

1. Introduction

- In both the Phase 2b NEFIGAN and the Phase 3 NeflgArd clinical trials, **Nefecon was found to significantly reduce proteinuria and preserve eGFR at 9 months** compared with placebo in patients with IgAN¹⁻³
- The targeted-release formulation of budesonide, Nefecon, is designed to deliver budesonide to the GALT of the terminal ileum, a major site of IgA production³
- 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 activation⁴
- 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 NeflgArd trial, in which 9 months of treatment with Nefecon led to a reduction in proteinuria at 9 months ($p=0.0003$)² and a reduction in loss of eGFR at 24 months ($p<0.0001$) compared with placebo³

2. Objective

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

3. Methods

- The NeflgArd study was a randomized, double-blind, placebo-controlled, Phase 3 trial in patients with IgAN, comprising two parts:^{2,3}
 - 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 NeflgArd 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 $p<0.05$

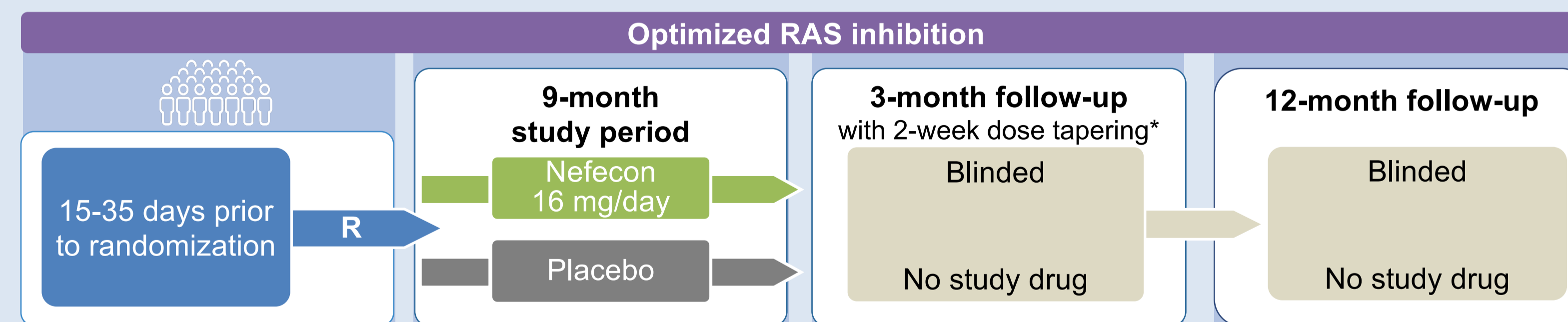


Figure 1. NeflgArd study design.

Results from part A of the multi-center, double-blind, randomized, placebo-controlled NeflgArd trial, which evaluated targeted-release formulation of budesonide for the treatment of primary immunoglobulin A nephropathy

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NeflgArd Part A²

Biomarker analysis (n=160)

*Patients had their blinded treatment reduced from 4 (16 mg/day) to 2 (8 mg/day) capsules.

BAFF, B-cell activating factor; CD, cluster of differentiation; eGFR, estimated glomerular filtration rate; GALT, gut-associated lymphoid tissue; Ig, immunoglobulin; IgAN, immunoglobulin A nephropathy; R, randomization; sCD, soluble cluster of differentiation; TRF, targeted release formulation.

1. Fellström B, et al. *Lancet* 2017;389:2117-2127. 2. Barratt J, et al. *Kidney Int* 2023;103:391-402. 3. Lafayette R, et al. *Lancet* 2023;402:859-870. 4. Wimbury D, et al. *Kidney Int* 2023 [Manuscript submitted for publication].

4. Results

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

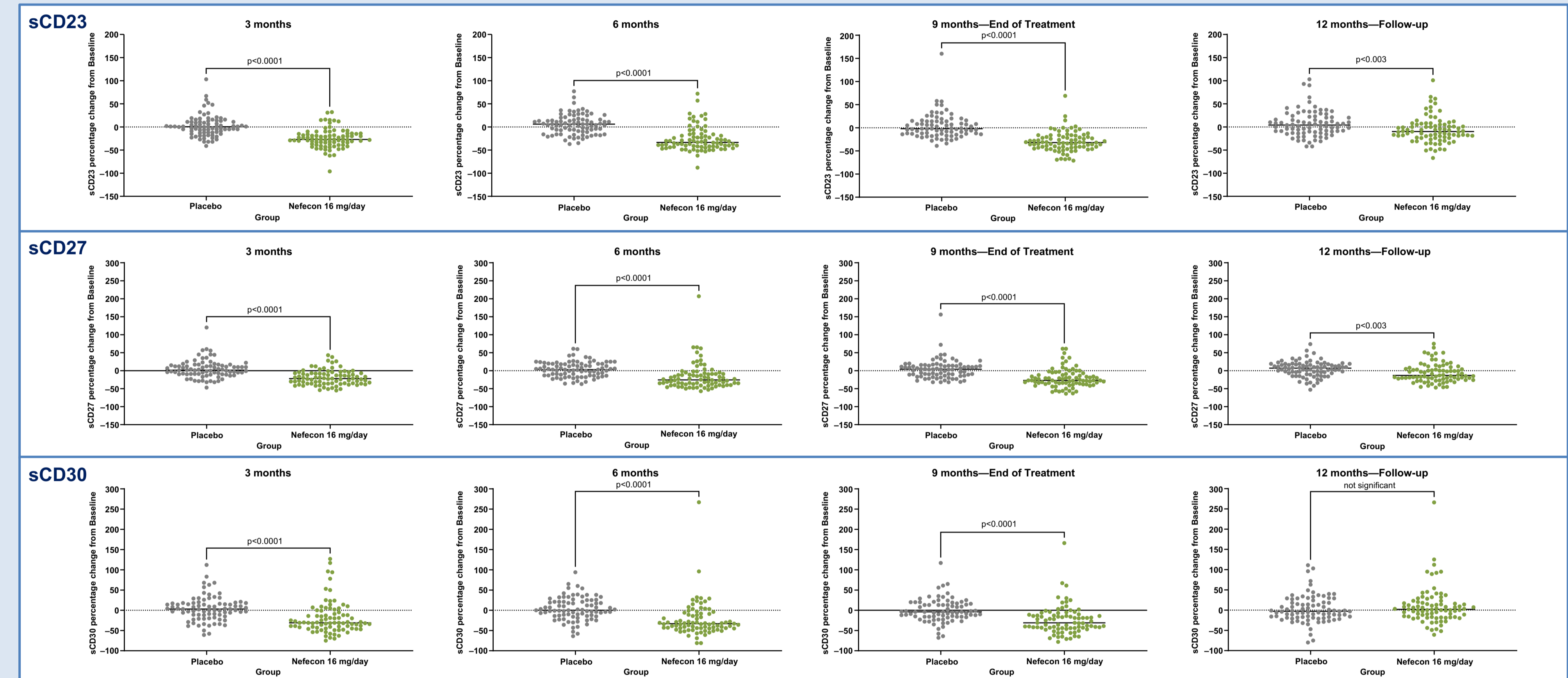


Figure 2. Levels of biomarkers of lymphocyte activation in the serum of patients in the NeflgArd trial.

- 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 $p<0.003$). sCD30 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

5. Discussion

- 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 interactome and immune complex formation

Scan to view other Nefecon presentations, posters, and materials



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