Data previously presented at the 61st ERA Congress, 23-26 May 2023 in Milan, Italy

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

11:15-12:15, September 30, 2023 (JST)

Tokyo, Japan

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Date of preparation: September 2023

Nefecon has not been approved by the Japanese Pharmaceuticals and Medical Devices Agency.

The 17th International Symposium on IgA Nephropathy

C O I disclosure

presenter : *Richard Lafayette*

I have the following relationships to disclose any COI for this research presentation within the period of 36 months.

* Employment/Leadership position/Advisory role: Calliditas Therapeutics
* Stock ownership or options:
* Patent royalties/licensing fees:
* Honoraria (e.g. lecture fees):
* Manuscript fees:
* Research funding: Calliditas Therapeutics
* Subsidies or donations:
* Endowed departments by commercial entities:
* Travel fees, gifts, and others:

Introduction

- Nefecon is a novel, oral, targeted-release budesonide formulation specifically designed to treat IgAN by inhibiting IgA formation in the Peyer's-patch–rich distal ileum[1,2]
- An interim analysis of the Phase 3 NefIgArd trial (N=199) demonstrated that Nefecon reduced proteinuria (27%, p=0.0003) and had an eGFR treatment benefit of 3.87 mL/min/1.73 m^2 compared with placebo after 9 months[2]
  - These findings led to FDA and EMA approval of Nefecon in patients with primary IgAN[3,4]
- Changes in microhematuria can be measured to determine the efficacy of IgAN treatments[5]
- Here, we present results from a secondary analysis of microhematuria data from the complete 2-year NefIgArd study (N=364)

eGFR, estimated glomerular filtration rate; EMA, European Medicines Agency; FDA, Food and Drug Administration; IgAN, immunoglobulin A nephropathy.

1. Barratt J, *et al. Kidney Int Rep* 2020;5:1620-1624. 2. Barratt J, *et al. Kidney Int* 2023;103:391-402. 3. Calliditas Therapeutics AB. Tarpeyo (Nefecon) US PI. 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215935s000lbl.pdf (accessed September 2023). 4. STADA Arzneimittel. Kinpeygo (Nefecon) SmPC. 2023. https://www.ema.europa.eu/en/medicines/human/EPAR/kinpeygo (accessed September 2023). 5. Coppo R & Fervenza FC. *J Am Soc Nephrol* 2017;28:2831-2834.

Methods

NeflgArd: A Phase 3, two-part, randomized, double-blind, placebo-controlled study

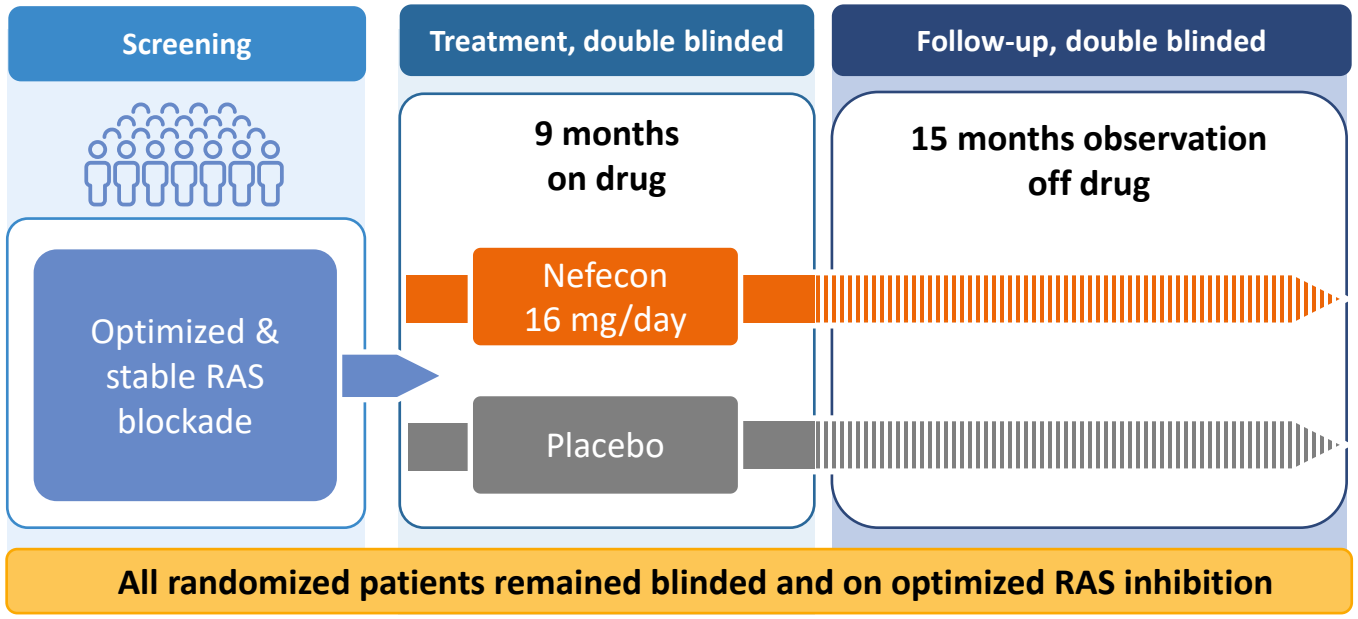
Aim of the analysis: To assess the effect of Nefecon 16 mg/day on microhematuria in patients with IgAN over the 9-month treatment period and 15-month observational follow-up period of the Phase 3 NeflgArd trial

