KIDNEY WEEK 2025

Pegcetacoplan for 52 weeks results in sustained proteinuria reduction to remission (≤0.5 g/g) and normalization (≤0.2 g/g): Phase 3 VALIANT trial

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Disclosures

- **CN** is the Associate Director for Molecular Otolaryngology and Renal Research Laboratory; receives NIH grant support (2R01DK110023-07); serves on advisory boards for Novartis, Apellis, Biocryst, and Alexion; participates as a site investigator for Novartis, Apellis, Biocryst, and Retrophin; is a member of the data safety monitoring board for Kira; serves as Chair of a data safety monitoring board for FIT4KID; and receives author royalties for UpToDate.
- **FF** has received consulting fees from Apellis, Sobi, Novartis, Roche, Alexion, and AstraZeneca.
- **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.
- **ASB** has received consulting fees from Amgen, Apellis, Catalyst, Genentech, Kezar, Novartis, Q32, Silence Therapeutics, and Visterra.
- **CL** received consulting fees and honoraria from Alexion, Apellis, Sobi, Novartis, and Pfizer.
- **GR** has received consulting fees from BioCryst and Silence Therapeutics and speakers' bureau fees from Novartis.
- **NVDK** has received consulting fees from Alexion, Samsung, and Roche; and speakers fees from Sobi and Novartis.
- **KG** and **AM** are employees of Apellis and hold stock or stock options.
- **LQG** and **JS** are employees of Swedish Orphan Biovitrum AB and hold stock or stock options.
- **MCP** has received consulting fees from Alexion, Achillion, Annexon, Apellis, BioCryst, ChemoCentryx, Complement Therapeutics, Gemini, Gyroscope, MIRNA Therapeutics, Omeros, and Q32bio Pharma.

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C3G and primary IC-MPGN are driven by **complement dysregulation**[1,2]

- Complement dysregulation results in accumulation of **C3 deposits in the glomeruli** (in addition to immunoglobulins in IC-MPGN), which leads to inflammation and progressive **kidney damage** and **ultimately kidney failure**[1,2]
- Patients achieve **improved outcomes** with **proteinuria <1 g/g** or **proteinuria reduction ≥50%**[3]

- In the **phase 3 VALIANT trial** (NCT05067127), **pegcetacoplan** (a **targeted C3/C3b inhibitor**) led to **significant proteinuria reductions** in adolescents and adults with C3G and primary IC-MPGN in native or post-transplant kidneys[4]

- Here, we report **exploratory and post hoc analyses** related to **proteinuria changes**

1. Bomback AS, et al. *Kidney Int Rep*. 2024. 2. Mastrangelo A, et al. *Front Pediatr*. 2020. 3. Masoud S, et al. *Kidney Int*. 2025.
4. Fakhouri F, et al. 62nd ERA Congress. June 4–7, 2025.

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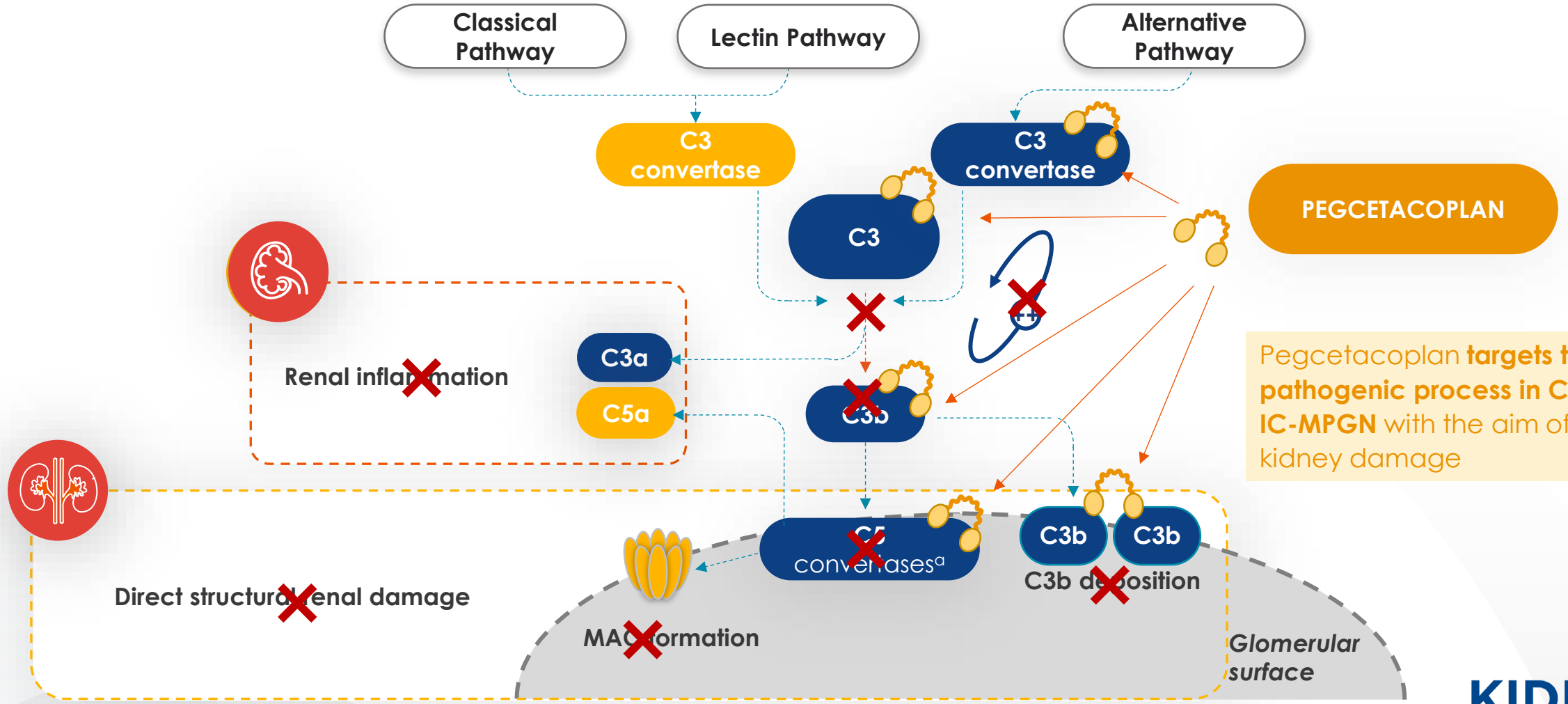
Pegcetacoplan blocks C3 dysregulation and downstream complement activation[1–7]

