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Hematuria reduction in patients with IgAN following Nefecon treatment: A secondary analysis of the full 2-year NeflgArd Phase 3 trial results

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INTRODUCTION

Immunoglobulin A nephropathy (IgAN) is a chronic autoimmune kidney disease characterized by IgA deposition in the glomeruli.[1]

Hematuria is a common clinical manifestation of IgAN, and changes in hematuria can be measured to determine the efficacy of IgAN treatments.[2]

Nefecon 16 mg/day was associated with, among other benefits, a reduction in microhematuria after a 9-month course of treatment and 3-month follow-up in the Phase 2b NEFIGAN trial.[3]

In the interim analysis of the Phase 3 NeflgArd trial (N=199), patients treated with Nefecon 16 mg/day in addition to optimized standard of care (SOC) had reduced proteinuria versus placebo and an estimated glomerular filtration rate (eGFR) treatment benefit of 3.87 mL/min/1.73 m^2 after a 9-month course of treatment.[4] These findings led to the Food and Drug Administration and European Medicines Agency approval of Nefecon in patients with primary IgAN.[4,5]

Here, we present results from the entire 2-year NeflgArd study consisting of the full dataset of 364 patients.

AIM

To assess the effect of 9 months of Nefecon 16 mg/day treatment on microhematuria in patients with IgAN during the subsequent 15-month, off-drug, observational follow-up period of the Phase 3 NeflgArd trial.

METHODS

NeflgArd was a 2-part randomized, double-blind, placebo-controlled study. Patients received Nefecon 16 mg/day or placebo, in addition to optimized SOC for 9 months, with a 2-week tapering period, followed by a 15-month blinded observational follow-up with continued optimized SOC (Figure 1).

Key inclusion criteria:

- Patients ≥18 years with biopsy-confirmed primary IgAN
- Urine protein-to-creatinine ratio (UPCR) ≥0.8 g/g or proteinuria ≥1 g/24 h, despite optimized renin–angiotensin system blockade
- eGFR of 35-90 mL/min/1.73 m^2

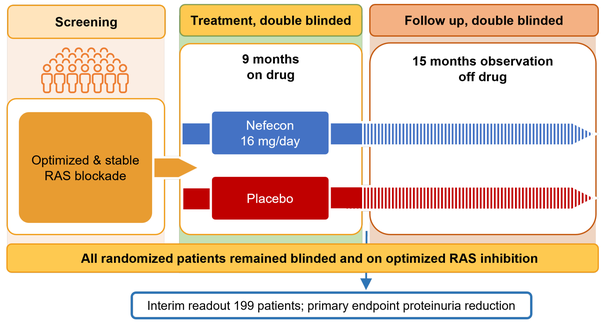
Key exclusion criteria:

- Other glomerulopathies
- Kidney transplant
- Systemic diseases that may cause mesangial IgA deposition
- Poorly controlled blood pressure (≥140/90 mmHg)

METHODS (CONT.)

Presence of microhematuria (a secondary efficacy endpoint for this trial) was defined as presenting a positive urine dipstick result in at least 2 of the follow-up visits assessed at 12, 18, and 24 months after the first dose of Nefecon or placebo.

Figure 1: Study design for the full Phase 3 NeflgArd trial.



eGFR, estimated glomerular filtration rate; RAS, renin–angiotensin system.

- Odds ratio was estimated using logistic regression model with treatment, log-baseline UPCR, log-baseline eGFR, and geographic region as covariates; confidence interval (CI) was estimated using a profile likelihood approach and the p-value was from a likelihood-ratio test.

RESULTS

- Baseline characteristics were **well balanced** for the Nefecon 16 mg and placebo groups (Table 1)
- Of the 364 patients in the full analysis set, **158/182 patients in the Nefecon group and 152/182 patients in the placebo group had ≥2 valid urine dipstick results** during the observational follow-up period
- At randomization, **the proportion of patients with microhematuria was similar in the Nefecon (68%) and placebo (70%) groups** (Table 1)
- **The proportion of patients with microhematuria in the Nefecon group decreased from 66.5% at baseline to 40.5% during follow-up,** compared with a decrease from 67.8% to 61.2% in the placebo group at the same time points (Figure 2)

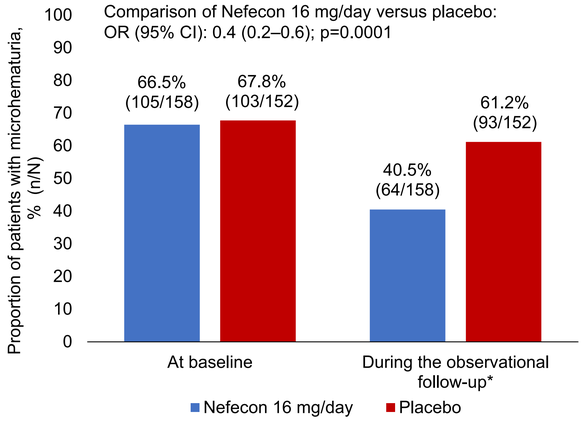
RESULTS (CONT.)

Table 1: Patient demographics and baseline characteristics in the NeflgArd full analysis set.

	Nefecon 16 mg (n=182)	Placebo (n=182)
Age, years, median (range)	43 (21-69)	42 (20-73)
Sex, male, n (%)	117 (64)	123 (68)
Race, White, n (%)	138 (76)	137 (75)
Race, Asian, n (%)	43 (24)	40 (22)
Systolic BP, median (range)	126 (121-132)	124 (117-130)
Diastolic BP, median (range)	79 (76-84)	79 (74-84)
UPCR, g/gram, median (IQR)	1.28 (0.9-1.8)	1.25 (0.9-1.7)
eGFR CKD-EPI, mL/min/1.73 m^2, median (IQR)	56.1 (46-71)	55.1 (46-68)
Patients with microhematuria at randomization, n (%)	123 (68)	127 (70)

BP, blood pressure; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR; estimated glomerular filtration rate; IQR, interquartile range; UPCR, urine protein-to-creatinine ratio.

Figure 2: Proportion of patients with microhematuria at different time points during the observational follow-up.



**Patients with a positive urine dipstick result in at least 2 of the following time points: 12, 18, and 24 months following the first dose of study drug.*

CI, confidence interval; OR, odds ratio.

CONCLUSIONS

This secondary analysis shows that after 9 months of Nefecon 16 mg/day treatment, a clinically relevant and durable reduction in microhematuria was seen in patients with primary IgAN. These results provide further evidence for the disease-modifying effect of Nefecon.

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