

Time is Kidney: **The Impact of Timely Management in Children with C3G and Primary IC-MPGN**

Sobi Industry Symposium
ESPN 2026

Thursday, 1 October 2026
13:30-14:30 CET

NP-54110

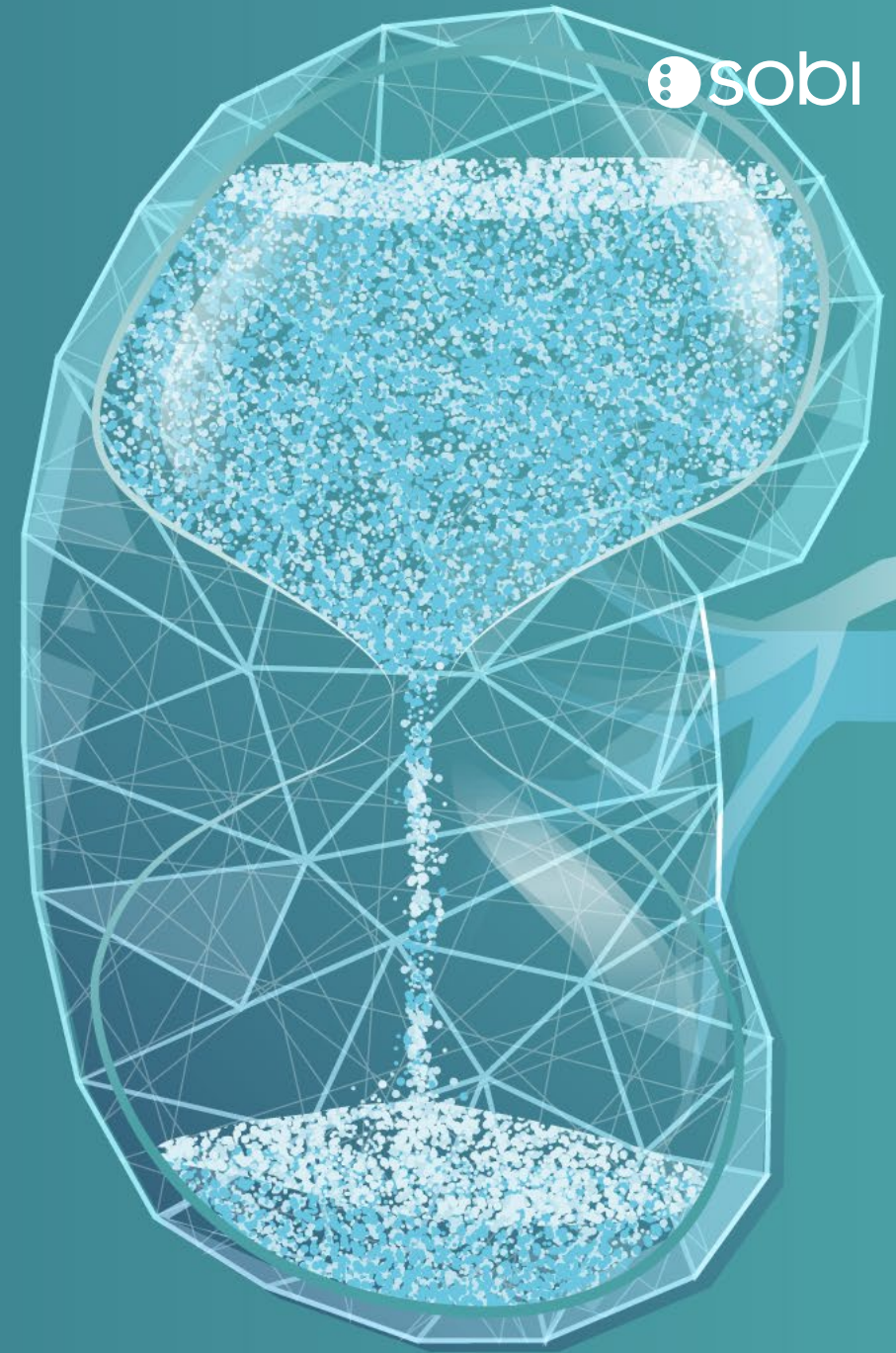
Date of preparation: September 2026



Welcome and introduction

Marina Vivarelli

Bambino Gesù Children's Hospital
Rome, Italy



Disclosures



Consultancy fees	Novartis, Sobi, Travers, Roche, Apellis, Alexion, PureSpring, Sanegene, Santhera, Alexion
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Speaker’s fees	Sobi, Novartis, Samsung Bioepis, Roche, Alexion

Disclaimer & important information



This presentation serves **educational purposes** and is intended to provide information and **stimulate discussion on** the rare immunological diseases, complement 3 glomerulopathy (C3G) and primary immune complex-mediated membranoproliferative glomerulonephritis (IC-MPGN).

The intent is **not to provide** medical or any other type of **advice**. All **treatment decisions should be up to the discretion of the healthcare provider** and the patient, as each patients' situation may vary. **No identifiable patient-specific information** is included.

The **content, discussion, and answers reflect the personal opinion of the speaker** and may not represent those of Sobi.

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Introductions



Marina Vivarelli

Bambino Gesù Children's Hospital,
Rome, Italy



Nabil Melhem

Evelina London Children's Hospital
Guy's and St. Thomas' NHS Trust,
London, UK



Olivia Boyer

Necker Children's Hospital,
Paris, France

Agenda



Time is Kidney: The Impact of Timely Management in Children with C3G and Primary IC-MPGN

Time	Presentation	Speaker
13:30-13:38	Welcome and introduction	Marina Vivarelli (Chair)
13:38-13:50	Getting it right early: Treatment decisions for optimal outcomes	Nabil Melhem
13:50-14:05	What can and cannot be recovered after chronic kidney damage	Olivia Boyer
14:05-14:20	Navigating treatment sequencing: Individualised decisions in practice	Marina Vivarelli (Chair)
14:20-14:30	Q&A, panel discussion and closing remarks	All (moderated by Chair)

C3G, C3 glomerulopathy; IC-MPGN, immune complex membranoproliferative glomerulonephritis.

C3G and primary IC-MPGN remain diseases with significant unmet need

Typical disease progression

Excessive glomerular C3 deposition¹⁻⁴

Glomerular inflammation and structural damage²⁻⁴

Persistent C3 dysregulation causes scarring, tubular atrophy and glomerulosclerosis, leading to CKD and kidney failure^{2,3}

Non-targeted treatment does not address the root cause of disease

Supportive care addresses symptoms only (e.g. renoprotective therapy, such as RAASi)^{1,3}

Immunosuppression does not target C3 dysregulation and carries significant treatment burden (e.g. glucocorticoids and MMF*)^{1,5}

Supportive care and non-targeted immunosuppression form conventional standard of care

Kidney failure in up to 20% of paediatric and adolescent patients within 10-15 years⁶⁻⁸

High rates of recurrence after kidney transplant¹⁰

Dialysis has a detrimental impact on QoL⁹

* MMF is not approved by the EMA specifically for the treatment of C3G or primary IC-MPGN.¹¹

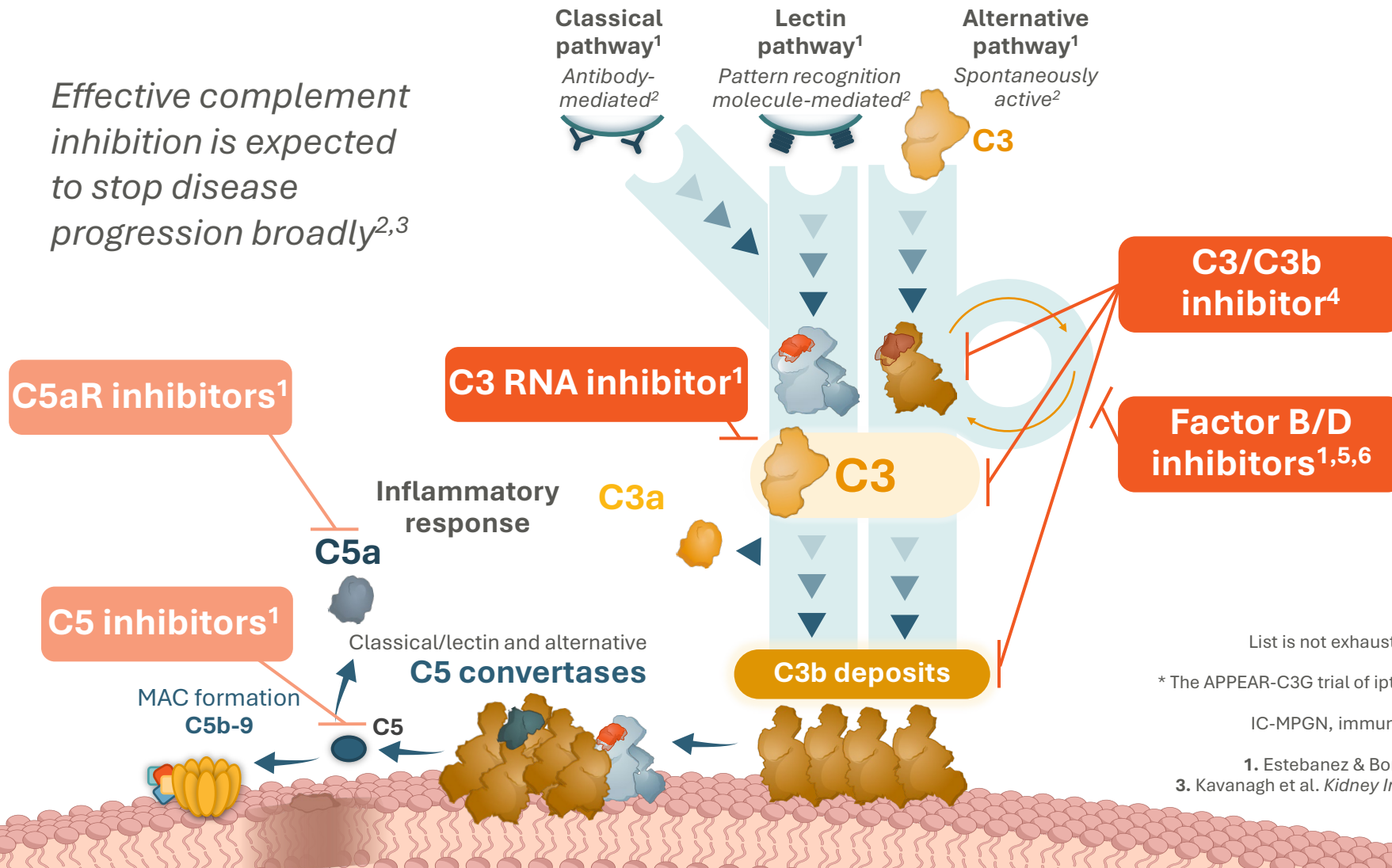
C3, complement 3; C3G, C3 glomerulopathy; CKD, chronic kidney disease; EMA, European Medicines Agency; GBM, glomerular basement membrane; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; MMF: mycophenolate mofetil; RAASi, renin-angiotensin system inhibition, QoL, quality of life.

1. Noris & Remuzzi *Nephrol Dial Transplant* 2024 2. Smith et al. *Nat Rev Nephrol* 2019 3. Caravaca-Fontán et al. *Nephron* 2020 4. Willows et al. *Clin Med* 2020 5. Jefferson *Clin J Am Soc Nephrol* 2018

6. Kirpalani et al. *Kidney Int Rep* 2020 7. Wong et al. *Clin J Am Soc Nephrol* 2021 8. Fakhouri et al. *N Engl J Med* 2025 9. Himmelfarb et al. *Nat Rev Nephrol* 2020 10. Patry et al. *Pediatr Nephrol* 2024 11. CellCept SmPC 2026.

Complement pathway therapeutic targets in C3G and primary IC-MPGN

Effective complement inhibition is expected to stop disease progression broadly^{2,3}



Availability of complement-targeted treatments and further understanding of the disease may prompt an update in the current guidelines with potential new treatment pathways³

Pegcetacoplan, a C3/C3b inhibitor, is the only targeted therapy currently approved for use in adolescents ≥12 years old with C3G or primary IC-MPGN*⁴

List is not exhaustive of emergent therapies; not all pipeline products are included.

Not all treatments are approved in all countries.

* The APPEAR-C3G trial of iptacopan (NCT04817618) in adolescents ≥12 years old is ongoing.⁹

C3G, C3 glomerulopathy; C5aR, C5a receptor;

IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis;

MAC, membrane attack complex; RNA, ribonucleic acid.