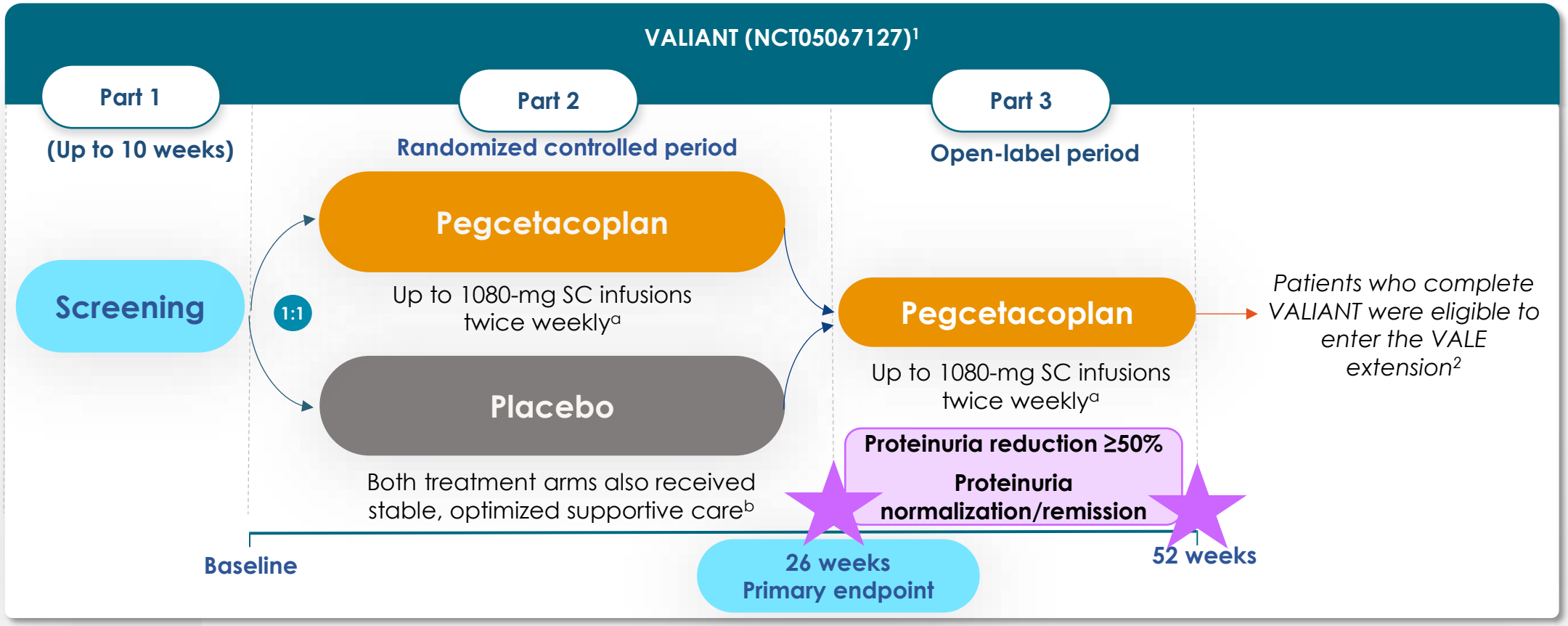


Pegcetacoplan **targets the pathogenic process in C3G/primary IC-MPGN** with the aim of stopping kidney damage

[a] C5 convertases: C4b2aC3b and C3bBbC3b.

