1. Introduction

• Nefecon, the targeted release formulation of budesonide, is delivered to the GALT of the terminal ileum, a major site of IgA production. Results from the Phase 2b NEFIGAN and Phase 3 NefIgArd trials demonstrated that treatment with Nefecon 16 mg/day significantly reduces proteinuria and loss of eGFR compared with placebo. A number of serum biomarkers have been measured in the 2 trials and many of those identified to be modulated by Nefecon in the Phase 2b study have now been validated in Part A of the NefIgArd study. The aim of this study was to determine biological pathways modulated by Nefecon treatment using the data currently available from the Part A biomarker analysis program.

2. Methods

• NefIgArd is a Phase 3 double-blind, randomized, controlled clinical trial designed to determine the efficacy of Nefecon in patients with IgAN at high risk of progressive kidney disease despite optimized supportive care. The trial comprised 9 months of treatment with placebo or Nefecon 16 mg/day, and a 3-month (Part A) or 12-month (Part B) off drug observational follow-up period (15 months off drug in total). An interactome analysis was performed incorporating all serum proteins significantly modulated by treatment with Nefecon 16 mg/day in Part A of the NefIgArd study using the STRING PPI database, which contains known and predicted protein interactions, to determine which biological processes and pathways are modulated by Nefecon treatment.

3. Results

• Consistent with the Phase 2b findings, functional analysis demonstrated that serum biomarkers significantly modulated by Nefecon treatment in Part A of the NefIgArd trial are enriched for proteins involved in the Kyoto Encyclopedia of Genes and Genomes pathway database for intestinal immune network for IgA production, and biological processes involved in B-cell activation, indicating the mechanism of action of Nefecon is, at least in part, driven by an effect within the GALT.

4. Conclusion