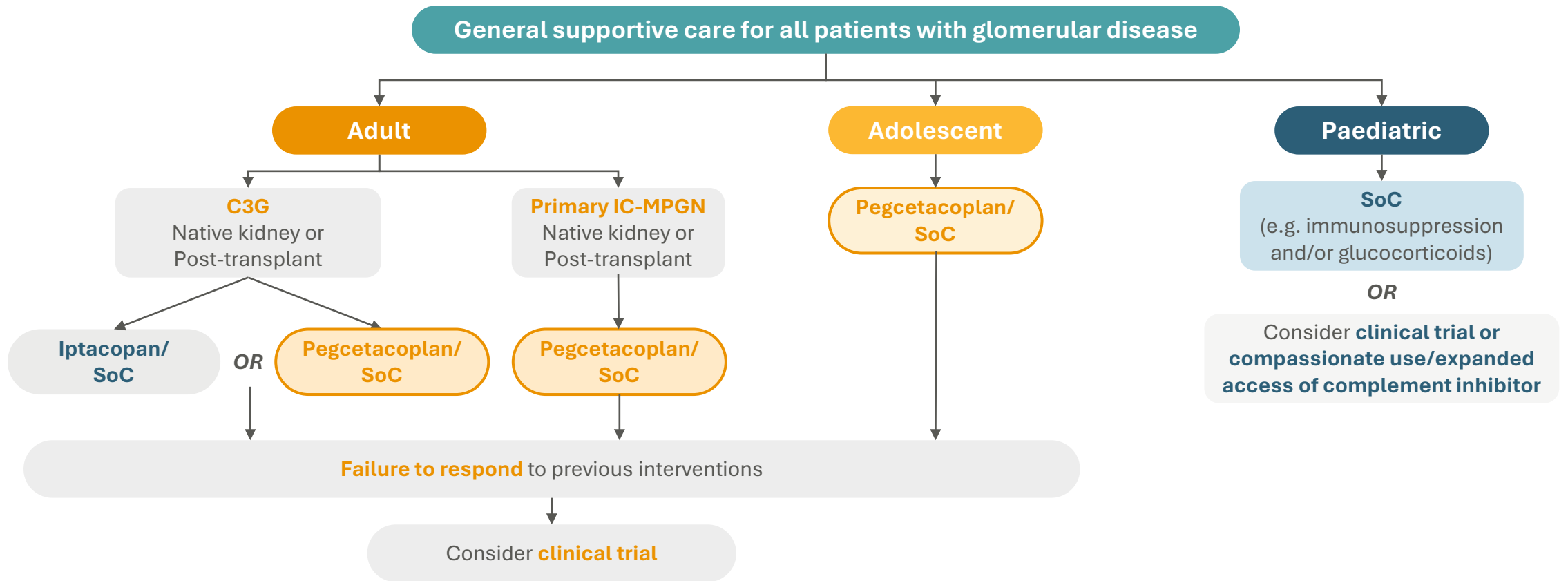
1. Estebanez & Bomback *Kidney Int Rep* 2024 2. Vivarelli et al. *Pediatr Nephrol* 2022

3. Kavanagh et al. *Kidney Int Rep* 2025 4. Empaveli (pegcetacoplan). Prescribing information

5. Fabhalta (iptacopan) Prescribing information

6. Clinicaltrials.gov NCT04817618.

A recently proposed potential new treatment pathway for the era of targeted treatments¹



It remains to be seen whether there is a continued role for immunosuppression and/or glucocorticoids in addition to complement inhibition in certain patient subpopulations

SoC includes supportive treatment ± non-targeted immunosuppression.

Figure adapted from Kavanagh et al. *Kidney Int Rep* 2025.

C3G, complement 3 glomerulopathy; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; SoC, standard of care.

1. Kavanagh et al. *Kidney Int Rep* 2025.

There is a growing evidence base for pegcetacoplan in paediatric and adolescent patients with C3G and primary IC-MPGN

The VALIANT study^{1,2}



VALIANT included a **broad patient population**, including **44% adolescents** (n=55/124)^{1,2}

Pegcetacoplan led to **significant proteinuria reduction** and to **eGFR stabilisation** in **adolescent patients** at 26 weeks, consistent with the overall population^{1,2}

Real-world case studies and series³⁻⁹



Paediatric patients **<12 years of age***⁴⁻⁷



Patients with **early**³ and **late-stage** disease^{3,6-8}



Patients **on dialysis** due to acute disease^{6,8,9}



Combination with/switch from **other complement inhibitors**^{3,7,9}



Pre-kidney **transplant**⁷

Case studies and series provide further **insights into** pegcetacoplan use in young patients with **clinically complex presentations**³⁻⁹

* Not included in the approved labels for pegcetacoplan.

C3G, complement 3 glomerulopathy; HCRU, healthcare resource utilisation; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; eGFR, estimated glomerular filtration rate.

1. Fakhouri et al. *N Engl J Med* 2025 2. Vivarelli et al. *Clin J Am Soc Nephrol* 2026 3. Mancuso et al. *Pediatr Nephrol* 2025 4. Román Ortiz et al. *Pediatr Nephrol* 2025 5. Guzman et al. *Nephrology (Carlton)* 2025

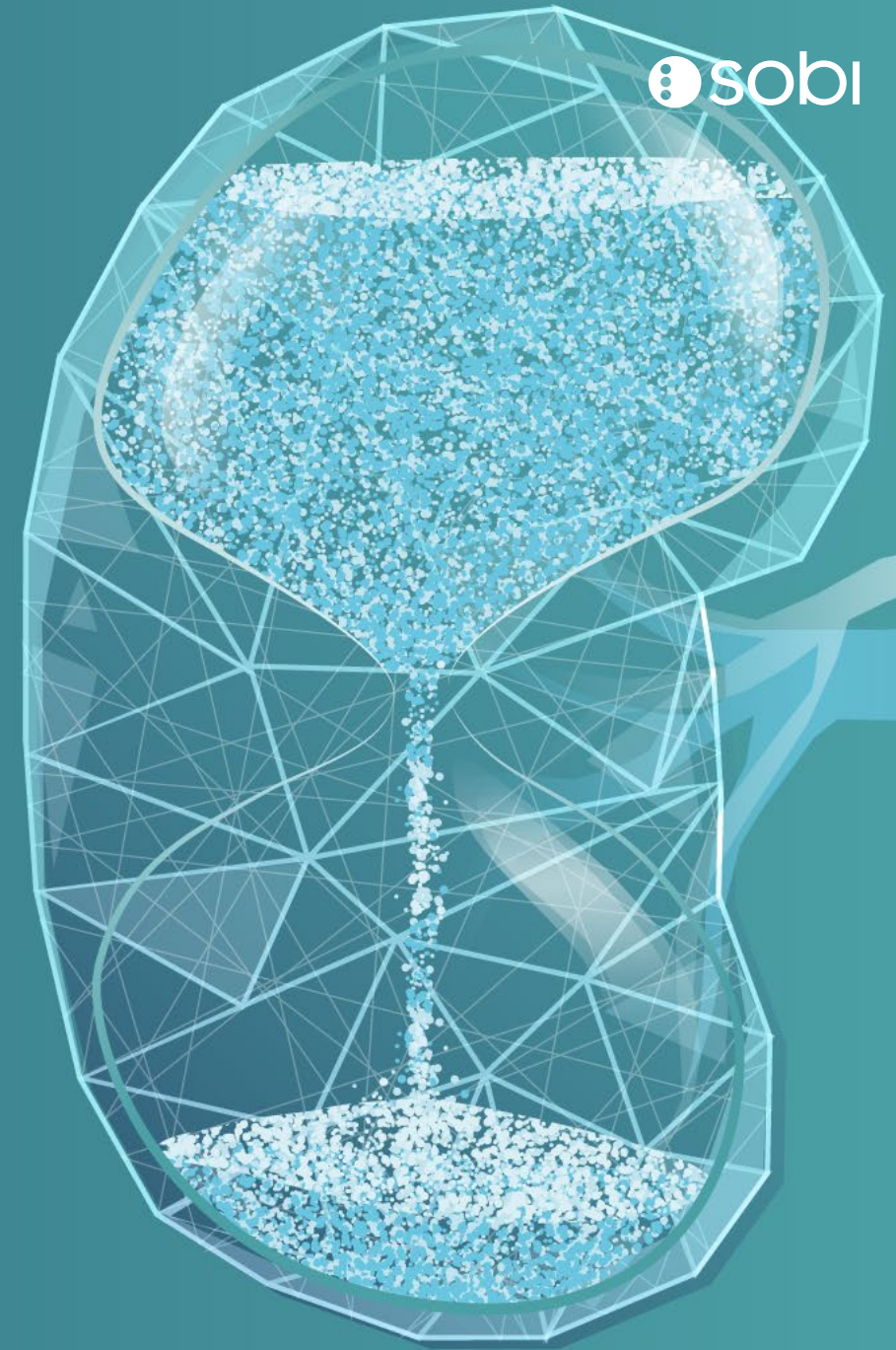
6. Alrasheed et al. *Front Med* 2025 7. Busutti et al. *Kidney Int* 2026 8. Levar et al. *Pediatr Nephrol* 2025 9. Bassanese et al. *Kidney Int* 2026.

Getting it right early: Treatment decisions for optimal outcomes

Nabil Melhem

Evelina London Children's Hospital Guy's and
St. Thomas' NHS Trust

London, UK



Disclosures



Consultancy	Sobi, SERB Pharmaceuticals
Speaker’s fees	Sobi



Patient case: 6-year-old female



Initial presentation

2014

6-year-old female

Presented with microscopic haematuria

- Low C3
- Elevated antistreptolysin O titre (800 IU/mL)
- Thought to be post-infectious glomerulonephritis but proteinuria worsening

Complex comorbidity spectrum including mental health issues

- Mild pulmonary valve stenosis
- Neuromuscular scoliosis
- Autism spectrum disorder
- Attention deficit hyperactivity disorder



Patient case: Diagnosis of C3 glomerulopathy and initial treatment



First kidney biopsy

February 2016

Diagnosis

Findings consistent with C3 glomerulopathy

Ultrastructural examination:
Dense deposit disease (DDD)

Initial treatment

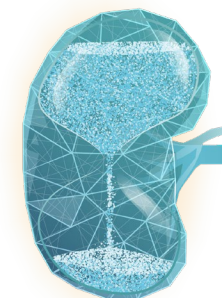
Lisinopril

Lisinopril is not approved by the EMA specifically for the treatment of C3G/DDD and is used as supportive therapy to manage hypertension and proteinuria.¹

C3G, C3 glomerulopathy; EMA, European Medicines Agency.

1. Zestril SmPC 2004.

Patient case courtesy of Nabil Melhem.



Patient case: Clinical deterioration and repeated kidney biopsy



February 2016

2016 to 2021
Progressive/worsening proteinuria
despite treatment with lisinopril

Repeat kidney biopsy

February 2021

- C3 glomerulopathy (DDD)
- Secondary focal segmental glomerulosclerosis
- No evidence of active tubulointerstitial nephritis
- **Minimal chronic damage**

Lisinopril is not approved by the EMA specifically for the treatment of C3G/DDD and is used as supportive therapy to manage hypertension and proteinuria.¹

C3G, C3 glomerulopathy; EMA, European Medicines Agency.

1. Zestril SmPC 2004.

Patient case courtesy of Nabil Melhem.



Patient case: Mycophenolate mofetil treatment commenced

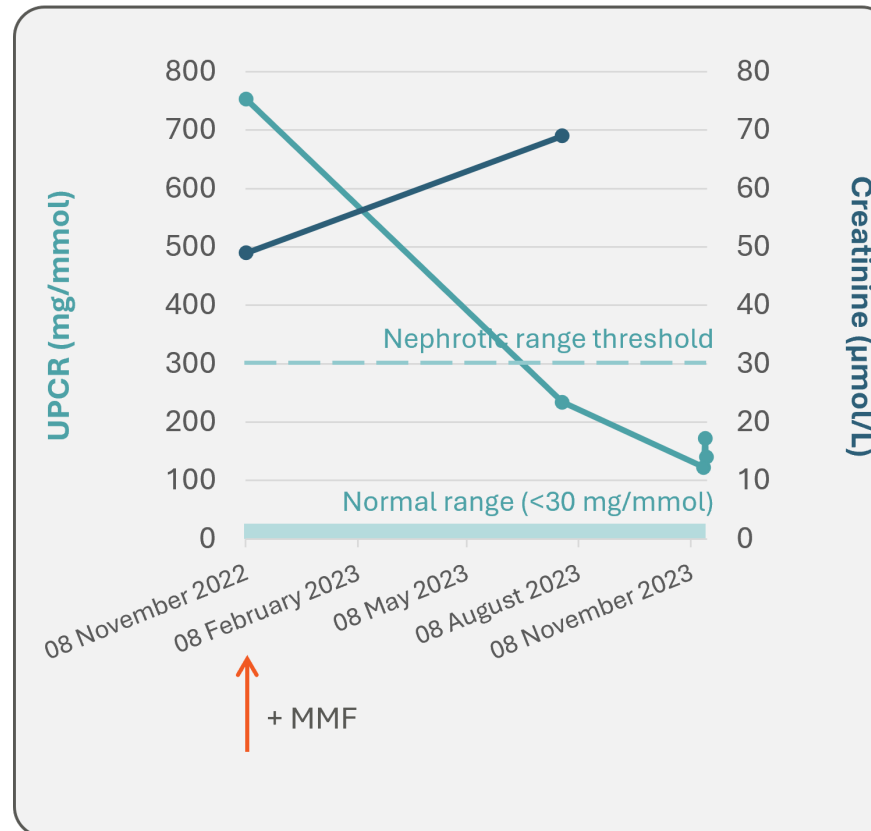
Treatment update

November 2022 – November 2023

Additional treatment

- **MMF**
- Continued **lisinopril**

- Proteinuria reduction with adequate MMF and lisinopril dosing
- **However:**
 - Ongoing proteinuria remains significant
 - Low serum C3 levels
 - Seeking alternative to oral medications



Immunosuppressive therapies have a significant treatment burden¹

Common AEs include disorders of the brain, CV system, metabolism, and bone, nephrotoxicity, GI bleeding, infection, and cataracts¹

