



**KIDNEY
WEEK** 20
26

Pegcetacoplan for 76 weeks maintains proteinuria reduction and stabilized kidney function in C3G or primary IC-MPGN

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C3G and primary (idiopathic) IC-MPGN are rare, chronic, and heterogeneous complement-mediated diseases with a high unmet need



C3

C3G and primary (idiopathic) IC-MPGN are driven by **C3 dysregulation resulting in glomerular deposition of C3 breakdown products**, along with immunoglobulins in IC-MPGN, leading to **inflammation and progressive kidney damage**^{1,2}

Traditional nonspecific **immunosuppressive therapies** (such as corticosteroids and MMF) **do not target underlying complement pathway dysregulation**, and **inflammation and glomerular damage persist despite treatment**³



Persistent complement dysregulation drives **ongoing glomerular injury** that can progress to irreversible scarring. Consistent with this, **interstitial fibrosis and glomerulosclerosis** are associated with **poor renal outcomes**, underscoring the importance of controlling disease activity before substantial chronic damage accumulates⁴



Up to 50% of patients progress to kidney failure within 10 years despite current standard-of-care treatments that do not address the underlying pathologic mechanism^{3,5}

An **early, definitive diagnosis** and **immediate, pathway-specific therapeutic interventions** are needed to **prevent long-term kidney damage**³



Pegcetacoplan is the only treatment approved to slow the loss of kidney function in C3G and primary IC-MPGN⁶