Key inclusion criteria:

- ≥18 years old with biopsy-confirmed primary IgAN
- UPCR ≥0.8 g/g or proteinuria ≥1 g/24h, despite optimized RAS inhibition
- eGFR 35-90 mL/min/1.73 m^2

Key exclusion criteria

- Secondary form of IgAN or non-IgAN glomerulonephritis
- Kidney transplant
- Systemic diseases that may cause mesangial IgA deposition
- Poorly controlled BP (≥140/90 mmHg)
- Poorly controlled T1D or T2D



Primary efficacy endpoint: Time-weighted average of eGFR over 2 years

Secondary efficacy endpoint: Proportion of patients without microhematuria* in at least 2 follow-up visits at 12, 18, and 24 months

*A patient was defined as without microhematuria if the urine dipstick returned a result of negative or trace. The proportion of patients without microhematuria was analyzed using a logistic regression model including treatment, log-baseline UPCR, log-baseline eGFR, and geographic region as covariates. Patients without at least two valid results from 12 months onwards were excluded from the analysis. BP, blood pressure; eGFR, estimated glomerular filtration rate; IgA, immunoglobulin A; IgAN, immunoglobulin A nephropathy; RAS, renin–angiotensin system; T1D, type 1 diabetes; T2D, type 2 diabetes; UPCR, urine protein-creatinine ratio.

