1. Introduction

- In both the Phase 2b NEFIGAN and the Phase 3 NefIgArd clinical trials, Nefecon was found to significantly reduce proteinuria and preserve eGFR at 9 months compared with placebo in patients with IgAN.
- The targeted-release formulation of budesonide, Nefecon, is designed to deliver budesonide to the GALT of the terminal ileum, a major site of IgA production.
- In the Phase 2b NEFIGAN trial, treatment with Nefecon significantly reduced serum levels of galactose-deficient IgA1, IgA/IgG immune complexes, and cytokines involved in B-cell activation.
- This study investigated the effect of Nefecon on biomarkers of lymphocyte activation in the Part A population of the Phase 3 double-blind, randomized controlled NefIgArd trial, in which 9 months of treatment with Nefecon led to a reduction in proteinuria at 9 months (p<0.0003) and in loss of GFR at 9 months (p=0.0001) compared with placebo.

2. Objective

- To investigate the effect of Nefecon 16 mg/day on circulating levels of sCD23, sCD27, and sCD30 in the NefIgArd study population.

3. Methods

- The NefIgArd study was a randomized, double-blind, placebo-controlled, Phase 3 trial in patients with IgAN, comprising two parts:
  - Part A: 9-month treatment period with 3-month observational follow-up period off study drug (Figure 1)
  - Part B: 12-month additional observational follow-up period off study drug
- Levels of sCD23, sCD27, and sCD30 were measured using Luminex technology in 160 NefIgArd Part A participants using serum samples collected at baseline and 3, 6, 9, and 12 months after randomization.
- Comparisons between placebo- and Nefecon-treated groups were made at each time point using unpaired t-tests, with a significance level of p<0.05.

4. Results

- Levels of sCD23, sCD27, and sCD30 were all significantly reduced by Nefecon compared with placebo (Figure 2).

5. Discussion

- Treatment with Nefecon 16 mg/day resulted in a significant reduction in the levels of sCD23 and sCD27 at 3, 6, and 9 months (all p<0.0001), and at 12 months (both p<0.0003), sCD23 levels were also significantly reduced at 3, 6, and 9 months (all p<0.0001), but statistical significance was not achieved at 12 months. These findings broadly confirm those of the NEFIGAN trial.
- The extent of sCD23, sCD27, and sCD30 suppression correlated with the magnitude of BAFF reductions at each time point. sCD30 reductions at 6 and 9 months correlated with the magnitude of reductions in IgA/IgG immune complexes.
- These data validate the findings from the Phase 2b NEFIGAN study and further support a disease-modifying action of Nefecon in IgAN, specifically an action on the BAFF-lymphocyte interaction and immune complex formation.

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