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european society for paediatric nephrology
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Paediatric Kidney Week

Pegcetacoplan treatment response in VALIANT/VALE: Impact of genetic and acquired complement dysregulation and disease type in C3G and primary IC-MPGN

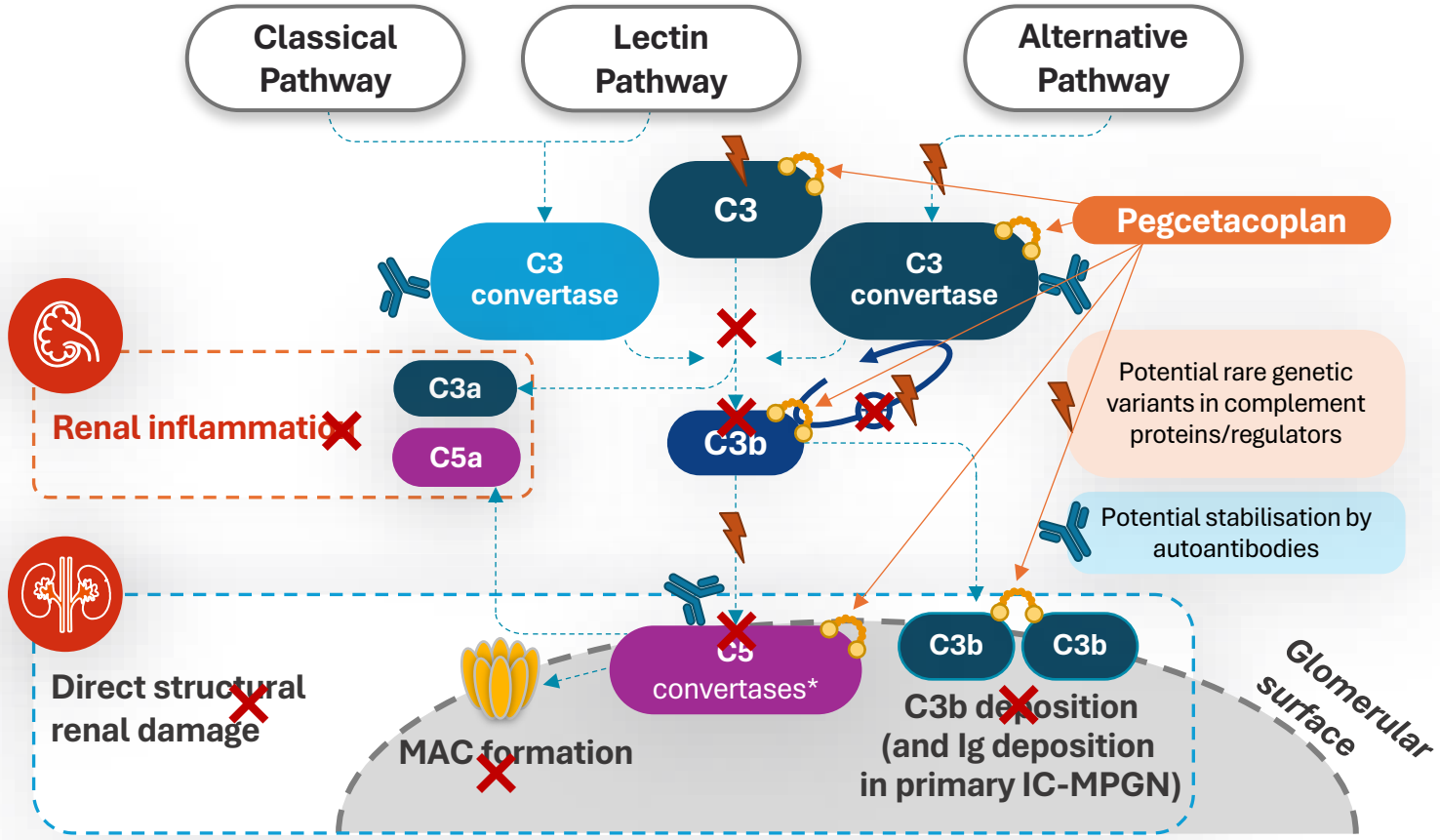
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Declaration of conflict of interest