Baseline characteristics

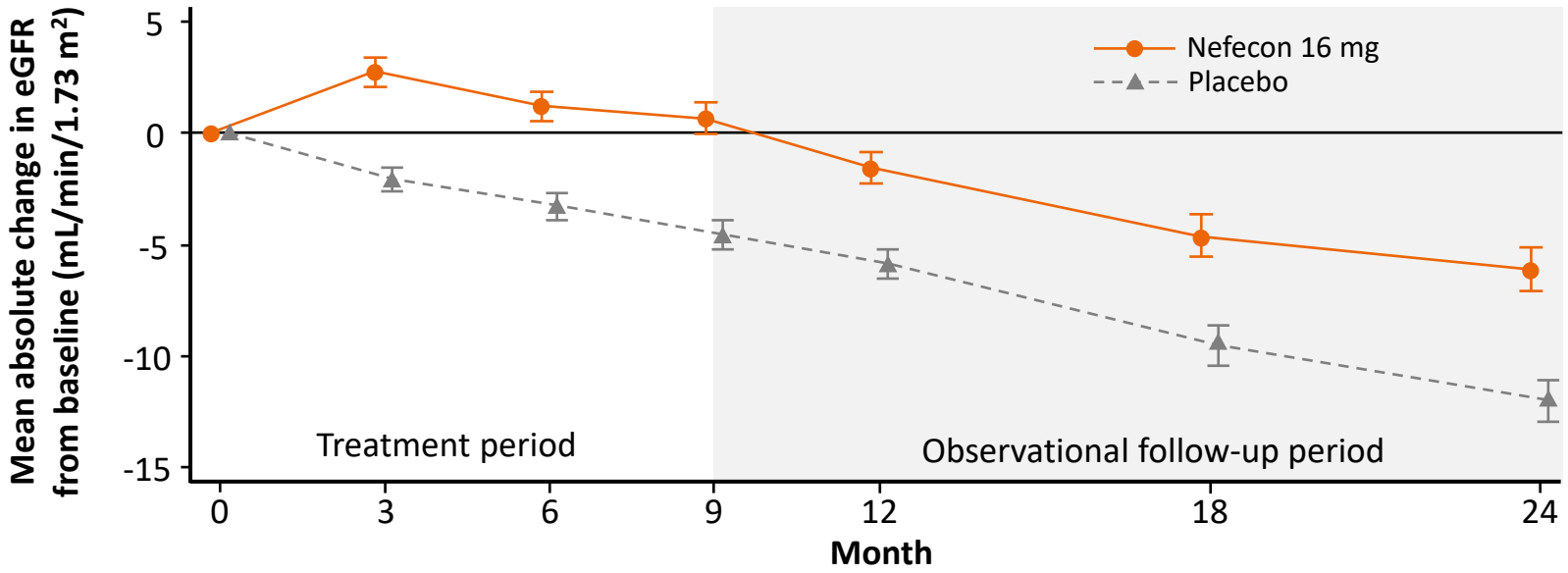
	Nefecon 16 mg (n=182)	Placebo (n=182)
Age, years, median (range)	43 (21-69)	42 (20-73)
Sex, male, n (%)	117 (64.3)	123 (67.6)
Race, White, n (%)	138 (75.8)	137 (75.3)
Race, Asian, n (%)	43 (23.6)	40 (22.0)
Systolic BP, median (IQR)	126 (121-132)	124 (117-130)
Diastolic BP, median (IQR)	79 (76-84)	79 (74-84)
UPCR, g/gram, median (IQR)	1.28 (0.90-1.76)	1.25 (0.88-1.74)
eGFR CKD-EPI, mL/min/1.73 m^2, median (IQR)	56.1 (45.5-71.0)	55.1 (46.0-67.7)

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

Primary endpoint: Time-weighted eGFR change

For additional details on the primary results from NeflgArd please scan here:

Primary endpoint: Time-weighted average change from baseline in eGFR over the 2-year period



Nefecon 16 mg/day, mL/min/1.73 m^2	+0.66	-1.52	-6.11
Placebo, mL/min/1.73 m^2	-4.56	-5.85	-12.00
Absolute difference, mL/min/1.73 m^2 (95% CI)	5.21 (3.35, 7.58)	4.33 (2.44, 6.66)	5.89 (3.35, 9.15)

