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# Nefecon treatment response in Asian and White patient populations with immunoglobulin A nephropathy: A 2-year analysis of the Phase 3 NefIgArd trial

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## INTRODUCTION

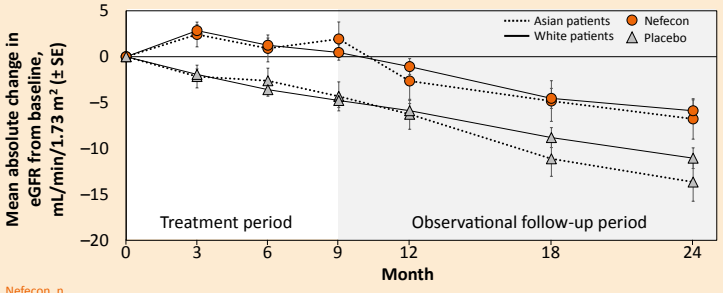
- People of **East Asian** ancestry **have the highest likelihood of all race categories to progress to kidney failure** as a result of IgAN[1]
- **Nefecon** is a novel, oral, targeted-release budesonide formulation specifically designed to treat IgAN **by acting locally in the distal ileum**[2]
- Nefecon has received full FDA approval to **reduce the loss of kidney function in adults with primary IgAN who are at risk for disease progression, irrespective of proteinuria levels**, whereas the EMA indication requires patients to have UPCR ≥1.5 g/g[3,4]
- In the **interim analysis** of the Phase 3 NefIgArd trial, treatment with Nefecon 16 mg/day for 9 months resulted in a significant reduction in UPCR and significant eGFR benefit compared with placebo at 3 months post treatment[5]
  - The observed **benefits were maintained** over a further 12-month period off treatment[6]
- Here, we present the **full 2-year NefIgArd trial data** to assess responses to Nefecon treatment **in patients identifying as Asian or White**

## METHODS

- The **Phase 3 NefIgArd trial** was designed to assess whether **9 months of treatment with Nefecon 16 mg/day** leads to a significant reduction in kidney function decline compared with placebo over 2 years; the trial comprised **9 months of treatment and 15 months of observational follow-up**
- **Inclusion criteria** included patients aged ≥18 years with biopsy-proven primary IgAN; UPCR ≥0.8 g/g or proteinuria ≥1 g/24 h despite optimized RAS inhibitor blockade; and eGFR 35-90 mL/min/1.73 m²
- **Exclusion criteria** were poorly controlled diabetes or blood pressure (≥140/90 mmHg); any secondary form of IgAN or non-IgAN glomerulonephritis; systemic diseases that may cause mesangial IgA deposition; and having undergone a kidney transplant
- The **full analysis set** comprised **364 patients**: Asian (n=83), White (n=275), and other (n=6); race categories were defined based on those specified by the FDA
- **Outcomes of the subgroup race analysis** included time-weighted eGFR average over 2 years, changes in UPCR, time to 30% reduction in eGFR or kidney failure, microhematuria, and safety outcomes

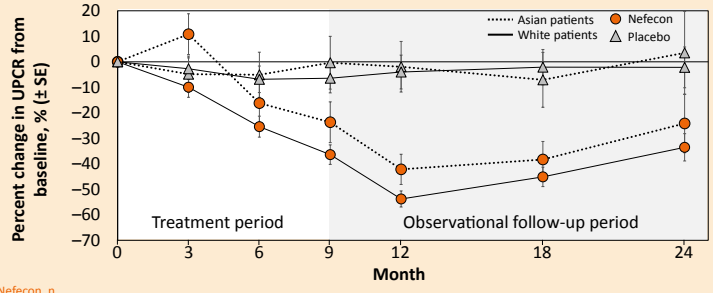
## RESULTS

**Figure 1: eGFR stratified by race and treatment**




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Nefecon, n (Asian; White) | 43; 138 | 39; 131 | 35; 131 | 37; 129 | 35; 117 | 31; 123 | 31; 117 |
| Placebo, n (Asian; White | 40; 137 | 40; 133 | 37; 129 | 37; 122 | 36; 121 | 31; 116 | 29; 114 |

