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JUNE 3-6, 2026
Challenge Your Thinking

Pegcetacoplan sustained clinical benefit in C3G and primary IC-MPGN through 1 year of therapy: Data from VALIANT/VALE

Fadi Fakhouri[1], Gema Ariceta[2], Matthew C Pickering[3], Moglie Le Quintrec[4], Marina Vivarelli[5], Carla M Nester[6], Bradley P Dixon[7], Virginia Taliadouros[8], Johan Szamosi[8], Kathryn Gordon[9], Anwesha Mukherjee[9], Christoph Licht[10]

[1]Centre Hospitalier Universitaire Vaudois, Lausanne, Vaud, Switzerland; [2]Hospital Universitari Vall d'Hebron, Barcelona, Catalunya, Spain; [3]Department of Immunology and Inflammation, Imperial College, London, United Kingdom; [4]Department of Nephrology, Centre Hospitalier Universitaire de Montpellier, Montpellier, France; [5]Ospedale Pediatrico Bambino Gesu IRCCS, Rome, Italy; [6]University of Iowa, Stead Family Children's Hospital, Iowa City, IA, United States; [7]University of Colorado Anschutz Medical Campus School of Medicine, Aurora, CO, United States; [8]Swedish Orphan Biovitrum AB, Stockholm, Sweden; [9]Apellis Pharmaceuticals, Inc., Waltham, MA, United States; [10]The Hospital for Sick Children, Toronto, Ontario, Canada.

Disclosures

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- **FF** has received consultancy honorarium from Alexion, Astra Zeneca, Apellis, Novartis, Sobi and Roche.
- **GA** received honoraria for lectures, educational events, or advisory boards for Astra Zeneca (Alexion), Recordati Rare Disease, Advicenne, Chiesi, Kyowa Kirin, Alnylam, and Dicerna; and served as site investigator for Apellis.
- **MCP** has received consulting fees from Alexion, Achillion, Annexon, Apellis, Biocryst, ChemoCentryx, Complement Therapeutics, Gemini, Gyroscope, MIRNA Therapeutics, Ormeros, Q32bio Pharma, and Sobi.
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- **VT** is an employee of Swedish Orphan Biovitrum AB and may hold stock or stock options.
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- **KG** is an employee of Apellis Pharmaceuticals and may hold stock or stock options.
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- **CL** has received consulting fees from Apellis, Sobi, Novartis, and Alexion AstraZeneca.