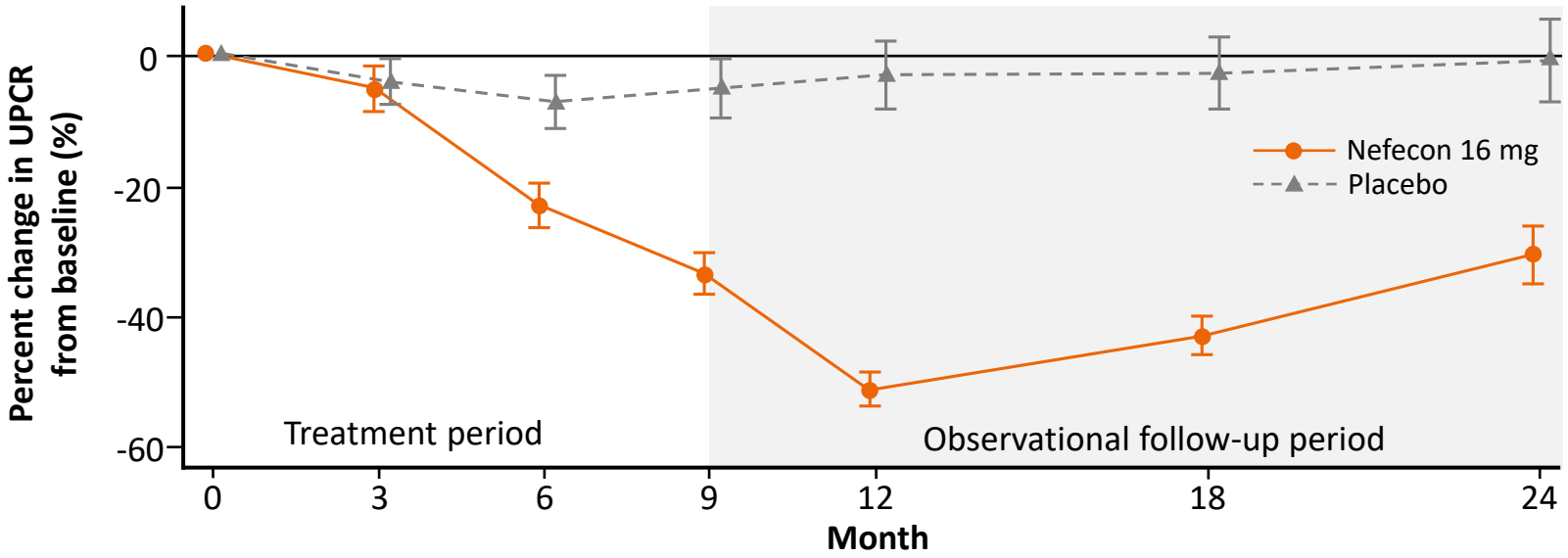
- **eGFR treatment benefit** of **5.05** (95% CI 3.24, 7.38) mL/min/1.73 m^2 with Nefecon 16 mg/day vs placebo (p<0.0001)
- eGFR benefit of Nefecon observed by 9 months of treatment was **maintained over 15 months of observational follow-up**

Error bars represent standard error.
CI, confidence interval; eGFR, estimated glomerular filtration rate.

Secondary endpoint: Change in UPCR

For additional details on the primary results from NeflgArd please scan here:

Mean percentage change in UPCR from baseline



Nefecon 16 mg/day, %	-34	-51	-31
Placebo, %	-5	-3	-1
Corresponding percentage reduction, % (95% CI)	30 (20, 39)	50 (42, 57)	30 (16, 41)

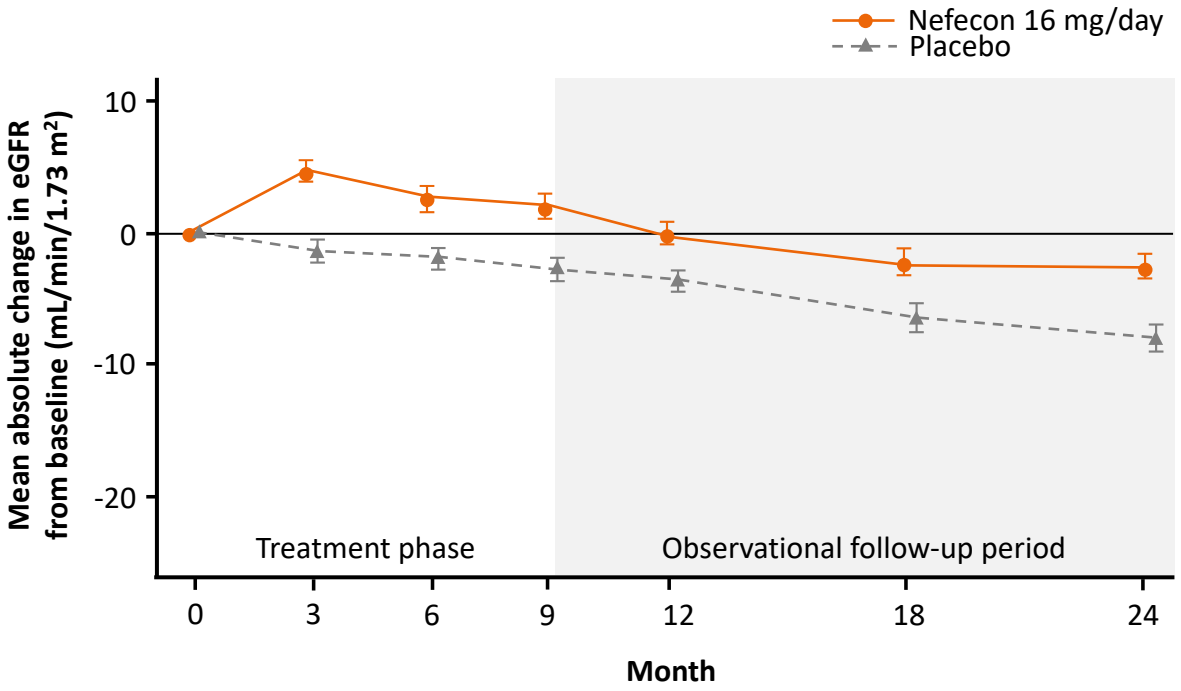
30% reduction in UPCR with Nefecon compared with placebo observed after the 9-month treatment period **sustained up to 2 years**

