Modeling based on NeflgArd 2-year eGFR total slope predicts long-term clinical benefit of Nefecon in a real-world IgAN population

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INTRODUCTION

• IgAN is a chronic autoimmune kidney disease associated with a high lifetime risk of kidney failure.1–3
• Kidney failure severely compromises patients’ quality of life, with poor long-term outcomes and high economic burden.2,3 It is vital to delay the time to kidney failure as long as possible in patients with IgAN.
• Nefecon is a novel, oral, targeted-release budesonide formulation designed to treat IgAN.
• Results from the full 2-year Phase 3 NeflgArd study demonstrated an eGFR treatment benefit vs placebo and durable proteinuria reduction after 9 months of treatment and 15 months of observational follow-up.4

AIM

• To predict the median time to the clinical outcome of kidney failure, eGFR <15 ml/min/1.73 m², or sustained doubling of serum creatinine with Nefecon compared with supportive care only based on the Nefecon 2-year eGFR total slope treatment effect5

METHODS

• Patient records from a long-term Leicester General Hospital (LGH) registry (n=804 patients), collected between 1992 and 2020, were used to model the estimated median time to the clinical outcome for a reference group receiving supportive care only (including renin-angiotensin system inhibitors, lifestyle modifications and blood pressure control).
• Each LGH patient generated multiple records over time with differing eGFR and UPCR values
• A total of 352 of the 364 patients recruited in the NeflgArd trial were each matched to a maximum of 5 distinct patients from the LGH registry, when their baseline UPGR was within 25% and their eGFR <5 ml/min/1.73 m² of an LGH patient record3
• If the same LGH patient record was matched to >1 NeflgArd patient, it was used only once in the modeling of LGH data
• The treatment benefit for 2-year eGFR total slope with Nefecon 16 mg per day vs placebo was applied to the linear regression analysis of 2-year eGFR total slope with the lag HR of clinical outcome, from a published meta-analysis involving 60,620 patients with chronic kidney disease to calculate an associated HR for time to clinical outcome6
• A Weibull model was fitted to the matched LGH data and the HR used to predict time to clinical outcome for Nefecon assuming a common shape parameter

RESULTS

• A total of 352 patients from the NeflgArd trial were matched to 886 unique records from 192 patients from LGH based on UPGR and eGFR values (Figure 1)

Table 1: Cohort demographics

<table>
<thead>
<tr>
<th>NeflgArd (n=352)</th>
<th>LGH (n=886)</th>
<th>Total (n=1238)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NeflgArd (n=352)</td>
<td>312</td>
<td>886</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>52.5 (13.1)</td>
<td>53.7 (13.1)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>51.0 (42.5;62.0)</td>
<td>52.0 (42.6;62.0)</td>
</tr>
<tr>
<td>UPGR (p&lt;0.05, n=312)</td>
<td>352</td>
<td>852</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.47 (0.83)</td>
<td>1.64 (0.96)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>1.26</td>
<td>1.27</td>
</tr>
</tbody>
</table>

The REED equation used for eGFR:

For a small number of cases, eGFR records were not available from the patient’s LGH registry, matching was based on UPGR.

• In the full 2-year NeflgArd trial, 2-year eGFR total slope was improved by 2.78 ml/min/1.73 m² per year (95% CI 1.39, 4.17) when analyzed using the 2-phase linear spline mixed-effect model. When applied to the linear regression of the model, the HR of 0.38 (95% CI 0.21, 0.63) was predicted for the clinical outcome (i.e., a 62% reduction) (Figure 2)
• This is consistent with the significantly reduced time to 30% eGFR reduction from baseline or kidney failure (HR 0.45 [95% CI 0.26, 0.75]) seen with Nefecon vs placebo in the NeflgArd trial7

DISCUSSIONS

• The proportion of patients who would be expected to have a clinical outcome event within 10 years was 24% in patients treated with Nefecon, compared with 52% in patients receiving supportive care only, a relative reduction of approximately 50%

CONCLUSIONS

• These modeling analysis findings, along with the positive impact seen in clinical outcomes in the full 2-year NeflgArd trial data, indicate that Nefecon exerts a substantial disease-modifying effect on IgAN, potentially delaying the onset of clinical outcomes by many years

REFERENCES


CONTACT INFORMATION

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