WCN24-AB-1774

eGFR decline in patients with IgAN treated with Nefecon or placebo: Results from the 2-year NefIgArd Phase 3 trial

Richard Lafayette,[1] Jens Kristensen,[2] Andrew Stone,[3] Jürgen Floege,[4] Vladimír Tesař,[5] Hernán Trimarchi,[6] Hong Zhang,[7] Necmi Eren,[8] Alexander Paliege,[9] Heather N. Reich,[10] Brad H. Rovin,[11] and Jonathan Barratt,[12] on behalf of the NefIgArd trial investigators

[1]Division of Nephrology, Department of Medicine, Stanford University, Stanford, CA, USA; [2]Calliditas Therapeutics AB, Stockholm, Sweden; [3]Stone Biostatistics Ltd., Crewe, UK; [4]Department of Nephrology and Clinical Immunology, Rheinisch Westfälische Technische Hochschule Aachen University Hospital, Aachen, Germany; [5]Department of Nephrology, First Faculty of Medicine and General University Hospital, Charles University, Prague, Czech Republic; [6]Nephrology Service, Hospital Británico de Buenos Aires, Buenos Aires, Argentina; [7]Renal Division, Peking University First Hospital, Peking University Institute of Nephrology, Beijing, China; [8]Department of Nephrology, Kocaeli University, Kocaeli, Turkey; [9]Division of Nephrology, Department of Internal Medicine III, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [10]Division of Nephrology, University Health Network, Department of Medicine, University of Toronto, Toronto, ON, Canada; [11]Division of Nephrology, The Ohio State University Wexner Medical Center, Columbus, OH, USA; [12]College of Medicine Biological Sciences and Psychology, University of Leicester, Leicester, UK

INTRODUCTION

- **Nefecon** is a novel, oral, targeted-release capsule formulation of budesonide, specifically designed to treat IgAN by **inhibiting IgA formation in the Peyer's patch–rich distal ileum**[1]
- Results from the full 2-year Phase 3 NefIgArd study evidenced an eGFR treatment benefit versus placebo and **durable reduction in proteinuria after 9 months of treatment and 15 months of observational follow-up**[1]
- 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[2,3]
- Here, we present **the 2-year results** for the **composite endpoint of time to confirmed 30% eGFR reduction or kidney failure** from the NefIgArd study

METHODS

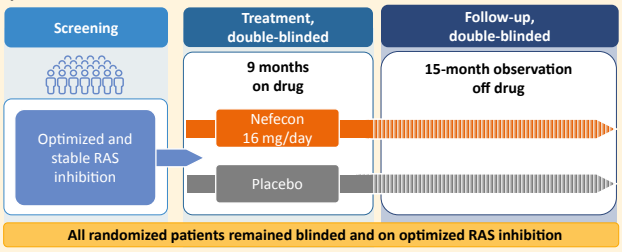
Key inclusion criteria[1]:
- Aged ≥18 years with biopsy-confirmed primary IgAN
- eGFR 35-90 mL/min/1.73 m²
- UPCR ≥0.8 g/g or proteinuria ≥1 g/24 h, despite optimized RAS inhibition

Key exclusion criteria[1]:
- Secondary form of IgAN or non-IgAN glomerulonephritis
- Poorly controlled BP (≥140/90 mmHg)
- Poorly controlled diabetes

Primary efficacy endpoint: Time-weighted eGFR average over 2 years[1]

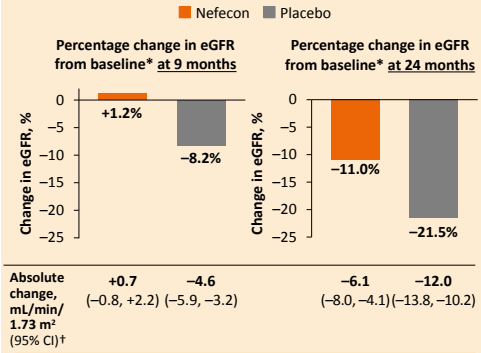
Secondary efficacy endpoint: Composite endpoint of time from randomization to confirmed 30% reduction in eGFR or confirmed kidney failure (dialysis for ≥1 month, kidney transplantation, sustained [≥1 month] eGFR <15 mL/min/1.73 m², or kidney-related death)[1]

Figure 1: NefIgArd – a Phase 3, two-part, randomized, double-blind, placebo-controlled trial[1]



RESULTS

Figure 2: Percentage change in eGFR from baseline at 9 and 24 months



- The **primary endpoint** of time-weighted average of eGFR over 2 years showed a difference of **5.05** mL/min/1.73 m² (95% CI 3.24, 7.38; p<0.0001) **in favor of Nefecon**
- Treatment with Nefecon 16 mg/day for 9 months resulted in approximately **50% less deterioration of kidney function** versus placebo at 24 months (Figure 2)