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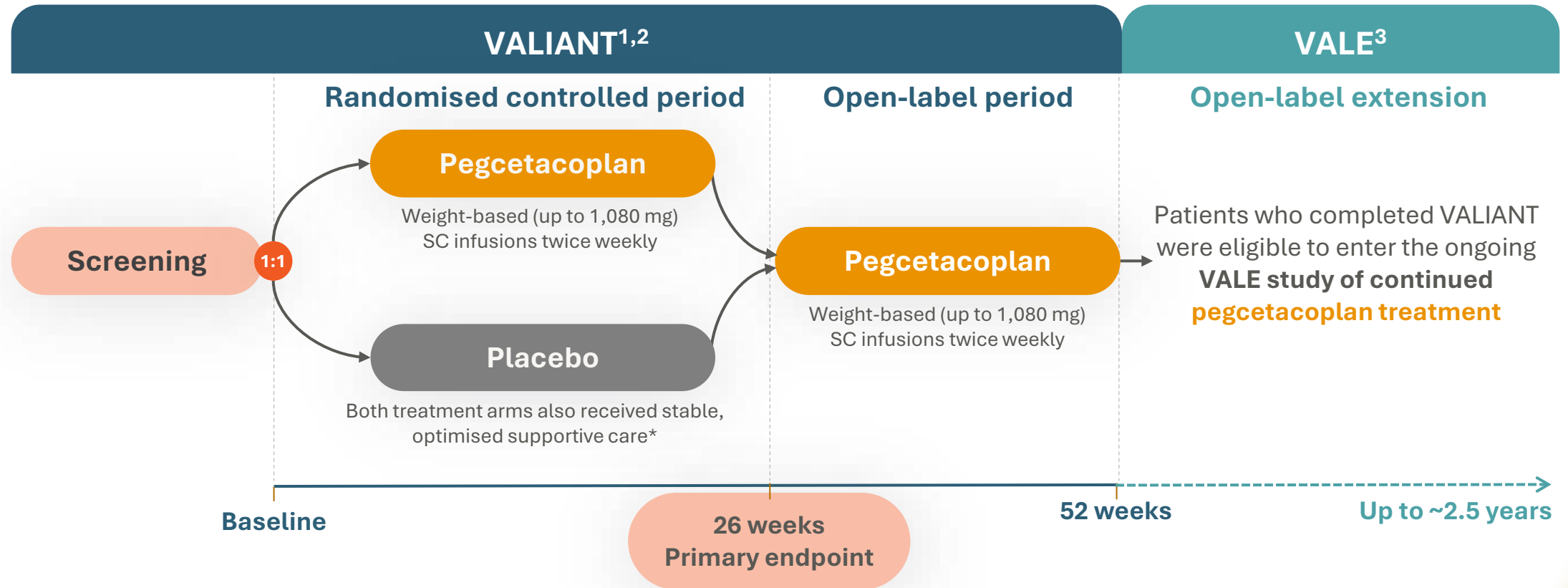
Lisinopril and MMF are not approved by the EMA specifically for the treatment of C3G/DDD.^{2,3}

AE, adverse event; C3G, C3 glomerulopathy; CV, cardiovascular; DDD, dense deposit disease; EMA, European Medicines Agency; GI, gastrointestinal; MMF, mycophenolate mofetil.

1. Jefferson et al. *Clin J Am Soc Nephrol* 2018 2. Zestril SmPC 2004 3. CellCept SmPC 2026. Patient case courtesy of Nabil Melhem.



VALIANT/VALE: Phase 3 study and open-label extension of pegcetacoplan for patients ≥ 12 years old with C3G and primary IC-MPGN¹



* 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 NCT05067127 3. ClinicalTrials.gov NCT05809531.



VALIANT included a **broad patient population**

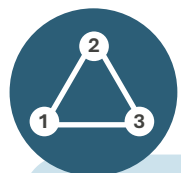
Baseline characteristic	Adolescents ¹ n=55		Overall population ¹ N=124	
	Pegcetacoplan (n=28)	Placebo (n=27)	Pegcetacoplan (n=63)	Placebo (n=61)
Age, mean (SD), years	14.6 (1.7)	14.8 (1.8)	28.2 (17.1)	23.6 (14.3)
Sex, female, n (%)	18 (64)	14 (52)	37 (59)	33 (54)
Underlying disease based on screening biopsy, n (%)				
C3G	21 (75)	17 (63)	51 (81)	45 (74)
Primary IC-MPGN	7 (25)	10 (37)	12 (19)	16 (26)
Baseline triplicate first-morning spot UPCR, mean (SD), g/g	3.5 (3.1)	2.6 (2.3)	3.1 (2.4)	2.5 (2.0)
Baseline eGFR, mean (SD), mL/min/1.73 m ²	92.8 (32.4)	94.0 (34.3)	78.5 (34.1)	87.2 (37.2)
Time since diagnosis, mean (SD), years	3.3 (2.5)	3.4 (3.5)	3.6 (3.5)	3.8 (3.6)
Post-transplant disease recurrence, n (%)	1 (4)	0	5 (8)	4 (7)
Immunosuppressant use at baseline, n (%)	22 (79)	21 (78)	47 (75)	42 (69)

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

1. Vivarelli et al. *Clin J Am Soc Nephrol* 2026.



VALIANT: Pegcetacoplan’s efficacy in adolescents with C3G and primary IC-MPGN was comparable to the overall population at 26 weeks



Kidney Health Initiative (KHI) consensus¹:

Favourable treatment effect on **histopathology, proteinuria and eGFR**

Glomerular C3 clearance

74%
achieved C3 staining reduction ≥ 2 OOM^{**}
vs placebo: 12%

Adults^{2||}

71%
showed no detectable deposits[†]

**Histopathology improvement:
C3 staining**

Proteinuria reduction

Primary endpoint
Relative reduction in UPCR vs placebo

Overall ²	68%	p<0.001
Adolescents ^{3§}	75%	p<0.001 nominal

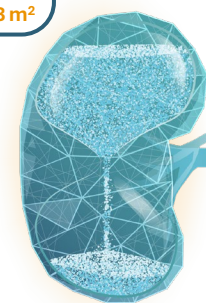
**eGFR stabilisation/
improvement**

Stabilisation of eGFR vs placebo^{**†}

Overall ²	+6.3 mL/min/1.73 m ²
Adolescents ^{3§}	+9.7 mL/min/1.73 m ²

* Key secondary endpoint.
† Post-hoc analysis, thus not powered to detect statistical significance.
‡ A fixed sequence testing strategy was used for key secondary endpoints. Key secondary histologic activity score endpoint was not met at week 26; therefore subsequent endpoints including C3 staining reduction and eGFR change were not formally tested and should be interpreted descriptively.
§ Pre-specified adolescent subgroup analysis; comparisons for all endpoints described were not corrected for multiplicity, therefore p values are nominal.
|| Biopsy was not mandated in adolescents (aged 12-17 years).
C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex membranoproliferative glomerulonephritis;
OOM, orders of magnitude, UPCR, urine protein-to-creatinine ratio.
1. Nester et al. *Clin J Am Soc Nephrol* 2024 2. Fakhouri et al. *N Engl J Med* 2025 3. Vivarelli et al. *Clin J Am Soc Nephrol* 2026.

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VALIANT: Pegcetacoplan was **well tolerated** by **adolescent patients** up to 26 weeks¹

n (%)	Adolescents n=55	
	Pegcetacoplan (n=28)	Placebo (n=27)
TEAEs	23 (82)	26 (96)
Mild	12 (43)	11 (41)
Moderate	9 (32)	14 (52)
Severe	2 (7)	1 (4)
Treatment-related TEAEs	13 (46)	11 (41)
Serious TEAEs	3 (11)	3 (11)
TEAEs leading to study discontinuation	0	1 (4)
Deaths	0	0

Frequency and severity of TEAEs was similar between arms and there were no cases of encapsulated meningococcal infection



Pegcetacoplan's efficacy in patients with C3G or primary IC-MPGN and **mild proteinuria at baseline**¹

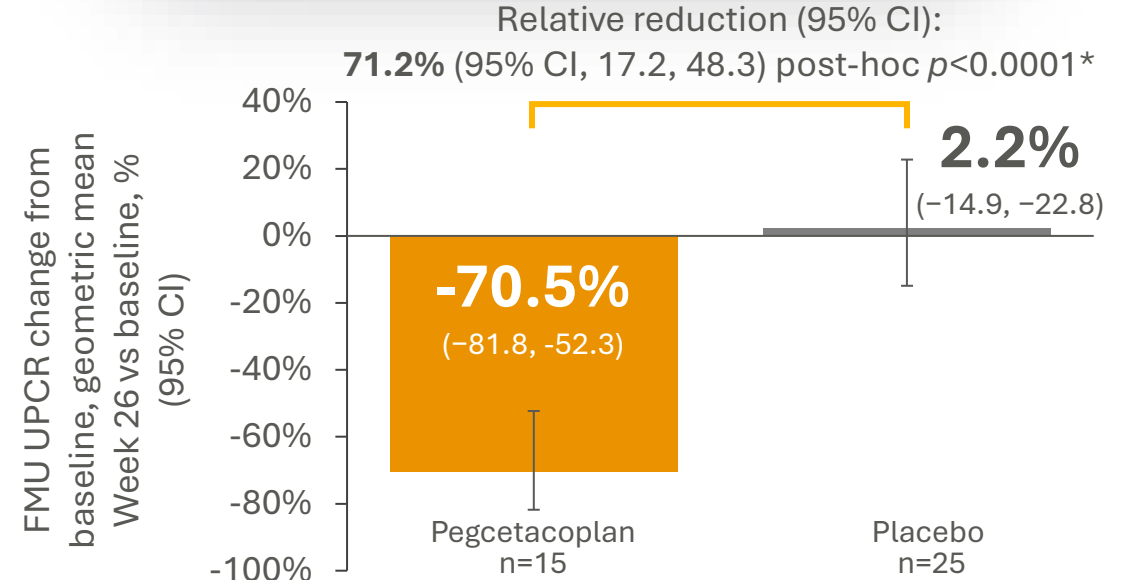


Post-hoc analysis of 40 patients with FMU UPCR of 1–1.5 g/g (median 1.1)

Although patients with lower levels of proteinuria are generally considered lower risk, **even modest proteinuria may confer substantial risk of kidney function decline** in C3G and primary IC-MPGN^{2,3}

In patients with mild proteinuria, pegcetacoplan was associated with **significant reduction in proteinuria, stabilisation of eGFR, and decrease in C3 staining**¹

Change from baseline in proteinuria at Week 26 (N=40, 18 adolescents)¹



* Post-hoc analysis, thus not powered to detect statistical significance.

C3G, C3 glomerulopathy; CI, confidence interval; eGFR, estimated glomerular filtration rate; FMU, first-morning urine; IC-MPGN, immune complex membranoproliferative glomerulonephritis; UPCR, urine protein-to-creatinine ratio.

1. Han et al. Poster 184 presented at WCN 2026 2. Caravaca-Fontán et al. *Kidney Int Rep* 2025 3. Caravaca-Fontán et al. *Nephrol Dial Transplant* 2022.



Patient case: Treatment with pegcetacoplan



Treatment update

Enrolled in VALIANT trial

- **Pegcetacoplan** twice weekly
- Continued lisinopril and MMF: Adherence to oral medication questionable throughout the trial

December 2023

June – July 2024

Continued pegcetacoplan treatment

- Transition to open-label pegcetacoplan
- Subsequent enrolment in VALE study

Surgery around time of transition to open-label pegcetacoplan:
T4-L3 posterior instrumented correction and fusion for adolescent idiopathic scoliosis

- **Pegcetacoplan** continued throughout
- **Stopped lisinopril and MMF:** Mental health difficulties worsened and adherence more apparently faltering
- *C. difficile* infection: Managed with oral vancomycin (14 days)

Lisinopril eventually restarted at a lower dose, but not MMF

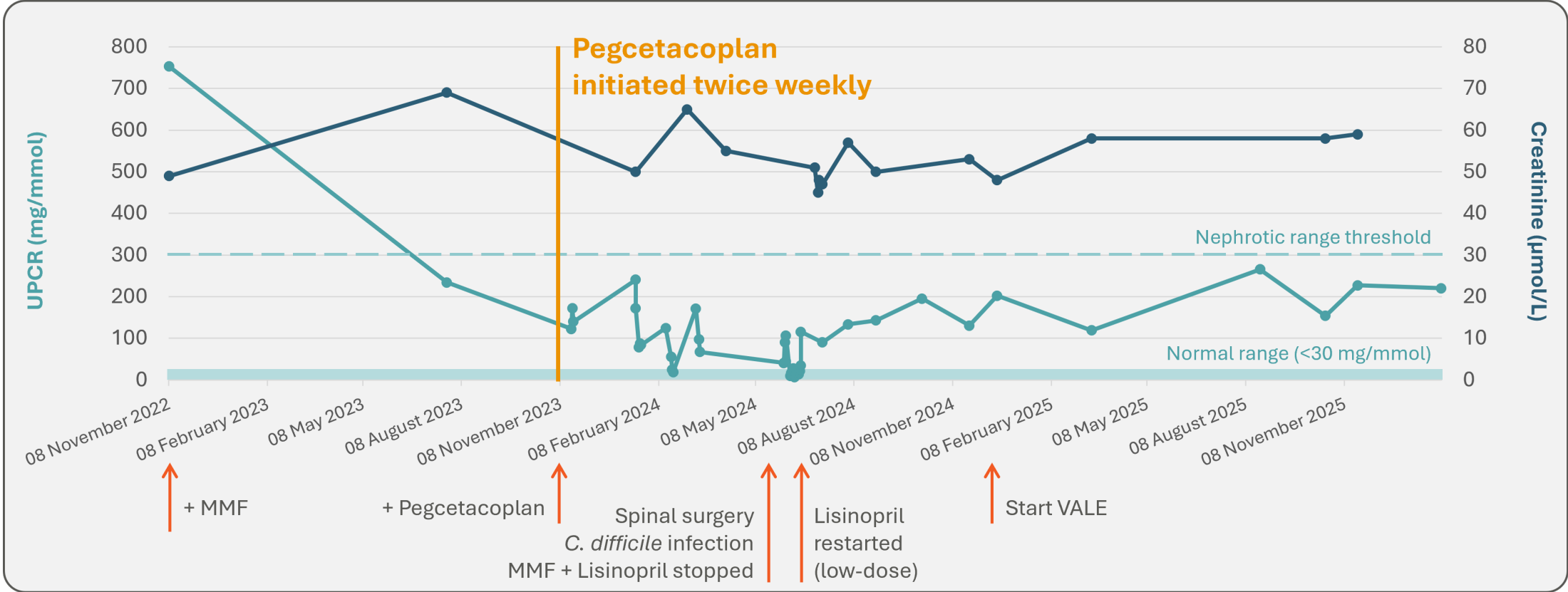


Patient case: Patient journey over treatment

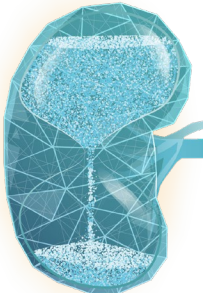


Clinical course

November 2022 – February 2026



Lisinopril and MMF are not approved by the EMA specifically for the treatment of C3G/DDD.^{1,2}
C3G, C3 glomerulopathy; DDD, dense deposit disease; MMF, mycophenolate mofetil; UPCR, urine protein-to-creatinine ratio. 1. Zestril SmPC 2004 2. CellCept SmPC 2026.
Patient case courtesy of Nabil Melhem.



