
C3 COMPLEMENT DYSREGULATION
IS CENTRAL TO THE DEVELOPMENT OF C3G AND PRIMARY IC-MPGN[1–3]
NOTE TO AFFILIATES:
TO PROVIDE LOCAL REPORTING INFORMATION
▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. You can help by reporting any side effects to Competent Authority or to Swedish Orphan Biovitrum AB by email:
PP-31580 February 2026
ASPAVELI® ▼
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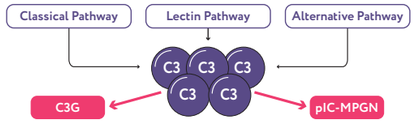
C3G, and pIC-MPGN, are progressive and severe kidney diseases, characterised by overactivation of the complement system[2,4,5]

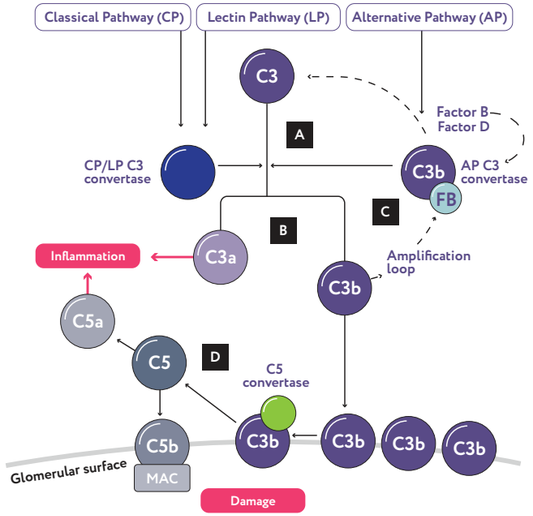
- The complement system is a regulated network within the immune system that plays an important role in host defense against infection[6]
- The complement cascade is composed of three pathways – classical, alternative and lectin[7]
- Complement proteins are the effectors in the pathways that are activated in response to pathogens or immune complexes[6]
- Activation of the complement occurs in a cascade reaction that enhances the immune response by:[7]
  - Opsonization – tagging pathogens for easier uptake by immune cells
  - Inflammatory signaling – recruiting immune cells to the site of infection
  - Cell lysis – directly destroying target cells
- The central protein within the complement system is C3[8]
- The rare kidney diseases, C3 glomerulopathy (C3G) and primary immune-complex membranoproliferative glomerulonephritis (pIC-MPGN), arise when the complement system becomes overactive or poorly regulated, resulting in excessive accumulation of C3 deposits and/or immunoglobulins[1,3,9,10]



C3 dysregulation leads to renal inflammation & damage[2,3]

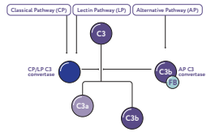
Overactivation of C3 by the complement system leads to complement dysregulation which is central to the pathogenesis of C3G and pIC-MPGN, and leads to renal inflammation and damage[2,7,11]

Dysregulation of the complement cascade in C3G and pIC-MPGN



A

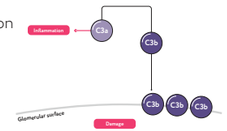
C3 is activated by the classical/lectin or the alternative C3 convertase, which can cleave C3 into C3a and C3b[7,12,13]



B

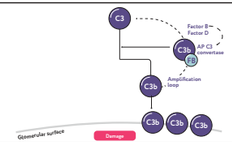
C3a is an anaphylatoxin involved in inflammation and chemotaxis of immune cells[7,12,13]

C3b is an opsonin that can deposit in the glomerular surface causing damage or injury[12,13]



C

C3b can also bind to Factor B to produce more alternative pathway C3 convertase, creating an amplification loop of C3 activation and deposition of C3b[7,12,13]

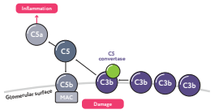


D

C3b also contributes to the formation of C5 convertases which cleave C5 into:[7,12,13]

C5a – an anaphylatoxin involved in inflammation[2,7,12]

C5b – which triggers the formation of the membrane attack complex (MAC), causing cell death and tissue damage[2,7,12]



Addressing complement dysregulation can help to halt renal damage[2]

C3 dysregulation leads to kidney damage resulting in:[2,9]

C3 deposition causing inflammation and structural damage (histopathology)

