# CHOOSE A NEW ROUTE FOR YOUR PATIENTS WITH IgA NEPHROPATHY[1]

**FABHALTA® is the first and only Factor B complement inhibitor that targets the overactivation of the alternative pathway.[1,2]**

FABHALTA® iptacopan ▼

**THE CLEAR PATH TO RAPID PROTEINURIA REDUCTION*[3]**

FABHALTA® is indicated for the reduction of proteinuria in adults with primary IgA nephropathy at risk of rapid disease progression, generally a UPCR ≥1.5 g/g.[2]
▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.
Prescribing information and adverse event reporting can be found via the PI button.

* Treatment with FABHALTA® led to reductions in proteinuria (UPCR-FMV) from baseline as early as Week 2 in the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study.[3]

© 2025 Novartis Pharma AG, CH-4002 Basel Switzerland. All rights reserved.
FA-11424493 | August 2025

## Abbreviations

FMV, first morning void; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; UPCR, urine protein-to-creatinine ratio.

## References

1. Rizk DV, et al. Kidney Int Rep. 2023;8:968–979.
2. FABHALTA® US Prescribing Information - PLACEHOLDER FOR CN LABEL.
3. Perkovic V, et al. N Engl J Med. 2025;392:531–543.

# IgA nephropathy is a heterogeneous disease[1,2]

The heterogeneity in clinical presentation makes early recognition and treatment difficult – many patients are diagnosed late, with significant proteinuria and impaired eGFR[2–4]

**Diagnose and treat early with targeted therapy to preserve kidney function[2]**

## Abbreviations

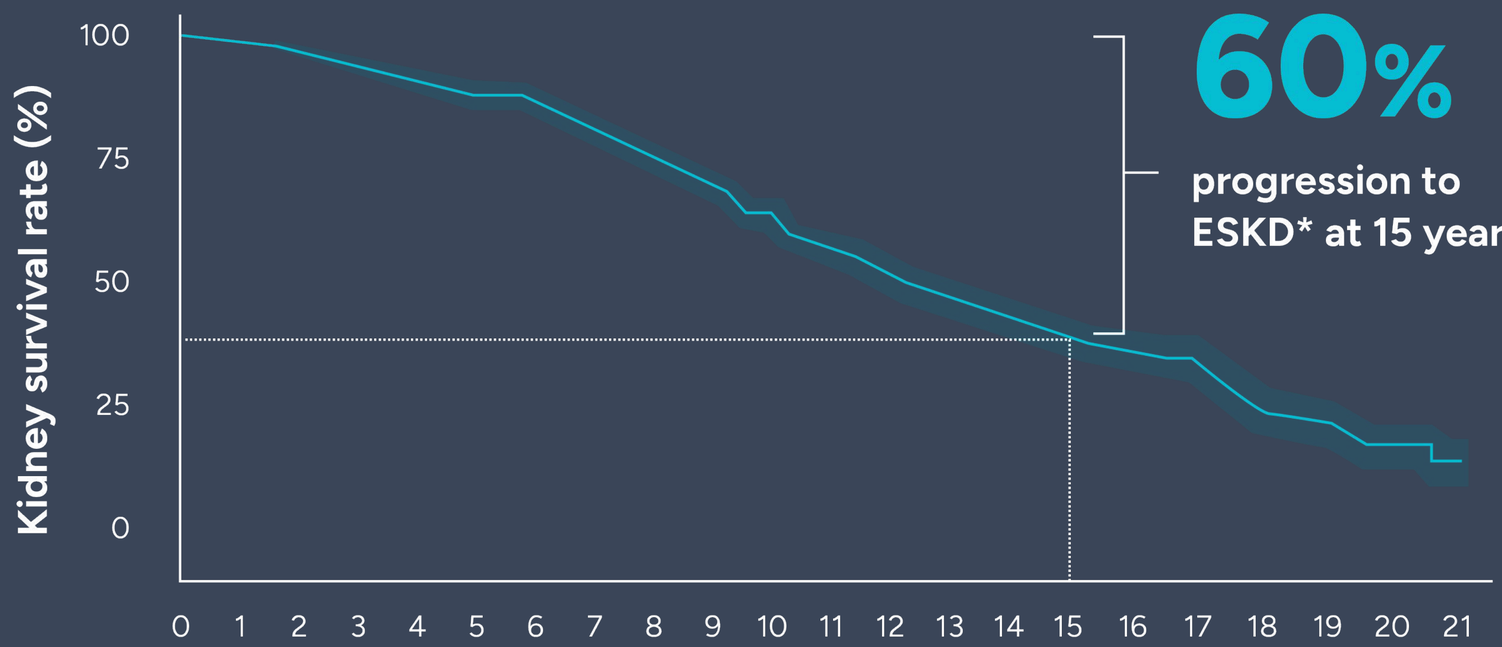
eGFR, estimated glomerular filtration rate; IgA, immunoglobulin A.

## References


1. El Karoui K, et al. J Am Soc Nephrol. 2024;35:103–116.
2. Barratt J, et al. Front Med. 2024;11:1461879.
3. Caster DJ, et al. Kidney Int Rep. 2023;8:1792–1800.
4. Kwon CS, et al. J Health Econ Outcomes Res. 2021;8:36–45.
5. Rout P. Treasure Island (FL): StatPearls Publishing; 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538214/. Last accessed August 2025.
6. Rajasekaran A, et al. Am J Med Sci. 2021;361:176–194.
7. Perkins P, et al. Kidney International Reports. 2022;7:POS-050.
8. IgA Nephropathy. Available at: https://rarediseases.org/rare-diseases/iga-nephropathy/#symptoms. Last accessed August 2025.

# 60% of patients progressed to ESKD* within 15 years of biopsy, despite supportive care†‡[1]

## Kaplan-Meier survival curve of time to ESKD from an observational cohort study in China†‡[1]




**60%**

**progression to ESKD* at 15 years[1]**

The fear of progression, and an uncertain future, means many patients experience emotional and social difficulties[1–3]

**Act early to mitigate risk of disease progression[1,4]**

- Median age at ESKD* onset was just 40 years[1]

Adapted from Shen X, et al. Nephrol Dial Transplant. 2024.[1]

* ESKD: eGFR <15 mL/min/1.73m² or the need for kidney replacement therapy, including maintenance dialysis or kidney transplantation.[1] † Data from an observational cohort study at Peking University First Hospital (N=2141).[1] ‡ Medications: 91% RASi, 43% corticosteroids, 26% immunosuppressants and 27% hydroxychloroquine.[1]

## Abbreviations

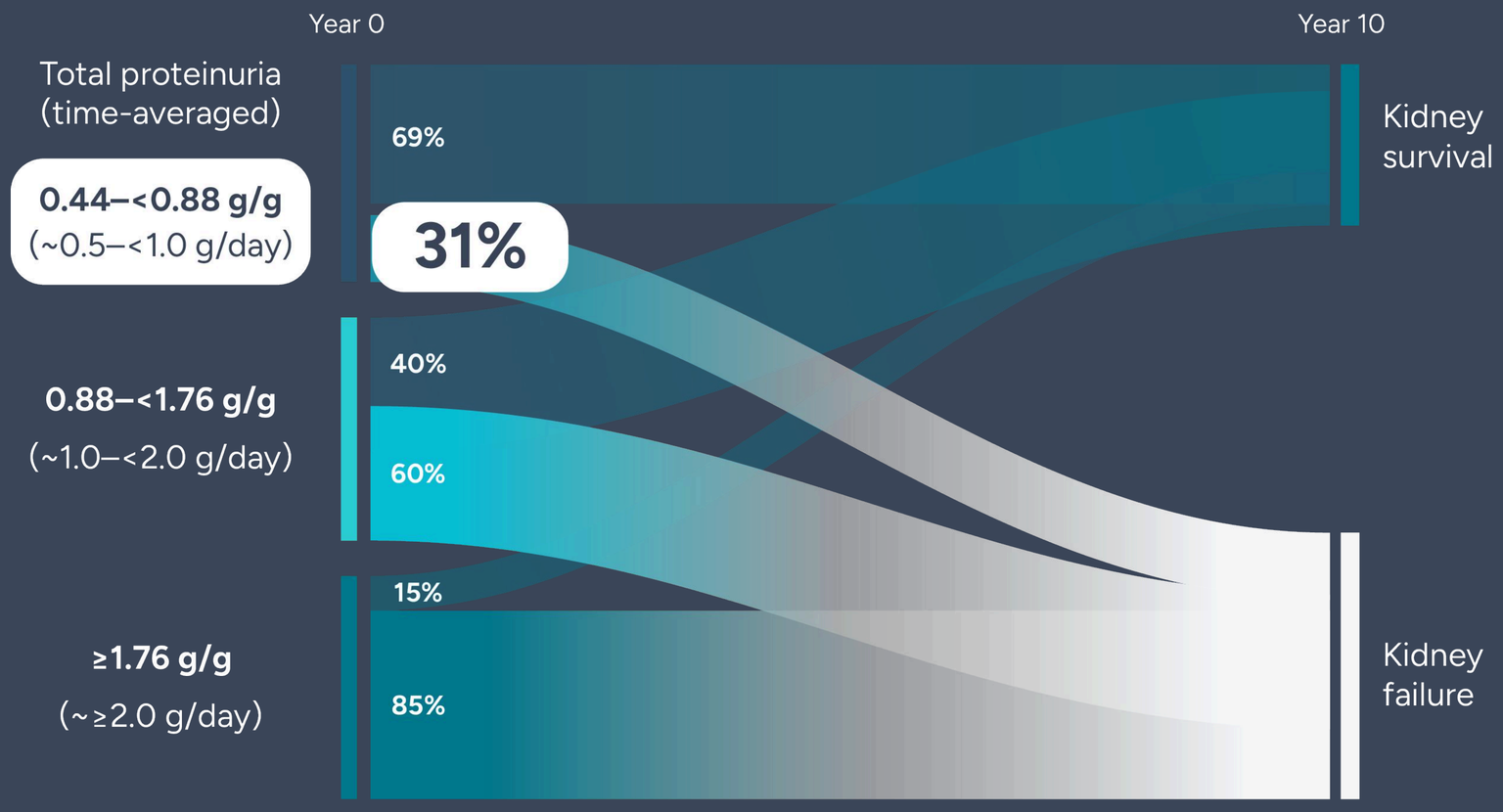
eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; RASi, renin-angiotensin system inhibitor.

## References

1. Shen X, et al. Nephrol Dial Transplant. 2025;40:1137–1146.
2. Kwon CS, et al. J Health Econ Outcomes Res. 2021;8:36–45.
3. National Kidney Foundation. Voice of the Patient 2020. Available at: https://nkf.egnyte.com/dl/aHGCS6tPNM. Last accessed August 2025.
4. Barratt J, et al. Front Med. 2024;11:1461879.