- **NvdK** received consultancy fees from Roche, Novartis, Alexion, Sobi and Samsung.
- **MN** has had consultancy agreement and research grant from Alexion Pharmaceuticals Inc, Biocryst Pharmaceuticals, and Novartis; speaker honoraria/travel reimbursement from Sobi, Novartis.
- **DPG** chairs the Rare Diseases Committee of the UK Kidney Association and reports fees for consulting and presenting from Novartis, Alexion, Calliditas, Sanofi, Britannia, and Travere.
- **SC** has received honoraria for consulting and lectures from Novartis, CSL Vifor, and Sobi and support attending meetings from Novartis.
- **FCF** received consultancy fees from Novartis, Apellis, Sobi, and AstraZeneca.
- **JW-M** has nothing to declare.
- **BPD** has received consultancy fees from Alexion Astra Zeneca Rare Disease, Novartis Pharmaceuticals, Apellis Pharmaceuticals, Roche Genentech, and Arrowhead Pharmaceuticals, and has received research funding (clinical trials support) from Alexion Astra Zeneca Rare Disease, Novartis Pharmaceuticals, Apellis Pharmaceuticals, Roche Genentech, and Ultragenyx Pharmaceuticals.
- **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.
- **LQ-G** is an employee of Swedish Orphan Biovitrum AB and may hold stock or stock options.
- **JS** is an employee of Swedish Orphan Biovitrum AB and may hold stock or stock options.
- **KG** is an employee of Apellis Pharmaceuticals and may hold stock or stock options.
- **AM** is an employee of Apellis Pharmaceuticals and may hold stock or stock options.
- **FF** has received consultancy honorarium from Alexion, Astra Zeneca, Apellis, Novartis, Sobi and Roche.

C3G and primary IC-MPGN are heterogeneous complement-related diseases in which **excessive glomerular C3 deposition drives inflammation, scarring, and irreversible kidney damage**[1,2]



- **Genetic risk factors** and **acquired autoantibodies** have been identified in up to **20%** and **40-80%** of patients, respectively[4,5]
  - The impact of rare genetic variants and autoantibodies on patient outcomes remains unclear[3]
- In the remaining patients, the disease trigger remains unknown[2]

Pegcetacoplan binds C3 and C3b:[1,2,6]