1. Smith RJH, et al. *Nat Rev Nephrol.* 2019. **2.** Zipfel PF, et al. *Front Immunol.* 2019. **3.** Meuleman MS, et al. *Semin Immunol.* 2022. **4.** Dixon BP, et al. *Kidney Int Rep.* 2023. **5.** EMPAVELI (pegcetacoplan). Apellis Pharmaceuticals, Inc.; 2024. **6.** ASPAVELI (pegcetacoplan). Swedish Orphan Biovitrum AB; 2024. **7.** Lamers C, et al. *Nat Commun.* 2022.

VALIANT: Double-blind phase 3 study that included patients ≥12 years old with native or post-transplant disease



[a] All adults and adolescents weighing ≥50 kg self administered 1080 mg/20 mL. Adolescent patients weighing 30–34 kg received 540 mg/10 mL for the first 2 doses, then 648 mg/12 mL. Adolescent patients weighing 35–49 kg received 648 mg/12 mL for the first dose, then 810 mg/15 mL.
[b] Stable, optimized antiproteinuric regimens: ACEis, ARBs, SGLT2is, MMF, and corticosteroids (prednisone ≤20 mg/d or equivalent) were permitted.

1. Dixon BP, et al. ASN Kidney Week 2023. Nov. 2–5, 2023. Abstract INFO12-SA. **2.** https://clinicaltrials.gov/study/NCT05809531. Accessed Sep 8, 2025.

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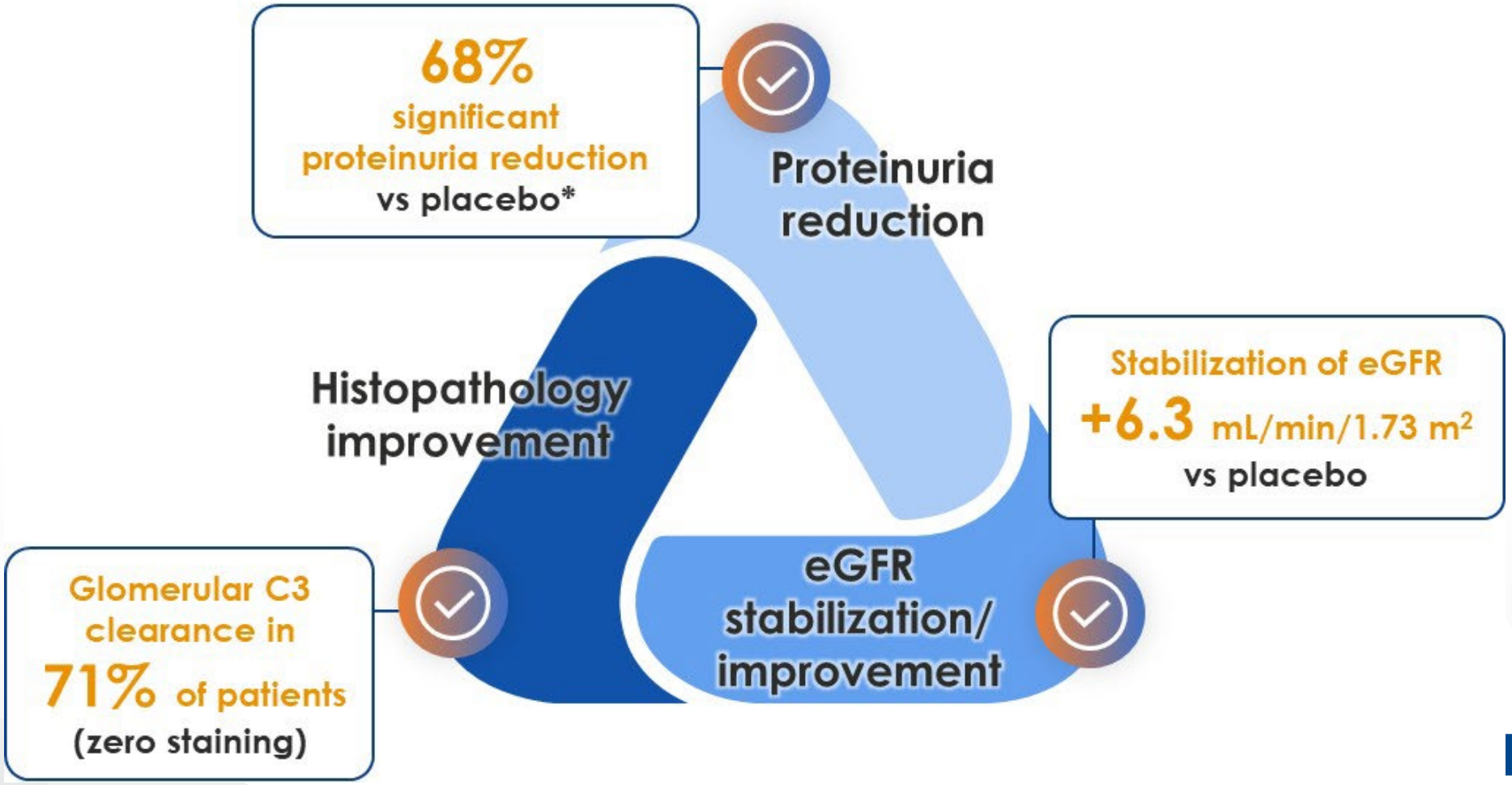
At week 26, **pegcetacoplan** demonstrated **robust and clinically meaningful** impacts on **histopathology**, **proteinuria**, and **eGFR**[1]



* Consistent across subgroups (age, disease type, transplant status).