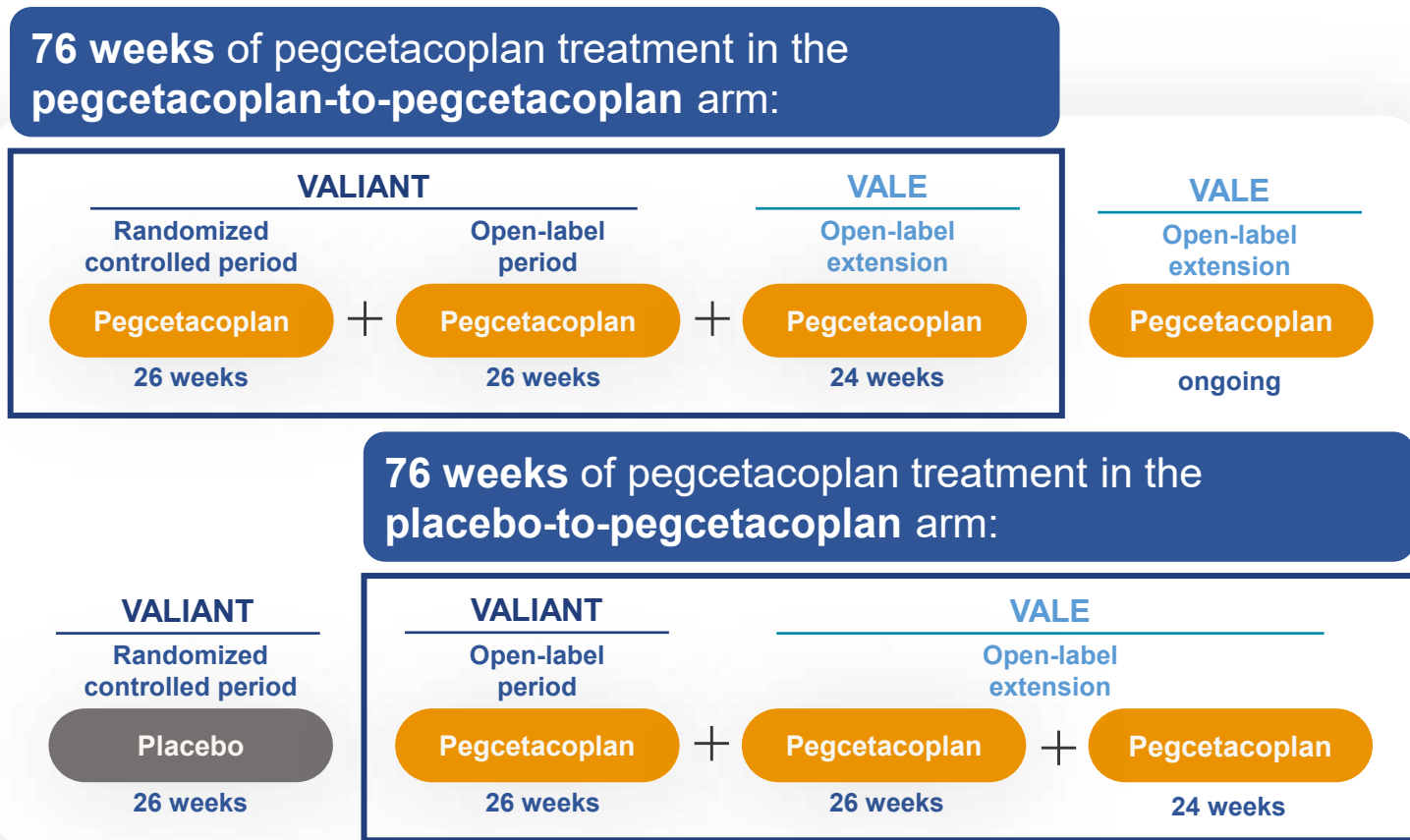


1. Bomback AS, et al. *Kidney Int Rep.* 2025. 2. Kavanagh D, et al. *Kidney Int Rep.* 2025. 3. Dixon BP, et al. *Clin J Am Soc Nephrol.* 2026. 4. Ghaddar M, et al. *Clin J Am Soc Nephrol.* 2025. 5. Smith RJH, et al. *Nat Rev Nephrol.* 2019. 6. Apellis pharmaceuticals. Prescribing Information. 2026.

Aim: To evaluate 76 weeks of efficacy and safety of pegcetacoplan in the total VALIANT population

METHOD (POST HOC):

- Patients in VALIANT were supplemented with treatment data from the VALE extension study to achieve 76 weeks of pegcetacoplan treatment *
- All data were time-aligned, with baseline defined as the date of pegcetacoplan initiation for all patients



* No histology data are available for this analysis, as histological assessment was not mandatory at 52 weeks in VALIANT and not included in the VALE study protocol.