Figure 3: Time to composite endpoint of confirmed 30% eGFR reduction from baseline or kidney failure‡

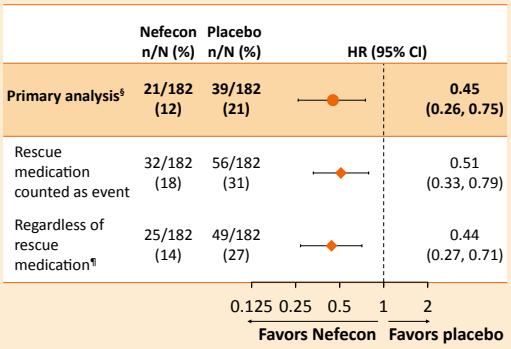
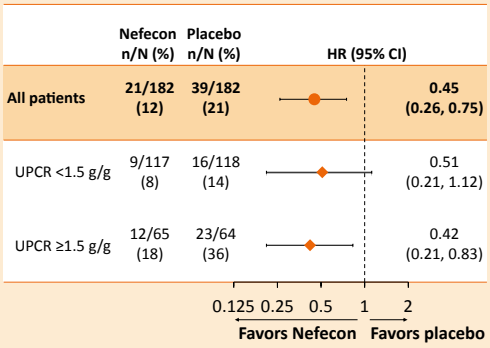


Figure 4: Time to composite endpoint of confirmed 30% eGFR reduction from baseline or kidney failure by UPCR subgroup‡,§



- **Time to confirmed 30% eGFR reduction or kidney failure** was **significantly delayed with Nefecon** versus placebo:‡,§
  - **HR 0.45** (95% CI 0.26, 0.75); **p=0.0014** (1-sided)
- **Nefecon treatment effect** was **similar irrespective of handling of rescue medication** (Figure 3)
- **Nefecon treatment effect** on risk of 30% eGFR reduction or kidney failure was **consistent irrespective of baseline UPCR category** (Figure 4)

- During the 9-month treatment period, **Nefecon 16 mg/day was well tolerated**, with an **expected safety profile for a locally acting oral budesonide product**

*Percentage change in eGFR from baseline = (geometric LS mean of ratio of postbaseline value/baseline value for each treatment arm – 1) ×100. †Estimated absolute change from baseline = baseline geometric mean for total × (geometric LS mean of postbaseline value/baseline value for each treatment arm – 1). ‡A 30% reduction in eGFR was confirmed by two values over ≥4 weeks. To prevent informative censoring, death from a renal-related event, patients who experienced dialysis for at least 1 month, kidney transplantation or kidney failure (defined as a sustained eGFR <15 mL/min/1.73m² prior to a 30% reduction) were included as having had a clinical event occurring at that time. §In an IPCW analysis, patients who received rescue medication or other prohibited immunosuppressive medications were censored at the time of their last eGFR measurement before receiving the medication. ¶Post hoc analysis using a standard Cox model.

CONCLUSIONS

- The time from randomization to confirmed 30% eGFR reduction or kidney failure was **significantly delayed with Nefecon** versus placebo
  - HR 0.45 (95% CI 0.26, 0.75); p=0.0014 (1-sided)
- **The Nefecon versus placebo treatment effect was similar, irrespective of the handling of rescue medication**
  - Rescue medication counted as an event: HR 0.51 (95% CI 0.33, 0.79)
  - Regardless of rescue medication: HR 0.44 (95% CI 0.27, 0.71)
- **The treatment effect of Nefecon versus placebo was consistent, irrespective of baseline UPCR category**
  - UPCR <1.5 g/g: HR 0.51 (95% CI 0.21, 1.12)
  - UPCR ≥1.5 g/g: HR 0.42 (95% CI 0.21, 0.83)
- These findings strongly indicate that **Nefecon preserved kidney function** and provide support for **Nefecon as a disease-modifying therapy in patients with IgAN**

Scan to view Nefecon presentations, posters, and materials

REFERENCES

1. Lafayette R, *et al. Lancet* 2023;402:859-870. 2. Calliditas Therapeutics AB. Tarpeyo (Nefecon) US PI. 2023. 3. STADA Arzneimittel. Kinpeygo (Nefecon) SmPC. 2023.

ABBREVIATIONS

BP, blood pressure; 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; IPCW, inverse probability of censoring weights; LS, least squares; RAS, renin–angiotensin system; UPCR, urine protein–creatinine ratio.

DISCLOSURES

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. **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. **JB** is a consultant to Calliditas and reports grants as well as consultancy and personal fees from Arzneimittel AG, Everest Medicines, Calliditas, and STADA.

Calliditas Therapeutics