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

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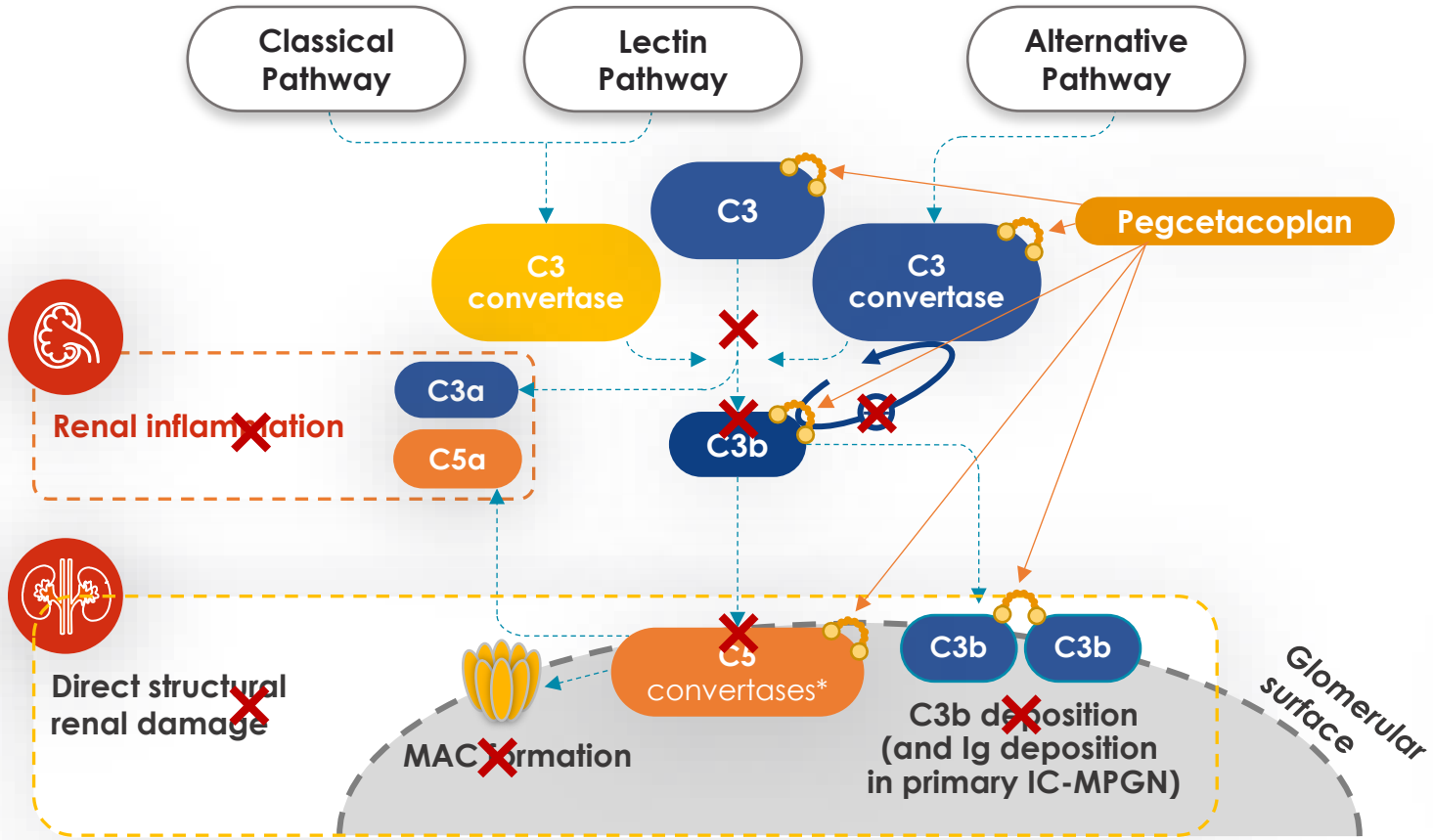

- Both diseases are **characterised by C3 dysregulation** resulting in **glomerular deposition of C3** breakdown products (and immunoglobulins in IC-MPGN)[1,2]
- Up to **50% of patients progress to kidney failure** within 10 years despite current standard of care treatments that do not address the underlying pathologic mechanism[3]

Pegcetacoplan binds C3/C3b to target the pathogenic process in C3G/primary IC-MPGN with the aim of stopping kidney damage[2,4]

C3G, C3 glomerulopathy; IC-MPGN, immune complex membranoproliferative glomerulonephritis; Ig, immunoglobulin; MAC, membrane attack complex.

1. Bomback et al. *Kidney Int Rep* 2025 **2.** Kavanagh et al. *Kidney Int Rep* 2025 **3.** Smith et al. *Nat Rev Nephrol* 2019 **4.** Fakhouri et al. *N Engl J Med* 2025.

VALIANT was a Phase 3 study of pegcetacoplan in C3G and primary IC-MPGN patients ≥12 years old with native or transplanted kidneys[1]