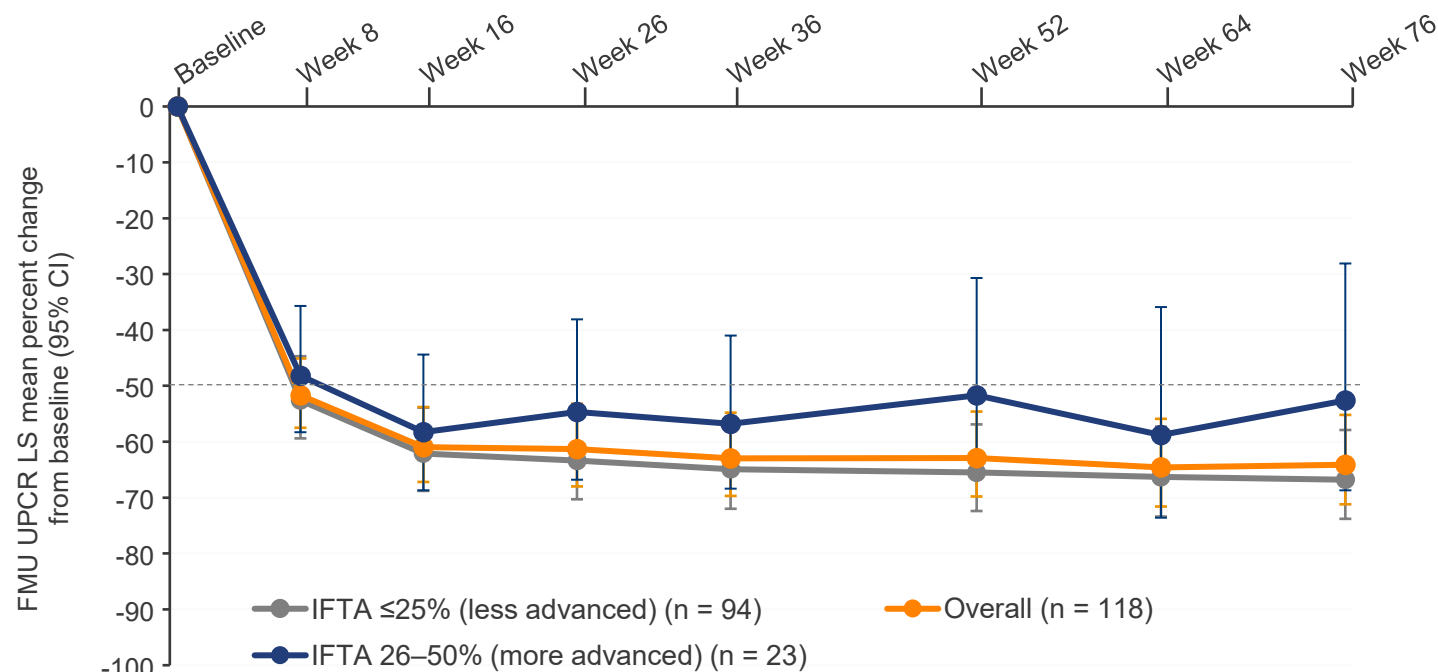
Participants in the realigned VALIANT/VALE analysis represented a broad patient population

Baseline characteristic	Overall (N = 120)
Age group, n (%)	
≤17 years	53 (44.2)
18–65 years	65 (54.2)
>65 years	2 (1.7)
Age, mean (SD), years	26.2 (16.1)
Sex, female, n (%)	68 (56.7)
Baseline triplicate first-morning spot UPCR, mean (SD), g/g	2.9 (2.4)
Baseline eGFR, mean (SD), mL/min/1.73 m²	79.0 (34.8)

For participants who received pegcetacoplan during the randomized controlled period of VALIANT, the realigned baseline was defined as the baseline value used in VALIANT. For participants who received placebo during the randomized controlled period of VALIANT, the realigned baseline was defined as the last available non-missing assessment prior to enrolling into the open-label period of VALIANT. Results were based on post-hoc analyses.

Pegcetacoplan led to a clinically meaningful proteinuria reduction regardless of baseline disease chronicity

Geometric mean change from time-aligned baseline in proteinuria over 76 weeks of pegcetacoplan treatment by baseline disease chronicity



Change from baseline to Week 76:

Overall
–64.1%

(95% CI, –71.2 to –55.2)

IFTA ≤25%
–66.8%

(95% CI, –73.8 to –57.9)

