Lung function, pharmacokinetics, and tolerability of indacaterol maleate and acetate in asthma patients

David Miller¹, Juergen Jauernig², Soniya Vaidya³, Brian Ethell⁴, Kristina Olsson⁵, Rajkumar Radhakrishnan⁶, Hans-Christian Tillmann⁷

¹Northeast Medical Research Associates Inc at North Dartmouth, United States; ²Novartis AG, Basel, Switzerland; ³Novartis Institutes for Biomedical Research, Cambridge, MA, United States; ⁴Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States; ⁵Novartis Healthcare Pvt. Ltd., Hyderabad, India; ⁶Novartis Institutes for Biomedical Research, Basel, Switzerland

Introduction

Asthma is a chronic inflammatory disorder of the airways, associated with excess airway responsiveness leading to recurrent episodes of wheezing, breathlessness, and coughing. (ClinicalTrials.gov number, NCT03257995)

Endpoints

• Through FEV₁ following indacaterol maleate and acetate inhalation, versus placebo at Day 14 was measured to assess the primary endpoint.

• Safety profile after 14 days of treatment in each treatment period

• Indacaterol maleate and acetate in combination for asthma, the acetate salt of indacaterol was used instead of the maleate salt

Methods

Study design

This was a double-blind, placebo-controlled, three-period, parallel-group, one-time study in patients with asthma (ClinicalTrials.gov number, NCT03257995).

Results

Patients

Of the 54 patients randomized, 51 patients completed the study:

• One patient discontinued due to a serious adverse event (SAD) and two discontinued due to deviations from study protocol.

Lung function

• After 14 days of treatment, both indacaterol maleate and indacaterol acetate showed a clinically relevant and statistically significant improvement in trough FEV₁ compared with placebo (P < 0.001) (Figures 2 and 3).

Systemic pharmacokinetics

• In both indacaterol maleate and acetate systems showed comparable systemic plasma concentration-time profiles on Day 14 (Figure 5).

Table 1. Summary statistics of plasma PK parameters for indacaterol salts on Day 14

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Indacaterol maleate</th>
<th>Indacaterol acetate</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC (L·h·mg⁻¹)</td>
<td>150·5·6 (45·2)</td>
<td>150·5·6 (45·2)</td>
</tr>
<tr>
<td>Cmax (µg·h·mL⁻¹)</td>
<td>1·2·4 (0·9·1)</td>
<td>1·2·4 (0·9·1)</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>1·3·4 (0·9·1)</td>
<td>1·3·4 (0·9·1)</td>
</tr>
</tbody>
</table>

Figure 2. Significant improvement in trough FEV₁ with indacaterol maleate and acetate versus placebo at Day 14

Figure 3. Improvement in FEV₁, AUC₀₋₂₄h (L) with indacaterol maleate and acetate versus placebo at Day 14

Figure 5. Plasma concentration—time profiles for indacaterol maleate and indacaterol acetate on Day 14

Conclusions

• In patients with asthma, both indacaterol maleate and acetate achieved significant improvements in lung function compared with placebo and exhibited comparable systemic exposure.

Acknowledgements

The authors wish to thank all the participating centres and their staff as well as the study patients. Safety was assessed in preparation of this paper by Jürgen Jauernig and Arjan Meuleman (Novartis).

References