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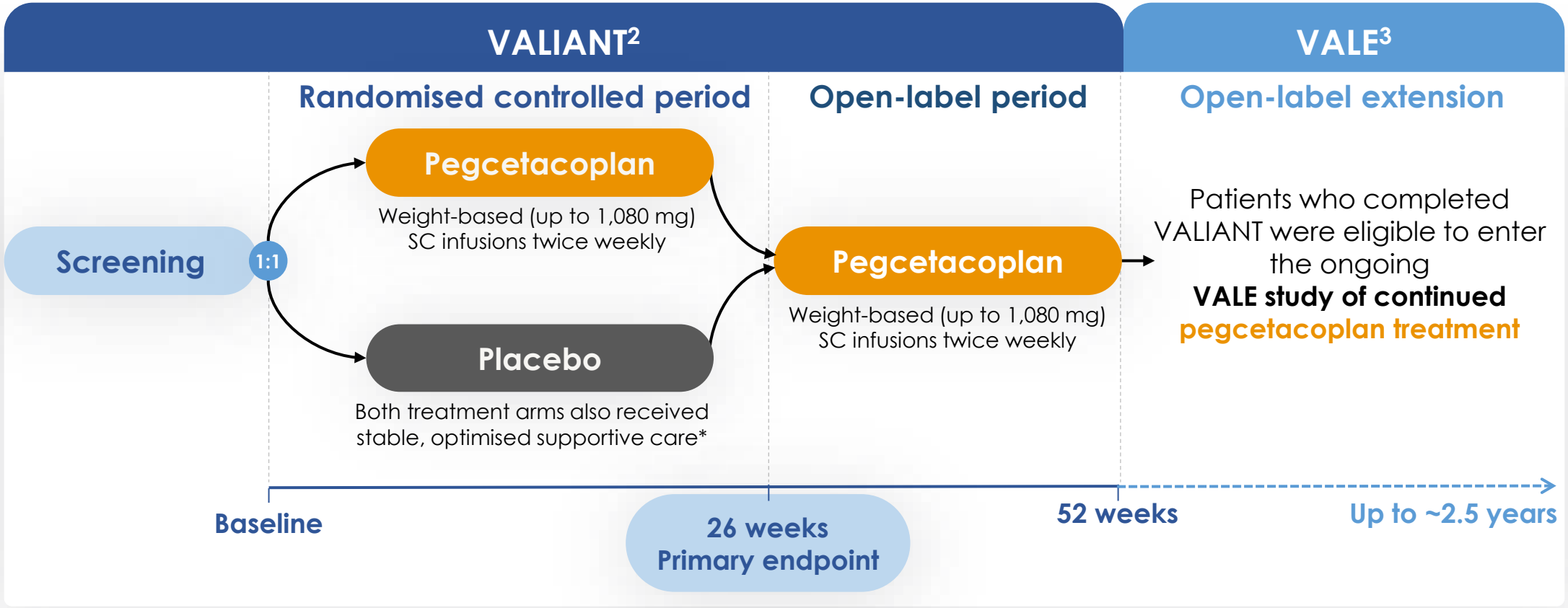

* Stable, optimised antiproteinuric regimens: ACEis, ARBs, SGLT2is, MMF, and corticosteroids (prednisone ≤20 mg/d or equivalent) were permitted, provided doses were stable 12 weeks prior and throughout randomised controlled period.
ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; C3G, C3 glomerulopathy; IC-MPGN, immune complex membranoproliferative glomerulonephritis; MMF, mycophenolate mofetil; SC, subcutaneous; SGLT2is, sodium-glucose cotransporter-2 inhibitors.

1. Fakhouri et al. *N Engl J Med* 2025 **2.** ClinicalTrials.gov. VALIANT. clinicaltrials.gov/study/NCT05067127 **3.** ClinicalTrials.gov. VALE. clinicaltrials.gov/study/NCT05809531.

VALIANT: **Pegcetacoplan's efficacy** in C3G and primary IC-MPGN[1]

26 weeks

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Kidney Health Initiative (KHI) consensus[2]:
Favourable treatment effect on **histopathology, proteinuria and eGFR**

68%
significant proteinuria reduction
vs placebo*

Proteinuria reduction

Histopathology improvement

Glomerular C3 clearance in 71% of patients (zero staining)

Stabilisation of eGFR
+6.3 mL/min/1.73 m²
vs placebo

eGFR stabilisation/ improvement

60% of patients achieved ≥50% proteinuria reduction from baseline

51% of patients with UPCR <1 g/g compared to 8% at baseline

* Consistent across subgroups (age, disease type, transplant status).
C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex membranoproliferative glomerulonephritis; UPCR, urine protein:creatinine ratio.
1. Fakhouri et al. *N Engl J Med* 2025 **2.** Nester et al. *Clin J Am Soc Nephrol* 2024 **3.** Kavanagh et al. *Kidney Int Rep* 2025.