# 31% of patients with proteinuria ~0.5 to <1.0 g/day* progressed to kidney failure within 10 years†[1]

## Risk of kidney failure 10 years after diagnosis†‡[1]




**Treat to achieve new proposed target of proteinuria ≤0.3 g/day to minimise loss of kidney function[2]**

Adapted from Pitcher D, et al. Clin J Am Soc Nephrol. 2023.[1]

* Time-averaged proteinuria 0.44 to <0.88 g/g (~0.5 to <1.0 g/day).‡[1] † Data from a retrospective cohort of the UK National Registry of Rare Kidney Diseases (RaDaR); N=2439.[1]
‡ UPCR cannot be directly compared with 24-hour proteinuria.[3] UACR values converted to UPCR using UPCR=UACR/0.7. A UPCR of 0.88 g/g may be considered comparable with protein excretion of 1 g/day.[1]

## Abbreviations

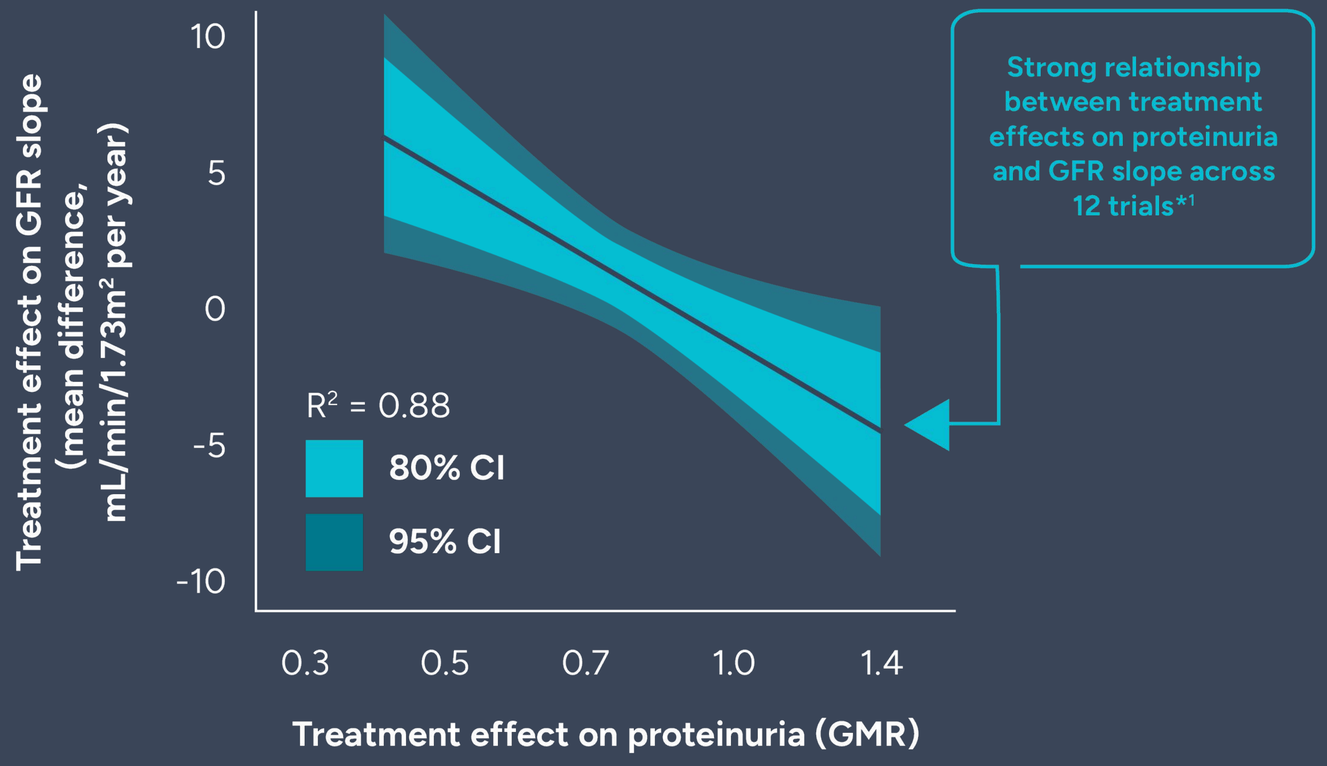
UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

## References

1. Pitcher D, et al. Clin J Am Soc Nephrol. 2023;18:727–738.
2. Floege J, et al. Kidney Int. 2025;107:640–651.
3. Yang F, et al. BMC Nephrol. 2022;23:49.

# A reduction in proteinuria is associated with better kidney outcomes[1]

## Association between treatment effects on proteinuria at 6 months and 3-year GFR slope*†[1]




**Strong relationship between treatment effects on proteinuria and GFR slope across 12 trials*[1]**

**Proteinuria reduction is considered a 'reasonably likely' surrogate endpoint for a treatment's effect on progression to ESKD in clinical trials, supporting conditional approval for an IgA nephropathy therapy[1–4]**

Adapted from Inker LA, et al. Am J Kidney Dis. 2021.[1]

* As demonstrated in an individual patient-level meta-analysis of a pooled dataset of 1037 individuals from twelve randomised controlled trials in IgA nephropathy.[1]
† The graph shows the relationship between estimated treatment effects on the 3-year GFR slope on the vertical axis to estimated treatment effects on the change in urine protein on the horizontal axis. Treatment effects on GFR slope are expressed as mean difference in treatment and control and expressed in mL/min/1.73m²/year. Treatment effects on urine protein are expressed as geometric mean ratios.[1]

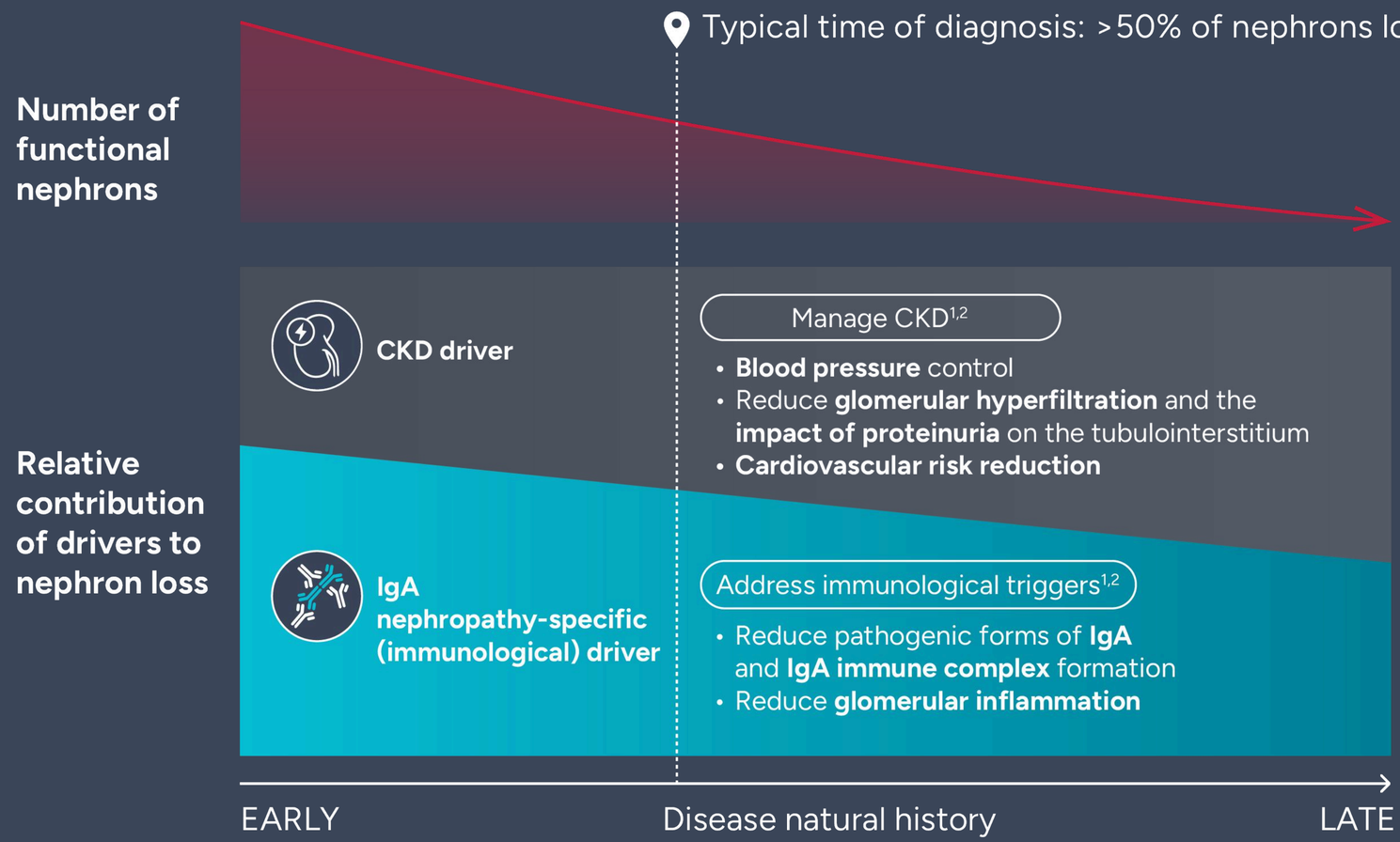
## Abbreviations

CI, confidence interval; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; GMR, geometric mean ratio; IgA, immunoglobulin A.

## References

1. Inker LA, et al. Am J Kidney Dis. 2021;78:340–349.
2. Floege J, et al. Kidney Int. 2025;107:640–651.
3. Thompson A, et al. Clin J Am Soc Nephrol. 2019;14:469–481.
4. Barbour SJ, et al. KI Reports. 2025;10:1283–1287.

# There are two fundamental drivers of nephron loss in IgA nephropathy[1,2]




**Both drivers should be addressed simultaneously at diagnosis[1,2]**

**Targeted therapies are needed to address the IgA nephropathy-specific driver and prevent kidney failure[1,2]**

**Stylised representation for illustrative purposes.**

Adapted from Barratt J, et al. Front Med. 2024.[1]

## Abbreviations

CKD, chronic kidney disease; IgA, immunoglobulin A.

## References

1. Barratt J, et al. Front Med. 2024;11:1461879.
2. Floege J, et al. Kidney Int. 2025;107:640–651.

# Patients like Mei experience uncertainty due to the looming risk of disease progression[1–3]

## Patient profile: Mei

"My treatment has helped my IgA nephropathy, but I still feel fatigued a lot. I'm afraid that I may face kidney failure and end up on dialysis in the future. Having to go on dialysis would change everything."

**Fictitious patient profile and quote for illustrative purposes only.**

### At diagnosis

- Confirmed by biopsy
  - MEST-C score: M1/E1/S1/T0/C1
  - C3 positive
- **Proteinuria:** 1.8 g/day
- **eGFR:** 77 mL/min/1.73m²
- **BP:** 125/80 mmHg
- **Haematuria:** Microscopic

### 12 months since diagnosis

- Treated with:
  - ACEi
  - SGLT2i
- **Proteinuria:** 1.5 g/day
- **eGFR:** 75 mL/min/1.73m²
  Rate of decline: 1–3 mL/min/1.73m²/year
- **BP:** 122/78 mmHg
- **Haematuria:** Persistent, microscopic

Treatment journey ›

Biopsy findings ›

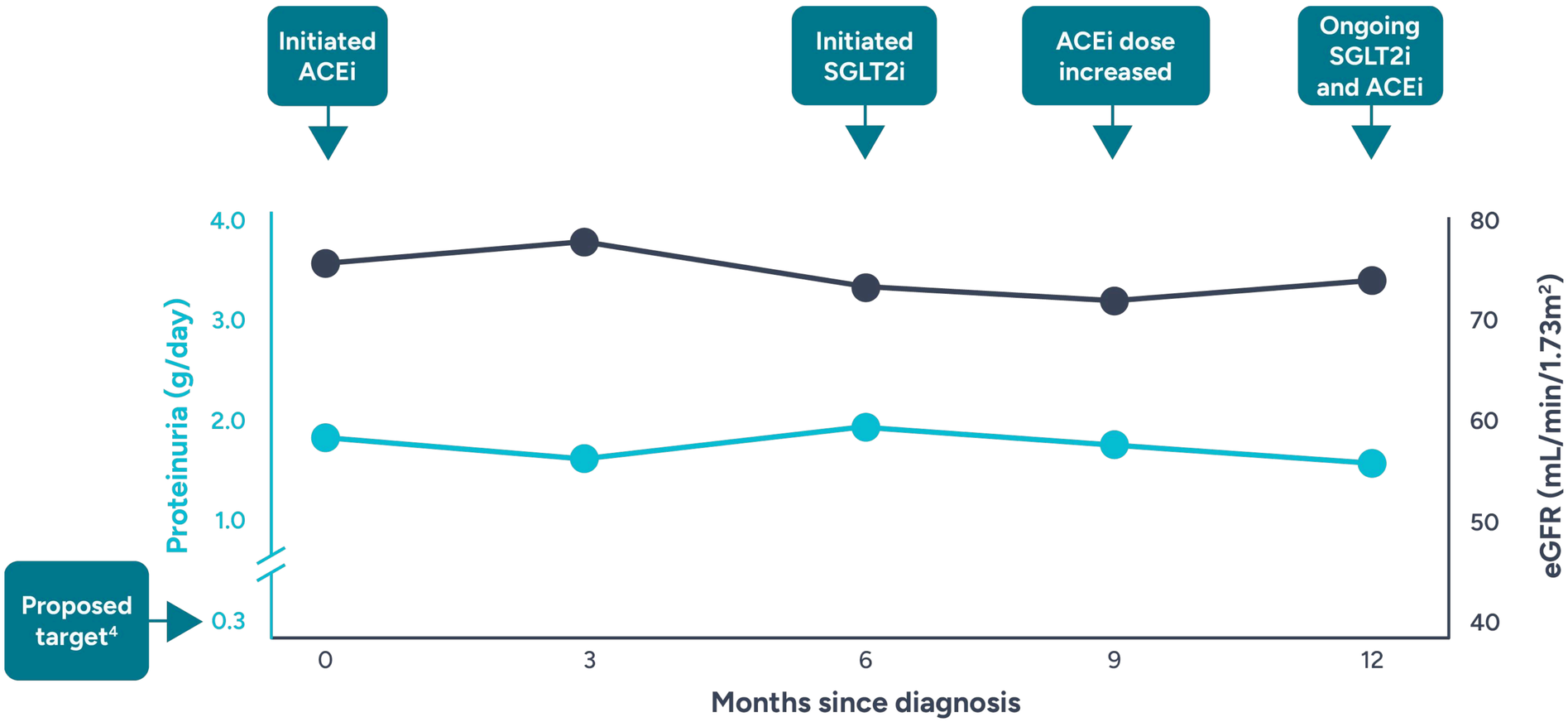
## Abbreviations

ACEi, angiotensin-converting enzyme inhibitor; BP, blood pressure; C3, complement component 3; eGFR, estimated glomerular filtration rate; IgA, immunoglobulin A; MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

## References

1. Kwon CS, et al. J Health Econ Outcomes Res. 2021;8:36–45.
2. Shen X, et al. Nephrol Dial Transplant. 2025;40:1137–1146.
3. National Kidney Foundation. Voice of the Patient 2020. Available at: https://nkf.egnyte.com/dl/aHGCS6tPNM. Last accessed August 2025.