Error bars represent standard error.
CI, confidence interval; UPCR, urine protein-creatinine ratio.

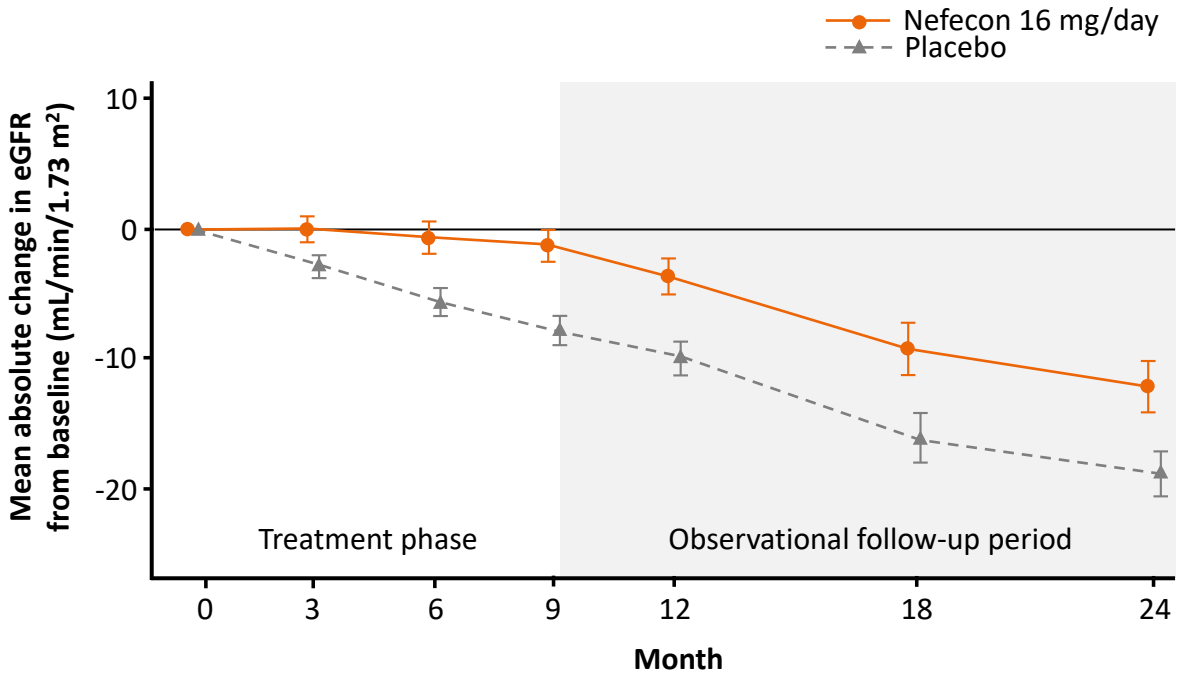
Secondary endpoint: eGFR benefit by baseline UPCR

For additional details on the primary results from NeflgArd please scan here:

