PRESERVE-C3Tx, a Phase 3b Pilot Study Design: Evaluating the Effect of Pre-emptive Pegcetacoplan Use on Recurrence of C3G or Primary IC-MPGN after Kidney Transplant

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CONCLUSIONS

- This pilot study will describe the recurrence and safety outcomes of pegcetacoplan in patients with C3 glomerulopathy (C3G) or primary (idiopathic) immune complex membranoproliferative glomerulonephritis (IC-MPGN) after kidney transplantation, generating initial evidence around pegcetacoplan's ability to prevent disease recurrence and kidney damage in this setting
- PRESERVE-C3Tx is expected to start recruitment by the end of 2026 with data to be presented over the coming years

INTRODUCTION

- C3G and primary IC-MPGN are rare diseases characterized by uncontrolled C3 activation and excessive glomerular deposition of C3 breakdown products, leading to kidney failure in up to 50% of patients within 10 years[1–3]
- Kidney transplantation is an option for patients with C3G or primary IC-MPGN and kidney failure, however, as the underlying disease mechanism remains, up to 89% of patients experience disease recurrence[4] leading to a high unmet need for therapeutic strategies that improve long-term graft outcomes
- Pegcetacoplan, a targeted C3/C3b inhibitor, has demonstrated benefits in patients with native kidney or post-transplant recurrent C3G and primary IC-MPGN.[3,5–7] 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[5,6]
- However, the role of pre-emptive pegcetacoplan on the development of recurrent disease has not been established. This single-arm, open-label, multicenter pilot study (Sobi.PEGCET-404) will describe disease recurrence, graft and safety outcomes associated with pre-emptive pegcetacoplan initiated after kidney transplantation

OBJECTIVES

- We describe the design and methodology of PRESERVE-C3Tx – a pilot study to explore and describe incidence and timing of protocol-defined recurrence and graft outcomes following post-kidney transplant initiation of pegcetacoplan in patients with C3G or primary IC-MPGN, including an assessment of safety and disease-specific biomarkers to better understand disease progression, treatment response, and relapse risk in these patients

References: **1.** Dixon BP, et al. *Kidney Int Rep*. 2023;8(11):2284–2293. **2.** Smith RJH, et al. *Nat Rev Nephrol*. 2019;15:129–143. **3.** Fakhouri F, et al. *N Eng J Med*. 2025;393(22):2210–2220. **4.** Ruiz-Cabello JE, et al. *Kidney Int Rep*. 2026;11:103682. **5.** ASPAVELI (pegcetacoplan) 1080 mg solution for infusion. Summary of Product Characteristics. Updated January 2026. **6.** EMPAVELI (pegcetacoplan) injection for use. Prescribing Information. Updated July 2025. **7.** Bomback AS, et al. *Kidney Int Rep*. 2025;10(1):87–98.

Abbreviations: C3, complement 3 protein; C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; IC-MPGN, immune-complex membranoproliferative glomerulonephritis; UPCR, urine protein-to-creatinine ratio; UK, United Kingdom; US, United States.

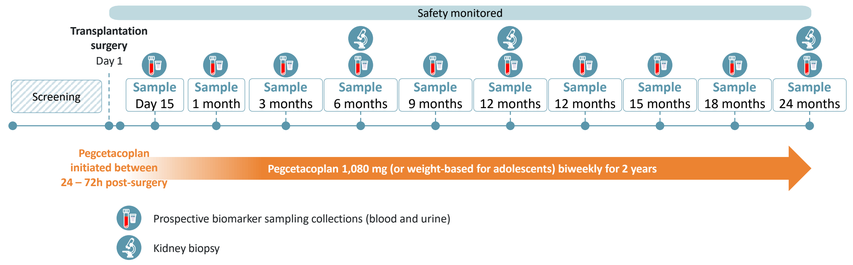
Acknowledgements: The study is funded by Sobi (Swedish Orphan Biovitrum AB). Medical writing and editorial support was funded by Sobi. The authors acknowledge David Kavanagh for his input on the study protocol.