# Patients like Mei experience uncertainty due to the looming risk of disease progression[1–3]




ACEi, angiotensin-converting enzyme inhibitor; eGFR, estimated glomerular filtration rate; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

**References: 1.** Kwon CS, et al. J Health Econ Outcomes Res. 2021;8:36–45. **2.** Shen X, et al. Nephrol Dial Transplant. 2025;40:1137–1146. **3.** National Kidney Foundation. Voice of the Patient 2020. Available at: https://nkf.egnyte.com/dl/aHGCS6tPNM. Last accessed August 2025. **4.** Floege J, et al. Kidney Int. 2025;107:640–651.

# Despite supportive care, patients like Hao have persistent proteinuria and ongoing disease progression[1,2]

## Patient profile: Hao

"Despite 12 months of my current treatment my fatigue has worsened recently, and I now regularly need time off work sick. My doctor suggested glucocorticoids but I am worried about the possible side effects. I'm frightened about what the future holds if my disease continues to worsen at this pace."

**Fictitious patient profile and quote for illustrative purposes only.**

### At diagnosis

- Confirmed by biopsy
  - MEST-C score: M1/E1/S1/T2/C1
  - C3 positive
- **Proteinuria:** 4.0 g/day
- **eGFR:** 44 mL/min/1.73m²
- **BP:** 130/90 mmHg
- **Haematuria:** Microscopic

### 12 months since diagnosis

- Treated with:
  - ARB
  - Buyi Ganshen Recipe*
- **Proteinuria:** 2.9 g/day
- **eGFR:** 40 mL/min/1.73m²
  Rate of decline: 3–5 mL/min/1.73m²/year
- **BP:** 119/81 mmHg
- **Haematuria:** Persistent, microscopic

Treatment journey ›

Biopsy findings ›

* Sheng Di (*Radix rehmanniae*), Shan Yu Rou (*Pulp of cornus*), Gou Qi Zi (*Fructus lycii*), Nv Zhen Zi (*Ligustrum lucidum ait*), Han Lian Cao (*Herba eclipta*).[3]

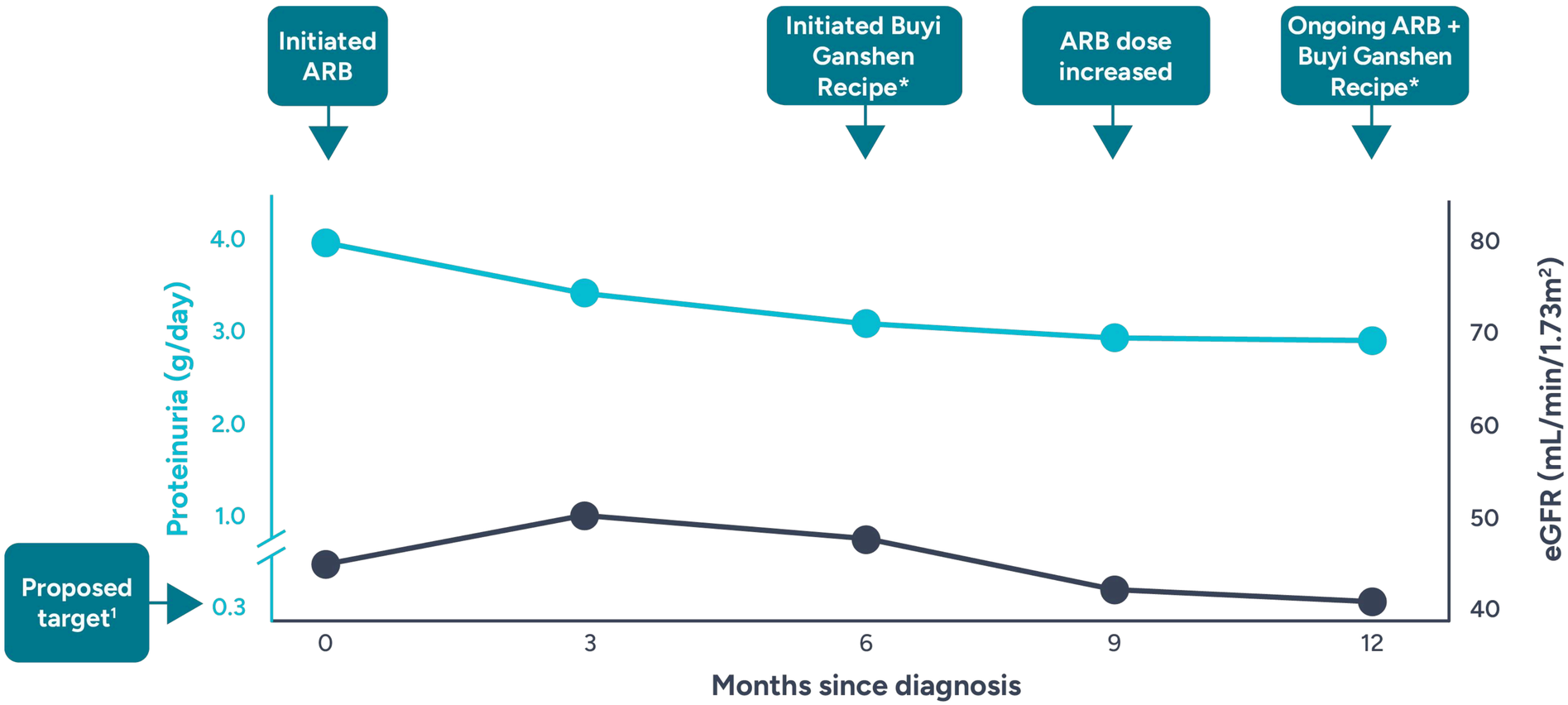
## Abbreviations

ARB, angiotensin receptor blocker; BP, blood pressure; C3, complement component 3; eGFR, estimated glomerular filtration rate;
MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents.

## References

1. Floege J, et al. Kidney Int. 2025;107:640–651.
2. Cheung CK, et al. J Clin Med. 2021;10:2493.
3. Wang X-H, et al. J Transl Int Med. 2021;9:161–167.

# Despite supportive care, patients like Hao have persistent proteinuria and ongoing disease progression[1,2]




* Sheng Di (*Radix rehmanniae*), Shan Yu Rou (*Pulp of cornus*), Gou Qi Zi (*Fructus lycii*), Nv Zhen Zi (*Ligustrum lucidum ait*), Han Lian Cao (*Herba eclipta*).[3]

ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate.

**References: 1.** Floege J, et al. Kidney Int. 2025;107:640–651. **2.** Cheung CK, et al. J Clin Med. 2021;10:2493. **3.** Wang X-H, et al. J Transl Int Med. 2021;9:161–167.

# Interpreting Mei and Hao's biopsy findings

## E1 and C1 in MEST-C (showing leukocyte infiltration) may indicate glomerular inflammation[1–3]

| MEST-C scoring system[1] | Mesangial hypercellularity | Endocapillary hypercellularity* | Segmental glomerulosclerosis | Tubular atrophy / interstitial fibrosis | Cellular / fibrocellular crescents† |
|---|---|---|---|---|---|
| | M0 <50% / M1 >50% of the glomeruli | E0 Absent / E1 Present | S0 Absent / S1 Present | T0 0–25% / T1 26–50% / T2 >50% of cortical area | C0 None / C1 <25% / C2 ≥25% of the glomeruli |
| Mei | M1 | E1 | S1 | T0 | C1 |
| Hao | M1 | E1 | S1 | T2 | C1 |

### C3 on biopsy indicates complement activation[5,6]

C3b/iC3b/C3c

C3dg

Representative biopsy images showing C3 deposition.[6]

Adapted from Medjeral-Thomas NR, et al. Sem Immunopathol. 2021.[6]

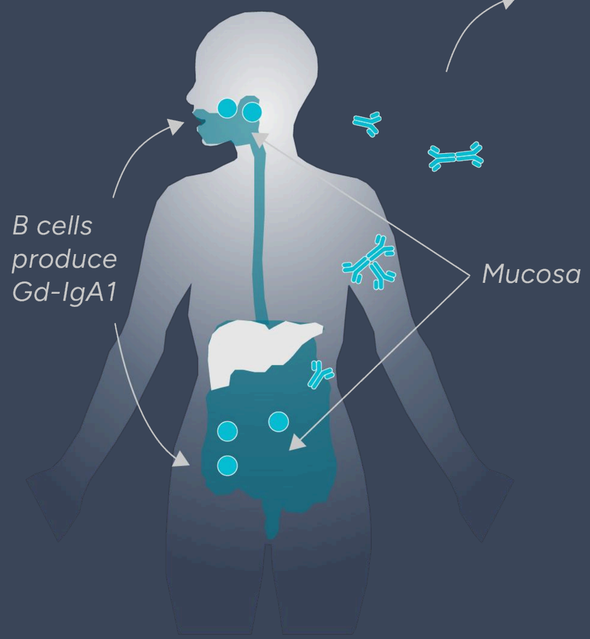
* Due to increased number of cells within glomerular capillary lumina causing narrowing of the lumina.[4] † Due to extracapillary proliferation of parietal and visceral epithelial cells and intermixed mononuclear leukocytes within the Bowman space.[1]

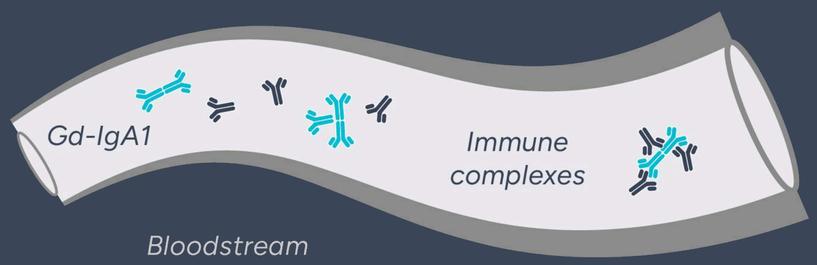
C3, complement component 3; iC3b, inactivated C3b; MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents.

**References: 1.** Markowitz G. Nat Rev Nephrol. 2017;13:385–386. **2.** Trimarchi H, et al. Kidney Int. 2017;91:1014–1021. **3.** Moriyama T, et al. Sci Rep. 2020;10:11151.
**4.** Cattran DC, et al. Kidney Int. 2009;76:534–545. **5.** Cattran DC, et al. Kidney Int Rep. 2023;8:2515–2528. **6.** Medjeral-Thomas NR, et al. Sem Immunopathol. 2021;43:679–690.