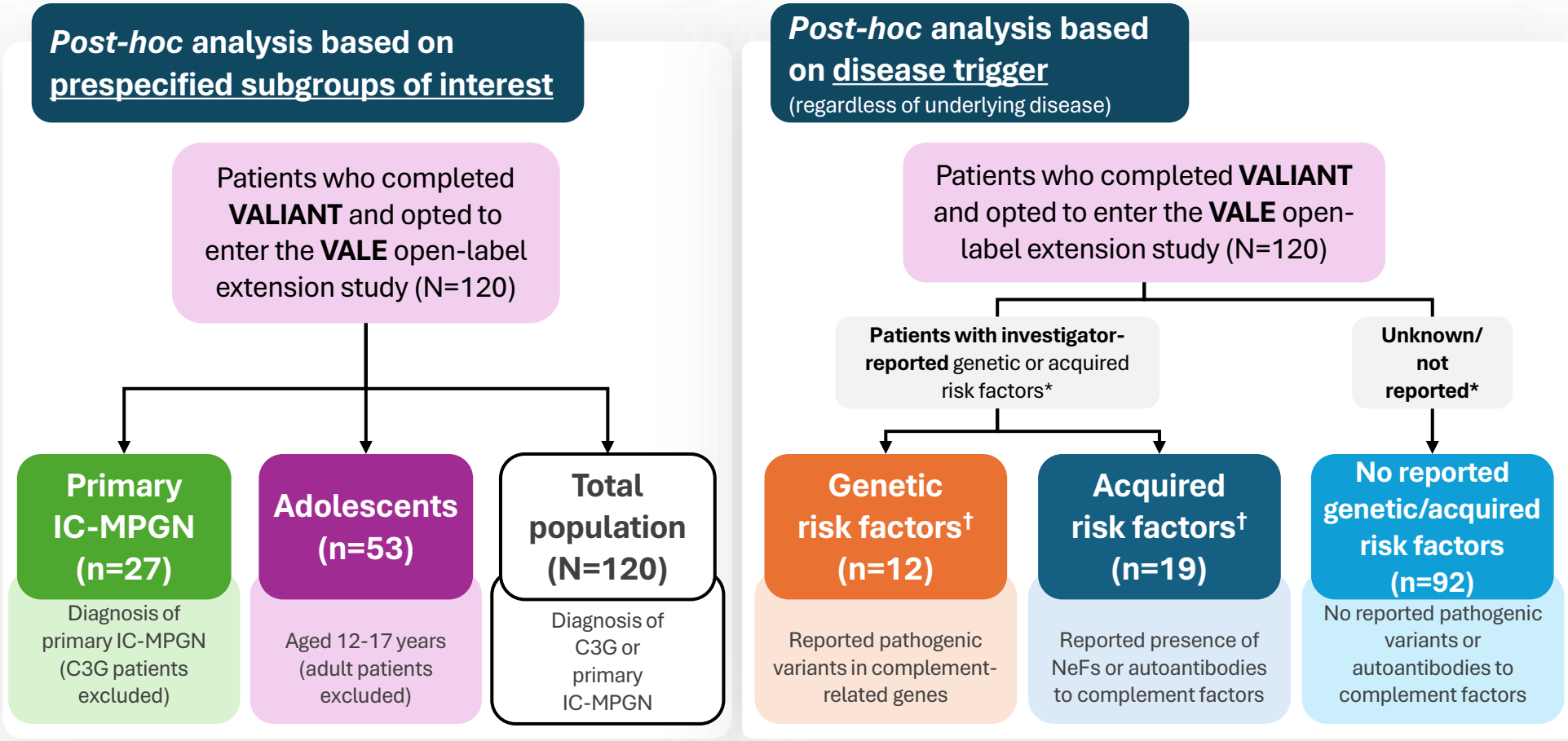
1. **Prevents C3 activation** through all complement pathways and upstream autoantibodies
2. **Blocks the C3 amplification loop** by inhibiting alternative pathway
3. **Prevents C3 deposits** and downstream effectors

* Including classical/lectin pathway C5 convertase and alternative pathway C5 convertase.
C3G, C3 glomerulopathy; IC-MPGN, immune complex membranoproliferative glomerulonephritis; Ig, immunoglobulin; MAC, membrane attack complex.
1. Fakhouri et al. *N Engl J Med* 2025 **2.** Kavanagh et al. *Kidney Int Rep* 2025 **3.** Bomback et al. *Kidney Int Rep* 2025
4. Meuleman *Clin J Am Soc Nephrol* 2023 **5.** Vivarelli *Kidney Int* 2024 **6.** Simon-Tillaux et al. ASN 2019; poster SA-PO609.

Aim: To evaluate **1-year pegcetacoplan** treatment effects in **patient subgroups of particular interest**

Method:

- Data from the Phase 3 VALIANT trial and its open-label extension (VALE) were pooled to enable a uniform evaluation of 1 year of pegcetacoplan exposure across all patients
- All data were time-aligned such that baseline represented pegcetacoplan initiation for all patients



* Testing for genetic and acquired risk factors was not mandatory for inclusion in VALIANT. Genetic and acquired risk factors were optionally reported by investigators and not assessed within the trial.
† Patients with reported genetic risk factors may also have had reported acquired risk factors, and *vice versa*.
C3G, C3 glomerulopathy; IC-MPGN, immune complex membranoproliferative glomerulonephritis; NeF, nephritic factor.