METHODS

Study overview and population

- PRESERVE-C3Tx is an international (ex-US), multicenter, interventional study that will follow patients for ≥2 years (**Figure 1**)
- The study aims to recruit 30 patients from approximately 30 sites worldwide including: Brazil, Canada, Saudi Arabia, UK, France, Finland, Italy, Spain, Germany and Switzerland; enrolment to commence end of 2026
- With an expected 2-year recruitment period and planned prospective study duration for each patient of 2 years, the study is expected to close in 2031

Figure 1. Study design



Key inclusion criteria

- Male or female patients ≥12 years with diagnosis of C3G or primary IC-MPGN with plan to undergo kidney transplantation
- Patients assessed as having a high risk of disease recurrence after kidney transplantation (based on either having a previous allograft loss due to recurrence of C3G or primary IC-MPGN, or assessed as having a high risk by the Investigator)
- Up to date with vaccination requirements

Key exclusion criteria

- A known secondary cause of MPGN
- History of malignancy or invasive meningococcal disease
- Enrolment in another concurrent interventional trial, or received an investigational treatment within 3 months of scheduled kidney transplant surgery
- Use of complement inhibitor within 1 month prior to scheduled surgery

Data collection and study endpoints

- **Biomarker sampling:** blood and urine biomarker data will be collected prospectively at scheduled time points relating to the initiation or discontinuation of pegcetacoplan treatment (**Figure 1**) and measured in a central laboratory. Biomarkers to be assessed include disease etiology markers, complement pathway biomarkers and kidney injury biomarkers. Study endpoints and corresponding data collection measures are outlined in **Table 1**
- **Protocol biopsies:** Biopsy samples will be taken at regular timepoints (6, 12, 24 months) after transplantation and assessed with light microscopy, immunofluorescence and electron microscopy
- **Other data:** patient demographics, disease characteristics, medical and treatment history, concurrent medication details, pegcetacoplan treatment details (including start/stop date, dosing regimen), dialysis details, clinical outcomes and safety, will be collected prospectively and through routine clinic visits

Table 1. Summary of study endpoints and data collection to inform study endpoints

Data collection to inform study endpoints	
Category	**Measures**
Renal function	Urinary protein-to-creatinine ratio (UPCR); serum creatinine (and calculation of eGFR); hematuria assessment;
Biomarkers	Disease etiology (genetic factors/nephritic factors); complement tests: plasma soluble C5b-9 (sC5b-9) and C3; kidney injury markers; kidney biopsy (including Ig and C3c staining)
Safety	AESI (serious/severe infections, malignancies, AKI); SAEs; inflammatory markers where available
Study endpoints	
Primary endpoint	
	• Histological evidence of recurrent disease within 2 years after transplantation based on the histopathological assessment of the kidney biopsy at the study center, **and** • Clinical evidence of disease recurrence, based on at least 1 of the following as judged by the Investigator: clinically significant increase in UPCR without other plausible causes; clinically significant decrease in eGFR without other plausible causes; clinically significant hematuria without other plausible causes
Secondary endpoints	
	• Time from kidney transplantation surgery to onset of clinically significant recurrence of C3G or IC-MPGN • Histological evidence of recurrent disease within 2 years of kidney transplantation, based on the histopathological assessment of a kidney biopsy at the study center • Time from kidney transplantation surgery to histological evidence of recurrent disease • The incidence of SAEs and AESIs
Exploratory endpoints	
	• Changes in proteinuria, eGFR, and hematuria • Incidence of delayed graft function; frequency of acute rejection episodes; frequency of graft failure; frequency and time course of graft failure due to clinically significant disease recurrence • Change during/to the end of the study (EOS) in: C3 and sC5b-9 levels; renal biopsy findings during the study period based on a local site assessment; proteinuria from clinically significant disease recurrence to EOS; eGFR from clinically significant disease recurrence to EOS

AESI, adverse events of special interest; AKI, acute kidney injury; C3, complement 3; eGFR, estimated glomerular filtration rate; Ig, immunoglobulin; SAE, serious adverse event; sC5b-9, soluble complement 5b-9; UPCR, urine protein-to-creatinine ratio.

Presented at the American Society of Nephrology Kidney Week, October 21–25 2026, Denver, CO, USA

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