# IgA nephropathy results from a multi-hit pathogenic process[1–3]

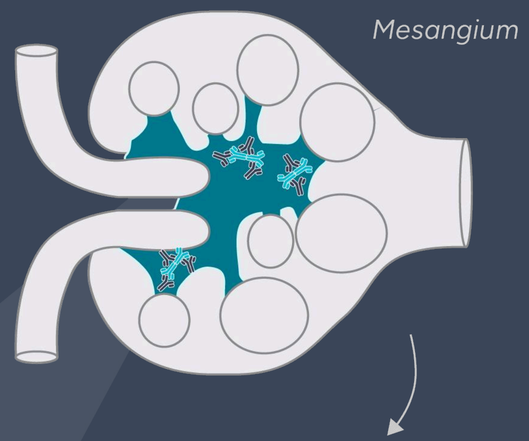
**Hit 1**
Increase in Gd-IgA1 in the systemic circulation




**Hit 2 & Hit 3**
Increased autoantibodies recognise and bind to Gd-IgA1, forming immune complexes

**Hit 4**
Immune complexes deposit in the kidney's glomerular mesangium



Mesangial deposition in Hit 4 triggers proinflammatory and profibrotic responses, including overactivation of the alternative complement pathway, leading to permanent kidney damage

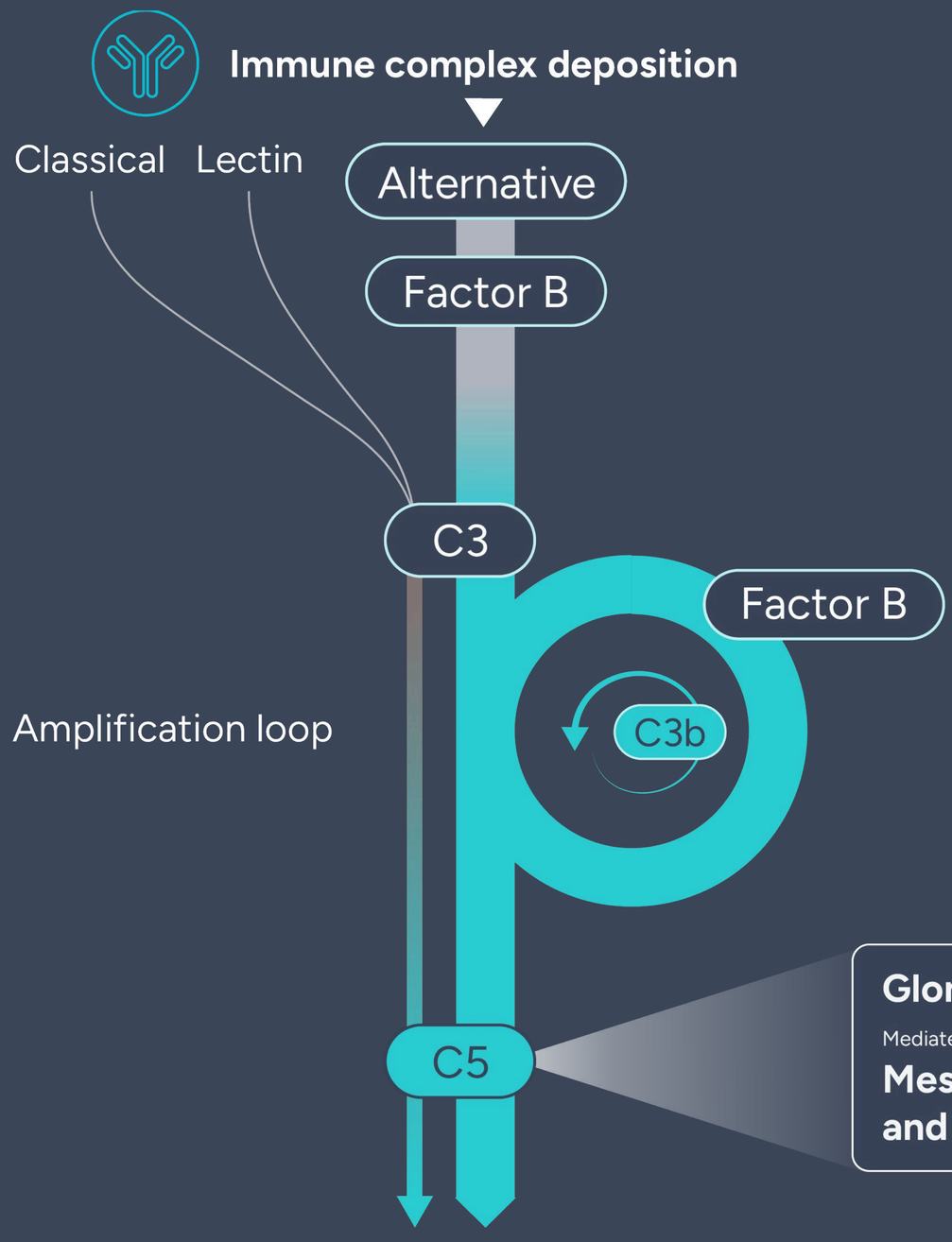
**AP overactivation is observed in >90% of patients with IgA nephropathy[4]**

## Abbreviations

AP, alternative pathway; Gd-IgA1, galactose-deficient immunoglobulin A1; IgA, immunoglobulin A.

## References

1. El Karoui K, et al. J Am Soc Nephrol. 2024;35:103–116.
2. Tesař V, et al. Kidney Int Rep. 2023;8:1730–1740.
3. Selvaskandan H, et al. Int J Immunogenet. 2022;49:8–21.
4. Duval A, et al. Nephrol Dial Transplant. 2023;38:2685–2693.




# AP overactivation is one of the key drivers of glomerular inflammation and disease pathogenesis[1,2]

Complement inhibitors targeting the AP may reduce immune complex-mediated glomerular inflammation and kidney injury[3]

Adapted from Karoui KE, et al. J Am Soc Nephrol. 2024[1] and Tesař V, et al. Kidney Int Rep. 2023.[2]

* C3b increases complement activity across all three pathways. C3a independently amplifies inflammation and tissue damage.[2]

## Abbreviations

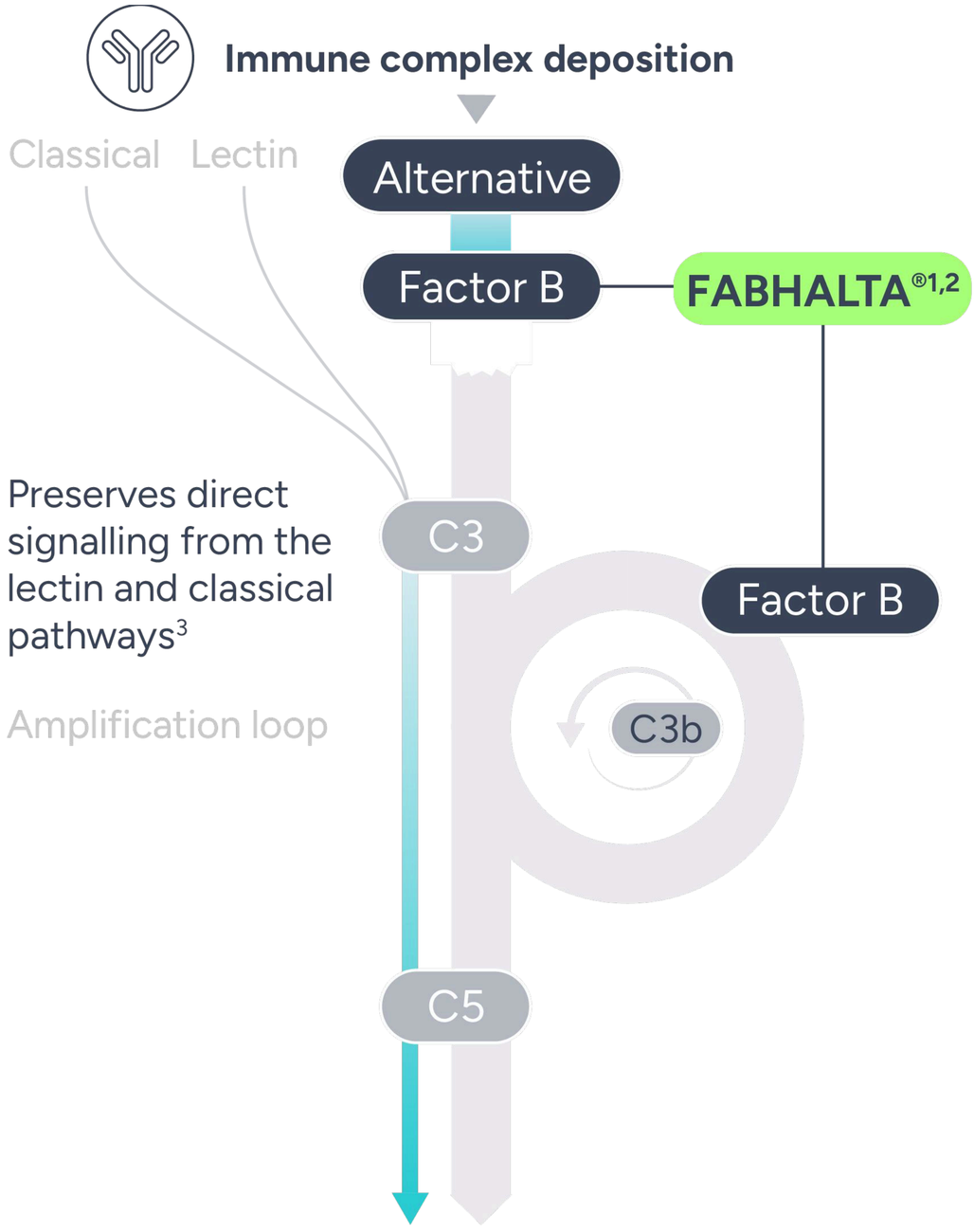
AP, alternative pathway; C3, complement component 3; C5, complement component 5.

## References


1. El Karoui K, et al. J Am Soc Nephrol. 2024;35:103–116.
2. Tesař V, et al. Kidney Int Rep. 2023;8:1730–1740.
3. Zhang H, et al. Kidney Int. 2024;105:189–199.
4. Yeo SC, et al. Pediatr Nephrol. 2018;33:763–777.

# FABHALTA®: The first and only approved treatment for IgA nephropathy that targets the AP[1,2]

A complement inhibitor that specifically binds to Factor B, inhibiting the AP with the aim of reducing glomerular inflammation* and complement-mediated kidney injury[1–4]




## Act on AP overactivation with FABHALTA®[1,3]

Adapted from Karoui KE, et al. J Am Soc Nephrol. 2024[5] and Tesař V, et al. Kidney Int Rep. 2023.[6]

* Based on proteomics analysis and a Phase 2 study.[3,4]

## Abbreviations

AP, alternative pathway; C3, complement component 3; C5, complement component 5; IgA, immunoglobulin A.

## References

1. Rizk DV, et al. Kidney Int Rep. 2023;8:968–979.
2. FABHALTA® US Prescribing Information - PLACEHOLDER FOR CN LABEL.
3. Zhang H, et al. Kidney Int. 2024;105:189–199.
4. Grioni A, et al. J Am Soc Nephrol. 2023;34(11S):p598.
5. El Karoui K, et al. J Am Soc Nephrol. 2024;35:103–116.
6. Tesař V, et al. Kidney Int Rep. 2023;8:1730–1740.

# FABHALTA®: Act on overactivation of the AP in IgA nephropathy[1,2]

**Target the IgA nephropathy-specific driver of nephron loss, with the aim of reducing glomerular inflammation* and complement-mediated kidney injury[2–4]**

**Rapid and sustained reduction in proteinuria†‡, a key marker of kidney outcomes in IgA nephropathy[3,5–7]**

**Improvement in haematuria†§, a proposed marker of glomerular inflammation[5,8,9]**

200 mg

**Convenient twice-daily oral dosing[10]**

**Choose a new route for your patients with IgA nephropathy[1,5,10]**

* Based on proteomics analysis and a Phase 2 study.[2,4] † Interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[5] ‡ Rapid – as early as Week 2. Sustained – continued through to Month 9.[5] § Based on a *post-hoc* analysis.[8]

## Abbreviations

AP, alternative pathway; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy.

## References

1. Rizk DV, et al. Kidney Int Rep. 2023;8:968–979.
2. Zhang H, et al. Kidney Int. 2024;105:189–199.
3. Floege J, et al. Kidney Int. 2025;107:640–651.
4. Grioni A, et al. J Am Soc Nephrol. 2023;34(11S):p598.
5. Perkovic V, et al. N Engl J Med. 2025;392:531–543.
6. Inker LA, et al. Am J Kidney Dis. 2021;78:340–349.
7. Thompson A, et al. Clin J Am Soc Nephrol. 2019;14:469–481.
8. Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.
9. Bobart SA, et al. Nephrol Dial Transplant. 2021;36:840–847.
10. FABHALTA® US Prescribing Information - PLACEHOLDER FOR CN LABEL.