1. Fakhouri F, et al. 62nd ERA Congress. June 4–7, 2025.

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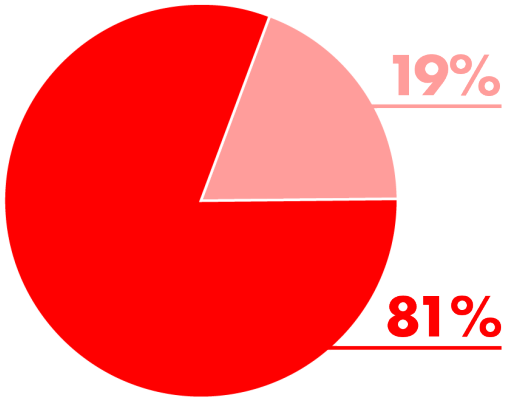
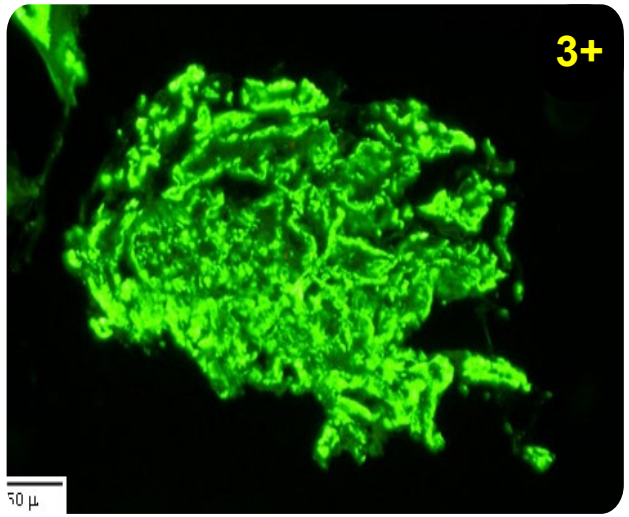
Pegcetacoplan led to **glomerular C3 clearance** at week 26

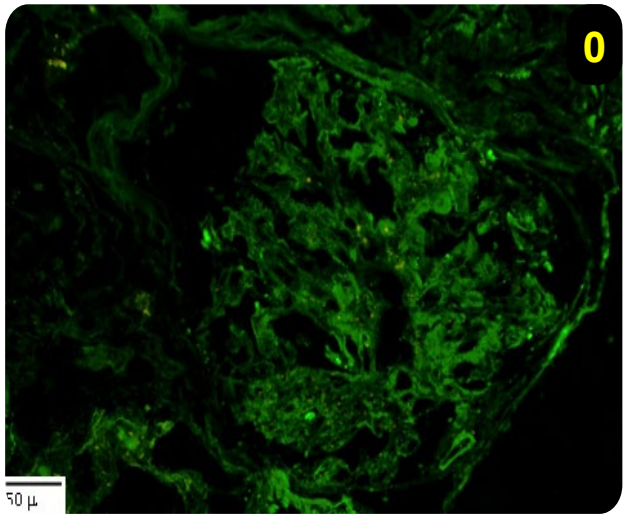
Biopsies from a C3G native kidney patient who received pegcetacoplan

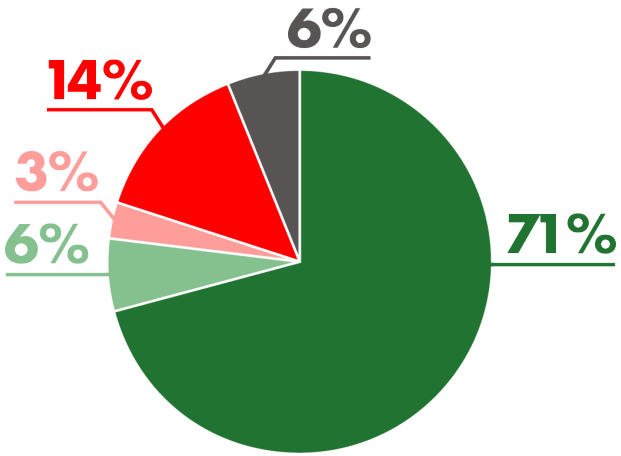
Baseline





Week 26





C3 staining: 0 | 1+ | 2+ | 3+ | Missing

KEY SECONDARY END POINT:
Reduction in C3 staining of at least 2 orders of magnitude

