METHODS *(cont.)*

- Key end points are shown in **Table 3**

Table 3. Key outcomes to be assessed in the VALE extension trial

Key outcomes
Primary efficacy end point
▪ Log-transformed ratio of UPCR over time versus pretreatment baseline
Secondary efficacy end points
▪ Change from pretreatment in eGFR values over time ▪ Proportion of patients with a UPCR reduction of ≥50% from the pretreatment value over time ▪ Proportion reaching proteinuria of <1 g/day over time ▪ Change from pretreatment in the FACIT-Fatigue Scale score over time ▪ Time to progression to a composite clinical outcome (≥1 of the following: sustained doubling of serum creatinine, progression to chronic kidney disease stage 5 or ESRD, kidney transplant, death from kidney or cardiovascular disease)
Key safety end points
▪ Incidence and severity of TEAEs and changes from baseline in vital signs, clinical laboratory tests, and ECG results

ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy – Fatigue; TEAEs, treatment-emergent adverse events; UPCR, urine protein-to-creatinine ratio.

RESULTS

- Of 114 patients who completed VALIANT, 113 enrolled in VALE
- As of June 2025, 101 of the 113 (89%) patients who entered VALE remain in VALE
- Results of this ongoing study are not yet available

References: 1. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. *Kidney Int*. 2021;100(4S):S1–276. **2.** Medjeral-Thomas NR, et al. *Clin J Am Soc Nephrol*. 2014;9:46–53. **3.** Kovala M, et al. *Cells*. 2023;12(5):712. **4.** Noris M, et al. *Nephrol Dial Transplant*. 2023;38:283–90. **5.** Dixon B, et al. *Kidney Int Rep*. 2023;8(11):2284–93. **6.** Smith RJH, et al. *Nat Rev Nephrol*. 2019;15:129–43. **7.** Fakhouri F, et al. In progress. **8.** Empaveli® Prescribing information. Apellis; 2025. **9.** ClinicalTrials.gov. VALE. Accessed August 21, 2025. clinicaltrials.gov/study/NCT05809531.

ABBREVIATIONS: C3G, C3 glomerulopathy; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy – Fatigue; IC-MPGN, immune-complex membranoproliferative glomerulonephritis; SC, subcutaneous; TEAEs, treatment-emergent adverse events; UPCR, urine protein-to-creatinine ratio.

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