Patient case: Learnings



Considerations for ongoing management

Patient continues pegcetacoplan treatment

Adherence with pegcetacoplan has not faltered and UPCR remains stable

Significant adherence issues with oral medications

- Irregular use of MMF and lisinopril
- Stopped lisinopril following spinal surgery and very reluctant to restart

Complex comorbidity spectrum including mental health difficulties alongside ADHD and ASD

General medication nonadherence in adolescents may be as high as 80%, which may be exacerbated by mental health comorbidities¹

Nonadherence may increase morbidity, complications, and contribute to poorer QoL^{1,2}

Psychiatric AEs may occur during immunosuppressive therapy,³⁻⁸ impacting patient QoL

MMF and corticosteroids are commonly associated with confusion, depression, insomnia, and anxiety,³⁻⁵ while corticosteroids are additionally associated with adverse behavioural effects⁶⁻⁸

Lisinopril and MMF are not approved by the EMA specifically for the treatment of C3G/DDD.^{9,10}

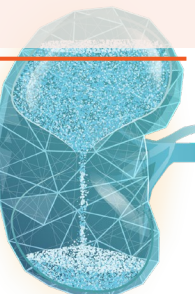
AE, adverse event; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; C3G, C3 glomerulopathy; DDD, dense deposit disease;

MMF, mycophenolate mofetil; UPCR, urine protein-to-creatinine ratio; QoL, quality of life.

1. Werner et al. *J Pediatr Psychol* 2026 2. Taddeo et al. *Paediatr Child Health* 2008 3. Mycophenolate mofetil (CellCept) SmPC 2026 4. Arkin et al. *Pediatr Dermatol* 2016

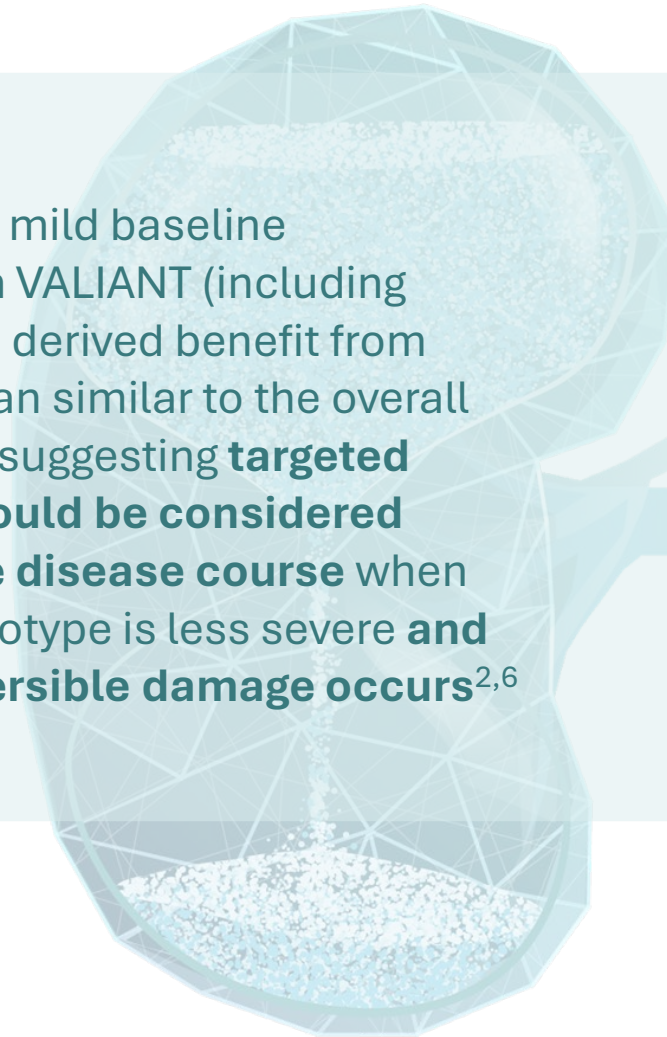
5. Draper. *Pharmacotherapy* 2008 6. Warrington & Bostwick *Mayo Clin Proc* 2006 7. Soliday et al. *Pediatrics* 1999 8. Hall et al. *Pediatr Nephrol* 2003 9. Zestril SmPC 2004 10. CellCept SmPC 2026.

Patient case courtesy of Nabil Melhem.



Key takeaways

- Conventional **immunosuppressive treatments** used for C3G and primary IC-MPGN are **non-specific**, with **variable efficacy** and **potentially significant treatment burden**^{1,2}
- **Adherence to oral medications can be challenging** for adolescent patients, particularly in the setting of mental health difficulties³
- Targeted C3/C3b inhibition with **pegcetacoplan** was associated with **significant proteinuria reduction**, as well as **eGFR stabilisation** in **adolescents** in VALIANT⁴ – effective targeted therapy may reduce reliance on non-targeted treatments such as immunosuppression²



Patients with mild baseline proteinuria in VALIANT (including adolescents) derived benefit from pegcetacoplan similar to the overall population⁵, suggesting **targeted treatment could be considered earlier in the disease course** when clinical phenotype is less severe **and before irreversible damage occurs**^{2,6}

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

1. Jefferson et al. *Clin J Am Soc Nephrol* 2018 **2**. Kavanagh et al. *Kidney Int Rep* 2025 **3**. Werner et al. *J Pediatr Psychol* 2026

4. Vivarelli et al. *Clin J Am Soc Nephrol* 2026 **5**. Han et al. Poster 184 presented at WCN 2026 **6**. Wallace et al. Poster 3319 presented at ERA 2026.

What can and cannot be recovered after chronic kidney damage

Olivia Boyer

Necker Children's Hospital

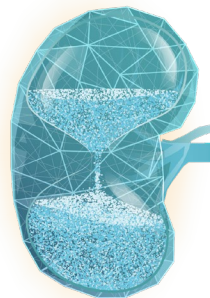
Paris, France



Disclosures



Speaker’s fees	Alexion, Alnylam, Biocodex, Chiesi, Novartis, Samsung, Sobi, Takeda
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Pegcetacoplan efficacy through 52 weeks in adolescent patients in VALIANT¹

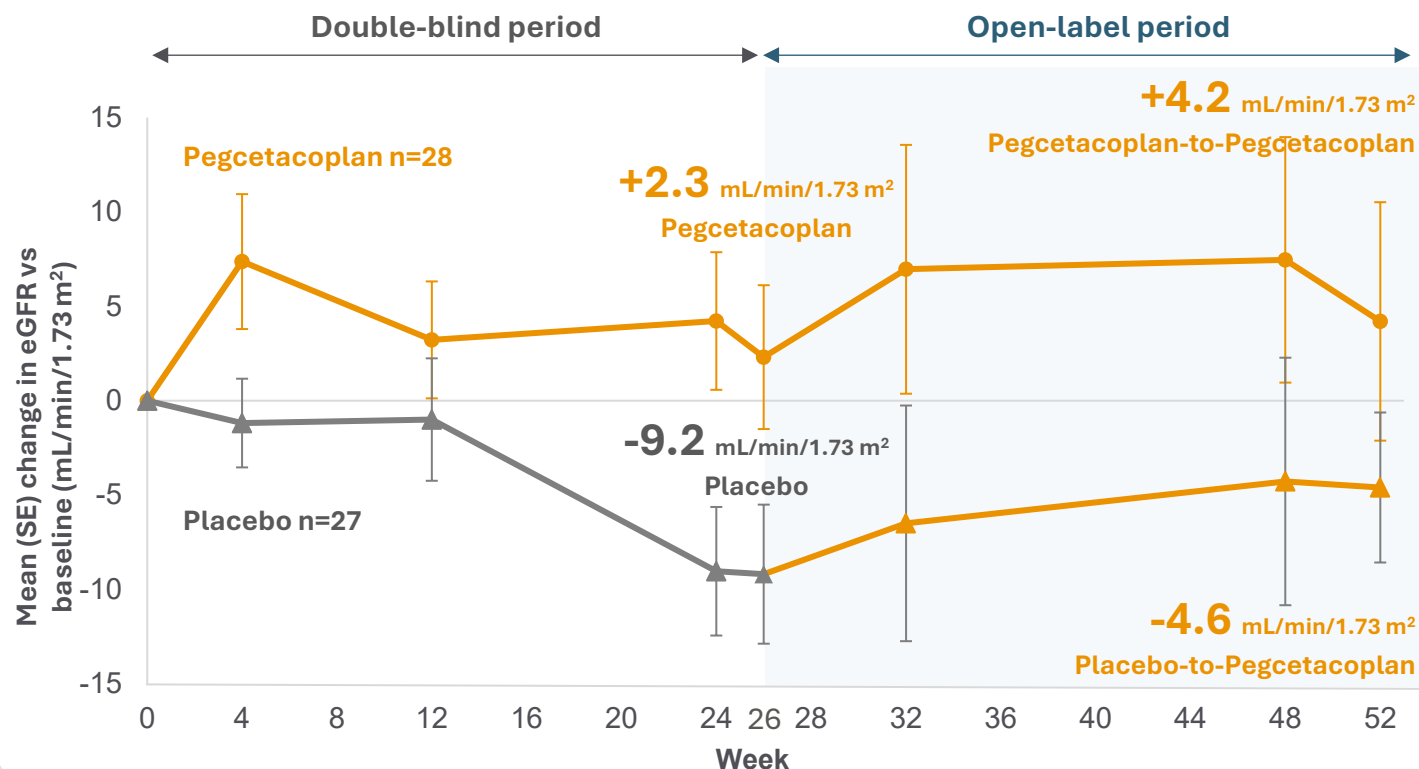
After 1 year of follow-up in VALIANT, pegcetacoplan was associated with sustained efficacy in adolescent patients:¹

Rapid and sustained improvement of serum complement biomarkers

71.6% reduction in proteinuria, with similar improvement after crossover from placebo to pegcetacoplan

Stabilisation of eGFR

Change in eGFR over 52 weeks in adolescent patients¹



Updated 1-year data from VALIANT and the VALE extension study will be presented in Hall A tomorrow

Licht C, et al. Friday 2 October, 12:00–13:25 CET

Subgroup analyses were exploratory and not powered to detect statistically significant differences. 52-week efficacy analyses were exploratory.

eGFR, estimated glomerular filtration rate; SE, standard error.

1. van de Kar et al. Oral presented at ESPN 2025.



Patient case: 14-year-old male



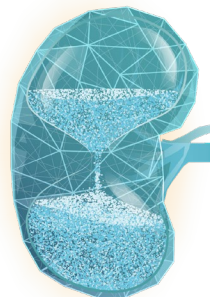
Initial presentation



October 2025

14-year-old male	Biology / Complement	
- Viral-induced asthma exacerbation - Blood tests performed because of generalised oedema Microhaematuria, severe nephrotic syndrome, acute kidney injury C3NeF+	Proteinuria	23 g/L (1600 mg/mmol)
	Serum creatinine	124 µmol/L
	eGFR	51 mL/min/1.73 m²
	Serum albumin	11 g/L
	C3	0.849 g/L (N)
	C3NeF	positive
	sC5b-9	230 ng/mL (N)
	Auto-Abs Factor B	Neg (ANCA, anti-PLA2R) 0.132 g/L (0.190–0.455)

ANCA, anti-neutrophil cytoplasmic antibodies; anti-PLA2R, anti-phospholipase A2 receptor antibodies; Auto-Abs, autoantibodies; C3NeF, C3 nephritic factor; eGFR, estimated glomerular filtration rate; N, normal; Neg, negative, sC5b9, soluble C5b-9.
Patient case courtesy of Dr Mathilde Mauras.