VALIANT: **Pegcetacoplan's efficacy** in C3G and primary IC-MPGN[1]

52 weeks

in the pegcetacoplan-to-pegcetacoplan arm

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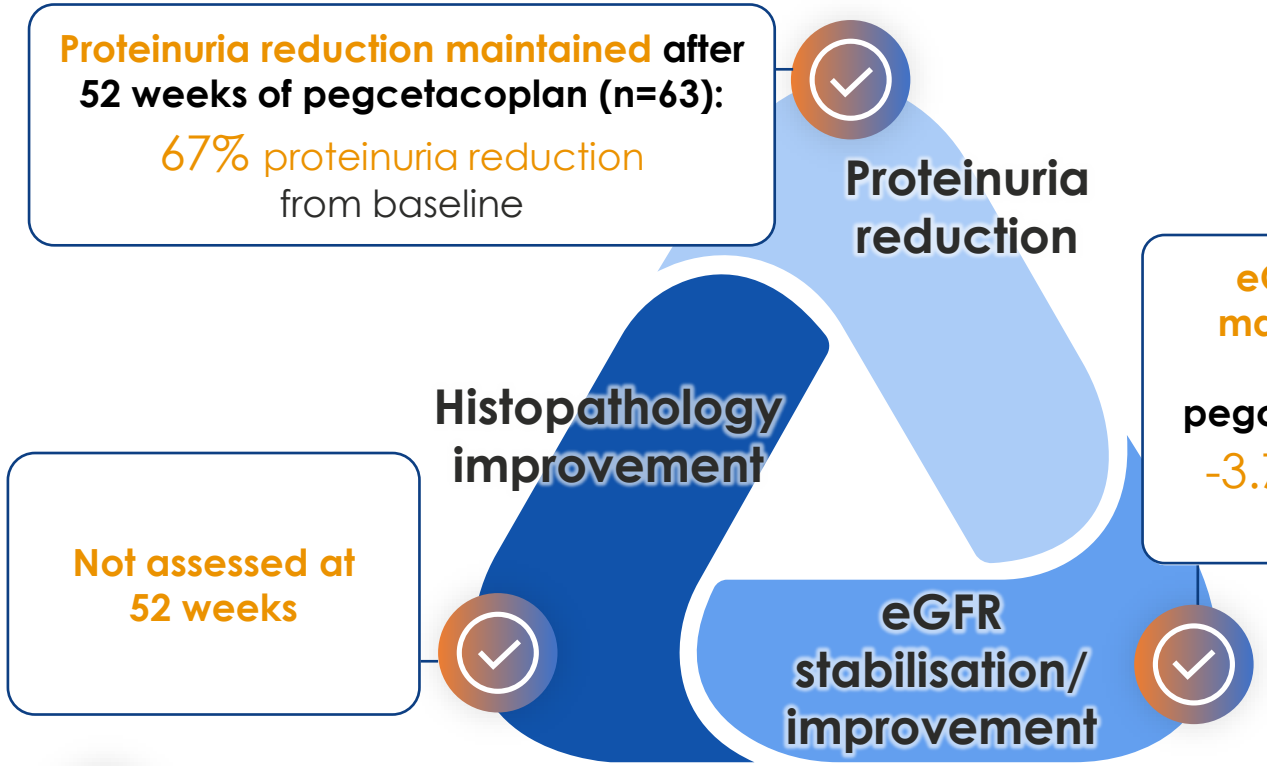
Assessment of treatment effects over time, particularly eGFR, are likely to be **more robust with long-term follow-up and in a larger patient population**[2,3]

Proteinuria reduction maintained after 52 weeks of pegcetacoplan (n=63):
67% proteinuria reduction from baseline



eGFR stabilisation maintained after 52 weeks of pegcetacoplan (n=63):
-3.7 mL/min/1.73 m^2 from baseline

Not assessed at 52 weeks

51% of patients achieved ≥50% proteinuria reduction from baseline

C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex membranoproliferative glomerulonephritis.
1. Fakhouri et al. ERA 2025; oral **2.** Nester et al. *Clin J Am Soc Nephrol* 2024 **3.** Kavanagh et al. *Kidney Int Rep* 2025.