Proteinuria

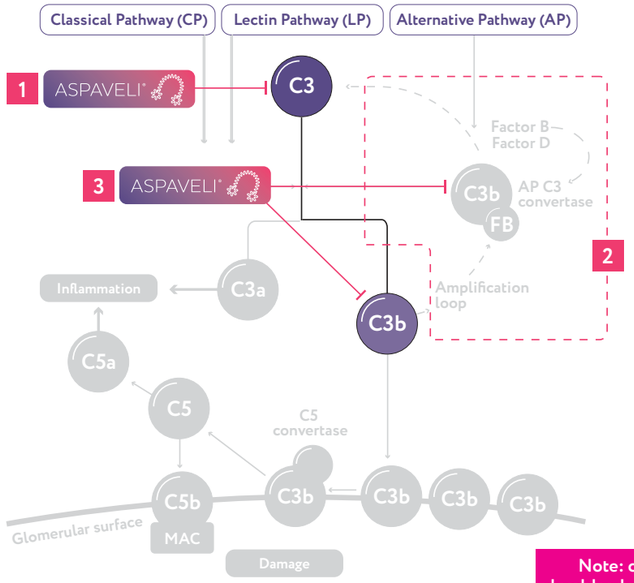
Scarring/fibrosis with progressive loss of kidney function (eGFR decline)

- Damage like glomerulosclerosis and scarring may not be reversible in patients, but control of C3 dysregulation and the complement cascade may prevent further build-up of C3 deposits, protecting the kidneys from further damage and preserving their function[2,14]
- As C3 is common to the three pathways, targeting C3 may prevent dysregulation across the complement system[2]

C3 dysregulation drives kidney failure in C3G and pIC-MPGN – targeted intervention is critical[1,15]

- The prognosis for people living with C3G and pIC-MPGN has been poor, with nearly 50% **progressing to renal failure within 10 years of diagnosis**[1]
- Early targeted intervention is important as **ongoing complement-mediated injury can drive progression** to chronic kidney disease and irreversible kidney failure[9,15,16]
- **C3 complement dysregulation** is the key driver of C3G and pIC-MPGN, so targeting C3 is critical to treating these conditions[2,17]

Aspaveli is the first and only approved targeted C3 and C3b inhibitor to directly target C3 complement dysregulation[10,18]



ASPAVELI is indicated for the treatment of adult and adolescent patients aged 12 to 17 years with C3G or pIC-MPGN in combination with a renin-angiotensin system (RAS) inhibitor, unless RAS inhibitor treatment is not tolerated or contraindicated.[18]

Aspaveli acts on the 3 key steps of C3 dysregulation, by:

1. Blocking C3 cleavage by all C3 convertases[10,18]
2. Blocking C3 convertase and the amplification loop[18,19]
3. Blocking C3b, preventing glomerular C3 deposition and generation of downstream effectors of kidney inflammation and damage[10,18]

Note: content on this page should only be used post approval – to be adapted at the country level

C3 dysregulation drives kidney failure in C3G and pIC-MPGN – targeted intervention is critical[1,15]

- The KHI recommends that any complement pathway intervention aiming to treat immune-related renal disease should demonstrate clinically meaningful improvements in key disease outcomes, including:[20†]
  - reduction in proteinuria
  - stabilisation or improvement in eGFR
  - improvement in kidney histopathology
- Only Aspaveli delivers on the KHI expert consensus of efficacy endpoints, with beyond-target proteinuria reduction*[14,16,20,21]

Footnote:

*The VALIANT Phase 3 trial was a randomised, double-blind, placebo-controlled study in 124 adolescents and adults (≥12 yrs) with C3G or pIC-MPGN. The primary endpoint was the log-transformed change in urine protein-to-creatinine ratio (UPCR) at Week 26 compared with baseline. Aspaveli met the primary endpoint, demonstrating a statistically significant and clinically meaningful 68% relative reduction in proteinuria vs placebo at Week 26 ($p<0.0001$). Renal function was also stabilised, with a +6.3 mL/min/1.73 m² difference in eGFR versus placebo at Week 26 (95% CI: 0.5–12.1). In addition, 71.4% of Aspaveli-treated patients achieved complete clearance of glomerular C3 deposits at 6 months.[14]

† The KHI identifies these domains as key outcomes but does not define numeric thresholds.

Notes


“I need my kidneys to function. Once they stop functioning, life is never the same again.”
Patient with C3G[22]

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Abbreviations

C3, complement 3; **C5**, complement 5; **C3G**, C3 glomerulopathy; **eGFR**; estimated glomerular filtration rate; **pIC-MPGN**, primary immune complex-mediated membranoproliferative glomerulonephritis; **KHI**, Kidney Health Initiative; **MAC**, membrane attack complex.

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