Pegcetacoplan vs **placebo:**
74.3% vs 11.8%
P<.001

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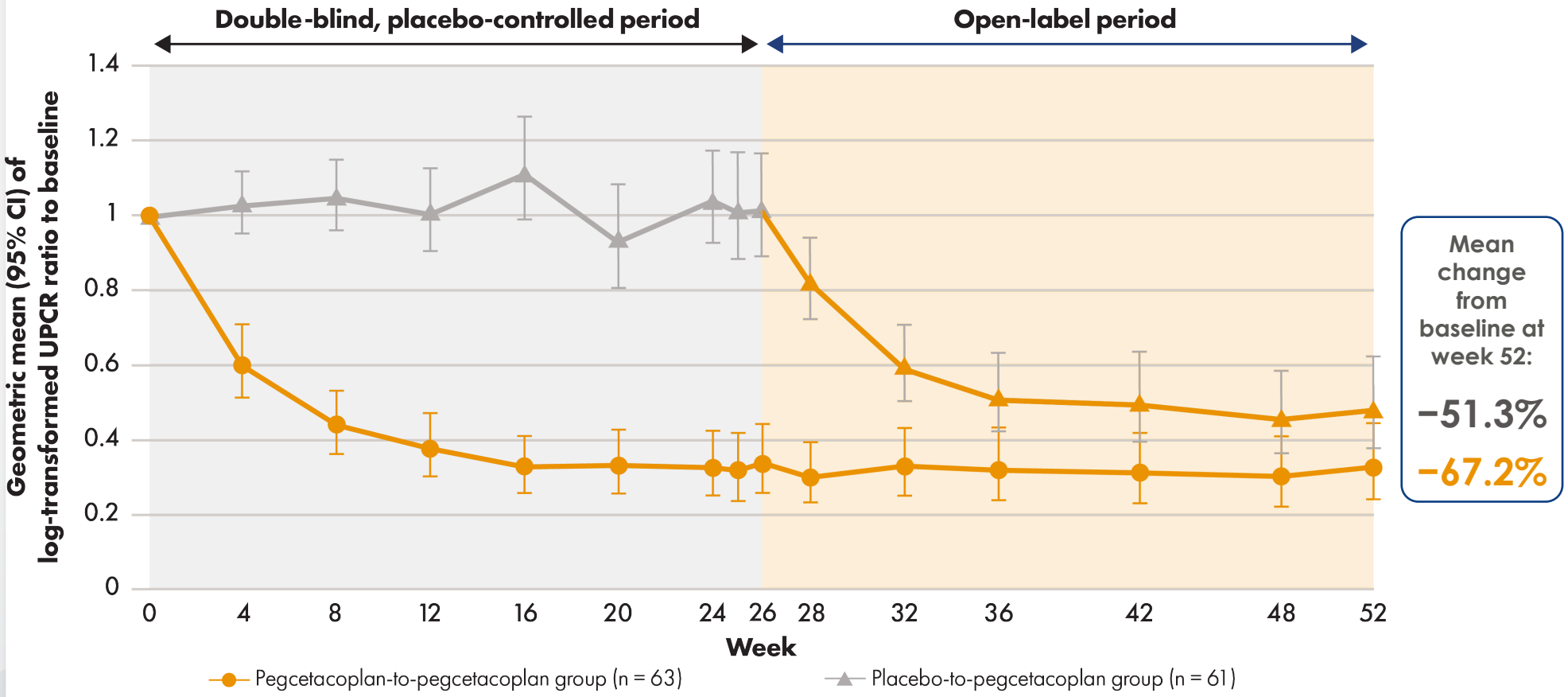
Statistically significant **proteinuria reduction** at week 26 **was maintained** through week 52