Aim: To evaluate **1-year efficacy and safety of pegcetacoplan** in a **larger population** than previously reported

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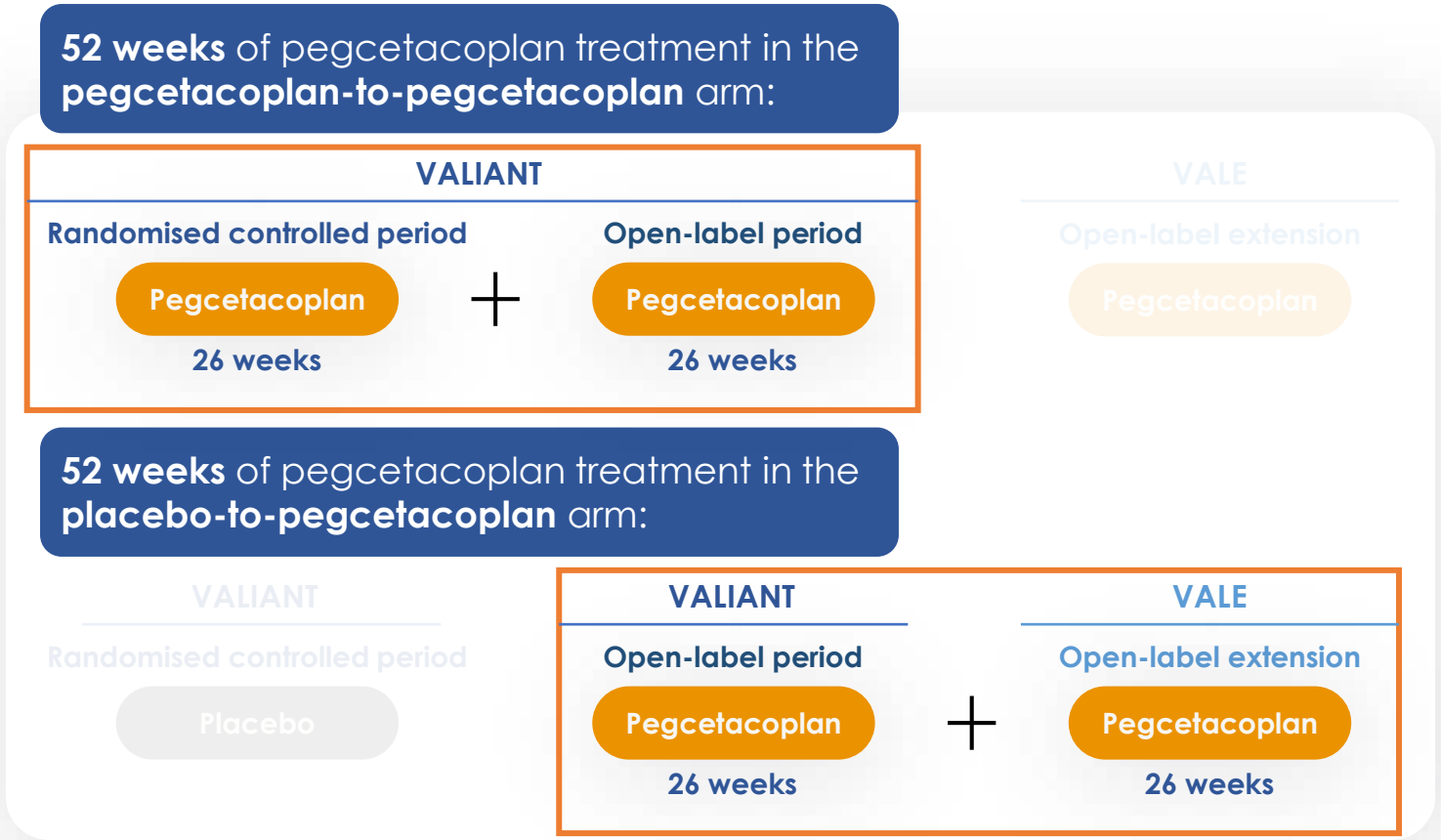
Method:

- Patients in VALIANT with <52 weeks of pegcetacoplan treatment were supplemented with up to 6 months of treatment data from the VALE extension study*
- All data were time-aligned such that baseline represented pegcetacoplan initiation for all patients



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

VALIANT included a **broad patient population** and **most patients opted to continue into VALE**