**Figure 2: UPCR stratified by race and treatment**




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Nefecon, n (Asian; White) | 43; 138 | 42; 130 | 37; 131 | 36; 129 | 35; 121 | 31; 123 | 31; 113 |
| Placebo, n (Asian; White | 40; 137 | 40; 131 | 38; 127 | 38; 122 | 37; 119 | 31; 117 | 29; 110 |

- Nefecon significantly differed from placebo in the time-weighted average change in eGFR over 2 years for Asian (p=0.0082*) and White (p<0.0001*) patients,[†] with a **favorable estimated absolute mean change in eGFR** over 2 years of 5.5 mL/min/1.73 m² in Asian patients and 4.8 mL/min/1.73 m² in White patients (Figure 1)
- Nefecon showed a **significant reduction in UPCR** versus placebo at 9 months in both race groups (Asian patients: 23.4%, p=0.0472*; White patients: 32.0%, p<0.0001*), and at 24 months in White patients (Asian patients: 26.7%, p=0.1014*; White patients: 32.1%, p=0.0003*) (Figure 2)
- The **time to a confirmed 30% reduction in eGFR or kidney failure event was significantly delayed** with Nefecon versus placebo, irrespective of race (Asian patients: HR 0.32, 95% CI 0.09, 0.91; p=0.0239*; White patients: HR 0.48, 95% CI 0.28, 0.83; p=0.0046*)
- Nefecon significantly **reduced the likelihood of microhematuria** in both Asian (OR 3.5, 95% CI 1.2, 11.7; p=0.0303) and White patients (OR 2.3, 95% CI 1.3, 3.9; p=0.0030) (Figure 3)
- Rates of **TEAEs were broadly similar** across groups, although with a slightly higher overall rate of TEAEs in Asian patients (Table 1)

**Figure 3: Proportion of patients with microhematuria[‡] stratified by race and treatment**

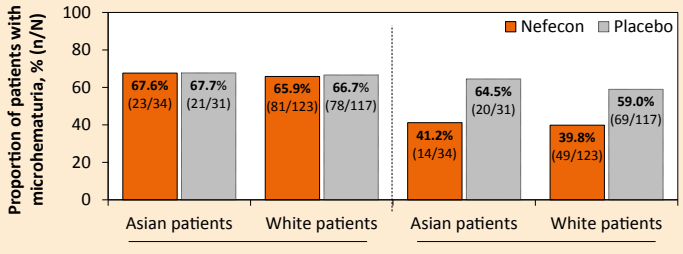



**Table 1: TEAEs and AEs during the 9-month treatment period, stratified by race and treatment**

| n (%) | Asian (n=83) | | White (n=275) | |
|---|---|---|---|---|
| | Nefecon (n=43) | Placebo (n=40) | Nefecon (n=138) | Placebo (n=137) |
| **All TEAEs** | 43 (100) | 29 (72.5) | 115 (83.3) | 92 (67.2) |
| Mild | 22 (51.2) | 19 (47.5) | 71 (51.4) | 53 (38.7) |
| Moderate | 20 (46.5) | 10 (25.0) | 36 (26.1) | 36 (26.3) |
| Severe | 1 (2.3) | 0 (0) | 8 (5.8) | 3 (2.2) |
| **Serious TEAEs** | 4 (9.3) | 0 (0) | 14 (10.1) | 8 (5.8) |
| Treatment-related | 3 (7.0) | 0 (0) | 1 (0.7) | 4 (2.9) |
| **AEs leading to death** | 0 (0) | 0 (0) | 1 (0.7)[§] | 0 (0) |
| **TEAEs leading to treatment discontinuation** | 7 (16.3) | 0 (0) | 10 (7.2) | 3 (2.2) |

*One-sided p-values. [†]Data analyzed using ratios of geometric least square means.[‡]A patient was defined as without hematuria if the urine dipstick returned a result of negative or trace. Patients without at least two valid results from 12 months onwards were excluded from the analysis. [§]There was one death reported during treatment with Nefecon(a fatal coronavirus infection that was considered unrelated to study treatment).