Patient case: Diagnosis of C3G



Initial presentation

October 2025

14-year-old male	Biology / Complement		Kidney biopsy
- Viral-induced asthma exacerbation - Blood tests performed because of generalised oedema - Microhaematuria, severe nephrotic syndrome, acute kidney injury - C3NeF+	Proteinuria	23 g/L (1600 mg/mmol)	C3 glomerulopathy with an MPGN pattern of injury GBM double contours Moderate endocapillary proliferation 20% global glomerulosclerosis, 20% fibrocellular crescents, 30% interstitial fibrosis C4d+, C3+++ . No humps
	Serum creatinine	124 µmol/L	
	eGFR	51 mL/min/1.73 m²	
	Serum albumin	11 g/L	
	C3 C3NeF	0.849 g/L (N) positive	
	sC5b-9	230 ng/mL (N)	
	Auto-Abs Factor B	Neg (ANCA, anti-PLA2R) 0.132 g/L (0.190–0.455)	

ANCA, anti-neutrophil cytoplasmic antibodies; anti-PLA2R, anti-phospholipase A2 receptor antibodies; Auto-Abs, autoantibodies; C3G, C3 glomerulopathy; C3NeF, C3 nephritic factor; eGFR, estimated glomerular filtration rate; GBM, glomerular basement membrane; MPGN, membranoproliferative glomerulonephritis; N, normal; Neg, negative; sC5b-9, soluble C5b-9. Patient case courtesy of Dr Mathilde Mauras.



Patient case: Initial management



Initial management

October 2025

- **IV methylprednisolone pulses** 1 g/1.73 m², 3 doses, then oral prednisone
- **MMF** 600 mg/m²/12 h (target AUC 35)
- **Albumin infusion** 1 g/kg/48 h

MMF is not approved by the EMA specifically for the treatment of C3G.¹

Methylprednisolone is not approved by the EMA specifically for the treatment of C3G and is used to manage inflammation.²

Albumin infusion is not approved specifically for the treatment of C3G and is used as supportive therapy to manage fluid retention.³

AUC, area under the curve; C3G, C3 glomerulopathy; EMA, European Medicines Agency; IV, intravenous; MMF, mycophenolate mofetil.

1. CellCept SmPC 2026 2. Solu-Medrone SmPC 2026 3. Human albumin solution SmPC 2018.

Patient case courtesy of Dr Mathilde Mauras.



Patient case: Treatment with pegcetacoplan



Treatment update

November 2025

- **Pegcetacoplan** twice weekly
- Expert Committee approval
- Continued corticosteroids and MMF
- Albumin infusion 1 g/kg three times weekly

MMF is not approved by the EMA specifically for the treatment of C3G.¹

Albumin infusion is not approved specifically for the treatment of C3G and is used as supportive therapy to manage fluid retention.²

C3G, C3 glomerulopathy; EMA, European Medicines Agency; MMF, mycophenolate mofetil.

1. CellCept SmPC 2026 2. Human albumin solution SmPC 2018.

Patient case courtesy of Dr Mathilde Mauras.

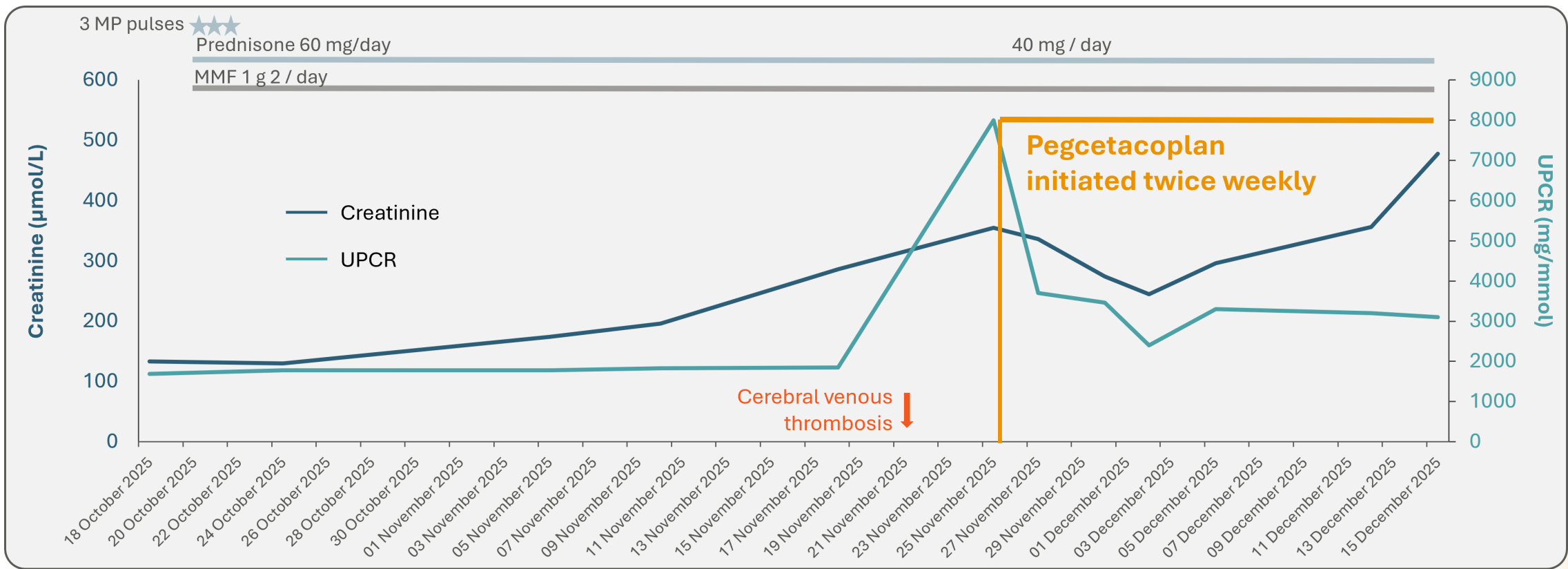


Patient case: Treatment with pegcetacoplan



Clinical course

October – December 2025



MMF is not approved by the EMA specifically for the treatment of C3G.¹
C3G, C3 glomerulopathy; EMA, European Medicines Agency; MMF, mycophenolate mofetil; MP, methylprednisolone; UPCR, urine protein-to-creatinine ratio.
1. CellCept SmPC 2026. Patient case courtesy of Dr Mathilde Mauras.



Patient case: Initial improvement, followed by clinical deterioration and pegcetacoplan withdrawal



1 month post-pegcetacoplan

December 2025

Initial improvement of eGFR and negative C3NeF, then clinical deterioration

Peritoneal dialysis initiated December 2025 →
No renal recovery

Treatment:

- MMF, prednisone, amlodipine, acebutolol, ACEi, albumin infusions twice weekly
- **Pegcetacoplan temporarily discontinued** because of dialysis and no immediate transplantation plan

Within 15 days of pegcetacoplan withdrawal →
Recurrent generalised oedema with worsening of serum albumin <20 g/L

Restarting pegcetacoplan → Rapid improvement, serum albumin increasing to 30 g/L within 10 days

MMF is not approved by the EMA specifically for the treatment of C3G.¹

Amlodipine and acebutolol are not approved by the EMA specifically for the treatment of C3G and is used as supportive therapy to manage hypertension.^{2,3}

Albumin infusion is not approved specifically for the treatment of C3G and is used as supportive therapy to manage fluid retention.⁴

ACEi, angiotensin-converting enzyme inhibitor; C3G, C3 glomerulopathy; EMA, European Medicines Agency; C3NeF, C3 nephritic factor; eGFR, estimated glomerular filtration rate; MMF, mycophenolate mofetil.

1. CellCept SmPC 2026 2. Norvasc SmPC 2012 3. Acebutolol SmPC 2024 4. Human albumin solution SmPC 2018. Patient case courtesy of Dr Mathilde Mauras.



Patient case: Rapid improvement after restarting pegcetacoplan



6 months post-pegcetacoplan

May 2026

Current treatment:

- MMF 1 g twice daily
- Prednisone, slowly tapered
- **Pegcetacoplan 1080 mg twice weekly SC**

- Persistent nephrotic-range proteinuria but **no further requirement for albumin infusions**
- **C3NeF remained negative**
- Treatment extension approved by the French National Health Insurance
- **Kidney transplantation planned**

Despite progression to kidney failure, **pegcetacoplan** appeared to provide **meaningful clinical benefit** by **improving serum albumin, controlling oedema**, and ultimately **eliminating the need for albumin infusions**, thereby helping maintain clinical stability while awaiting transplantation

It cannot be excluded that reduction in eGFR and subsequent dialysis contributed to improvement in proteinuria and oedema

MMF is not approved by the EMA specifically for the treatment of C3G.¹

C3G, C3 glomerulopathy; C3NeF, C3 nephritic factor; eGFR, estimated glomerular filtration rate; EMA, European Medicines Agency; MMF, mycophenolate mofetil; SC, subcutaneous.

1. CellCept SmPC 2026.

Patient case courtesy of Dr Mathilde Mauras.



Patient case: Open questions



Considerations for ongoing management

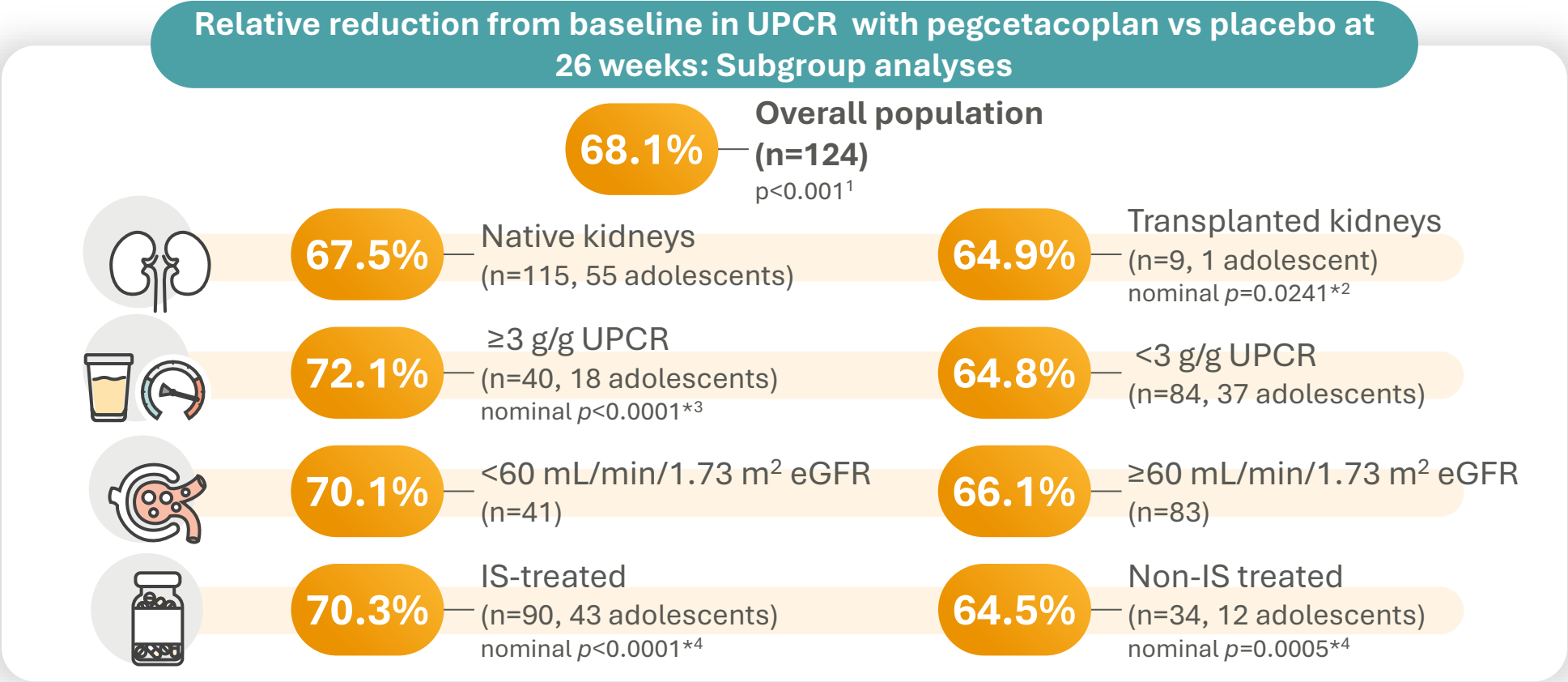
Results of **genetic testing** are pending

- Should **pegcetacoplan** be continued **long term**?
- What can be expected **beyond 6 months of treatment**?
- What is the **optimal strategy for pegcetacoplan around kidney transplantation**?

C3G is a disease with a **high risk of recurrence after transplantation, ranging from 30–89% and usually occurring early^{1–3}**



Pegcetacoplan efficacy was maintained in prespecified subgroup analyses at 26 weeks in VALIANT¹



VALIANT included a broad patient population, with consistent proteinuria reduction demonstrated between subgroups¹

* Prespecified subgroup analysis; Comparisons for all subgroups described were not corrected for multiplicity, therefore p values are nominal.
eGFR, estimated glomerular filtration rate; IS, immunosuppressant; UPCR, urine protein-to-creatinine ratio.
1. Fakhouri et al. *N Engl J Med* 2025 2. Oosterveld et al. Poster 3482 presented at ERA 2025 3. Vivarelli et al. Oral 3265 presented at ERA 2025 4. Kavanagh et al. Oral 288 presented at ERA 2025.

