

Real-world effectiveness and safety of pegcetacoplan in patients with C3 glomerulopathy or primary immune-complex membranoproliferative glomerulonephritis: PRISM-C3, a multi-country Phase 4 study

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David Kavanagh;^{1,2} Matthew Pickering;³ Terence Cook;³ Marina Vivarelli;⁴ Moglie Le Quintrec;⁵ Veronique Fremeaux-Bacchi;⁶ Virginia Taliadouros;⁷ Elena Surova;⁷ Nicholas Webb;⁷ Fadi Fakhouri⁸

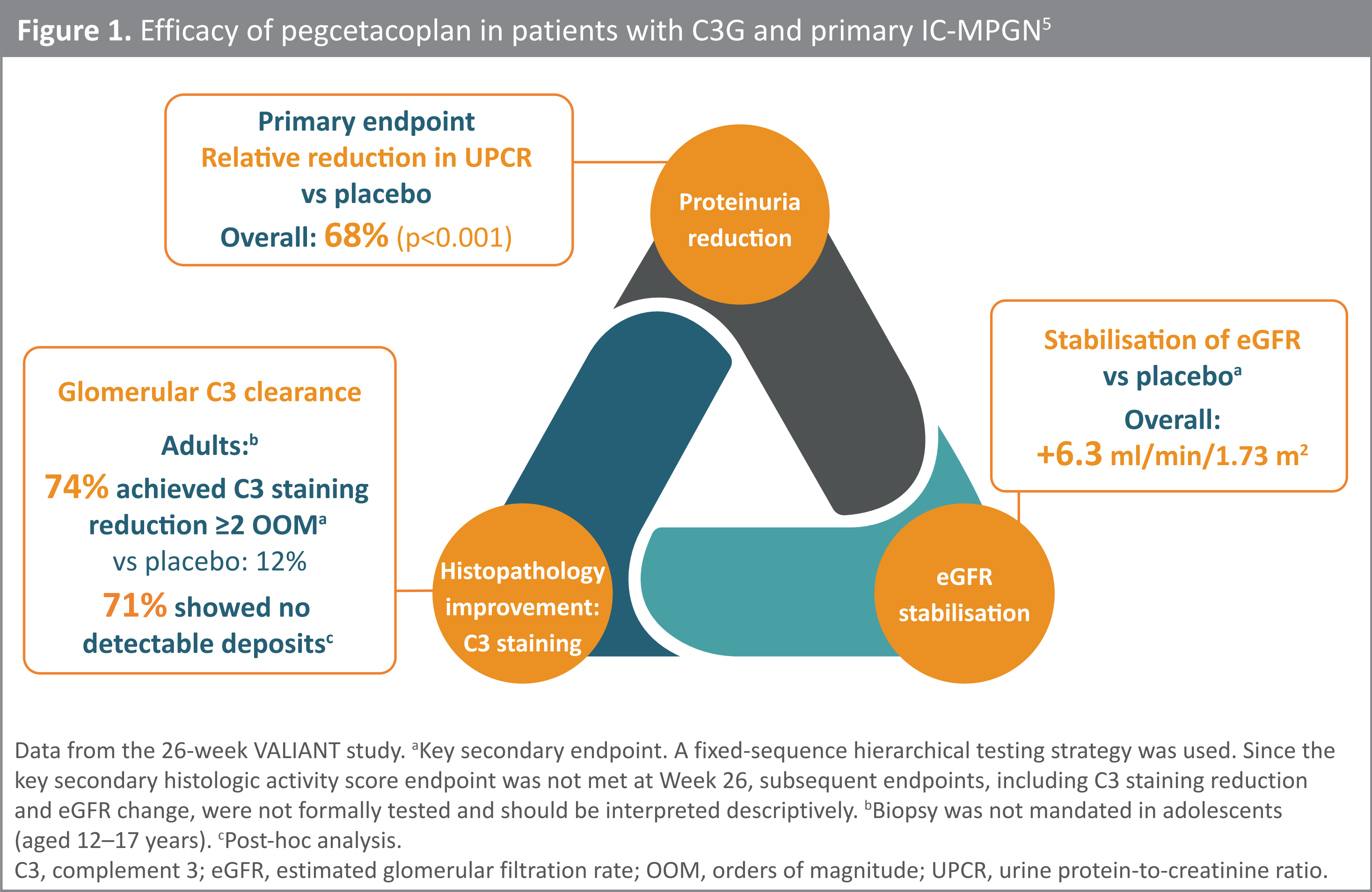
¹Newcastle University, Newcastle upon Tyne, UK; ²National Renal Complement Therapeutics Centre, Royal Victoria Infirmary, Newcastle upon Tyne, UK; ³Department of Immunology and Inflammation, Imperial College, London, UK; ⁴Laboratory of Nephrology and Clinical Trial Center, IRCCS Bambino Gesù Children’s Hospital, Rome, Italy; ⁵Montpellier University, Nephrology Department, Centre Hospitalier Universitaire Lapeyronier, Montpellier, France; ⁶Department of Immunology Biology, Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Paris, France; ⁷Swedish Orphan Biovitrum AB, Stockholm, Sweden; ⁸Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