# APPLAUSE-IgAN: Phase 3, multicentre, randomised, double-blind, placebo-controlled study[1]

Study design | Baseline characteristics

**Study population: enrolled patients had proteinuria (24h-UPCR) ≥1 g/g despite maximally tolerated RASi for ≥90 days, with or without SGLT2i[1,2]**

**Other key inclusion criteria:[1,2]**

- Aged ≥18 years with biopsy-confirmed IgA nephropathy*
- eGFR ≥30 mL/min/1.73m$^2$

**Selected key exclusion criteria:[2]**

- Any secondary IgA nephropathy
- Prior IS treatment within 90 days before study treatment

Randomised 1:1

**FABHALTA® 200 mg BID + optimised supportive care†** (n=125‡)

**Placebo + optimised supportive care†** (n=125‡)

End of study

Option to roll over in open-label extension study

**Prespecified interim analysis**

**Final analysis**

**Screening period**

**Day 1**

**Month 9**
**Primary endpoint**
24h-UPCR at Month 9

**Month 24**
**Primary endpoint**
eGFR slope over 24 months

Adapted from Perkovic V, et al. N Engl J Med. 2025[1] and Perkovic V, et al. N Engl J Med. 2025. (Suppl).[2]

* Biopsy within 5 years for eGFR ≥45 mL/min/1.73m$^2$; biopsy within 2 years (with <50% tubulointerstitial fibrosis) for eGFR 30 to <45 mL/min/1.73m$^2$.[2] † Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[2] ‡ n values are for the interim efficacy analysis – the first 250 randomised patients from the main trial population who completed the Month 9 visit or discontinued by Month 9 as of the data cut-off.[1]

BID, twice daily; eGFR, estimated glomerular filtration rate; h, hour; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; IS, immunosuppressive; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**References: 1.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. **2.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

# APPLAUSE-IgAN: Baseline demographic and disease characteristics were balanced across arms*[1]



| Parameter | FABHALTA® n=125† | Placebo n=125† |
|---|---|---|
| **Age [years] – mean (SD)** | 39.3 (12.4) | 39.6 (12.6) |
| Male – n (%) | 71 (56.8) | 60 (48.0) |
| Female – n (%) | 54 (43.2) | 65 (52.0) |
| **Region** | | |
| Asia – n (%) | 64 (51.2) | 64 (51.2) |
| Non-Asia – n (%) | 61 (48.8) | 61 (48.8) |
| **Baseline 24h-UPCR [g/g] – median (IQR)** | 1.8 (1.4, 2.7) | 1.9 (1.5, 2.8) |
| <2 g/g – n (%) | 71 (56.8) | 67 (53.6) |
| ≥2 g/g – n (%) | 54 (43.2) | 58 (46.4) |
| **Baseline eGFR [mL/min/1.73m$^2$] – mean (SD)** | 62.7 (26.0) | 65.5 (26.7) |

Adapted from Perkovic V, et al. N Engl J Med. 2025.[1]

* Abbreviated table.[1] † Interim efficacy analysis population.[1] ‡ Not all MEST-C components were available for all patients.[1] § Summarised for 249 patients with measurements available in sitting position.[1] || Haematuria was defined as a dipstick reading of more than 1+.[1] ¶ Number not shown to prevent unblinding of individual patient information.[1] ** Patients receiving glucocorticoids (in doses of >7.5 mg/day of prednisone equivalent) or other immunosuppressive medications had to stop taking these agents within 90 days before starting the trial regimen.[1]

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; h, hour; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; IQR, interquartile range; MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents; SD, standard deviation; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**Reference: 1.** Perkovic V, et al. N Engl J Med. 2025;392:531–543.

# APPLAUSE-IgAN: Baseline demographic and disease characteristics were balanced across arms*[1]



| Parameter | FABHALTA® n=125† | Placebo n=125† |
|---|---|---|
| **Region** | | |
| Asia – n (%) | 64 (51.2) | 64 (51.2) |
| Non-Asia – n (%) | 61 (48.8) | 61 (48.8) |
| **Baseline 24h-UPCR [g/g] – median (IQR)** | 1.8 (1.4, 2.7) | 1.9 (1.5, 2.8) |
| <2 g/g – n (%) | 71 (56.8) | 67 (53.6) |
| ≥2 g/g – n (%) | 54 (43.2) | 58 (46.4) |
| **Baseline eGFR [mL/min/1.73m²] – mean (SD)** | 62.7 (26.0) | 65.5 (26.7) |
| 30 to <45 mL/min/1.73m² – n (%) | 36 (28.8) | 34 (27.2) |
| ≥45 mL/min/1.73m² – n (%) | 89 (71.2) | 91 (72.8) |
| **Time from kidney biopsy to baseline [years] – median (IQR)** | 1.3 (0.5, 2.8) | 0.8 (0.3, 2.6) |

Adapted from Perkovic V, et al. N Engl J Med. 2025.[1]

* Abbreviated table.[1] † Interim efficacy analysis population.[1] ‡ Not all MEST-C components were available for all patients.[1] § Summarised for 249 patients with measurements available in sitting position.[1] || Haematuria was defined as a dipstick reading of more than 1+.[1] ¶ Number not shown to prevent unblinding of individual patient information.[1] ** Patients receiving glucocorticoids (in doses of >7.5 mg/day of prednisone equivalent) or other immunosuppressive medications had to stop taking these agents within 90 days before starting the trial regimen.[1]

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; h, hour; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; IQR, interquartile range; MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents; SD, standard deviation; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**Reference: 1.** Perkovic V, et al. N Engl J Med. 2025;392:531–543.

Study design | Baseline characteristics

# APPLAUSE-IgAN: Baseline demographic and disease characteristics were balanced across arms*[1]

| Parameter | FABHALTA® n=125† | Placebo n=125† |
|---|---|---|
| **Baseline eGFR [mL/min/1.73m²] – mean (SD)** | 62.7 (26.0) | 65.5 (26.7) |
| 30 to <45 mL/min/1.73m² – n (%) | 36 (28.8) | 34 (27.2) |
| ≥45 mL/min/1.73m² – n (%) | 89 (71.2) | 91 (72.8) |
| **Time from kidney biopsy to baseline [years] – median (IQR)** | 1.3 (0.5, 2.8) | 0.8 (0.3, 2.6) |
| **MEST-C score‡ – %** | | |
| M1 / M0 | 60.8 / 32.0 | 64.0 / 31.2 |
| E1 / E0 | 28.8 / 63.2 | 28.8 / 64.8 |
| S1 / S0 | 69.6 / 22.4 | 71.2 / 23.2 |
| T1 or T2 / T0 | 38.4 / 54.4 | 42.4 / 53.6 |
| C1 / C2 / C0 | 26.4 / 1.6 / 60.8 | 16.0 / 1.6 / 68.0 |

Adapted from Perkovic V, et al. N Engl J Med. 2025.[1]

* Abbreviated table.[1] † Interim efficacy analysis population.[1] ‡ Not all MEST-C components were available for all patients.[1] § Summarised for 249 patients with measurements available in sitting position.[1] || Haematuria was defined as a dipstick reading of more than 1+.[1] ¶ Number not shown to prevent unblinding of individual patient information.[1] ** Patients receiving glucocorticoids (in doses of >7.5 mg/day of prednisone equivalent) or other immunosuppressive medications had to stop taking these agents within 90 days before starting the trial regimen.[1]

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; h, hour; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; IQR, interquartile range; MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents; SD, standard deviation; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**Reference: 1.** Perkovic V, et al. N Engl J Med. 2025;392:531–543.

# APPLAUSE-IgAN: Baseline demographic and disease characteristics were balanced across arms*[1]



| Parameter | FABHALTA® n=125† | Placebo n=125† |
|---|---|---|
| S1 / S0 | 69.6 / 22.4 | 71.2 / 23.2 |
| T1 or T2 / T0 | 38.4 / 54.4 | 42.4 / 53.6 |
| C1 / C2 / C0 | 26.4 / 1.6 / 60.8 | 16.0 / 1.6 / 68.0 |
| **Systolic blood pressure§ [mmHg] – mean (SD)** | 121.9 (10.7) | 122.6 (10.8) |
| **Diastolic blood pressure§ [mmHg] – mean (SD)** | 77.7 (8.1) | 78.3 (8.8) |
| **Haematuria at baseline‖ – n (%)** | 97 (77.6) | 90 (72.0) |
| **ACEi/ARB use at baseline – %** | >98¶ | >98¶ |
| **SGLT2i use at baseline – n (%)** | 18 (14.4) | 14 (11.2) |
| **Previous glucocorticoids for IgA nephropathy** – n (%)** | 37 (29.6) | 36 (28.8) |
| **Previous use of other immunosuppressants for IgA nephropathy** – n (%)** | 19 (15.2) | 11 (8.8) |

Adapted from Perkovic V, et al. N Engl J Med. 2025.[1]

* Abbreviated table.[1] † Interim efficacy analysis population.[1] ‡ Not all MEST-C components were available for all patients.[1] § Summarised for 249 patients with measurements available in sitting position.[1] ‖ Haematuria was defined as a dipstick reading of more than 1+.[1] ¶ Number not shown to prevent unblinding of individual patient information.[1] ** Patients receiving glucocorticoids (in doses of >7.5 mg/day of prednisone equivalent) or other immunosuppressive medications had to stop taking these agents within 90 days before starting the trial regimen.[1]

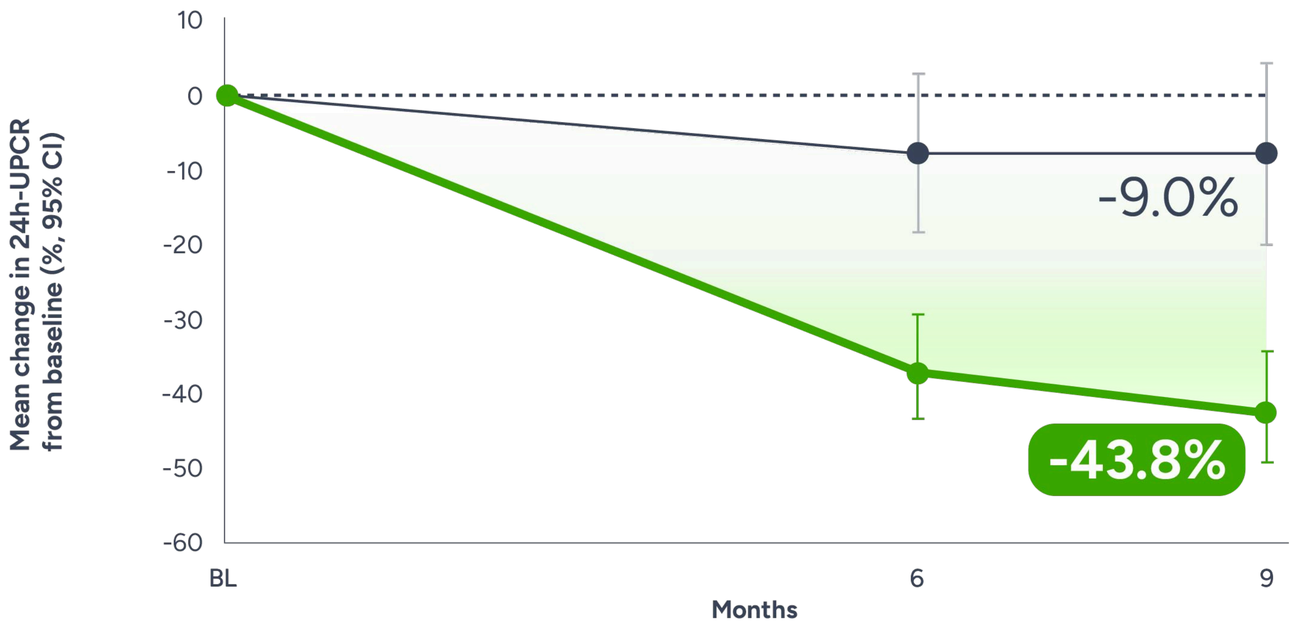
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; h, hour; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; IQR, interquartile range; MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents; SD, standard deviation; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**Reference: 1.** Perkovic V, et al. N Engl J Med. 2025;392:531–543.