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Baseline characteristic	Pegcetacoplan (n=63)	Placebo (n=61)	Overall (n=124)
Age group, n (%)			
Adolescents (12–17 years) Adults (≥18 years)	28 (44.4) 35 (55.6)	27 (44.3) 34 (55.7)	55 (44.4) 69 (55.6)
Age, mean (SD), years			
Adolescents (12–17 years) Adults (≥18 years)	14.6 (1.7) 39.1 (15.9)	14.8 (1.8) 30.6 (15.9)	14.7 (1.7) 35.0 (16.4)
Sex, female, n (%)	37 (58.7)	33 (54.1)	70 (56.5)
Underlying disease based on screening biopsy, n (%)			
C3G Primary IC-MPGN	51 (81.0) 12 (19.0)	45 (73.8) 16 (26.2)	96 (77.4) 28 (22.6)
Baseline triplicate first-morning spot UPCR, mean (SD), g/g	3.1 (2.4)	2.5 (2.0)	2.8 (2.2)
Baseline eGFR, mean (SD), mL/min/1.73 m^2	78.5 (34.1)	87.2 (37.2)	82.8 (35.8)
Patients with up to 52 weeks of pegcetacoplan treatment in VALIANT/VALE, n	**63**	**57**	**120**

C3G, C3 glomerulopathy; IC-MPGN, immune complex membranoproliferative glomerulonephritis; eGFR, estimated glomerular filtration; SD, standard deviation; UPCR, urine protein:creatinine ratio.

Pegcetacoplan led to a **clinically meaningful proteinuria reduction, sustained through 52 weeks**

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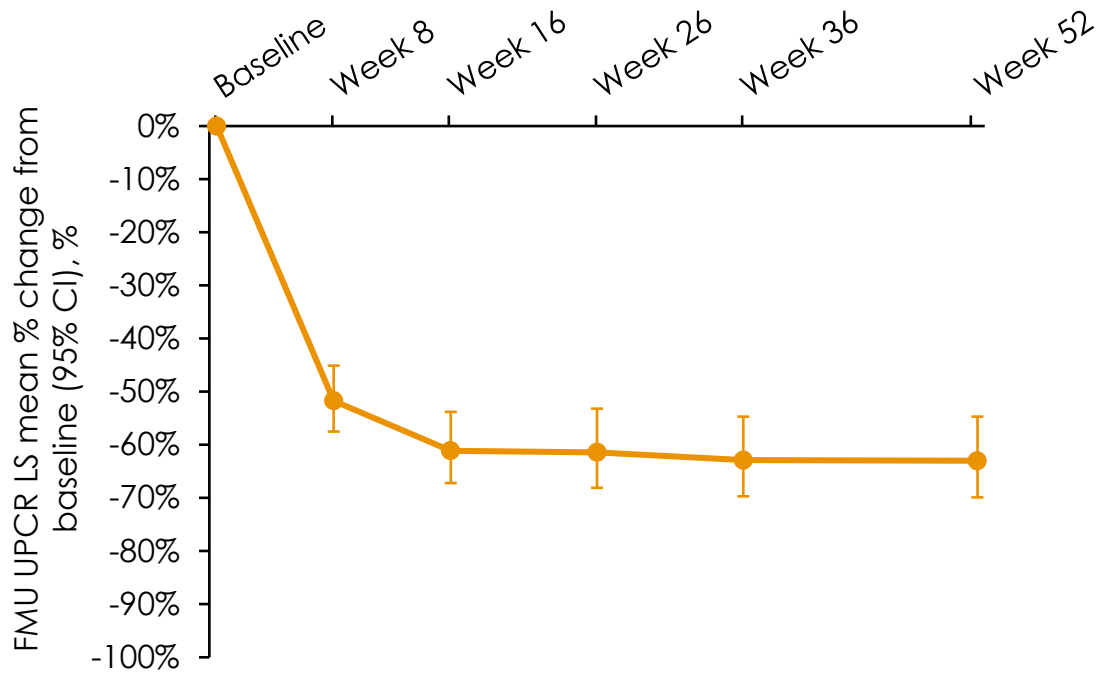
Change from time-aligned baseline in proteinuria over 52 weeks of pegcetacoplan treatment



n=118 included in the MMRM model*

Geometric mean change in proteinuria between baseline and 52 weeks:

-63.0%

(95% CI -69.9, -54.7)

* 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 utilised to analyse the log-transformed ratio of UPCR at each visit compared to VALIANT baseline.
CI, confidence interval; FMU, first morning urine; LS, least squares; MMRM, mixed model for repeated measures; UPCR, urine protein:creatinine ratio.