CONCLUSIONS

- The findings of this real-world study will support the long-term evaluation of the benefit–risk profile of pegcetacoplan in a broad population of patients with C3G or primary (idiopathic) IC-MPGN, and may help to optimise evidence-based clinical practice.
- Assessing disease-specific biomarkers is a novel and valuable addition to evaluating the real-world effectiveness of pegcetacoplan.

INTRODUCTION

- C3G and primary IC-MPGN are two chronic, heterogeneous, rare kidney diseases, driven by C3 dysregulation and uncontrolled deposition of C3 and its breakdown products in the glomeruli, resulting in progressive kidney damage and a high risk of kidney failure.^{1–4}
- Pegcetacoplan, a targeted C3/C3b inhibitor, has demonstrated compelling clinical efficacy (proteinuria reduction, eGFR stabilisation, and clearance of glomerular C3 deposits) and a favourable safety profile in patients with C3G or primary IC-MPGN, in controlled Phase 2 and 3 clinical trials (**Figure 1**).^{1,5,6}



- Pegcetacoplan is approved in the EU and the US for the treatment of adult and adolescent patients (aged ≥12 years) with C3G or primary IC-MPGN.^{7,8}
- Although randomised controlled trials are the gold standard for measuring the efficacy of interventions, their generalisability can be limited to specific settings or patient characteristics.⁹
- Therefore, real-world evidence for pegcetacoplan in the approved patient population would complement clinical trial data and support clinical decision-making.⁹