## IA: 24h-UPCR Primary endpoint[1]

# FABHALTA® significantly reduced proteinuria vs placebo at Month 9*[1]

### Change in 24h-UPCR from baseline to Month 9†[1]




| | | | |
|---|---|---|---|
| FABHALTA® | 125 | 115 | 118 |
| Placebo | 125 | 112 | 106 |

**38.3%**

**Relative UPCR reduction[1]**

(95% CI, 26.0, 48.6; p<0.001)

Prespecified subgroup analysis ›

Exploratory subgroup analysis ›

## Offer a clear route to proteinuria reduction with FABHALTA®[1]

Adapted from Perkovic V, et al. N Engl J Med. 2025.[1]

* Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[1] † Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[2]

## Abbreviations

BL, baseline; CI, confidence interval; h, hour; IA, interim analysis; IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

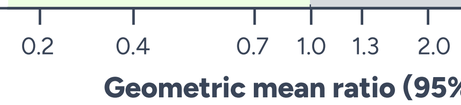
## References

1. Perkovic V, et al. N Engl J Med. 2025;392:531–543.
2. Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

## Prespecified subgroup analysis of primary endpoint[1]

# FABHALTA® delivered consistent proteinuria reductions vs placebo across subgroups at Month 9*[2,3]

| Group | FABHALTA® n/N† | Placebo n/N† | FABHALTA® | Placebo | FABHALTA® vs placebo % reduction in 24h-UPCR at Month 9 (95% CI) |
|---|---|---|---|---|---|
| **Overall** | 118/125 | 106/125 | | | 38.3 (26.0, 48.6) p<0.001‡ |
| **Gender** | | | | | |
| Male | 68/71 | 49/60 | | | 35.5 (17.4, 49.7) |
| Female | 50/54 | 57/65 | | | 42.6 (24.5, 56.4) |
| **Geographic region** | | | | | |
| Asia | 63/64 | 55/64 | | | 31.6 (13.4, 46.0) |
| Non-Asia | 55/61 | 51/61 | | | 45.5 (28.3, 58.5) |
| **Baseline 24h-UPCR category** | | | | | |
| ≥1.5 g/g | 73/80 | 76/91 | | | 41.2 (26.0, 53.2) |
| <1.5 g/g | 45/45 | 30/34 | | | 27.3 (2.4, 45.9) |




N: Number of all patients included in the analysis (with non-missing baseline and covariates).[2]
n: Number of patients with values non-missing/not imputed.[2]

Adapted from Perkovic V, et al. N Engl J Med. 2025[2] and Perkovic V, et al. N Engl J Med. 2025. (Suppl).[3]

* Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[3] † Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[2]
‡ Two-sided p-value.[2]

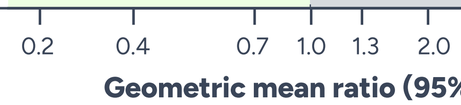
CI, confidence interval; eGFR, estimated glomerular filtration rate; h, hour; IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**References: 1.** Rizk DV, et al. NKF 2024, 14–18 May; Long Beach, CA. Oral 448. **2.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. **3.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

## Prespecified subgroup analysis of primary endpoint[1]

# FABHALTA® delivered consistent proteinuria reductions vs placebo across subgroups at Month 9*[2,3]

| Group | FABHALTA® n/N† | Placebo n/N† | FABHALTA® | Placebo | FABHALTA® vs placebo % reduction in 24h-UPCR at Month 9 (95% CI) |
|---|---|---|---|---|---|
| Asia | 63/64 | 55/64 | | | 31.6 (13.4, 46.0) |
| Non-Asia | 55/61 | 51/61 | | | 45.5 (28.3, 58.5) |
| **Baseline 24h-UPCR category** | | | | | |
| ≥1.5 g/g | 73/80 | 76/91 | | | 41.2 (26.0, 53.2) |
| <1.5 g/g | 45/45 | 30/34 | | | 27.3 (2.4, 45.9) |
| ≥2 g/g | 47/54 | 47/58 | | | 41.2 (20.9, 56.4) |
| <2 g/g | 71/71 | 59/67 | | | 35.0 (18.8, 48.0) |
| **Baseline eGFR category** | | | | | |
| 30 to <45 mL/min/1.73m² | 32/36 | 27/34 | | | 45.4 (25.3, 60.1) |
| ≥45 mL/min/1.73m² | 86/89 | 79/91 | | | 35.1 (19.0, 48.0) |




N: Number of all patients included in the analysis (with non-missing baseline and covariates).[2]
n: Number of patients with values non-missing/not imputed.[2]

Adapted from Perkovic V, et al. N Engl J Med. 2025[2] and Perkovic V, et al. N Engl J Med. 2025. (Suppl).[3]

* Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[3] † Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[2]
‡ Two-sided p-value.[2]

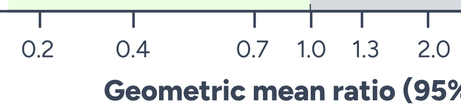
CI, confidence interval; eGFR, estimated glomerular filtration rate; h, hour; IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**References: 1.** Rizk DV, et al. NKF 2024, 14–18 May; Long Beach, CA. Oral 448. **2.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. **3.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

## Exploratory subgroup analysis of primary endpoint[1]

# FABHALTA® delivered consistent proteinuria reductions vs placebo across subgroups at Month 9*[2,3]

| Group | FABHALTA® n/N† | Placebo n/N† | FABHALTA® | Placebo | FABHALTA® vs placebo % reduction in 24h-UPCR at Month 9 (95% CI) |
|---|---|---|---|---|---|
| **Overall** | 118/125 | 106/125 | | | 38.3 (26.0, 48.6) p<0.001‡ |
| **Dipstick haematuria at baseline** | | | | | |
| ≥1 | 93/97 | 74/90 | | | 35.4 (21.8, 46.7) |
| Negative/trace | 20/23 | 28/30 | | | 42.8 (6.1, 65.2) |
| **MEST-C score** | | | | | |
| **M score§** | | | | | |
| M1 | 69/76 | 66/80 | | | 44.3 (28.7, 56.5) |
| M0 | 40/40 | 35/39 | | | 20.8 (-6.1, 40.9) |
| **E score§** | | | | | |
| E1 | 32/36 | 30/36 | | | 39.2 (19.1, 4.3) |




N: Number of all patients included in the analysis (with non-missing baseline and covariates).[2]
n: Number of patients with values non-missing/not imputed.[2]

Adapted from Perkovic V, et al. N Engl J Med. 2025[2] and Perkovic V, et al. N Engl J Med. 2025. (Suppl).[3]

* Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[3] † Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[2] ‡ Two-sided p-value.[2] § Based on qualifying biopsy as per inclusion criteria; assessed locally, documented by the investigator at screening.[2]

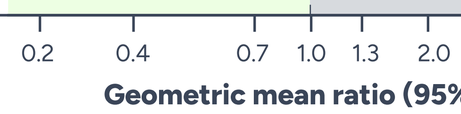
CI, confidence interval; h, hour; IgAN, immunoglobulin A nephropathy; MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**References: 1.** Rizk DV, et al. NKF 2024, 14–18 May; Long Beach, CA. Oral 448. **2.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. **3.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

## Exploratory subgroup analysis of primary endpoint[1]

# FABHALTA® delivered consistent proteinuria reductions vs placebo across subgroups at Month 9*[2,3]

| Group | FABHALTA® n/N† | Placebo n/N† | FABHALTA® | Placebo | FABHALTA® vs placebo % reduction in 24h-UPCR at Month 9 (95% CI) |
|---|---|---|---|---|---|
| E0 | 76/76 | 69/81 | | | 37.4 (20.1, 50.9) |
| **S score§** | | | | | |
| S1 | 81/87 | 81/89 | | | 35.3 (19.2, 48.2) |
| S0 | 27/28 | 19/29 | | | 39.4 (13.2, 57.7) |
| **T score§** | | | | | |
| T1 or T2 | 46/48 | 44/53 | | | 34.4 (15.0, 49.4) |
| T0 | 63/68 | 58/67 | | | 40.3 (21.8, 54.5) |
| **C score§** | | | | | |
| C1 or C2 | 32/35 | 17/22 | | | 45.5 (15.0, 65.0) |
| C0 | 72/76 | 72/85 | | | 32.5 (15.2, 46.2) |




N: Number of all patients included in the analysis (with non-missing baseline and covariates).[2]
n: Number of patients with values non-missing/not imputed.[2]

Adapted from Perkovic V, et al. N Engl J Med. 2025[2] and Perkovic V, et al. N Engl J Med. 2025. (Suppl).[3]

* Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[3] † Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[2] ‡ Two-sided p-value.[2] § Based on qualifying biopsy as per inclusion criteria; assessed locally, documented by the investigator at screening.[2]

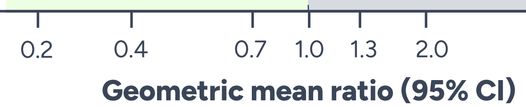
CI, confidence interval; h, hour; IgAN, immunoglobulin A nephropathy; MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**References: 1.** Rizk DV, et al. NKF 2024, 14–18 May; Long Beach, CA. Oral 448. **2.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. **3.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

## Exploratory subgroup analysis of primary endpoint[1]

# FABHALTA® delivered consistent proteinuria reductions vs placebo across subgroups at Month 9*[2,3]

| Group | FABHALTA® n/N† | Placebo n/N† | FABHALTA® | Placebo | FABHALTA® vs placebo % reduction in 24h-UPCR at Month 9 (95% CI) |
|---|---|---|---|---|---|
| **SGLT2i use at baseline** | | | | | |
| Yes | 16/18 | 12/14 | | | 36.7 (4.4, 58.1) |
| No | 102/107 | 94/111 | | | 38.1 (24.4, 49.2) |
| **Prior use of glucocorticoids** | | | | | |
| Yes | 36/37 | 30/36 | | | 28.7 (5.7, 46.0) |
| No | 82/88 | 76/89 | | | 42.5 (27.7, 54.3) |
| **Prior use of glucocorticoids/ immunosuppressants** | | | | | |
| Yes | 39/40 | 32/38 | | | 29.5 (7.9, 46.0) |
| No | 79/85 | 74/87 | | | 42.6 (27.4, 54.6) |




N: Number of all patients included in the analysis (with non-missing baseline and covariates).[2]
n: Number of patients with values non-missing/not imputed.[2]

Adapted from Perkovic V, et al. N Engl J Med. 2025[2] and Perkovic V, et al. N Engl J Med. 2025. (Suppl).[3]

* Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[3] † Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[2] ‡ Two-sided p-value.[2] § Based on qualifying biopsy as per inclusion criteria; assessed locally, documented by the investigator at screening.[2]

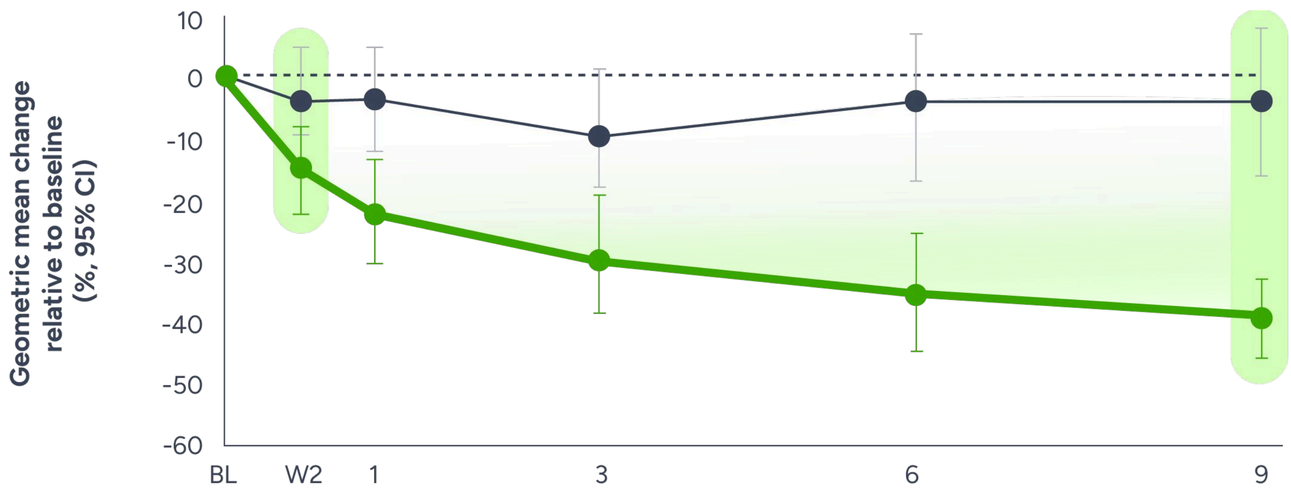
CI, confidence interval; h, hour; IgAN, immunoglobulin A nephropathy; MEST-C, Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

**References: 1.** Rizk DV, et al. NKF 2024, 14–18 May; Long Beach, CA. Oral 448. **2.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. **3.** Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

## IA: UPCR-FMV Supplementary analysis of primary endpoint

# FABHALTA® delivered rapid and sustained proteinuria reduction vs placebo*[1]

### Change from baseline in UPCR-FMV from baseline to Month 9†[1]




| | BL | W2 | 1 | 3 | 6 | 9 |
|---|---|---|---|---|---|---|
| FABHALTA® | 124 | 116 | 116 | 119 | 114 | 115 |
| Placebo | 123 | 120 | 114 | 133 | 110 | 104 |

**35.8%**

**Relative UPCR-FMV reduction[1]**

(95% CI, 22.6, 46.7; nominal p<0.0001)

## Proteinuria reductions were observed as early as Week 2 in the FABHALTA® arm and continued to decrease through to Month 9[1]

Adapted from Rizk DV, et al. NKF 2024.[1]

* Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[2] † Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[3]

## Abbreviations

BL, baseline; CI, confidence interval; FMV, first morning void; IA, interim analysis; IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio; W, week.