Baseline UPCR subgroup: <1.5 g/gram



Baseline UPCR subgroup: ≥1.5 g/gram

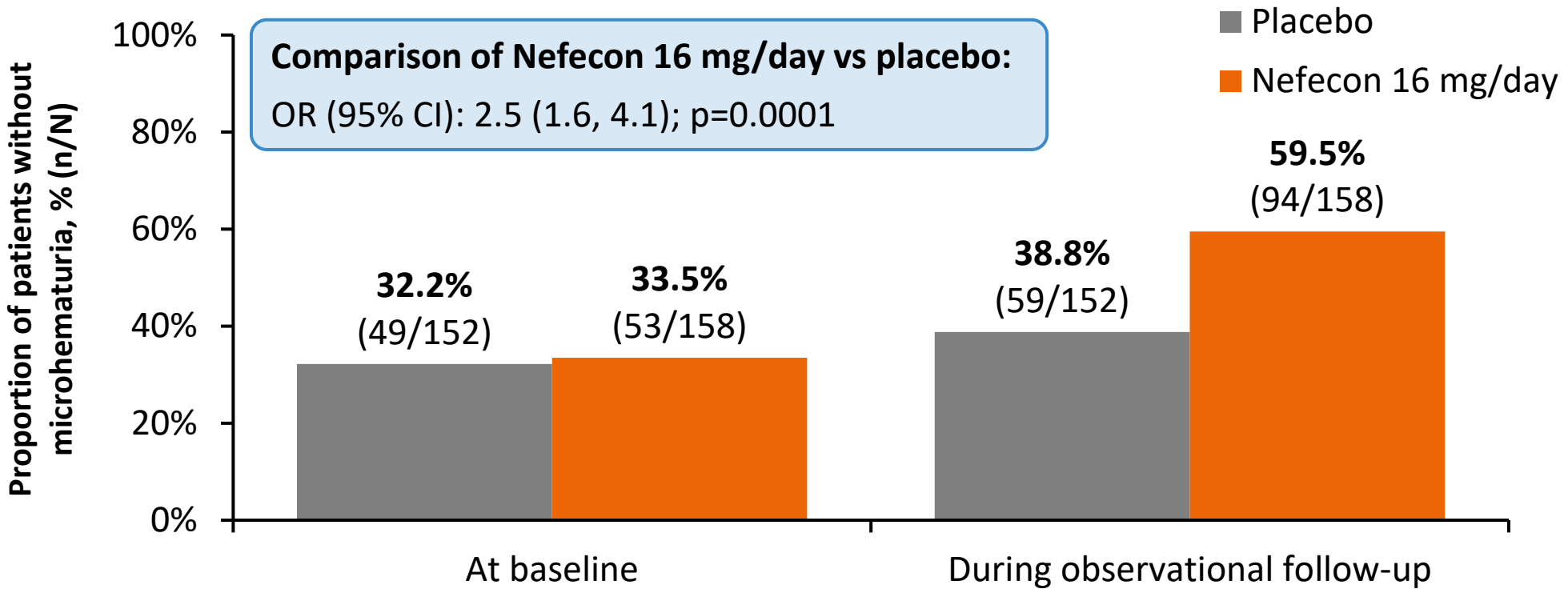


eGFR benefit with Nefecon vs placebo was **consistent irrespective of baseline UPCR**

Error bars represent standard error.
eGFR, estimated glomerular filtration rate; UPCR, urine protein-creatinine ratio.

Secondary endpoint: Proportion of patients without microhematuria

Proportion of patients without microhematuria at different time points during observational follow-up



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 at least two valid urine dipstick results during the observational follow-up period.
CI, confidence interval; OR, odds ratio.

Conclusions

- Patients receiving 9 months of Nefecon treatment were significantly less likely than those receiving placebo to have microhematuria up to 15 months after the end of treatment
  - The proportion of patients without microhematuria was 59.5% versus 38.8% (p=0.0001) during the observational follow-up for Nefecon and placebo, respectively
- These results may be due to a reduction in IgA immune complex-mediated inflammation in the glomeruli with Nefecon and provide further evidence for the disease-modifying effect of Nefecon

IgA, immunoglobulin A.