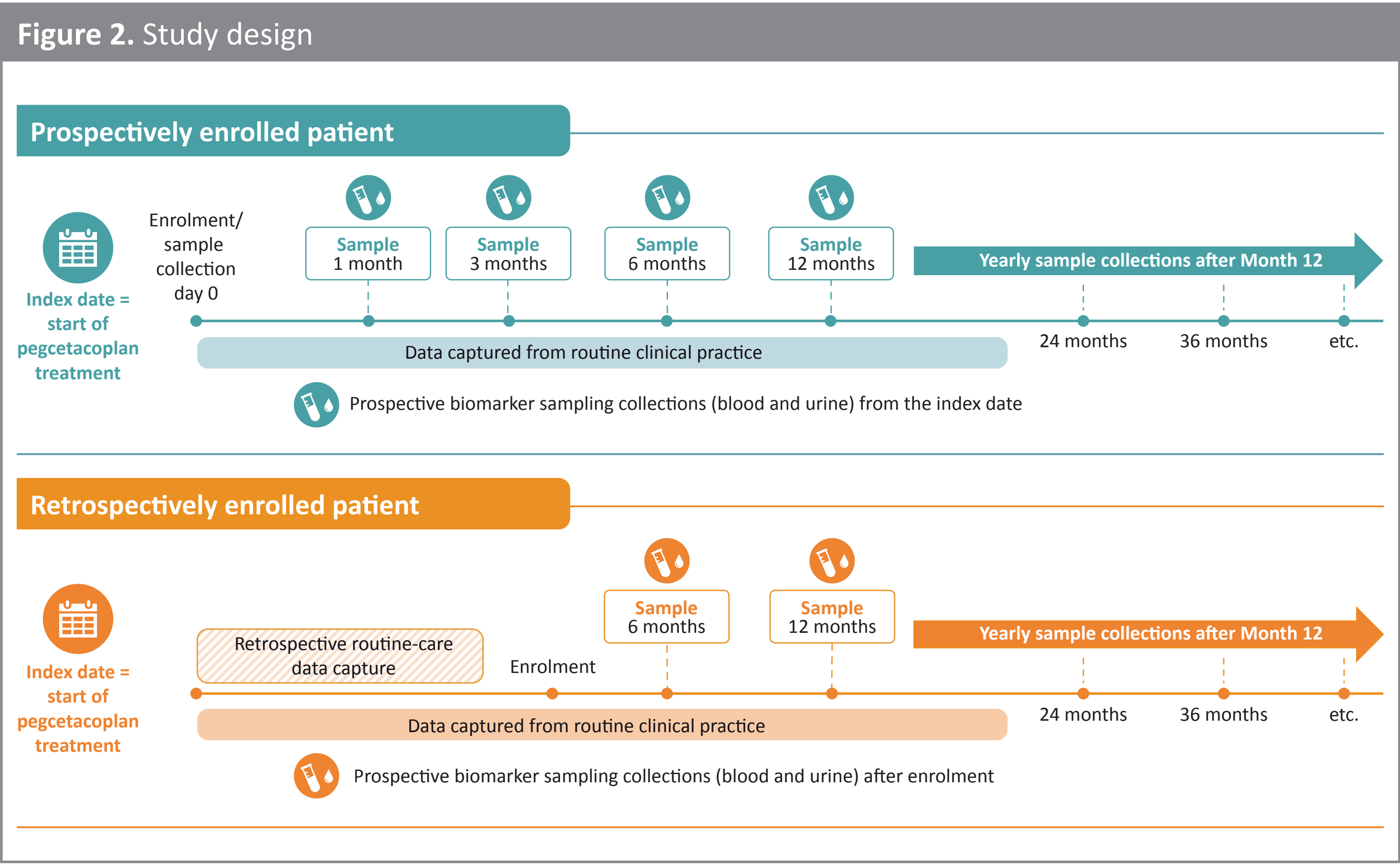
AIMS

- Here, we describe the design and methodology of PRISM-C3 – a real-world study to evaluate the effectiveness and safety of pegcetacoplan in patients with C3G or primary IC-MPGN,¹⁰ including an assessment of disease-specific biomarkers to better understand disease progression, treatment response, and relapse risk.

METHODS

Study overview

- PRISM-C3 is an international (ex-US), multicentre, Phase 4 study that will follow patients for ≥2 years (**Figure 2**).
- With an expected 3.5-year recruitment period, the planned prospective study duration for each patient will range from 2 years (for the last patient) to approximately 5.5 years (for the first patient).



Study population

- Patients who have initiated or plan to initiate pegcetacoplan treatment for C3G or primary IC-MPGN (native or post-transplantation recurrent disease) outside of interventional clinical studies are being recruited; enrolment commenced in August 2026.
- Patients are excluded if they have received an investigational treatment for C3G or primary IC-MPGN at the time of pegcetacoplan initiation, or if they have started treatment with pegcetacoplan in an interventional study.

Data collection and study endpoints

- **Observational part:** patient demographics, disease characteristics, medical and treatment (prior or concurrent C3G/primary IC-MPGN related) history, pegcetacoplan treatment details (including start/stop date, dosing regimen, reason for use), clinical outcomes, safety, PROs, and healthcare resource utilisation related to C3G/primary IC-MPGN will be collected from medical records both retrospectively and prospectively (through routine clinic visits).
- **Low interventional aspect:** blood and urine biomarker data will be collected prospectively at scheduled time points relating to the initiation or discontinuation of pegcetacoplan treatment (**Figure 2**) and measured in a central laboratory. Biomarkers to be assessed include disease aetiology markers, complement pathway biomarkers, and inflammatory and kidney injury biomarkers. Study endpoints and corresponding data collection measures are outlined in **Table 1**.