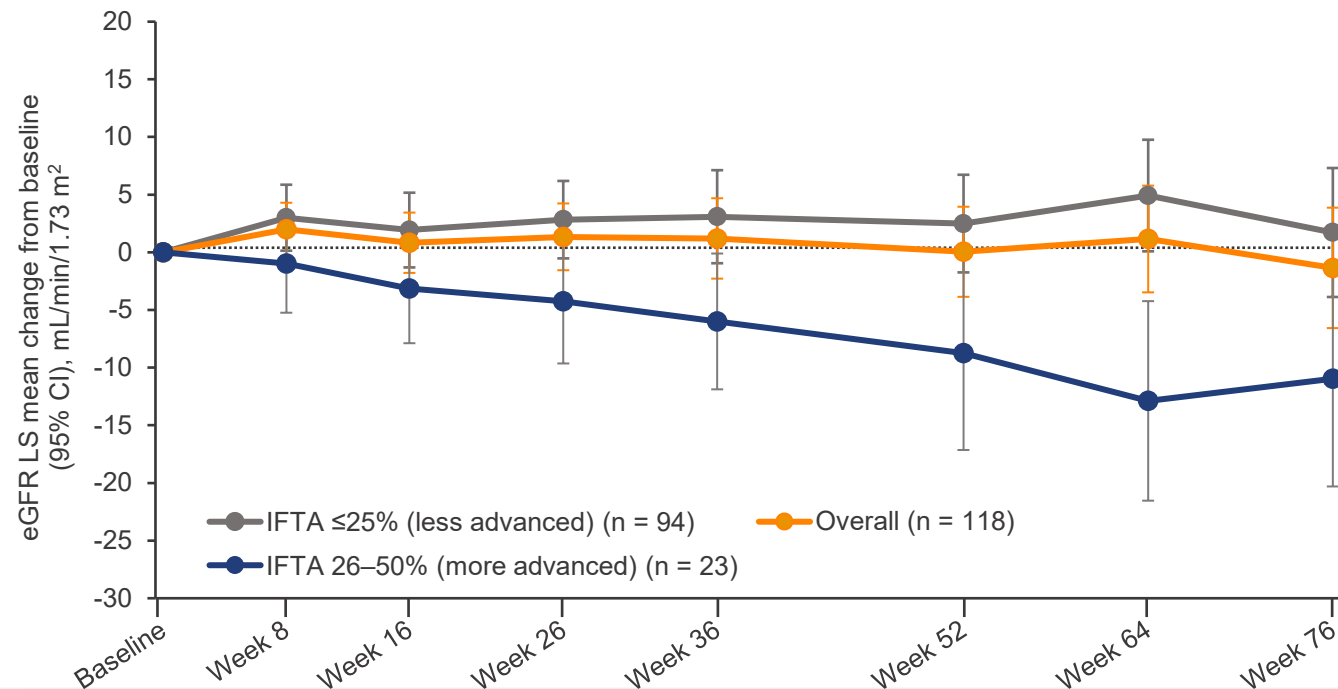
IFTA 26–50%
–52.6%

(95% CI, –68.7 to –28.1)

Results were based on post-hoc analyses. For the IFTA subgroup analysis, geometric means and % change estimated from exponentiated LS mean differences from an MMRM of log-transformed UPCR. MMRM model including the fixed categorical effect for visit, disease type, baseline immunosuppressants use, stratification factors, as well as the continuous fixed covariate of baseline log-transformed UPCR, was used to analyze the log-transformed ratio of UPCR compared with VALIANT baseline. For the overall population, geometric means and % change estimated from exponentiated LS mean differences from an MMRM of log-transformed UPCR. MMRM model including the fixed categorical effect for treatment group, visit, disease type, baseline immunosuppressants use, stratification factors, and the visit-by-treatment group interactions as well as the continuous fixed covariate of baseline log-transformed UPCR, is used to analyze the log-transformed ratio of UPCR at each visit compared with VALIANT baseline.

Pegcetacoplan was associated with eGFR stabilization through 76 weeks in less advanced disease

LS mean change from time-aligned baseline in eGFR over 76 weeks of pegcetacoplan treatment by baseline disease chronicity



Change from baseline to Week 76 (mL/min/1.73 m²):

Overall

-1.4 (95% CI, -6.6 to 3.9)

IFTA ≤25%

+1.7 (95% CI, -3.9 to 7.3)

IFTA 26–50%

-11.0 (95% CI, -20.3 to -1.6)

Annualized eGFR slope (SE) in post-treatment period: **-1.4 (1.7)** mL/min/1.73 m² per year

Results were based on post-hoc analyses. For IFTA subgroups, MMRM model including the fixed categorical effect for visit, disease type, and stratification factors, as well as the continuous, fixed covariate of baseline eGFR, was used to analyze mean change from baseline eGFR at each visit compared with VALIANT baseline. For the overall population, MMRM model including the fixed categorical effect for treatment group, visit, disease type, baseline immunosuppressant use, stratification factors, and the visit-by-treatment group interactions as well as the continuous, fixed covariate of baseline eGFR, is used to analyze change from baseline eGFR at each visit compared with VALIANT baseline. Results were based on post-hoc analyses. Baseline eGFR was the last eGFR assessment prior to the first dose of pegcetacoplan.