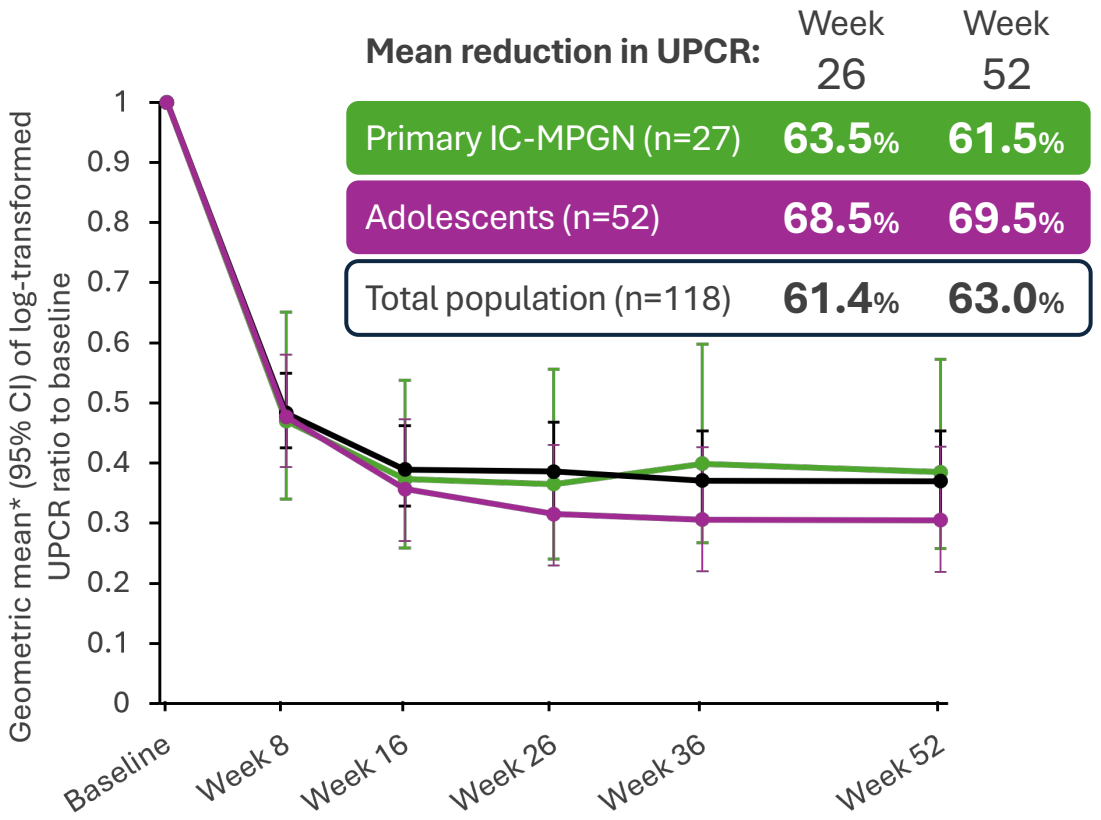
Baseline characteristics suggest **differences in disease duration and severity between subgroups**

Baseline characteristic	Primary IC-MPGN (n=27)	Adolescents (n=55*)	Total population (N=124*)	Genetic risk factors (n=12)	Acquired risk factors (n=19)	No reported genetic/ acquired risk factors (n=92)
Age, mean (SD), years	30.1 (19.2)	14.7 (1.7)	26.0 (15.9)	23.1 (12.5)	22.4 (14.5)	27.0 (16.6)
Sex, female, n (%)	16 (59.3)	32 (58.2)	70 (56.5)	9 (75.0)	12 (63.2)	50 (54.3)
Baseline triplicate first-morning spot UPCR, mean (SD), g/g	4.0 (3.3)	3.1 (2.8)	2.8 (2.2)	3.1 (2.3)	3.0 (2.0)	3.0 (2.5)
Baseline eGFR, mean (SD), mL/min/1.73 m^2	67.6 (34.3)	93.4 (33.1)	82.8 (35.8)	71.2 (42.5)	88.8 (32.5)	78.0 (34.3)
Time since diagnosis, mean (SD), years	3.2 (2.6)	3.3 (3.0)	3.7 (3.5)	5.1 (4.3)	2.6 (2.1)	3.3 (2.6)