50% of patients achieved **proteinuria ≤1 g/g with pegcetacoplan, sustained through 52 weeks**

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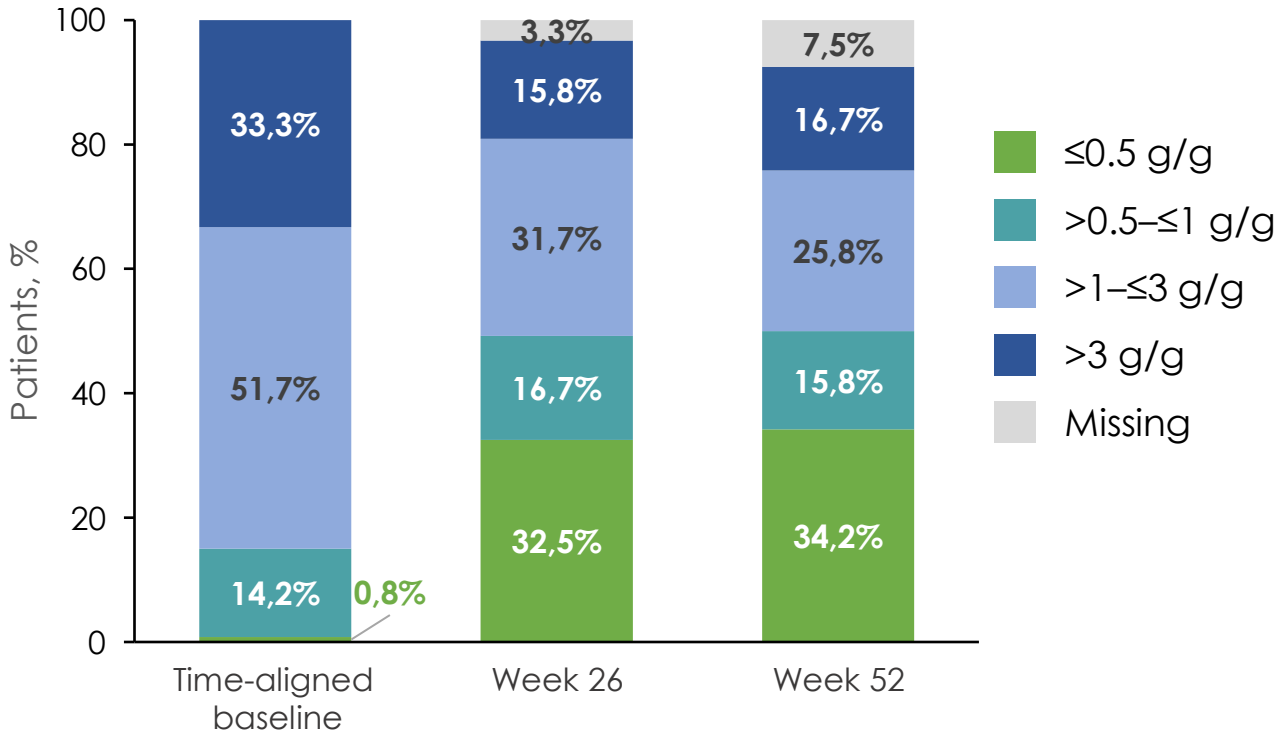
Proteinuria shift analysis based on FMU UPCR



Patients with UPCR ≤1 g/g at 52 weeks:

50.0%

n=60/120

Patients with UPCR ≤0.5 g/g at 52 weeks:

34.2%

n=41/120

FMU, first morning urine; UPCR, urine protein:creatinine ratio.