## References

1. Rizk DV, et al. NKF 2024, 14–18 May; Long Beach, CA. Oral 448.
2. Perkovic V, et al. N Engl J Med. 2025;392:531–543.
3. Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

## IA: secondary endpoint[1]

# ~2× more patients* achieved proteinuria <1 g/g with FABHALTA® vs placebo at Month 9†[2]

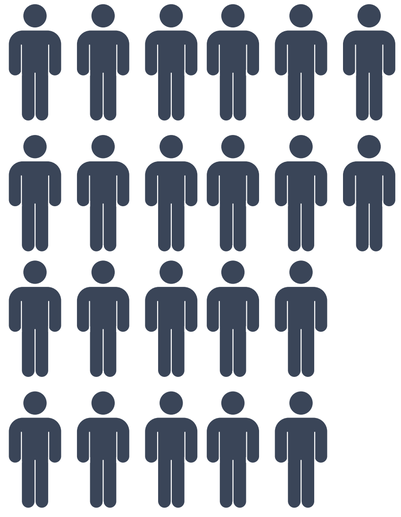
### Proportion of patients reaching 24h-UPCR <1 g/g at Month 9‡§[2]

**FABHALTA®**



**42.5%**
(95% CI, 34.5, 50.5)
n/N=54/119

**Placebo**



**21.9%**
(95% CI, 14.8, 29.0)
n/N=24/110

N: Number of patients with response variable defined and not imputed as per the intercurrent event handling strategy.[2]
n: Number of patients who reached the endpoint and were not imputed per the intercurrent event handling strategy.[2]

* Odds ratio 3.122; 95% CI, 1.684, 5.787; p=0.0002 (nominal one-sided p-value).[2] † Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[1] ‡ Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[3] § Without receiving alternative/rescue medication or initiating kidney replacement therapy.[2]

## Abbreviations

CI, confidence interval; h, hour; IA, interim analysis; IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

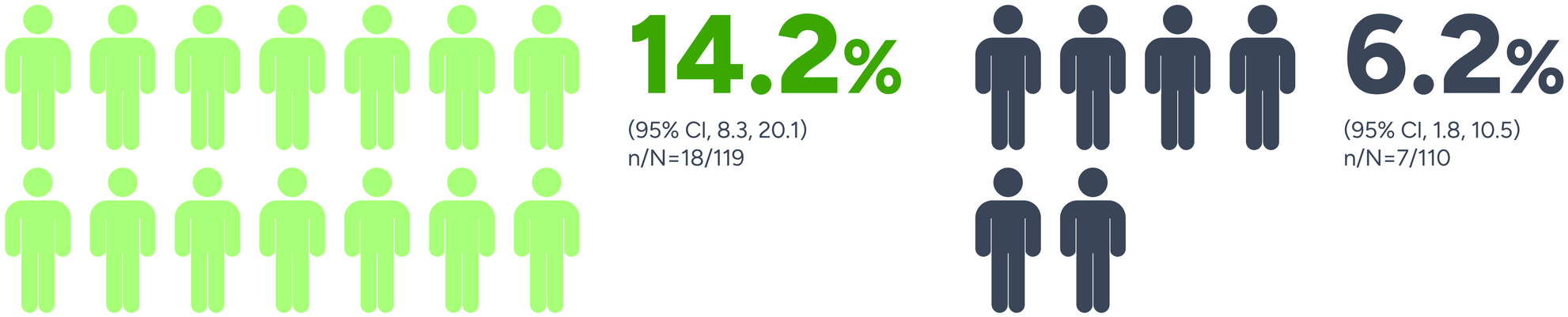
## References

1. Perkovic V, et al. N Engl J Med. 2025;392:531–543.
2. Rizk DV, et al. NKF 2024, 14–18 May; Long Beach, CA. Oral 448.
3. Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

## IA: supplementary analysis of secondary endpoint

# More than twice as many patients* achieved proteinuria <0.5 g/g with FABHALTA® vs placebo at Month 9†[1]

### Proportion of patients reaching 24h-UPCR <0.5 g/g at Month 9‡§[1]




N: Number of patients with response variable defined and not imputed as per the intercurrent event handling strategy.[1]
n: Number of patients who reached the endpoint and were not imputed per the intercurrent event handling strategy.[1]

* Odds ratio 2.656; 95% CI, 1.040, 6.781.[1] † Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[2] ‡ Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[1] § Without receiving alternative/rescue medication or initiating kidney replacement therapy.[1]

## Abbreviations

CI, confidence interval; h, hour; IA, interim analysis; IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

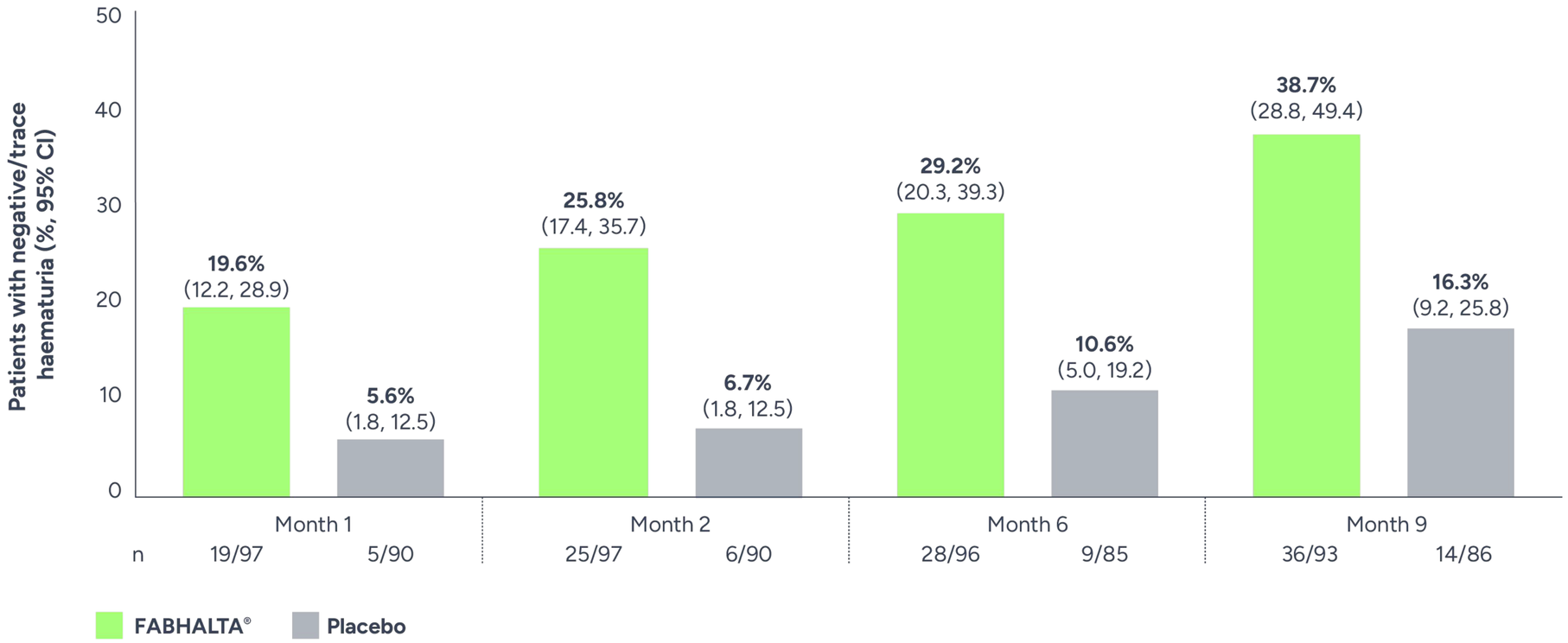
## References

1. Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.
2. Perkovic V, et al. N Engl J Med. 2025;392:531–543.

## IA: *post-hoc* analysis[1]

# More than one-third of patients achieved no/trace haematuria with FABHALTA® at Month 9*[1]

### Proportion of patients with dipstick haematuria of 1+ or more at baseline becoming negative/trace over time†[1]




n: Number of patients with non-missing values at each visit. At each post-treatment time point, only patients with a value at both baseline and that visit are counted.[1]

Adapted from Perkovic V, et al. N Engl J Med. 2025. (Suppl).[1]

* Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[2] † Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[1]

## Abbreviations

CI, confidence interval; IA, interim analysis; IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

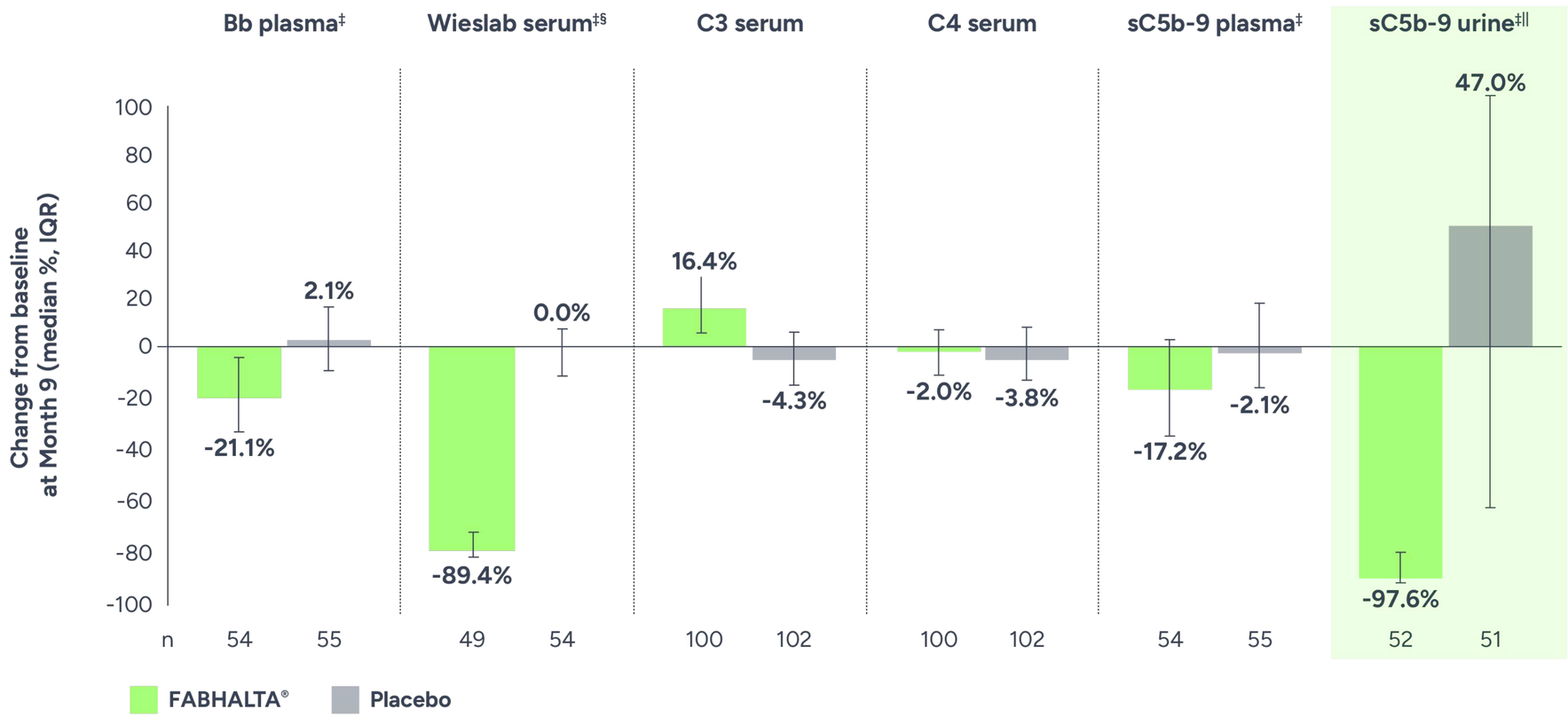
## References

1. Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.
2. Perkovic V, et al. N Engl J Med. 2025;392:531–543.