Change in proteinuria according to treatment group



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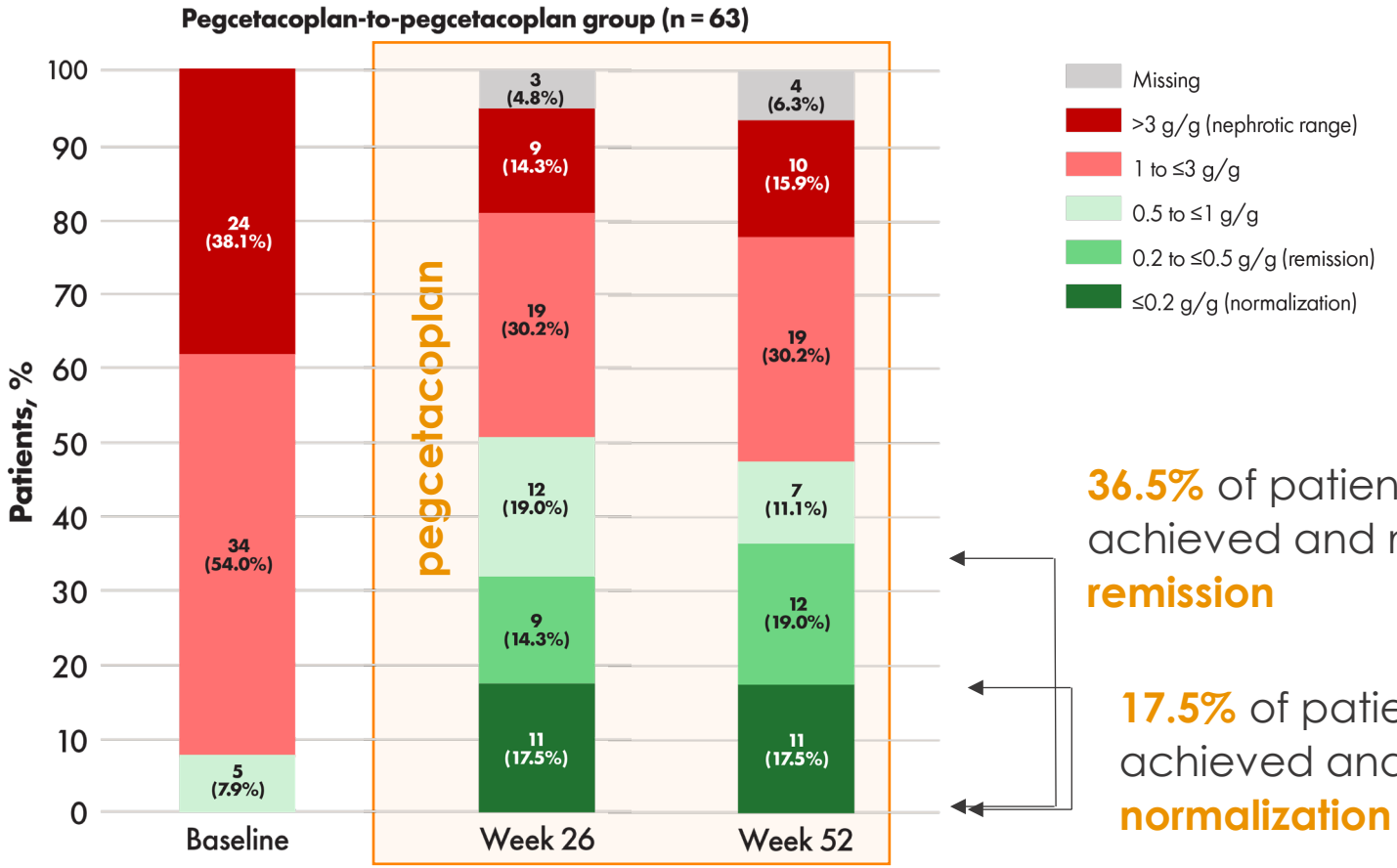
One-third of patients **achieved and maintained proteinuria remission (≤0.5 g/g) or normalization (≤0.2 g/g)*** with pegcetacoplan

Proportion of patients in proteinuria categories



36.5% of patients achieved and maintained **remission**

17.5% of patients achieved and maintained **normalization**

* Baseline UPCR value was calculated as the average of the UPCR measurements from at least 6 of the 9 FMU samples collected between the start of screening and day 1, inclusive. Week 26 and week 52 UPCR values were calculated using triplicate FMU collections.