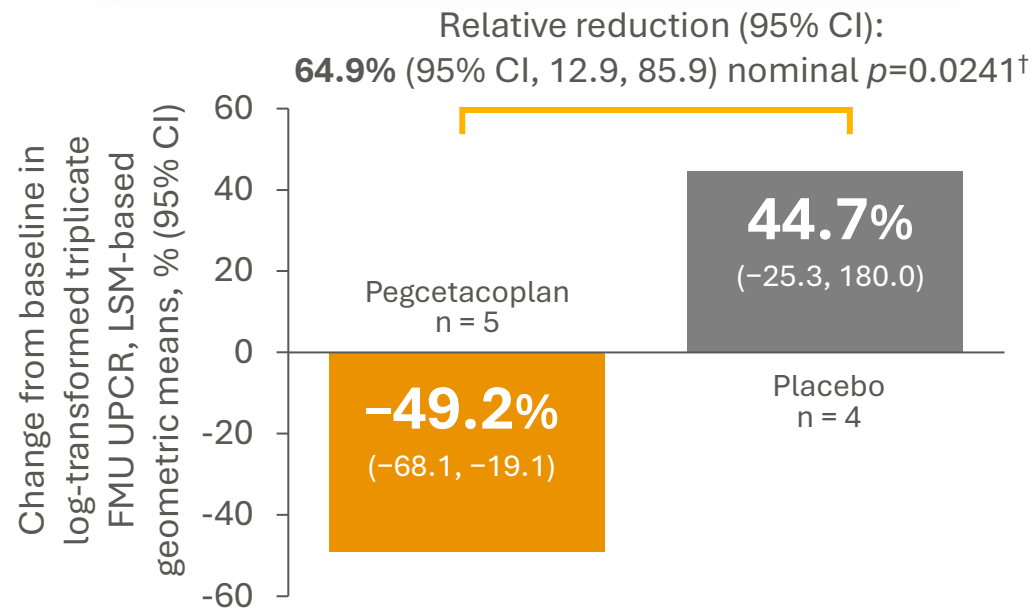


Pegcetacoplan was effective post-transplant^{1,*}

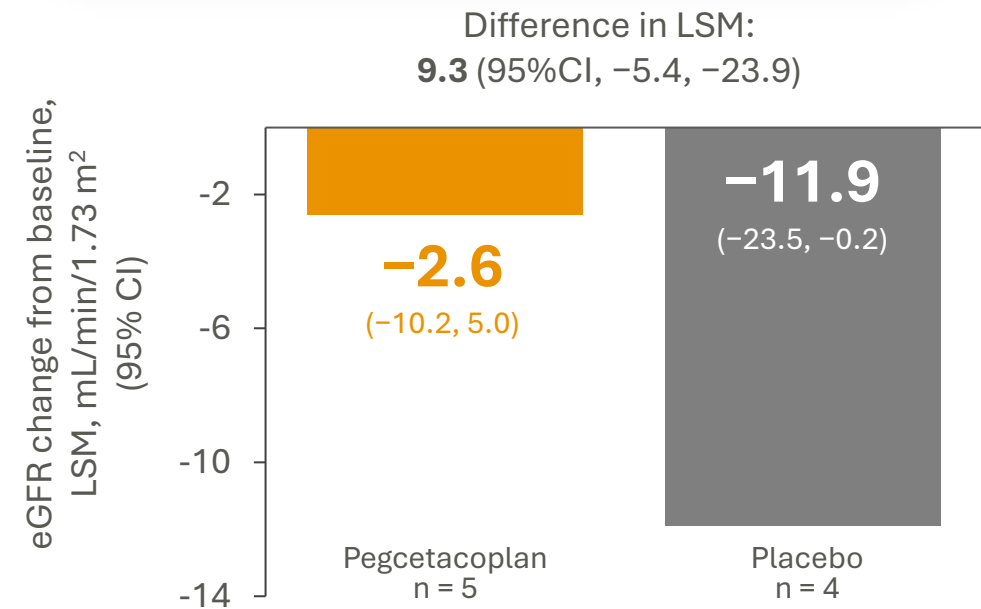


Subgroup analysis of patients with post-transplant recurrence (n=9/124)

Change from baseline in UPCR at Week 26 in post-transplant patients¹



Change from baseline in eGFR at Week 26 in post-transplant patients¹



Pegcetacoplan efficacy and safety in patients with post-transplant recurrence was consistent with the overall population^{1,2}

Subgroup analyses were exploratory and not powered to detect statistically significant differences between subgroups.

* Data cut-off date: June 20, 2024. [†] Prespecified subgroup analysis; Comparison was not corrected for multiplicity, therefore p value is nominal.

CI, confidence interval; eGFR, estimated glomerular filtration rate; FMU, first morning urine; LSM, least-squares mean; UPCR, urine protein-to-creatinine ratio.

1. Oosterveld et al. Poster 3482 presented at ERA 2025 2. Fakhouri et al. *N Engl J Med* 2025.

NP-54110

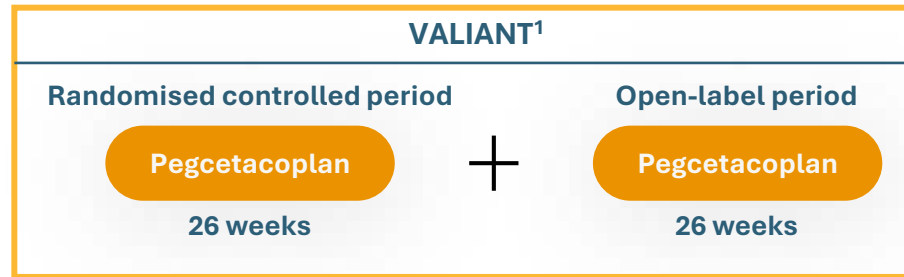


The **VALE extension study** has enabled exploratory analysis of **pegcetacoplan's 1-year efficacy in larger subgroups**

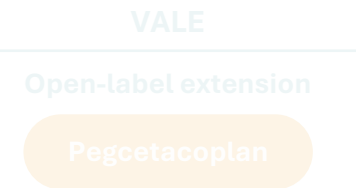
Patients in VALIANT with <52 weeks of pegcetacoplan treatment were **supplemented with up to 6 months of treatment data from the VALE extension study**

Data were time-aligned such that **baseline represented pegcetacoplan initiation** for all patients

52 weeks of pegcetacoplan treatment in the **pegcetacoplan-to-pegcetacoplan arm**:



52 weeks of pegcetacoplan treatment in the **placebo-to-pegcetacoplan arm**:



In VALIANT and VALE, patients with **less chronic kidney damage** showed **better preservation of kidney function** with pegcetacoplan¹

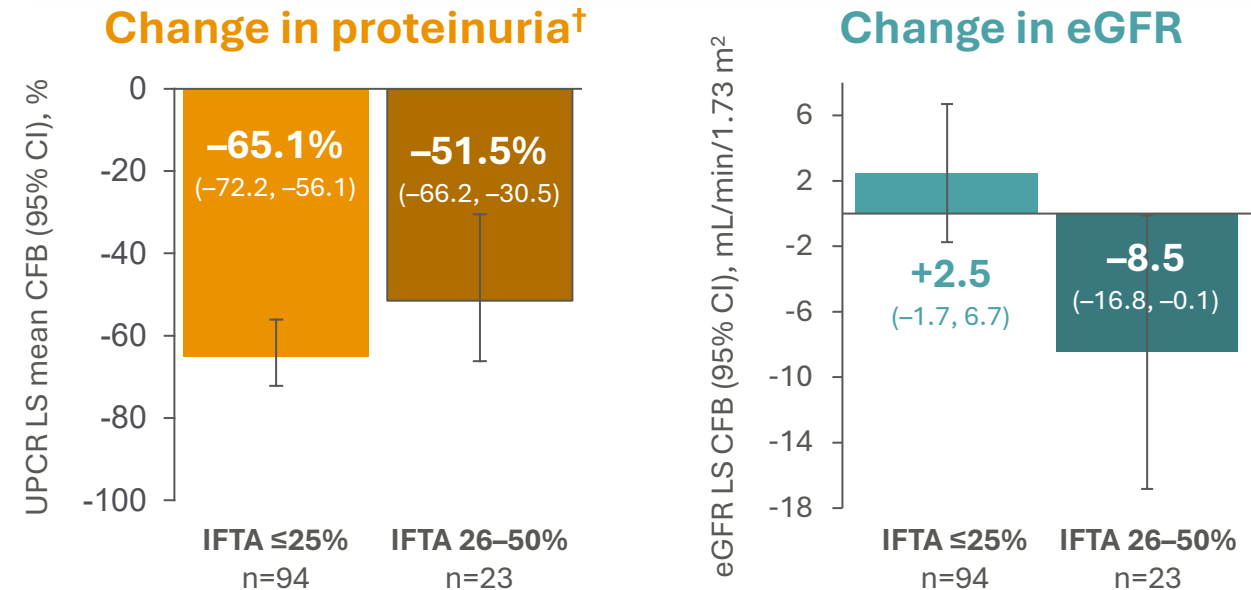
Post-hoc analysis stratified by IFTA at baseline ($\leq 25\%$ or $26-50\%$)*

Pegcetacoplan reduced proteinuria by **>50% regardless of baseline disease chronicity**

eGFR stabilisation at 52 weeks was **maximised** in patients with **baseline IFTA $\leq 25\%$**

Initiating targeted C3 inhibition before substantial fibrotic damage occurs can optimise durable preservation of kidney function in C3G and primary IC-MPGN

Change from baseline in UPCR and eGFR at Week 52 by IFTA at baseline



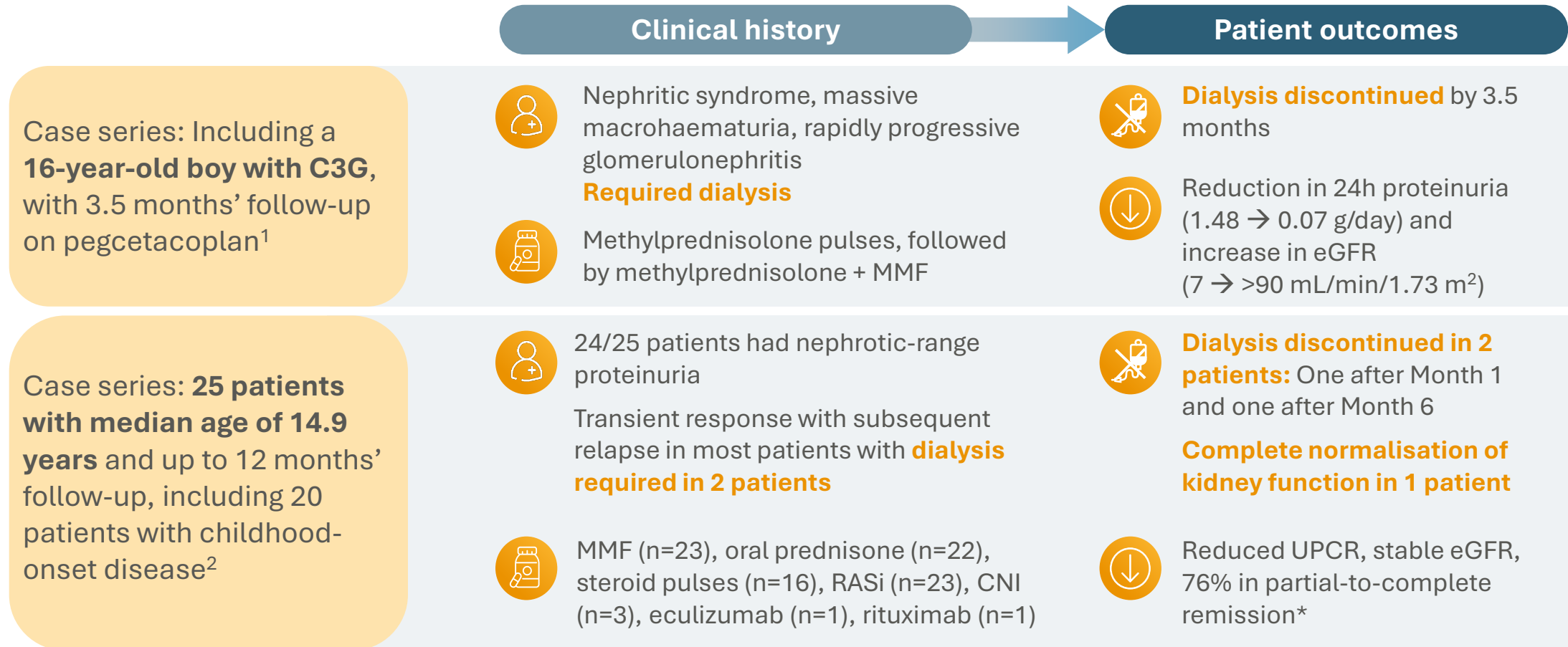
Post-hoc analysis, thus not powered to detect statistical significance.

* Patients with $>50\%$ IFTA were excluded from VALIANT. † Geometric means and % change estimated from exponentiated LS mean differences from a MMRM of log-transformed UPCR. C3G, C3 glomerulopathy; CFB, change from baseline; CI, confidence interval; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex membranoproliferative glomerulonephritis; IFTA, interstitial fibrosis/tubular atrophy; LS, least squares; MMRM, mixed model for repeated measures; UPCR, urine protein-to-creatinine ratio.

1. Wallace et al. Poster 3319 presented at ERA 2026.



Emerging evidence on dialysis discontinuation after pegcetacoplan treatment



MMF, eculizumab and rituximab are not approved by the EMA specifically for the treatment of C3G or primary IC-MPGN.³⁻⁵

Methylprednisolone is not approved by the EMA specifically for the treatment of C3G or primary IC-MPGN and is used to manage inflammation.⁶

* Complete proteinuria remission was defined as a UPCR ≤0.2 g/g in paediatric patients and ≤0.3 g/g in adults. Partial remission was defined as a reduction in UPCR of more than 50% from baseline with a final UPCR below the nephrotic range.

C3G, C3 glomerulopathy; CNI, calcineurin inhibitor; eGFR, estimated glomerular filtration rate; EMA, European Medicines Agency; IC-MPGN, immune complex membranoproliferative glomerulonephritis;

MMF, mycophenolate mofetil; RASi, renin-angiotensin system inhibitor; UPCR, urine protein-to-creatinine ratio.