Pegcetacoplan was well-tolerated and its safety profile was consistent with previous reports

Patients, n (%)		Pegcetacoplan for 76 weeks (n = 120)	
TEAEs		113 (94.2)	
Treatment-related		61 (50.8)	
Severe TEAEs		13 (10.8)	
Serious TEAEs		20 (16.7)	
Encapsulated meningococcal infections		0	
TEAE leading to study discontinuation		5 (4.2)	
Deaths		1* (0.8)	
Common TEAEs (occurring in ≥10% of patients)			
Headache	23 (19.2)	Nausea	14 (11.7)
Pyrexia	22 (18.3)	Pruritus	13 (10.8)
Diarrhea	18 (15.0)	Acute kidney injury	12 (10.0)
Nasopharyngitis	18 (15.0)	Anemia	12 (10.0)
Hypertension	17 (14.2)	Cough	12 (10.0)
Influenza	15 (12.5)	Upper respiratory tract infection	12 (10.0)
Vomiting	15 (12.5)		

Consistent with >4,200 patient-years of pegcetacoplan exposure[†]

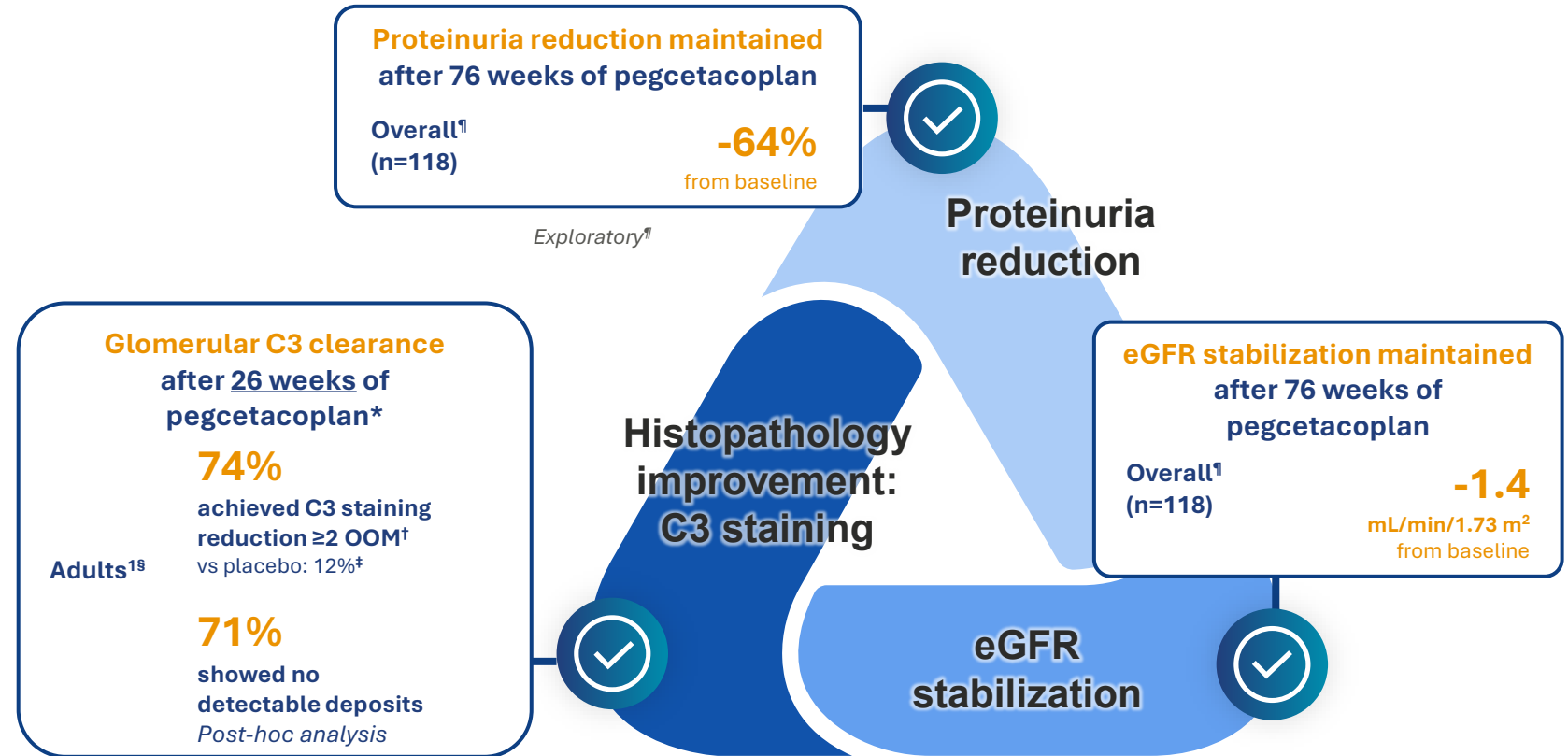
TEAEs defined as any new AE that began, or any preexisting condition that worsened in severity, after the first dose of study drug in either VALIANT or VALE and ≤56 days beyond the last dose of study drug. Results were based on post-hoc analyses. * One patient died of respiratory failure associated with Covid-19 pneumonia, which was considered unrelated to pegcetacoplan.¹ † As of 13 Aug 2026. Includes exposure in clinical trials and postmarketing experience across multiple indications.