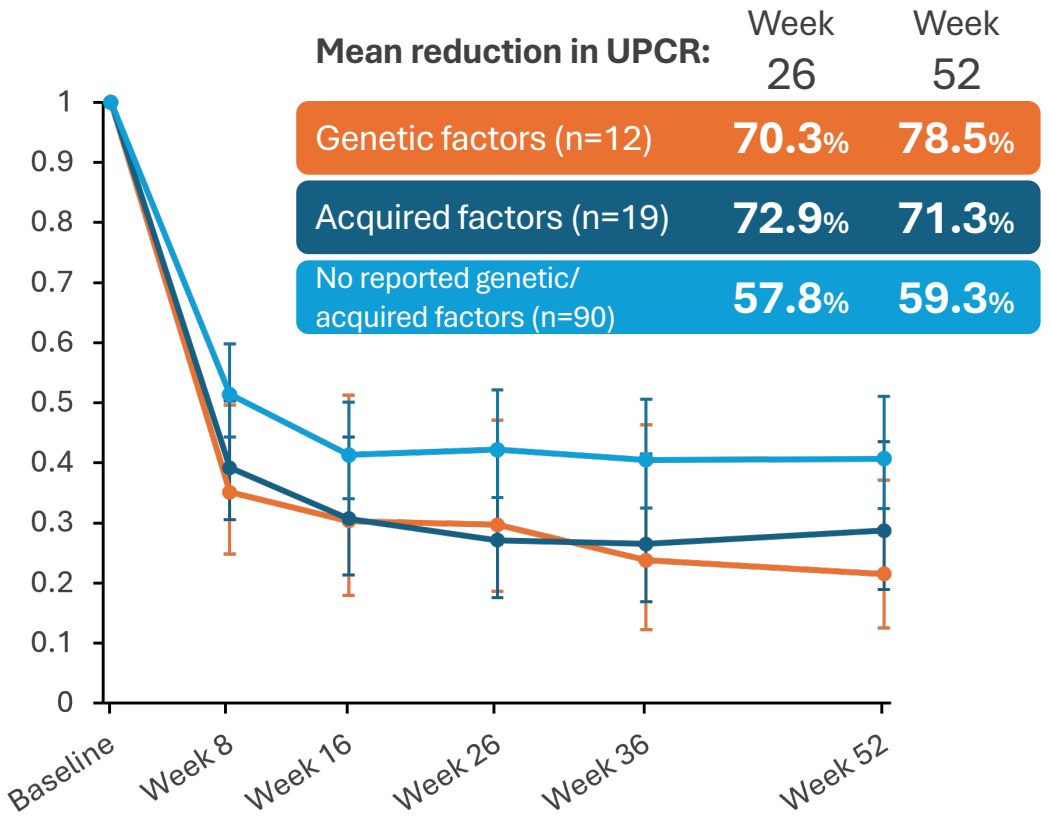
* Baseline characteristics at VALIANT study initiation.
IC-MPGN, immune complex membranoproliferative glomerulonephritis; eGFR, estimated glomerular filtration; SD, standard deviation; UPCR, urine protein:creatinine ratio.