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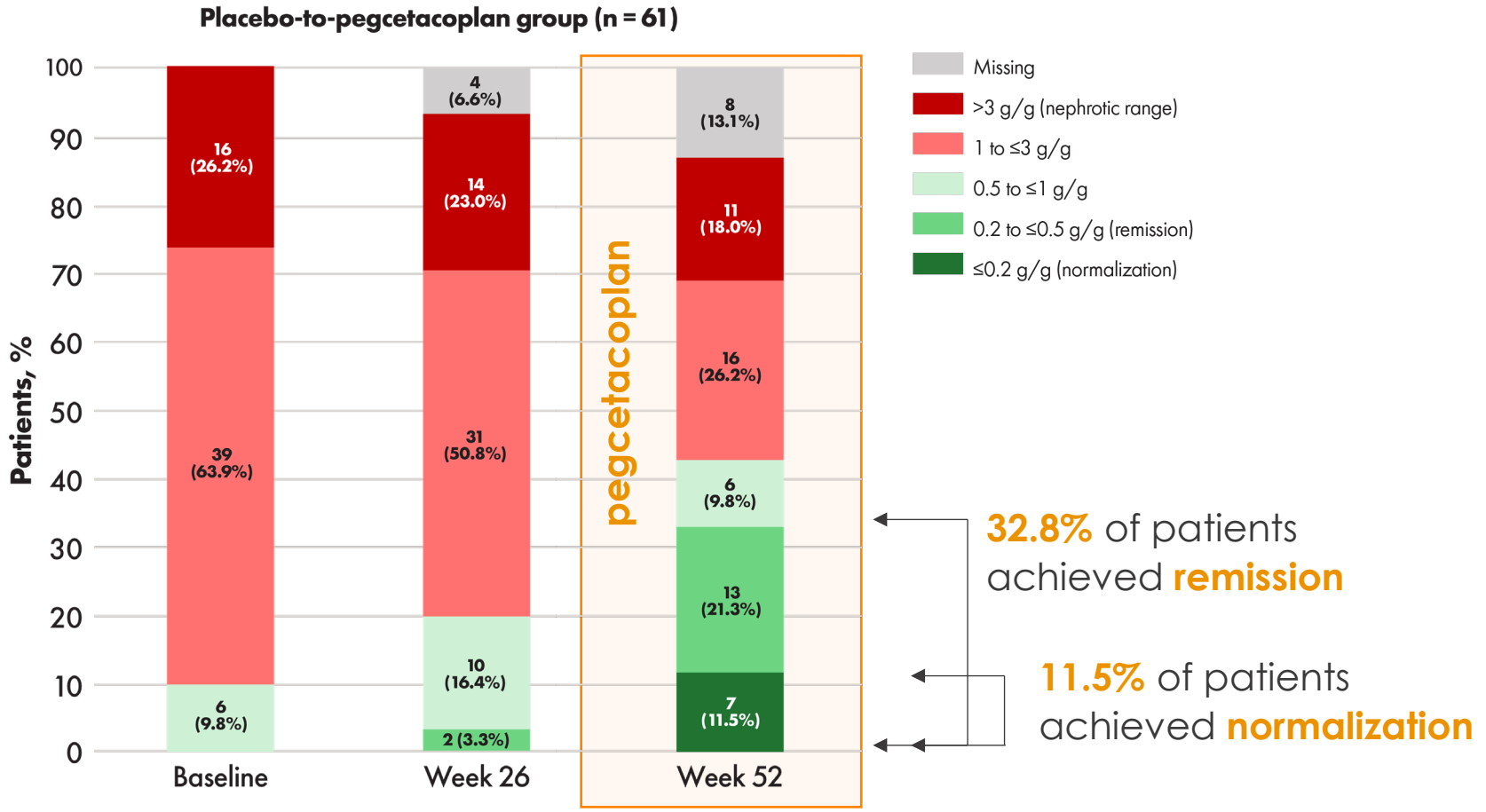
Patients who switched from **placebo to pegcetacoplan** achieved **similar results**

Proportion of patients in proteinuria categories



32.8% of patients achieved **remission**

11.5% of patients achieved **normalization**

* Baseline UPCR value was calculated as the average of the UPCR measurements from at least 6 of the 9 FMU samples collected between the start of screening and day 1, inclusive. Week 26 and week 52 UPCR values were calculated using triplicate FMU collections.

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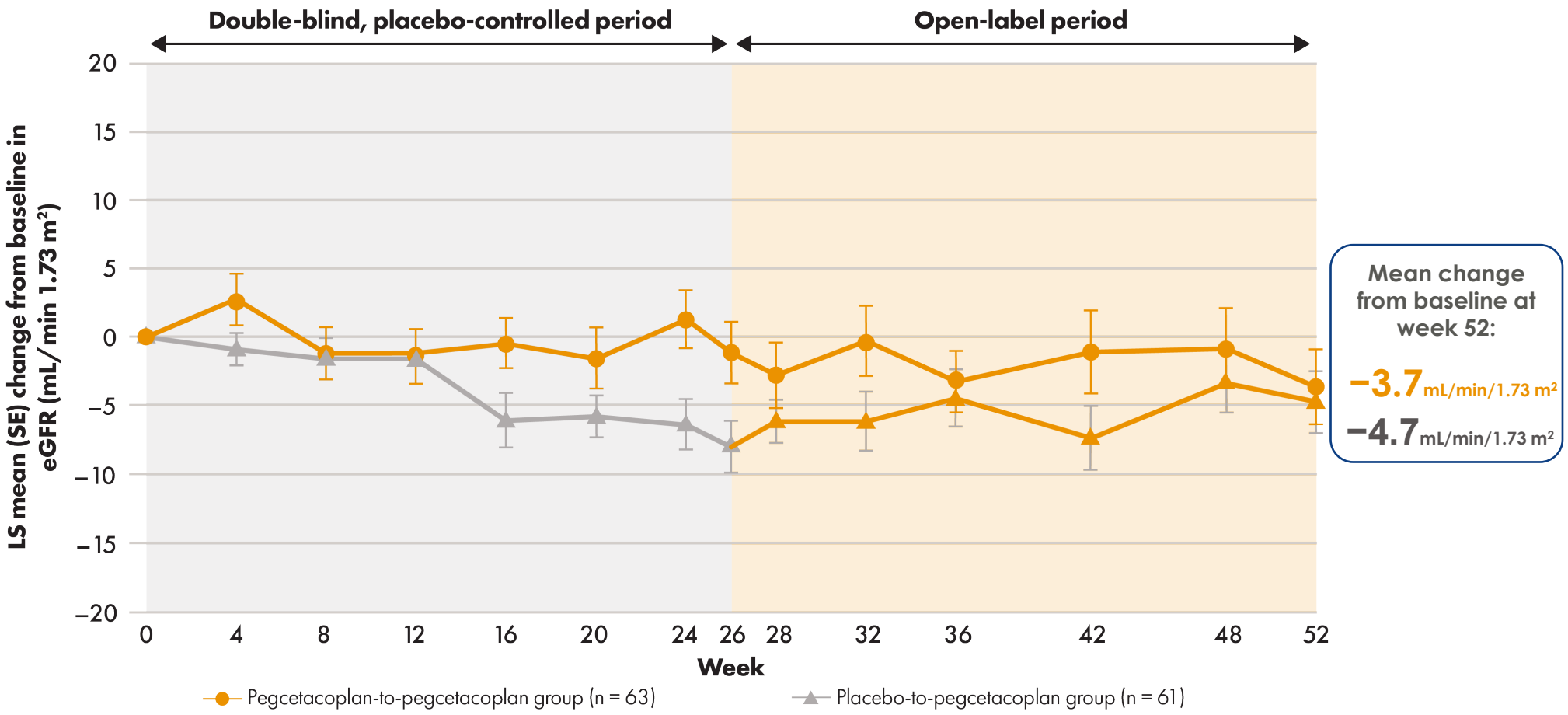
eGFR remained stable with 52 weeks of pegetacoplan treatment