Table 1: Summary of study endpoints and data collection to inform study endpoints	
Data collection to inform study endpoints	
Category	Measures
Renal function	UPCR; serum creatinine (and calculation of eGFR); urinalysis; serum albumin, lipids and lipoproteins; complement tests; kidney biopsy (including Ig and C3c staining)
Biomarkers	Disease aetiology; complement pathway; inflammatory and kidney injury
PROs	
Paediatrics (<18 years old)	Peds FACIT-Fatigue
Adults (≥18 years old)	FACIT-Fatigue; TSQM-9; WPAI
Healthcare resource utilisation	Number of inpatient/outpatient hospital visits; number of ICU admissions; number of emergency visits; length of hospital stay; length of ICU stay
Safety	AESI (serious/severe infections, malignancies, AKI); SAEs
Study endpoints	
	Primary endpoint • The proportion of patients achieving a UPCR of <1 g/g after 6 months of pegcetacoplan treatment.
	Secondary endpoints • Evaluation of renal function and disease characteristics, including disease progression prior to and during pegcetacoplan treatment. • Changes in biomarkers prior to and during pegcetacoplan treatment. • PROs during pegcetacoplan treatment. • Healthcare resource utilisation prior to and during pegcetacoplan treatment.
	Safety endpoints • Incidence of AESI and SAEs from pegcetacoplan initiation until 8 weeks after the end of treatment.
AESI, adverse events of special interest; AKI, acute kidney injury; C3, complement 3; eGFR, estimated glomerular filtration rate; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; ICU, intensive care unit; Ig, immunoglobulin; Peds FACIT-Fatigue, paediatric FACIT-Fatigue; PRO, patient-reported outcome; SAE, serious adverse event; TSQM-9, Treatment Satisfaction Questionnaire for Medication (9-item version); UPCR, urine protein-to-creatinine ratio; WPAI, Work Productivity and Activity Impairment Questionnaire.	

Sample size and statistical/data analyses

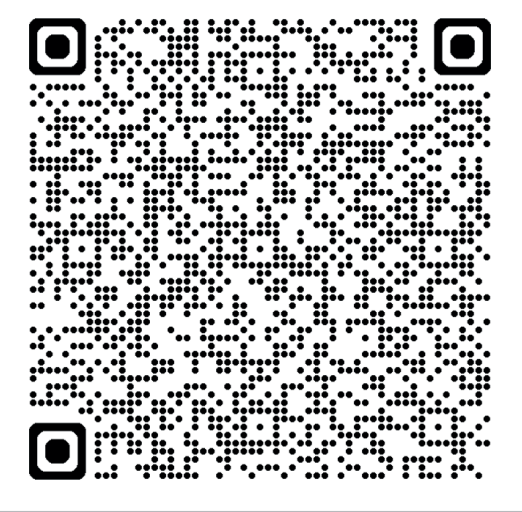
- The study aims to recruit approximately 150 patients with C3G or primary IC-MPGN, including ≥30 patients with post-transplantation recurrent disease.
- Study endpoints will be analysed for the overall population and for the following subgroups:
 - renal transplant status at the start of pegcetacoplan treatment: disease on native kidney or post-transplantation recurrence
 - age at the start of pegcetacoplan treatment: <18 years or ≥18 years
 - concomitant immunosuppressant use at the start of pegcetacoplan treatment: yes or no
 - primary diagnosis: C3G or primary IC-MPGN
 - UPCR at the start of pegcetacoplan treatment: <3 g/g or ≥3 g/g (nephrotic range).

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ABBREVIATIONS: C3, complement 3 protein; C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; EU, European Union; IC-MPGN, immune-complex membranoproliferative glomerulonephritis; PRO, patient-reported outcome; UPCR, urine protein-to-creatinine ratio; UK, United Kingdom; US, United States.

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