1. Levart et al. *Pediatr Nephrol* 2025;suppl 2. Bassanese et al. *Kidney Int* 2026 3. CellCept SmPC 2026 4. Soliris SmPC 2025 5. MabThera SmPC 2026 6. Solu-Medrone SmPC 2026.



Key takeaways

- **Early diagnosis and treatment, before the development of irreversible chronic kidney lesions,** are likely critical to maximise the therapeutic benefit of C3 inhibition¹
- **Prophylactic C3 inhibition may reduce the risk of C3G recurrence** following kidney transplantation^{2,3}
- Evidence from clinical studies and real-world experience suggests that **clinical benefit may be achieved with pegcetacoplan across a broad range of disease severity, including advanced disease, dialysis-dependent patients and post-transplant recurrence**^{1,4-7}

What can be recovered?²

- ✓ Complement activation and deposition
- ✓ Proteinuria
- ✓ Serum albumin and oedema
- ✓ Disease activity

What cannot be recovered?²

- ✗ Established interstitial fibrosis
- ✗ Glomerulosclerosis
- ✗ Advanced CKD

What may still be prevented?²

- ✓ Post-transplant recurrence

C3G, C3 glomerulopathy; CKD, chronic kidney disease.

1. Wallace et al. Poster 3319 presented at ERA 2026. 2. Based on the expert opinion of Olivia Boyer 3. Busutti et al. *Kidney Int.* 2026

4. Alrasheed et al. *Front Med* 2026 5. Levart et al. *Pediatr Nephrol* 2025;suppl 6. Bassanese et al. *Kidney Int* 2026 7. Oosterveld et al. Poster 3482 presented at ERA 2025

Navigating treatment sequencing: Individualised decisions in practice

Marina Vivarelli

Bambino Gesù Children's Hospital
Rome, Italy



Patient case: 12-year-old female



Initial presentation

April 2020

12-year-old female

- Post-infectious macrohaematuria with persistent microhaematuria
- Massive proteinuria (UPCR 20 g/g)
- Hypoalbuminaemia (1.8 g/dL)
- Normal serum creatinine
- Low C3 with normal C4
- ANA, ENA and anti-dsDNA negative



Patient case: Diagnosis of C3G



C3G diagnosis and immunosuppressive treatment

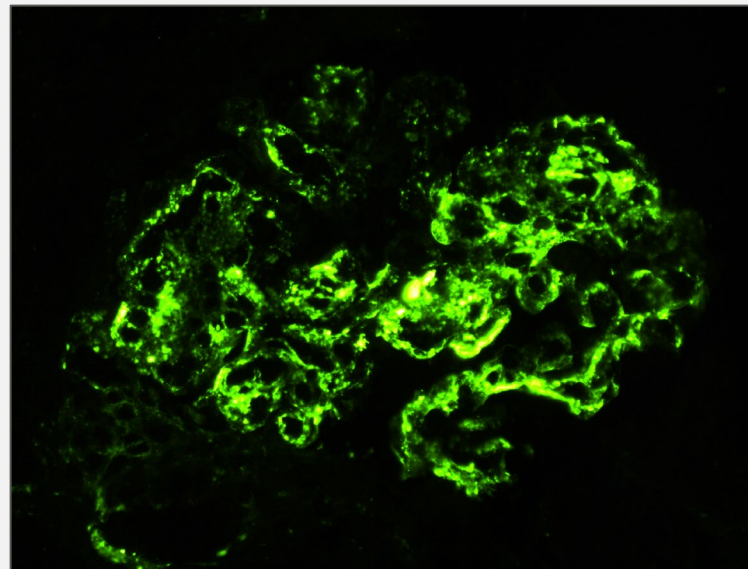
May 2020

Complement screening workup **negative**:

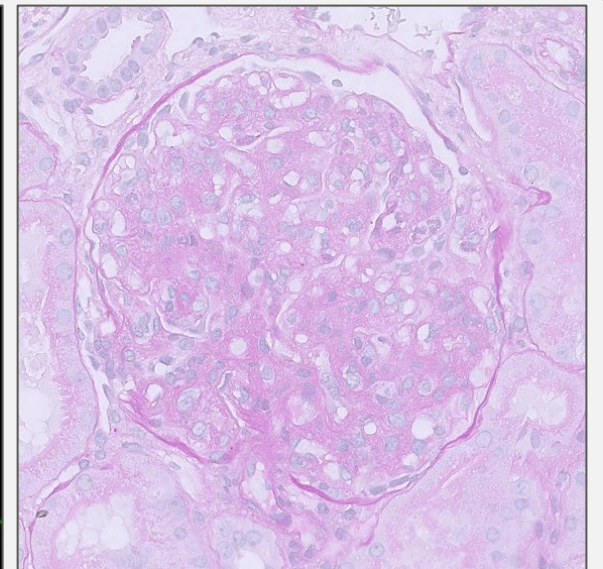
- No pathogenic complement gene variants
- C3NeF negative
- No drusen

Kidney biopsy: **C3G diagnosed, no chronic lesions/IFTA**

- Treated with IV methylprednisolone (×3), followed by 12 months of glucocorticoids
- MMF and ACEi therapy
- Persistent IV albumin dependence despite treatment



Immunofluorescence staining shows glomerular C3 deposits



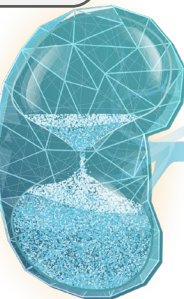
Light microscopy shows evidence of proliferative GN

MMF is not approved by the EMA specifically for the treatment of C3G.¹

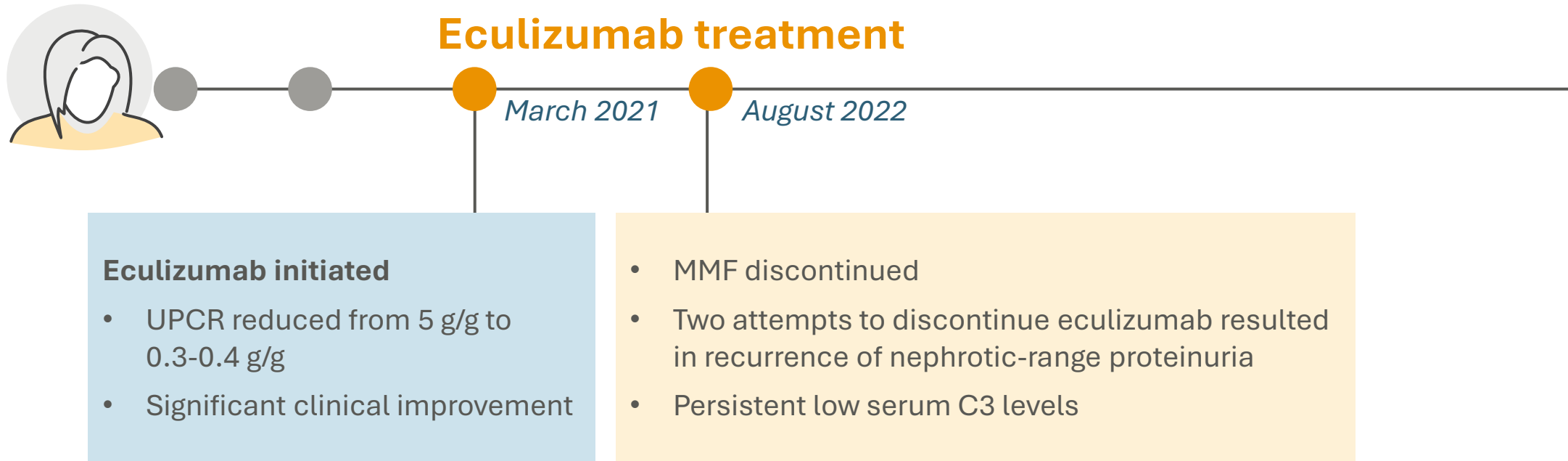
Methylprednisolone is not approved by the EMA specifically for the treatment of C3G and is used to manage inflammation.²

Albumin infusion is not approved specifically for the treatment of C3G and is used as supportive therapy to manage fluid retention.³

ACEi, angiotensin converting enzyme inhibitors; C3G, C3 glomerulopathy; C3NeF, C3 nephritic factor; EMA, European Medicines Agency; GN, glomerulonephritis; IFTA, interstitial fibrosis/tubular atrophy; IV, intravenous; MMF, mycophenolate mofetil. 1. CellCept SmPC 2026 2. Solu-Medrone SmPC 2026 3. Human albumin solution SmPC 2018. Patient case courtesy of Marina Vivarelli.



Patient case: Treatment with C5 inhibitors



Patient case: Treatment with C5 inhibitors



Ravulizumab treatment

January 2024

Maintenance C5 inhibition

- Switched to **ravulizumab**; clinical stability maintained
- Persistent low serum C3
- Mild increase in proteinuria from mid-2024 (UPCR 0.7-0.8 g/g), remaining below nephrotic range

Ravulizumab is not approved by the EMA specifically for the treatment of C3G.¹
C3G, C3 glomerulopathy; EMA, European Medicines Agency; UPCR, urine protein creatinine ratio.

1. Ultomiris SmPC 2026.

Patient case courtesy of Marina Vivarelli.



C5 inhibitors may provide clinical benefit to selected patients, but **do not target glomerular C3 deposition**¹⁻⁹

A Phase 2, single-arm clinical trial of eculizumab in C3G or primary IC-MPGN found:²

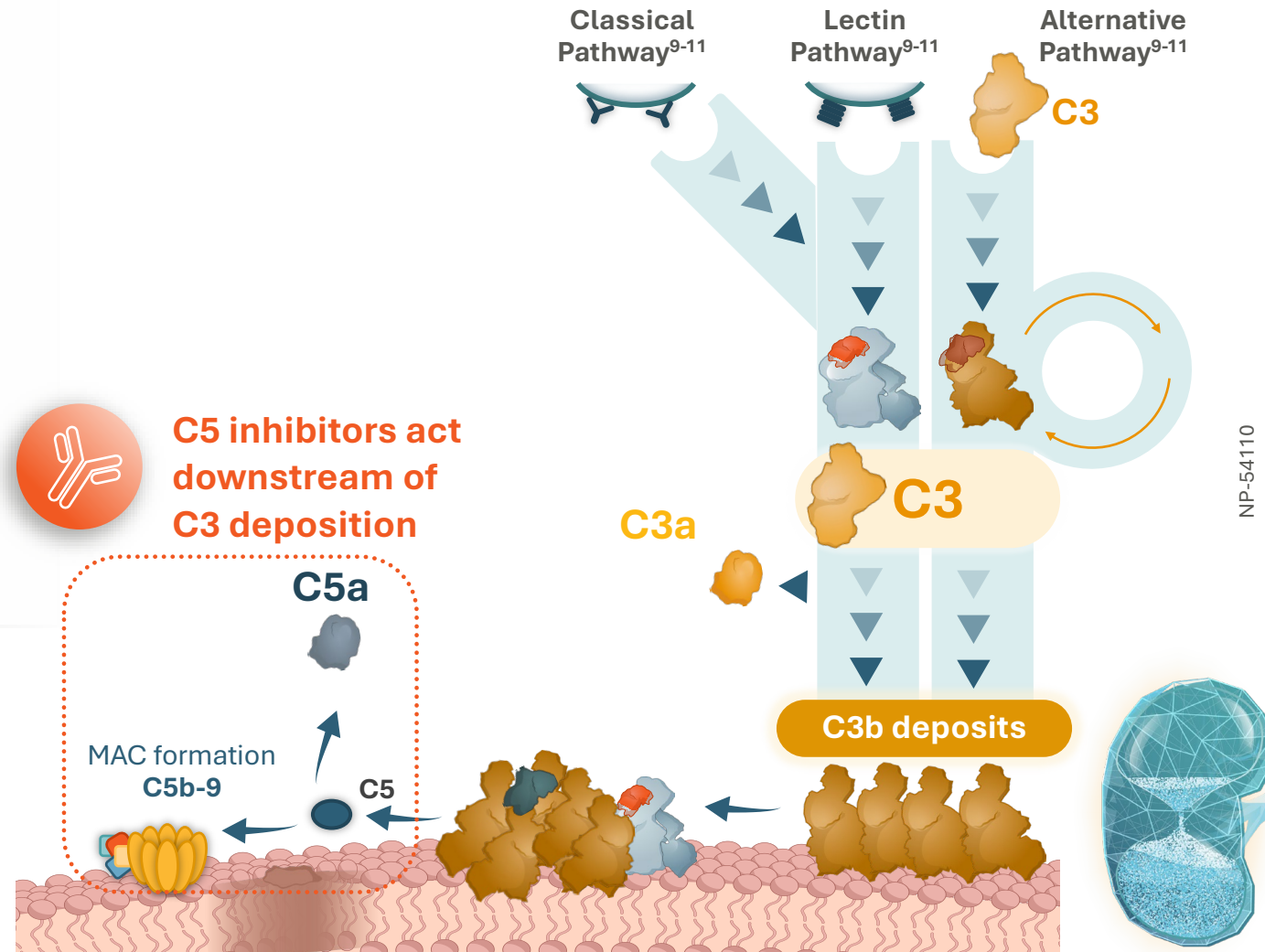
3/10
patients
responded

Persistent proteinuria response observed only in patients with **strong terminal complement pathway activation**

Retrospective studies and case reports support these findings, suggesting **inconsistent results and partial responses with eculizumab treatment**³⁻⁸

Eculizumab is not approved by the EMA specifically for the treatment of C3G or primary IC-MPGN.¹² C3G, C3 glomerulopathy; EMA, European Medicines Agency; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; MAC, membrane attack complex.