Change in eGFR according to treatment group



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With **1 year** of treatment, **pegcetacoplan** led to **sustained proteinuria remission and normalization** and **stable eGFR** for patients with C3G and primary IC-MPGN[1]

Proteinuria reduction:

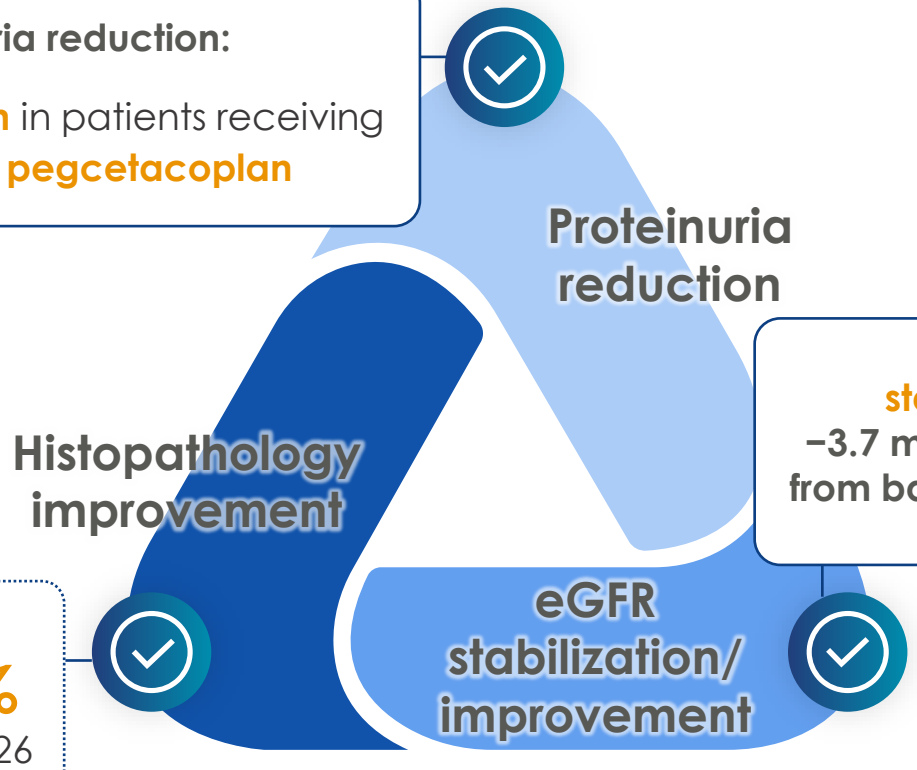
67% **reduction** in patients receiving **52 weeks of pegcetacoplan**

54% maintained proteinuria **reduction ≥50%**

47.6% achieved **proteinuria ≤1 g/g**

17.5% achieved **normalization** (≤0.2 g/g)

36.5% achieved **remission** (≤0.5 g/g)



eGFR:
stabilization of eGFR
−3.7 mL/min/1.73 m² change from baseline with 52 weeks of pegcetacoplan

Histopathology improvement:

glomerular C3 clearance in 71% of patients (zero staining) at week 26

Pegcetacoplan was well tolerated with no new safety signals

1. Fakhouri F, et al. 62nd ERA Congress. June 4–7, 2025.

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The authors thank the patients, investigators, and all other collaborators

This study was funded by Sobi (Swedish Orphan Biovitrum AB) and Apellis Pharmaceuticals, Inc.

Writing assistance was provided by Jennifer L. Gibson, PharmD (Kay Square Scientific, Butler, PA), and was funded by Sobi (Swedish Orphan Biovitrum AB) and Apellis Pharmaceuticals, Inc.

Abbreviations: C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; ERA, European Renal Association; FMU, first-morning urine; IC-MPGN, immune-complex membranoproliferative glomerulonephritis; LS, least-squares; UPCR, urine protein to creatinine ratio.

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