Durable proteinuria reduction over 2 years with Nefecon treatment: A secondary analysis of the full NefIgArd Phase 3 trial results

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INTRODUCTION

IgA nephropathy (IgAN) is a chronic autoimmune kidney disease characterized by IgA deposition in the glomerulus.1-4 Proteinuria is a common clinical manifestation of IgAN, and persistent proteinuria is a risk factor for progression to kidney failure. Changes in proteinuria can be measured to determine the efficacy of IgAN treatments.5,6 Previous findings from the Phase 2b NEFIGN trial showed that patients treated with Nefecon (targeted-release budesonide) versus placebo had a reduction in urine protein-to-creatinine ratio (UPCR) compared with placebo.7 In the interim analysis of the Phase 3 NefIgArd trial (N=199), patients treated with Nefecon 16 mg/day in addition to optimized standard of care (SOC) had reduced proteinuria versus placebo and an estimated glomerular filtration rate (eGFR) treatment benefit of 3.87 mL/min/1.73 m² after a 24-month follow-up.8,9 The pre-defined secondary analysis of durability of proteinuria reduction (as measured by UPCR and UACR) was seen in patients with IgAN treated with Nefecon 16 mg/day for 9 months, with a 3-month follow up, showing a reduction in urine protein-to-creatinine ratio (UPCR) compared with placebo.10 The pre-defined secondary analysis of durability of proteinuria reduction showed a reduction of 30.7% from baseline in the Nefecon group compared with placebo (95% CI 32–49%, p<0.0001; Table 2). These results lead to the FDA and EMA approval of Nefecon in patients with primary IgAN.11,12 Here, we present results from the entire 2-year NefIgArd study consisting of the full dataset of 364 patients with primary IgAN.

METHODS

Nefecon was a 2-part randomized, double-blind, placebo-controlled study. Patients received Nefecon 16 mg/day or placebo, in addition to optimized SOC for 9 months, with a 2-week tapering period, followed by a 15-month blinded observational follow-up with continued optimized SOC.

Key inclusion criteria:
- Patients aged ≥18 years with biopsy-confirmed primary IgAN
- UPCR ≥0.8 g/g or proteinuria ≥1 g/24 h, despite optimized renin-angiotensin system blockade
- eGFR of 35–90 mL/min/1.73 m²

Key exclusion criteria:
- Other glomerulopathies and nephrotic syndrome
- Kidney transplant
- Systemic diseases that cause mesangial IgA deposition
- Poorly controlled blood pressure (≥140/90 mmHg)

RESULTS

Baseline characteristics were well balanced for the Nefecon 16 mg and placebo groups (Table 1). Nefecon 16 mg Placebo

<table>
<thead>
<tr>
<th>Nefecon 16 mg (n=182)</th>
<th>Placebo (n=182)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (range)</td>
<td>43 (21–69)</td>
</tr>
<tr>
<td>Sex (n, % male)</td>
<td>117 (64)</td>
</tr>
<tr>
<td>Race (n, % white)</td>
<td>138 (76)</td>
</tr>
<tr>
<td>Race (n, % Asian)</td>
<td>43 (24)</td>
</tr>
<tr>
<td>Systolic BP, median (range)</td>
<td>126 (121, 122)</td>
</tr>
<tr>
<td>Diastolic BP, median (range)</td>
<td>70 (79, 84)</td>
</tr>
<tr>
<td>UPCR (g/g), median (Q1-Q3)</td>
<td>1.28 (0.9, 1.9)</td>
</tr>
<tr>
<td>UACR (mg/g), median (Q1-Q3)</td>
<td>0.90 (0.7, 1.4)</td>
</tr>
</tbody>
</table>

The pre-defined secondary analysis of durability of proteinuria reduction showed:
- UPCR was significantly reduced by 41% over 12–24 months in the Nefecon group compared with placebo (95% CI 32–49%, p<0.0001; Table 2)
- UACR was also significantly reduced by 46% over 12–24 months in the Nefecon group compared with placebo (95% CI 37–55%, p<0.0001; Table 2).

Table 2: Ratio of UPCR and UACR averaged over 12–24 months compared with placebo using MMRM (full analysis set).

CONCLUSIONS

These secondary analyses show that after 9 months of Nefecon 16 mg/day treatment, a clinically relevant reduction in proteinuria (as measured by UPCR and UACR) was seen in patients with primary IgAN. This effect was durable, being maintained throughout the 15 months’ off-drug observation period. A combination of efficacy and the clinical benefit of Nefecon as well as provide further evidence of a disease-modifying effect.

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REFERENCES


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