## CONCLUSIONS

- The **2-year full NefIgArd trial** demonstrated that treatment with Nefecon 16 mg/day for 9 months provided a statistically significant and **clinically relevant preservation of eGFR** compared with placebo[6]
  - Nefecon achieved a **durable reduction in proteinuria** when evaluated 15 months after end of treatment[6]
  - Nefecon was well tolerated, with a safety profile as expected for a locally acting oral budesonide product[6]
- The results from this subgroup race analysis indicate that, although the number of patients identifying as Asian was considerably lower than the number identifying as White, **Nefecon was efficacious and well tolerated, irrespective of White or Asian race**

**Scan to view Nefecon presentations, posters, and materials**

**REFERENCES**

1. KDIGO Glomerular Diseases Work Group. *Kidney Int* 2021;100:S1-S276. 2. Barratt J, *et al. Kidney Int Rep* 2020;5:1620-1624. 3. Calliditas Therapeutics AB. Tarpeyo (Nefecon) US PI. 2023. 4. STADA Arzneimittel. Kinpeygo (Nefecon) SmPC. 2023. 5. Barratt J, *et al. Kidney Int* 2023;103:391-402. 6. Lafayette R, *et al. Lancet* 2023;402:859-870.

**ABBREVIATIONS**

AE, adverse event; CI, confidence interval; eGFR, estimated glomerular filtration rate; EMA; European Medicines Agency; FDA, US Food and Drug Administration; HR, hazard ratio; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; OR, odds ratio; RAS, renin–angiotensin system; SE, standard error; TEAE, treatment-emergent adverse event; UPCR, urine protein–creatinine ratio.

**DISCLOSURES**

**JB** is a consultant to Calliditas and reports grants as well as consultancy and personal fees from Arzneimittel AG, Everest Medicines, Calliditas, and STADA. **JK** is a consultant for Calliditas. **AS** received support for the present study and reports consulting fees from AstraZeneca and Calliditas outside the submitted work. **JF** has received consultancy fees or honoraria from AstraZeneca, Bayer, Boehringer Ingelheim, Calliditas, Chinook, GSK, Novartis, Omeros, Otsuka, and Travere Therapeutics, and serves on data safety monitoring boards for Novo Nordisk and Visterra. **VT** has reported consultancy fees or honoraria from Calliditas, Novartis, Omeros, Otsuka, and Travere Therapeutics. **HT** has served on advisory boards for Calliditas and received grants, honoraria, consultancy fees, or travel support from Alexion, AstraZeneca, BioCryst, Calliditas, Chinook, George Clinical, Novartis, Omeros, Otsuka, Travere Therapeutics, and Vera Therapeutics. **HZ** has received consulting fees or honoraria from Calliditas, Chinook, Novartis, Omeros, and Otsuka. **NE** declares no competing interests. **AP** received honoraria and travel grants from Alexion, AstraZeneca, Bayer, Boehringer Ingelheim, GlaxoSmithKline, Otsuka, STADA Arzneimittel AG, and Vifor Pharma. **HNR** received support to serve as a member of the steering committee and funding for the execution of the study from Calliditas; has received grant support from the Kidney Foundation of Canada, Canadian Institutes of Health Research, and John and Leslie Pearson; has received fellowship support from the Louise Fast Foundation; reports consulting fees, honoraria, or travel support from Calliditas, Chinook, Novartis, Omeros, Pfizer, and Travere Therapeutics; served in advisory boards and steering committees for Chinook, Novartis, Omeros, Pfizer, and Travere Therapeutics; has been an investigator for Alnylam Pharmaceuticals, Calliditas, ChemoCentryx, Chinook, Omeros, Pfizer; and is Director of the Glomerulonephritis Fellowship, funded by the Louise Fast Foundation. **BHR** received support for the present study from Calliditas; reports consulting fees from Alpine Immune Sciences, Alexion, Calliditas, Novartis, Omeros, Otsuka/Visterra, Q32 Bio, Travere Therapeutics, and Vera Therapeutics; and is Co-Chair of Glomerular Diseases Guidelines for KDIGO. **RL** received support for the present study from Calliditas; reports institutional grants from Calliditas, ChemoCentryx, Omeros, Otsuka, Pfizer, Roche, Travere Therapeutics, Vera Therapeutics, and Visterra; and has served on advisory boards for Cara Therapeutics.

Calliditas Therapeutics