Pegcetacoplan led to a sustained mean **UPCR reduction greater than 50% across subgroups**

Change from time-aligned baseline in UPCR over time during pegcetacoplan treatment



Mean reduction in UPCR:	Week 26	Week 52
Primary IC-MPGN (n=27)	63.5%	61.5%
Adolescents (n=52)	68.5%	69.5%
Total population (n=118)	61.4%	63.0%

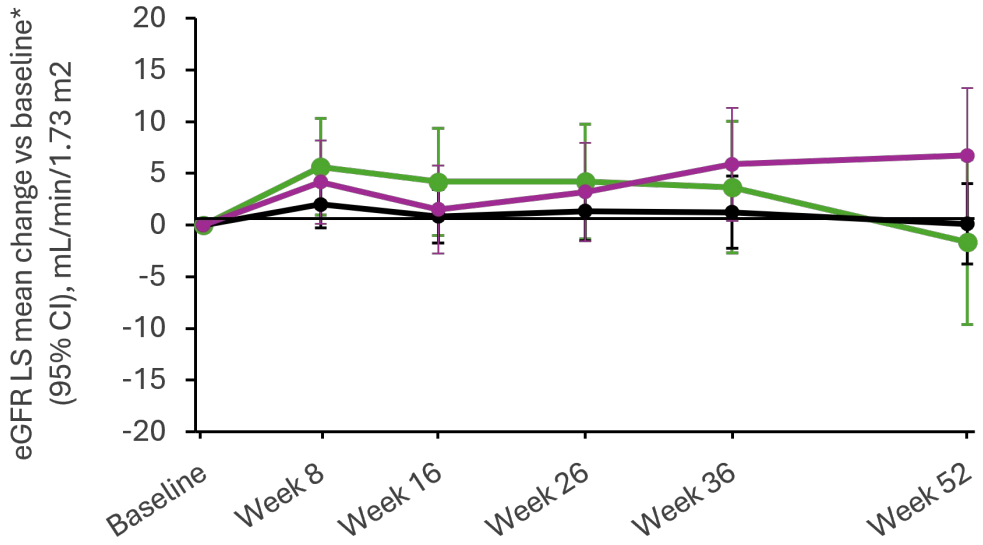


Mean reduction in UPCR:	Week 26	Week 52
Genetic factors (n=12)	70.3%	78.5%
Acquired factors (n=19)	72.9%	71.3%
No reported genetic/ acquired factors (n=90)	57.8%	59.3%

* Geometric means and % change estimated from exponentiated LS mean differences from an MMRM of log-transformed UPCR.
n=number of patients included in each model.
CI, confidence interval, FMU; first morning urine; IC-MPGN, immune complex membranoproliferative glomerulonephritis; LS, least-squares; MMRM, mixed model for repeated measures; UPCR, urine protein:creatinine ratio.

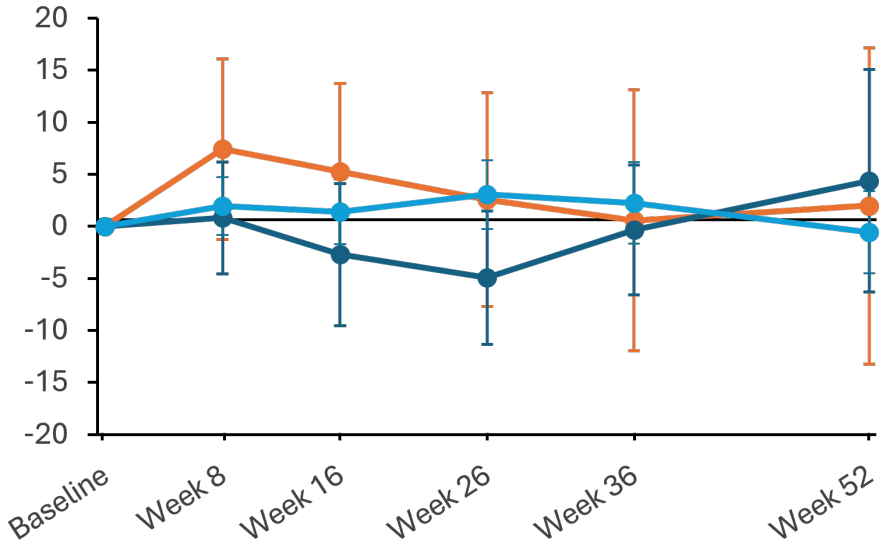
Pegcetacoplan led to **stabilisation of eGFR up to 1 year across subgroups**