1. Noris & Remuzzi *Nephrol Dial Transplant* 2024
2. Ruggenenti et al. *Am J Kidney Dis* 2019
3. Cappoli et al. *Pediatr Nephrol* 2024
4. Vivarelli et al. *N Engl J Med* 2012
5. Bomback et al. *Clin J Am Soc Nephrol* 2012
6. Le Quintrec *Am J Kidney Dis* 2018
7. Welte et al. *BMC Nephrol* 2023
8. Zubidat et al. *Clin Kidney J* 2026
9. Fakhouri et al. *Kidney Int* 2020
10. Meuleman et al. *Semin Immunol* 2022
11. Smith et al. *Nat Rev Nephrol* 2019
12. Soliris SmPC 2025.



Patient case: Improvement of clinical features, but not disease activity

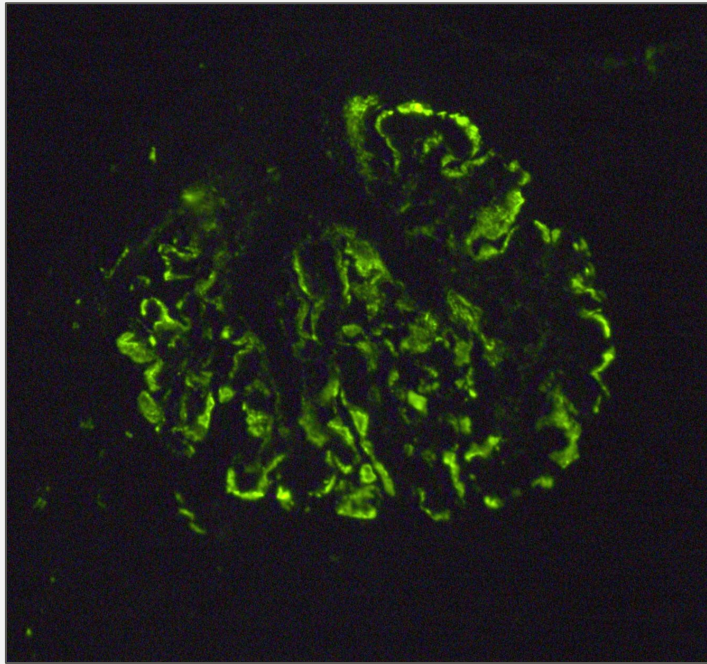


Repeat kidney biopsy

March 2025

- Intensely proliferative active lesions
- Persistent C3+++ staining on immunofluorescence

Active histological disease **despite** clinical response to C5 inhibition



Persistence of glomerular C3 deposits

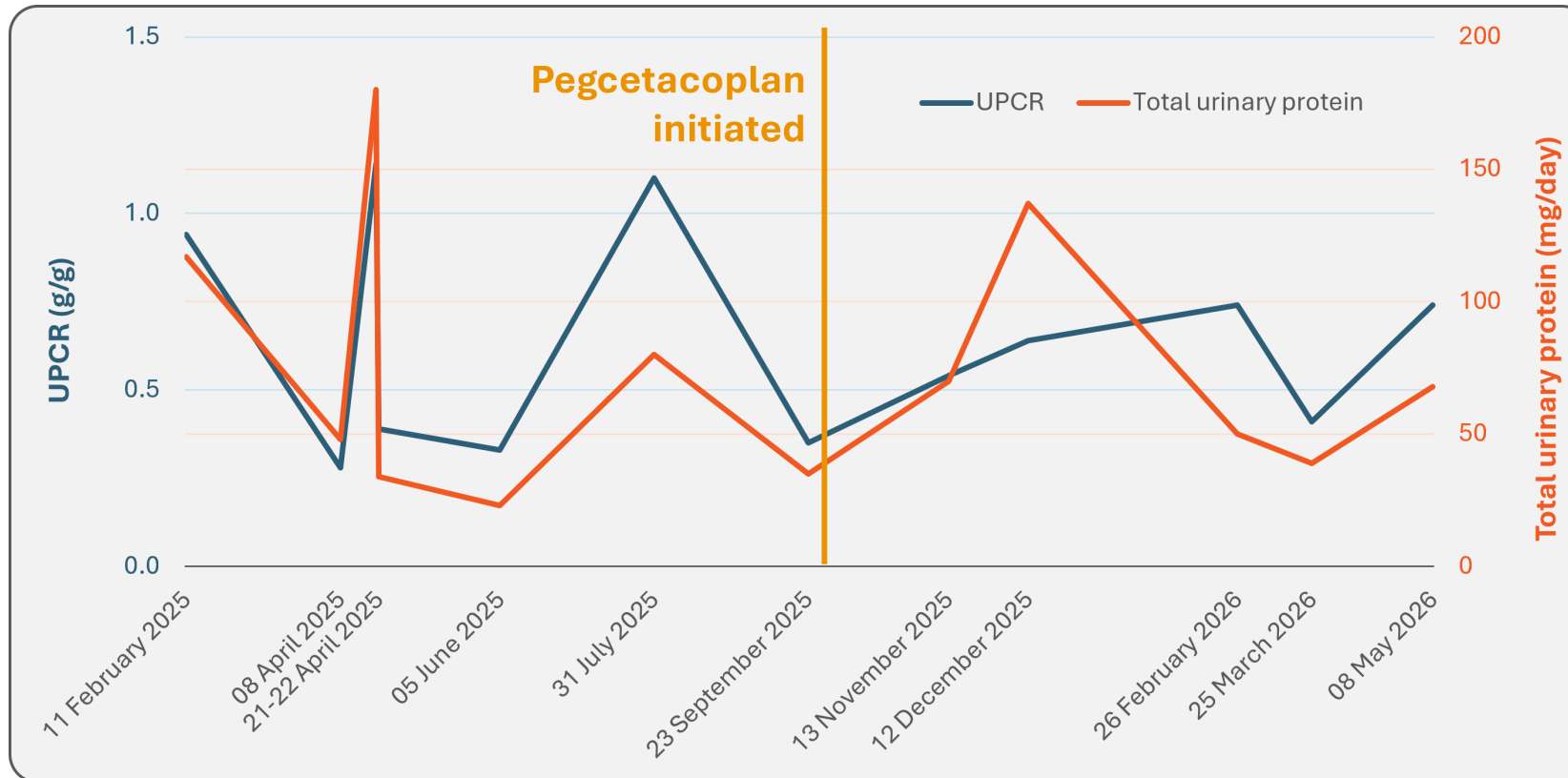


Patient case: Shift from C5 inhibition to C3/C3b inhibition with pegcetacoplan



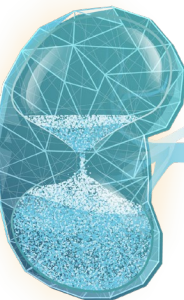
Treatment with pegcetacoplan

September 2025



Switched from C5 inhibition to **C3/C3b inhibition** with pegcetacoplan

Transition from C5 to C3/C3b inhibition was **well tolerated** and **maintained clinical remission**



Pegcetacoplan demonstrated effectiveness in a real-world cohort including children¹



A real-world, multicentre observational cohort study included 25 patients with biopsy-confirmed C3G or primary IC-MPGN

At pegcetacoplan initiation:

80%

patients aged <18 years
(n=20/25)

Underlying disease:

- C3GN (n=18)
- DDD (n=3)
- Primary IC-MPGN (n=4)

3.5 g/g

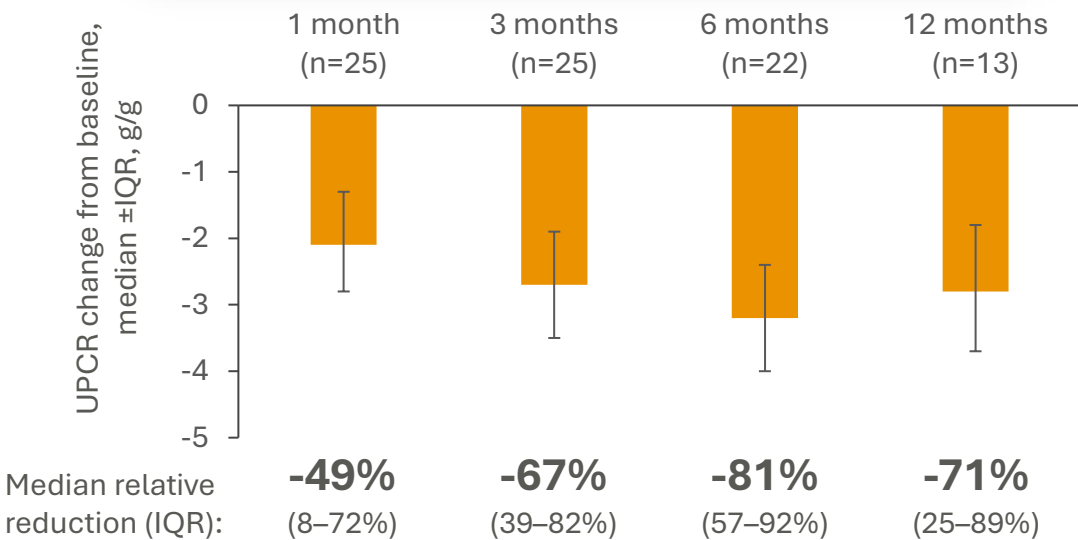
median UPCR
(IQR 2.5-6.0)

73.6 ml/min per 1.73 m²

mean eGFR
(SD 42.7)

Smaller studies and case reports also support real-world benefit of pegcetacoplan in children²⁻⁵

Change from baseline in UPCR

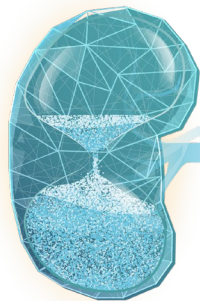


64% of patients achieved partial remission from proteinuria and **12%** achieved complete remission*

Mean **eGFR significantly increased** at 3 and 6 months, and remained stable at 12 months in patients with data available

* Complete proteinuria remission was defined as a UPCR ≤ 0.2 g/g in paediatric patients and ≤ 0.3 g/g in adults. Partial remission was defined as a reduction in UPCR of more than 50% from baseline with a final UPCR below the nephrotic range. C3G, C3 glomerulopathy; C3GN, C3 glomerulonephritis; DDD, dense deposit disease; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; IQR, interquartile range; SD, standard deviation; UPCR, urine protein-to-creatinine ratio.

1. Bassanese et al. *Kidney Int* 2026 2. Román Ortiz et al. *Pediatr Nephrol* 2025 3. Mancuso et al. *Pediatr Nephrol* 2025 4. Alrasheed et al. *Front Med* 2026 5. Levart et al. *Pediatr Nephrol* 2025;suppl.



Future perspectives

- Emerging **real-world evidence** suggests pegcetacoplan **effectiveness and safety** is **similar to that observed in clinical trials**¹⁻⁵
- **In-depth patient monitoring** during therapy is critical and can inform **continual evaluation of management options** – lack of response or incomplete response to previous therapy does not preclude response to a different targeted therapy⁶
- **Areas of uncertainty remain**, including standardisation of assays, how certain biomarkers should influence patient management, and duration of targeted therapy^{7,8}

PRISM-C3, an international Phase 4 study, is currently recruiting to evaluate the real-world efficacy and safety of pegcetacoplan in an even broader patient population⁹

What data will PRISM-C3 generate to support the community?⁹

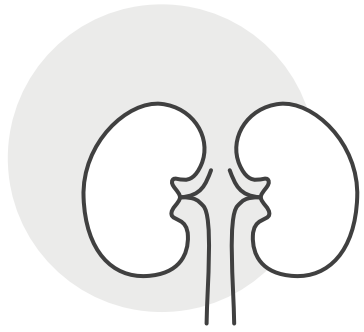
- ✓ Long-term real-world outcomes and impact of treatment duration
- ✓ Impact of patient characteristics and biomarkers on outcomes
- ✓ Impact of treatment on HCRU and patient QoL

HCRU, healthcare resource utilisation; QoL, quality of life.

1. Bassanese et al. *Kidney Int* 2026 2. Román Ortiz et al. *Pediatr Nephrol* 2025 3. Mancuso et al. *Pediatr Nephrol* 2025 4. Alrasheed et al. *Front. Med* 2026

5. Levart et al. *Pediatr Nephrol* 2025;suppl 6. Based on the expert opinion of Marina Vivarelli 7. Kavanagh et al. *Kidney Int Rep* 2025 8. Kavanagh et al. *Kidney Int* 2026 9. ClinicalTrials.gov NCT07746895.

Discussion points on treatment personalisation



Disease-related considerations

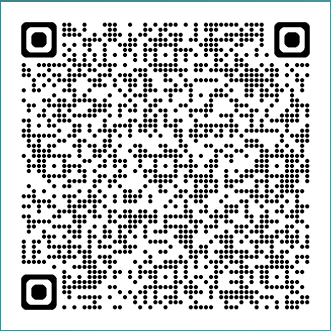
- Clinical severity and trajectory: proteinuria, haematuria and kidney function
- Histological activity and chronicity, including potential value of repeat biopsy
- Complement phenotype and underlying driver
- Previous treatment response, treatment dependence and disease recurrence
- Transplantation considerations



Patient and treatment-related considerations

- Age, comorbidities and concomitant treatments
- Safety profile, infection prevention and monitoring requirements
- Route, frequency and overall treatment burden
- Adherence, patient/family preferences and ability to self-administer
- Impact on daily life and practical access to treatment





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