1. Introduction

- Nefecon, the target-release formulation of budesonide, is delivered to the GALT of the terminal ileum, a major site of IgA production.
- The Phase 3 clinical trial, NefIgArd (NCT03643965), tested the efficacy of Nefecon in patients with IgAN at high risk of progressive kidney disease despite optimized supportive care.
- Treatment with Nefecon 16 mg/day significantly reduced proteinuria after 9 months of treatment compared with placebo (p<0.0003), and this effect was maintained, along with the preservation of eGFR (p=0.0001), over the 15-month off-drug observational follow-up period.

2. Objective

- This study investigated the effect of Nefecon treatment on circulating levels of dietary antigen-specific IgA, secretory IgA, and a marker of gut permeability, FABP2, in participants from Part A of the NefIgArd clinical trial.

3. Methods

- The NefIgArd study was a randomized, double-blind, placebo-controlled, Phase 3 trial, comprised of two parts:
  1. Part A: 9-month treatment period with 3-month off-drug observational follow-up
  2. Part B: 12-month additional observational follow-up period off study drug (Figure 1)
- Circulating levels of secretory IgA, anti-gliadin IgA, anti-casein IgA, and FABP2 were measured in baseline serum samples and 3, 6, 9, and 12 months after randomization during Part A of the NefIgArd trial using enzyme-based immunosorbent assays.
- 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.

4. Results

- Treatment with Nefecon 16 mg/day significantly reduced the levels of anti-gliadin IgA from baseline at 3 months (p=0.044), 6 months (p=0.529), 9 months (p=0.027; Figure 2B), and the levels of anti-casein IgA at 9 months (p=0.022; Figure 2C) compared to the placebo. These data are consistent with the Nefecon 16 mg/day results obtained in the Phase 2b NEFIGAN clinical trial (NCT01738035).
- No significant changes were seen in levels of secretory IgA (Figure 2A) or FABP2 (Figure 2D) from baseline to Nefecon 16 mg/day and placebo groups.

5. Discussion

- Reductions in IgA antibodies against mucosally encountered antibodies confirm a local mucosal effect of Nefecon in IgAN.
- This effect is likely mediated by a direct action on GALT B-cell IgA production rather than an effect on gut permeability and increased antigen exclusion.
- Additional cohort data are expected in the future.