Pegcetacoplan was associated with **eGFR stabilisation, sustained through 52 weeks**

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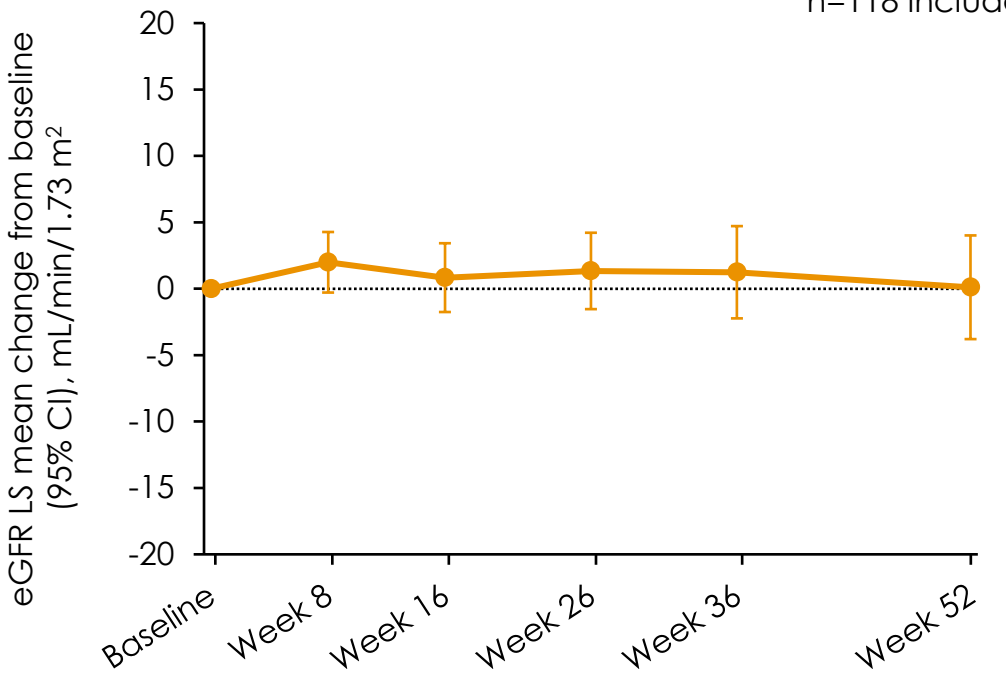
Change from time-aligned baseline in eGFR over 52 weeks of pegcetacoplan treatment

n=118 included in the MMRM model*



LS mean change in eGFR between baseline and 52 weeks:

+0.1

mL/min/1.73 m²

(95% CI -3.8, 4.0)

* 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 eGFR, is utilised to analyse change from baseline eGFR at each visit compared to VALIANT baseline.

CI, confidence interval; eGFR, estimated glomerular filtration rate; LS, least squares; MMRM, mixed model for repeated measures.

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

Patients, n (%)	Pegcetacoplan for 52 weeks (n=120)
TEAEs	106 (88.3)
Treatment-related TEAEs	53 (44.2)
Severe TEAEs	11 (9.2)
Serious TEAEs	17 (14.2)
Common TEAEs (occurring in ≥10% of patients)	
Infusion site reaction	41 (34.2)
Pyrexia	19 (15.8)
Headache	19 (15.8)
Diarrhoea	16 (13.3)
Nasopharyngitis	15 (12.5)
Influenza	13 (10.8)
Vomiting	12 (10.0)
Encapsulated meningococcal infections	0
TEAE leading to discontinuation	4 (3.3)
Deaths	1 (0.8)

Consistent with >3,500 patient-years of pegcetacoplan exposure*[1]

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.
* As of 13 February 2026. Includes exposure in clinical trials and post-marketing across multiple indications. AE, adverse event; TEAE, treatment-emergent AE.
1. Ayehu et al. NKF Spring Clinical Meetings 2026; poster.

Key takeaways

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

Early improvements in **proteinuria**, **eGFR** stabilisation, and overall **safety** observed at 26 weeks in VALIANT were **maintained through 52 weeks in a larger population** than previously assessed, indicating durable disease control

This *post-hoc* analysis supports the **potential of pegcetacoplan to provide sustained modification of disease progression** in C3G and primary IC-MPGN

C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex membranoproliferative glomerulonephritis.

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