INTRODUCTION

- **IgAN** is a chronic immune-mediated disease with significant patient burden, underscoring the need for disease-modifying therapies that prevent kidney function decline.
- **Nefecon** is a novel, oral, targeted-release capsule formulation of budesonide, designed to treat IgAN by reducing Gd-IgA1 antibody production at the Peyer’s patch-rich distal ileum.
- Nefecon is approved for use by the FDA to reduce the loss of kidney function in adult patients with primary IgAN at risk of rapid disease progression irrespective of proteinuria levels, whereas the EMA has an additional requirement of a UPCR ≥ 1.5 g/24 h.
- Previously published results from the 2-year global Nefgard trial demonstrated that treatment with Nefecon 16 mg/day for 9 months was associated with a significant reduction in time-weighted average change in eGFR over 2 years of 5.1 mL/min/1.73 m² versus placebo, and a significant 30% reduction in UPCR at 9 months and a 50% reduction at 12 months versus placebo.
- Here, we present the 2-year results of QoL analyses based on SF-36 assessments at 9 and 24 months.

METHODS

- **Nefgard** was a global, double-blind, randomized, placebo-controlled Phase 3 trial including patients with primary IgAN despite optimized renin-angiotensin system inhibition.
- Eligibility criteria included biopsy-confirmed primary IgAN, persistent proteinuria (UPCR ≥ 0.8 g/g or proteinuria ≥ 1 g/24 h in two consecutive measurements of the same parameter over ≥ 2 weeks), and an eGFR of 35-90 mL/min/1.73 m² estimated with the Chronic Kidney Disease Epidemiology Collaboration 2009 formula.
- Patients received a 9-month treatment course of Nefecon 16 mg/day or placebo in addition to optimized supportive care, followed by a 15-month, off-drug observational period.
- The SF-36 QoL questionnaire contains 36 questions, each of which are grouped into one of eight subscales: physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. Final scores for each subscale range from 0 to 100, with a higher score indicating better health and QoL.
- The mean re-coded scores for each of the eight subscales and overall physical and mental health component scores were summarized at baseline, 9 months, and 24 months.

RESULTS

- **SF-36 scores were similar between groups at baseline across all QoL domains.**
- **No clinically meaningful worsening or improvement in QoL measurements was observed at any timepoint, with SF-36 scores remaining consistent after 15 months of off-drug observational follow-up.**
- **These findings further support the benefit/risk profile of Nefecon, demonstrating that 9 months of treatment with Nefecon 16 mg/day did not result in changes in QoL at any measure, while providing significant benefit in preserving kidney function.**

CONCLUSIONS

- SF-36 scores were similar between groups at baseline across all QoL domains.
- No clinically meaningful worsening or improvement in QoL measurements was observed at any timepoint, with SF-36 scores remaining consistent after 15 months of off-drug observational follow-up.
- These findings further support the benefit/risk profile of Nefecon, demonstrating that 9 months of treatment with Nefecon 16 mg/day did not result in changes in QoL at any measure, while providing significant benefit in preserving kidney function.

REFERENCES


ABBREVIATIONS

eGFR, estimated glomerular filtration rate; EMA, European Medicines Agency; FDA, US Food and Drug Administration; Gd-IgA1, galactose-deficient immunoglobulin A1; IgAN, immunoglobulin A nephropathy; IQR, interquartile range; QoL, quality of life; SF-36, 36-Item Short Form Survey; UPCR, urine protein-creatinine ratio.

DISCLOSURES

JB is a consultant to Calitidas and reports grants as well as consultancy and personal fees from Arzneimittel AG, Everest Medicines, Calitidas, and STADA. JK is a consultant for Calitidas. AS received support for the present study and reports consulting fees from Astrazeneca and Calitidas outside the submitted work. IF has received consultancy fees or honoraria from Astrazeneca, Bayer, Boehringer Ingelheim, Calitidas, Chinoik, GSK, Novartis, Omeros, Otsuka, and Travere Therapeutics, and serves on data safety monitoring boards for Novo Nordisk and Vifor. VT has reported consultancy fees or honoraria from Calitidas, Novartis, Omeros, Otsuka, and Travere Therapeutics. HT has served on advisory boards for Calitidas and received grants, honoraria, consultancy fees, or travel support from Alexion, Astrazeneca, BioCyct, Calitidas, Chinoik, George Clinical, Novartis, Omeros, Otsuka, Travere Therapeutics, and Vifor Pharma. HZ has received consulting fees or honoraria from Calitidas, Chinoik, Novartis, Omeros, and Otsuka. NE declares no competing interests. AP received honoraria and travel grants from Alexion, Astrazeneca, Bayer, Boehringer Ingelheim, GlimaxSmithKline, 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 Calitidas, 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 Louis Fast Foundation; reports consulting fees, honoraria, or travel support from Calitidas, Chinoik, Novartis, Omeros, Pfizer, and Travere Therapeutics; served in advisory boards and steering committees for Chinoik, Novartis, Omeros, Pfizer, and Travere Therapeutics; has been an investigator for Alnylam Pharmaceuticals, Calitidas, ChemoCentrix, Chinoik, Omeros, Pfizer; and is Director of the Glomerulonephritis Fellowship, funded by the Louis Fast Foundation. BNR received support for the present study from Calitidas; reports consulting fees from Alpine Immune Sciences, Alexion, Calitidas, Novartis, Otsuka/Vistarisa; Q3 Bio, Travere Therapeutics, and Vifor Pharma; and is Co-Chair of Glomerular Diseases Guidelines for KDIGO. BL received support for the present study from Calitidas; reports institutional grants from Calitidas, ChemoCentrix, Omeros, Otsuka, Pfizer, Roche, Travere Therapeutics, Vera Therapeutics, and Visterra; and has served on advisory boards for Care Therapeutics.

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