Background

- Nefecon is the first treatment approved by the FDA and EMA for adult patients with primary IgAN at risk of rapid disease progression.
- Approval was based on the interim (Part A) results of the Phase 3, double-blind, randomized controlled NefeNef trial, which included a 9-month treatment course with Nefecon 16 mg/day or placebo, plus a 3-month follow-up period.\(^1\)
- The full results from the complete 2-year study, comprising 9 months of treatment and 15 months of follow-up, have been presented.\(^2\)
- This targeted-release formulation of budesonide, designed to deliver treatment to the ileal GALT, significantly reduced proteinuria and preserved eGFR at 9 months compared with placebo in both the Phase 2b NEFIGN and the Phase 3 NefeNef clinical trials.\(^3-4\)
- Nine months of treatment with Nefecon 16 mg/day also resulted in significant reductions in circulating levels of the key pathogenic biomarkers Golig and IgA/IgG immune complexes in the NEFIGN trial.\(^5\)
- These reductions were associated with a pattern of changes in serum chemokine and cytokine levels that, following pathway analysis, were congregated within the intestinal immune network for IgA production.\(^6\)

Objectives

- To investigate the effect of Nefecon 16 mg/day on circulating levels of three chemokines, CXCL5, CCL11, and CCL13, in the NefeNef interim (Part A) study population.

Materials and methods

- Levels of CXCL5, CCL11, and CCL13 were measured in serum samples (at baseline, 3-, 6-, and 9-months post-randomization) from 160 participants in the NefeNef trial (interim Part A results) using Luminex technology.
- Comparisons between placebo- and Nefecon-treated groups were made at each study time point using unpaired t-tests, with a significance level of p<0.05.

Results

- Treatment with Nefecon resulted in a significant reduction in the levels of CCL13 at end of treatment, compared with placebo (3 months, p<0.002; 6 months, p=0.0094; 9 months, p<0.004).
- Levels of CXCL5 were also significantly reduced by Nefecon compared with placebo (3 months, p=0.0056; 6 months, p=0.001; 9 months, p=0.0128).
- By contrast, Nefecon treatment resulted in significant increases in the levels of CCL11 compared with placebo (3 months, p=0.0036; 6 months, p=0.0027; 9 months, p=0.0004).
- These data confirm findings from the NEFIGN study that show treatment with Nefecon results in a coordinated pattern of responses in chemokines, cytokines, and B-cell survival factors that map to the Kyoto Encyclopedia of Genes and Genomes pathway for the intestinal immune network for IgA production.
- Further work will add to these analyses and validate Nefecon-mediated modulation of other key members of this network.

Conclusion

- These data provide further evidence for a mucosal mechanism of action of Nefecon in IgAN and support previous observations that disrupted lymphocyte trafficking and mucosal dysregulation are fundamental pathogenic pathways in IgAN.
- IgAN, estimated glomerular filtration rate: EMA, European Medicines Agency; FDA, US Food and Drug Administration; GALT, gut-associated lymphoid tissue; Golig, poorly characterized immunoglobulin A type 1; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; IgN, immunoglobulin N.