1. Fakhouri F, et al. *N Engl J Med*. 2025.

Clinical efficacy was sustained and maintained through 76 weeks of pegcetacoplan



Pegcetacoplan was well tolerated through 76 weeks of treatment, with no new safety signals



* Not assessed at Week 76. † Key secondary endpoint. ‡ A fixed sequence testing strategy was used for key secondary endpoints. Key secondary histologic activity score endpoint was not met at week 26; therefore subsequent endpoints including C3 staining reduction and eGFR change were not formally tested and should be interpreted descriptively. § Biopsy was not mandated in adolescents (aged 12-17 years). ¶¶ All Week 76 endpoints were exploratory and not powered to detect statistically significant differences. 1. Fakhouri F, et al. *N Engl J Med*. 2025;393:2210–20.

Clinical benefit of pegcetacoplan sustained through 76 weeks of treatment



Pegcetacoplan directly **targets** uncontrolled C3 activation, **addressing the underlying pathophysiology** of C3G and primary IC-MPGN beyond supportive therapies



Early improvements in **proteinuria**, **eGFR** stabilization, and overall **safety** observed at 26 weeks in VALIANT were **maintained through 76 weeks**, indicating durable disease control, with no new safety signals



A post hoc subgroup highlights that **eGFR stabilization with pegcetacoplan may be strongest in patients with $\leq 25\%$ IFTA**, suggesting a benefit of early detection and targeted C3 inhibition

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Abbreviations

- ACEis, angiotensin-converting enzyme inhibitors; AE, adverse event; ARBs, angiotensin receptor blockers; C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; FMU, first-morning urine; IC-MPGN, immune-complex membranoproliferative glomerulonephritis; IFTA, interstitial fibrosis and tubular atrophy; LS, least squares; MMF, mycophenolate mofetil; MMRM, mixed model for repeated measures; SC, subcutaneous; SE, standard error; SGLT2is, sodium-glucose cotransporter-2 inhibitors; TEAE, treatment-emergent AE; UPCR, urine protein-to-creatinine ratio.