## IA: exploratory endpoint[1]

# Biomarker changes demonstrated AP inhibition with FABHALTA® at Month 9*[1,2]

### Change in complement pathway biomarkers from baseline to Month 9†[2]




## Act on AP overactivation with FABHALTA®[2]

Adapted from Perkovic V, et al. N Engl J Med. 2025. (Suppl).[2]

* Data from the interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[1] † Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[2]
‡ Available only in a subset of patients.[2] § Serum Wieslab is a measure of AP activity.[2] || Urinary terminal MAC (sC5b-9) is a key contributor to kidney injury in IgA nephropathy.[1]

## Abbreviations

AP, alternative pathway; C3, complement component 3; C4, complement component 4; IA, interim analysis; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; IQR, interquartile range; MAC, membrane attack complex; RASi, renin-angiotensin system inhibitor; sC5b-9, soluble complement components 5b-9; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

## References

1. Perkovic V, et al. N Engl J Med. 2025;392:531–543.
2. Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

# FABHALTA® is well tolerated and has a favourable safety profile[1]

## APPLAUSE-IgAN: Interim analysis of safety at Month 9[1]

| Parameter | FABHALTA®* n=222†; n (%) | Placebo* n=221†; n (%) |
|---|---|---|
| **AEs‡** | | |
| Any AE | 138 (62.2) | 153 (69.2) |
| **AEs occurring in ≥5% of patients in either group‡** | | |
| COVID-19 | 31 (14.0) | 37 (16.7) |
| Upper respiratory tract infection | 20 (9.0) | 16 (7.2) |
| Nasopharyngitis | 11 (5.0) | 16 (7.2) |
| Headache | 9 (4.1) | 12 (5.4) |
| Hypertension | 4 (1.8) | 13 (5.9) |
| **Serious AEs‡** | 18 (8.1) | 11 (5.0) |
| **Severe AEs‡** | 7 (3.2) | 7 (3.2) |
| **AEs leading to treatment discontinuation** | 6 (2.7) | 6 (2.7) |
| **Death** | 0 | 0 |

- **The majority of AEs were mild to moderate in severity[1]**
- **No deaths were reported in either arm[1]**

Adapted from Perkovic V, et al. N Engl J Med. 2025.[1]

* Patients in both the FABHALTA® and placebo arms also received maximally tolerated RASi ± SGLT2i.[2] † Safety was assessed in all patients in the main trial population who received ≥1 dose of FABHALTA® or placebo at the time of data cut-off for the interim analysis.[1] ‡ Included are events that started during the treatment period, or events that were present before but increased in severity during the treatment period.[1]

## Abbreviations

AE, adverse event; COVID-19, coronavirus disease 2019; IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

## References

1. Perkovic V, et al. N Engl J Med. 2025;392:531–543.
2. Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.

# FABHALTA®: A single capsule taken orally twice a day[1]

Continuous treatment with FABHALTA® should be considered; discontinuation may lead to a return of proteinuria levels to near baseline within 30 days due to complement reactivation, based on a *post-hoc* analysis of pooled data from a Phase 2 study (N=26)[2]

**Twice-daily oral dosing[1]**

**No dose adjustments or titrations[1]**

**No food restrictions[1]**

## References

1. FABHALTA® US Prescribing Information - PLACEHOLDER FOR CN LABEL.
2. Barratt J, et al. ERA 2025, 4–7 June; Vienna, Austria and virtual. Oral 2626.

# Vaccination requirements when starting FABHALTA® to minimise the risk of serious infections[1]

**Required vaccinations:**

*N. meningitidis*[1]
*S. pneumoniae*[1]

**Recommended vaccinations:**

*H. influenzae* type B[1]
Where vaccines are available

Vaccinations are recommended[1]

At least 2 weeks **before** starting FABHALTA®

**OR**

As soon as possible **after** starting FABHALTA®
(with antibiotic prophylaxis until 2 weeks after vaccination)

**The use of complement inhibitors like FABHALTA® may predispose patients to serious, life-threatening or fatal infections caused by encapsulated bacteria[1]**

Please refer to the Prescribing Information for the full warnings and precautions.

## Reference

1. FABHALTA® US Prescribing Information - PLACEHOLDER FOR CN LABEL.

# Act on AP overactivation with FABHALTA® to help mitigate the uncertainty of IgA nephropathy[1–4]

**Target the IgA nephropathy-specific driver of nephron loss, with the aim of reducing glomerular inflammation* and complement-mediated kidney injury[4–6]**

**Rapid and sustained reduction in proteinuria†‡, a key marker of kidney outcomes in IgA nephropathy[5,7–9]**

**Improvement in haematuria†§, a proposed marker of glomerular inflammation[7,10,11]**

200 mg

**Convenient twice-daily oral dosing[12]**

**FABHALTA®: A new route for your patients with IgA nephropathy[1,7,12]**

* Based on proteomics analysis and a Phase 2 study.[4,6] † Interim efficacy analysis of the Phase 3 APPLAUSE-IgAN study at 9 months.[7] ‡ Rapid – as early as Week 2. Sustained – continued through to Month 9.[7] § Based on a *post-hoc* analysis.[10]

## Abbreviations

AP, alternative pathway; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy.

## References


1. Rizk DV, et al. Kidney Int Rep. 2023;8:968–979.
2. Kwon CS, et al. J Health Econ Outcomes Res. 2021;8:36–45.
3. Shen X, et al. Nephrol Dial Transplant. 2025;40:1137–1146.
4. Zhang H, et al. Kidney Int. 2024;105:189–199.
5. Floege J, et al. Kidney Int. 2025;107:640–651.
6. Grioni A, et al. J Am Soc Nephrol. 2023;34(11S):p598.
7. Perkovic V, et al. N Engl J Med. 2025;392:531–543.
8. Inker LA, et al. Am J Kidney Dis. 2021;78:340–349.
9. Thompson A, et al. Clin J Am Soc Nephrol. 2019;14:469–481.
10. Perkovic V, et al. N Engl J Med. 2025;392:531–543. Supplementary appendix.
11. Bobart SA, et al. Nephrol Dial Transplant. 2021;36:840–847.
12. FABHALTA® US Prescribing Information - PLACEHOLDER FOR CN LABEL.

# Prescribing Information

Lorem ipsum dolor sit amet consectetur adipiscing elit. Mus donec rhoncus eros lobortis nulla molestie mattis. Cras eleifend turpis fames primis vulputate ornare sagittis. Egestas iaculis massa nisl malesuada lacinia integer nunc. Finibus facilisis dapibus etiam interdum tortor ligula congue. Sit amet consectetur adipiscing elit quisque faucibus ex. Eros lobortis nulla molestie mattis scelerisque maximus eget. Fames primis vulputate ornare sagittis vehicula praesent dui. Nisl malesuada lacinia integer nunc posuere ut hendrerit. Etiam interdum tortor ligula congue sollicitudin erat viverra. Adipiscing elit quisque faucibus ex sapien vitae pellentesque. Molestie mattis scelerisque maximus eget fermentum odio phasellus. Ornare sagittis vehicula praesent dui felis venenatis ultrices. Integer nunc posuere ut hendrerit semper vel class. Ligula congue sollicitudin erat viverra ac tincidunt nam. Faucibus ex sapien vitae pellentesque sem placerat in. Maximus eget fermentum odio phasellus non purus est. Praesent dui felis venenatis ultrices proin libero feugiat. Ut hendrerit semper vel class aptent taciti sociosqu. Erat viverra ac tincidunt nam porta elementum a. Vitae pellentesque sem placerat in id cursus mi. Odio phasellus non purus est efficitur laoreet mauris. Venenatis ultrices proin libero feugiat tristique accumsan maecenas. Vel class aptent taciti sociosqu ad litora torquent. Tincidunt nam porta elementum a enim euismod quam. Placerat in id cursus mi pretium tellus duis. Purus est efficitur laoreet mauris pharetra vestibulum fusce. Libero feugiat tristique accumsan maecenas potenti ultricies habitant. Taciti sociosqu ad litora torquent per conubia nostra. Elementum a enim euismod quam justo lectus commodo. Cursus mi pretium tellus duis convallis tempus leo. Laoreet mauris pharetra vestibulum fusce erat viverra ac tincidunt. Venenatis ultrices proin libero feugiat tristique accumsan maecenas. Vel class aptent taciti sociosqu ad litora torquent. Tincidunt nam porta elementum a enim euismod quam. Placerat in id cursus mi pretium tellus duis. Purus est efficitur laoreet mauris pharetra commodo. Cursus mi pretium tellus duis convallis tempus leo. Laoreet mauris pharetra le vestibulum fusce erat viverra ac tincidunt

Libero feugiat tristique accumsan maecenas potenti ultricies habitant. Taciti sociosqu ad litora torquent per conubia nostra. Elementum a enim euismod quam justo lectus commodo. Cursus mi pretium tellus duis convallis tempus leo. Laoreet mauris pharetra vestibulum fusce dictum risus blandit. Accumsan maecenas potenti ultricies habitant morbi senectus netus. Litora torquent per conubia nostra inceptos himenaeos orci. Euismod quam justo lectus commodo augue arcu dignissim. Tellus duis convallis tempus leo eu aenean sed. Vestibulum fusce dictum risus blandit quis suspendisse aliquet. Ultricies habitant morbi senectus netus suscipit auctor curabitur. Conubia nostra inceptos himenaeos [illegible] penatibus. Lectus commodo augue arcu [illegible] imperdiet. [illegible] FPO [illegible] natoque penat[illegible] platea. Na[illegible] penatibus et magnis [illegible] nascetur. Aliqu[illegible] perdiet mollis nullam volutpat porttitor ull[illegible]per rutrum. Urna tempor pulvinar vivamus fringilla lacus nec me[illegible]. Sodales consequat magna ante condimentum neque at luctus. Cubilia curae hac habitasse platea dictumst lorem ipsum. Magnis dis parturient montes nascetur ridiculus mus donec. Nullam volutpat porttitor ullamcorper rutrum gravida cras eleifend. Vivamus fringilla lacus nec metus bibendum egestas iaculis. Ante condimentum neque at luctus nibh erat viverra ac tincidunt nullam varius natoque penatibus et magnis dis. Arcu dignissim velit aliquam imperdiet mollis nullam volutpat. Aenean sed diam urna tempor pulvinar vivamus fringilla. Suspendisse aliquet nisi sodales consequat magna ante condimentum. Auctor curabitur facilisi cubilia curae hac habitasse platea. Natoque penatibus et magnis dis parturient fringilla lacus metus bibendum iaculis. Ante condimentum neque at luctus

Vestibulum fusce dictum risus blandit quis suspendisse aliquet. Commodo augue arcu dignissim velit aliquam imperdiet mollis. Suscipit auctor curabitur facilisi cubilia curae hac habitasse. Urna tempor pulvinar vivamus fringilla lacus nec metus. Dis parturient montes nascetur ridiculus mus donec rhoncus. Neque at luctus nibh finibus facilisis dapibus etiam. Cras eleifend turpis fames primis vulputate ornare sagittis. Amet consectetur adipiscing elit quisque faucibus ex sapien. Lacinia integer nunc posuere ut hendrerit semper vel. Maximus eget fermentum odio phasellus non purus est. Viverra ac tincidunt nam porta elementum a enim. Proin libero feugiat tristique accumsan maecenas potenti ultricies. Cursus mi pretium tellus duis convallis tempus leo. Torquent per conubia nostra inceptos himenaeos orci varius. Mus donec rhoncus eros lobortis nulla molestie mattis. Cras eleifend turpis fames primis vulputate ornare sagittis. Egestas iaculis massa nisl malesuada lacinia integer nunc. Finibus facilisis dapibus etiam interdum tortor ligula congue. Sit amet consectetur adipiscing elit quisque faucibus ex. Eros lobortis nulla molestie mattis scelerisque maximus eget. Fames primis vulputate ornare sagittis vehicula praesent dui. Nisl malesuada lacinia integer nunc posuere ut hendrerit. Etiam interdum tortor ligula congue sollicitudin erat viverra. Adipiscing elit quisque faucibus ex sapien vitae pellentesque. Molestie mattis scelerisque maximus eget fermentum odio phasellus. Ornare sagittis vehicula praesent dui felis venenatis ultrices. Integer nunc posuere ut hendrerit semper vel class. Ligula congue sollicitudin erat viverra ac tincidunt nam. Faucibus ex sapien vitae pellentesque sem placerat in. Maximus eget fermentum odio phasellus non purus est. Praesent dui felis venenatis faucibus ex sapien. Lacinia integer nunc posuere ut hendrerit semper vel. Maximus eget fermentum odio phasellus non purus est. Viverra ac tincidunt nam porta elementum a enim. Proin libero feugiat tristique accumsan maecenas potenti ultricies. Cursus mi pretium tellus duis convallis tempus leo. Torquent per integer nunc. Finibus facilisis dapibus etiam interdum tortor ligula congue. Sit amet consectetur adipiscing elit quisque faucibus ex.

Healthcare professionals are asked to report any suspected adverse reactions via [insert local national reporting system information] and to Novartis via [insert local medical information].