Change from time-aligned baseline in eGFR over time during pegcetacoplan treatment



Mean change in eGFR between baseline and 52 weeks:

Primary IC-MPGN (n=27)	**-1.7** mL/min/1.73 m²
Adolescents (n=52)	**+6.7** mL/min/1.73 m²
Total population (n=118)	**+0.1** mL/min/1.73 m²



Mean change in eGFR between baseline and 52 weeks:

Genetic factors (n=12)	**+2.0** mL/min/1.73 m²
Acquired factors (n=19)	**+4.4** mL/min/1.73 m²
No reported genetic/ acquired factors (n=90)	**-0.6** mL/min/1.73 m²

* MMRM model of mean change from baseline in eGFR. n=number of patients included in each model.
CI, confidence interval; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex membranoproliferative glomerulonephritis; LS, least-squares; MMRM, mixed model for repeated measures.

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

Patients, n (%) *Note: Due to overlap between subgroup populations, the same TEAE may be reported in >1 subgroup*	Primary IC-MPGN (n=27)	Adolescents (n=53)	Total population (N=120)	Genetic risk factors (n=12)	Acquired risk factors (n=19)	No reported genetic/ acquired risk factors (n=92)
TEAEs	22 (81.5)	47 (88.7)	106 (88.3)	10 (83.3)	18 (94.7)	81 (88.0)
Treatment-related TEAEs	12 (44.4)	26 (49.1)	53 (44.2)	2 (16.7)	8 (42.1)	44 (47.8)
Severe TEAEs	5 (22.7)*	5 (9.4)	11 (9.2)	1 (10.0)†	1 (5.6)‡	9 (11.1)§
Serious TEAEs	5 (18.5)	8 (15.1)	17 (14.2)	3 (25.0)	3 (15.8)	12 (13.0)
Common TEAEs (occurring in ≥10% of all subgroups)						
Infusion site reaction	9 (33.3)	19 (35.8)	41 (34.2)	3 (25.0)	8 (42.1)	31 (33.7)
Nasopharyngitis	5 (18.5)	10 (18.9)	15 (12.5)	3 (25.0)	5 (26.3)	9 (9.8)
Influenza	5 (18.5)	6 (11.3)	13 (10.8)	2 (16.7)	3 (15.8)	10 (10.9)
Pyrexia	3 (11.1)	12 (22.6)	19 (15.8)	3 (25.0)	6 (31.6)	11 (12.0)
Encapsulated meningococcal infections	0	0	0	0	0	0
TEAE leading to discontinuation	3 (11.1)	1 (1.9)	4 (3.3)	0	0	4 (4.3)
Deaths‖	1 (3.7)	0 (0)	1 (0.8)	0	0	1 (1.1)

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.
* n=22 evaluable patients. † n=10 evaluable patients. ‡ n=18 evaluable patients. § n=81 evaluable patients.
‖ 1 death reported in total: due to COVID-19, unrelated to pegcetacoplan (counted in the "primary IC-MPGN" group, "total population" group, and in the "no reported genetic/acquired factors" group).
¶ As of 13 February 2026. Includes exposure in clinical trials and post-marketing across multiple indications.
AE, adverse event; IC-MPGN, immune complex membranoproliferative glomerulonephritis; TEAE, treatment-emergent AE.

1. Ayehu et al. NKF Spring Clinical Meetings 2026; poster.

Key takeaways

Pegcetacoplan treatment led to **sustained reductions in proteinuria** and **eGFR stabilisation** and overall **safety was consistent** across subgroups and with outcomes previously observed for the total VALIANT population

Pegcetacoplan provides **benefits** in **adult or adolescent** patients, with **C3G or primary IC-MPGN, irrespective of the aetiology of complement dysregulation**

This *post-hoc* analysis supports the **efficacy** of pegcetacoplan and its **mechanism of action** in a **broad patient population with different disease triggers**

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

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