Pharmacokinetics of indacaterol, glycopyrronium and mometasone furoate as a fixed-dose combination in Japanese and Caucasian healthy subjects

Hanns-Christian Tillmann,1 Satoru Inoue,1 Soniya Vaidya,1 Yohei Sakita,2 Surenda Machineni,3 Kiyoshi Kobayashi3, Kenichi Furutaka1

1Novartis Institutes for Biomedical Research, Basel, Switzerland; 2Novartis Pharma K.K., Tokyo, Japan; 3Novartis Institutes for Biomedical Research, Cambridge, MA, United States; 4Novartis Healthcare Pvt. Ltd., Hyderabad, India;
5-O_NPC, Clinic, Helsinki Medical Corporation, Tokyo, Japan

Methods

Study design
The aim of this non-comparative, single-centred, open-label, multiple-dose, multiple-ascending dose study was to investigate the safety, tolerability and PK of IND/GLY/MF on Day 1 and Day 36-49 following the administration of IND/GLY/MF 150/50/80 μg (medium-dose ICS) or 160 μg (high-dose ICS) and similarly of IND/GLY/MF 150/50/160 μg (medium-dose ICS) or 160 μg (high-dose ICS) delivered via o.d. the Breezhaler® inhalation device.

Table 1. Baseline demographics (safety analysis set)

<table>
<thead>
<tr>
<th>Age in years, median (range)</th>
<th>Japanese (N = 16)</th>
<th>Caucasian (N = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>100 (16/16)</td>
<td>85 (14/17)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>151 (150–160)</td>
<td>175 (172–180)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59 (57–62)</td>
<td>80 (75–85)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24 (23–26)</td>
<td>24 (23–26)</td>
</tr>
</tbody>
</table>

Patients

Key inclusion criteria
- Healthy subjects aged 20 to 65 years, weighing at least 50 kg and having a body mass index of 18-30 kg/m²
- Both, Japanese and Caucasian subjects included were of first generation ethnic origin

Exclusion criteria
- Inability to use the Breezhaler® inhalation device
- Female subjects who are pregnant or lactating
- Patients with a history of respiratory tract infection or asthma
- Patients with a history of bronchial asthma
- Patients with a history of allergy to any of the components of the study drug
- Patients with a history of allergy to any of the components of the study drug
- Patients with a history of allergy to any of the components of the study drug
- Patients with a history of allergy to any of the components of the study drug

Safety

Adverse events
- Headache, constipation and nasopharyngitis were the most frequent AEs.
- Overall, 10 subjects (30.3%) had ≥1 adverse event (AE); incidence of AEs in Japanese subjects was 23.8% compared with 36.4% in Caucasians.
- No serious or fatal events were reported. None of the AEs were considered to be related to the study treatment.

Conclusions

The authors thank the subjects and staff at the participating study centre.

References

1. Author’s name (year). Title of the article. Journal, 1(2), 1-10.

Acknowledgments

The authors acknowledge Ras Behari Koner (Novartis) for designing the poster layout and the authors thank the subjects and staff at the participating study centre.

Figure 1. Study design

Figure 2. Plasma concentration-time profiles of IND are comparable in Japanese and Caucasian subjects with IND/GLY/MF on Day 14

Figure 3. Plasma concentration-time profiles of GLY are comparable in Japanese and Caucasian subjects with IND/GLY/MF on Day 14

Figure 4. Plasma concentration-time profiles of MF are comparable in Japanese and Caucasian subjects with IND/GLY/MF on Day 14

Figure 5. Dose dependent plasma concentration-time profiles were observed for MF in Japanese versus Caucasian subjects on Day 14 following treatment with IND/GLY/MF

Figure 6. Dose dependent plasma concentration-time profiles were observed for MF in Japanese versus Caucasian subjects on Day 14 following treatment with IND/GLY/MF

Figure 7. Dose dependent plasma concentration-time profiles were observed for MF in Japanese versus Caucasian subjects on Day 14 following treatment with IND/GLY/MF

Table 2. Adjusted GMRs (Japanese vs. Caucasians) for AUC0–24h

Table 3. Summary statistics of plasma PK parameters for IND/GLY/MF after multiple dose on Day 14 (PK analysis set)

Table 4. Overall incidence of AEs (safety set)

Table 5. Summary statistics of plasma PK parameters for IND/GLY/MF after multiple dose on Day 14 (PK analysis set)