Significant reduction of hypoglycaemia in patients with type 1 diabetes with insulin degludec compared with insulin glargine U100: randomised, double-blind, crossover trial (SWITCH 1)

Introduction

- Inulin degludec (IDeg) is a basal insulin with a unique mode of action and a duration of action greater than 42 hours.
- The phase 3a development program included two trials in patients with type 1 diabetes (T1D), which demonstrated HbA1c (HbA1c) inferiority of IDeg to insulin glargine U100 (IGlar) with lower rates of nocturnal symptomatic hypoglycaemia.
- Potential limitations of the phase 3a data included the lack of blinding, inclusion of non-symptomatic hypoglycaemia, exclusion of patients with at least one risk factor for hypoglycaemia, and no recording of the timing of Klar administration.
- SWTCH 1 was designed to confirm the hypoglycaemia benefit previously seen, address these limitations, and assess the safe switch to IDeg from other insulins.

Aims

- Primary: To demonstrate non-inferiority in the rates of severe or blood glucose (BG)-confirmed symptomatic hypoglycaemia episodes for IDeg vs insulin apid (IGlar) as part of a full basal–bolus regimen.
- Secondary: To demonstrate non-inferiority in terms of severe or confirmed symptomatic nocturnal hypoglycaemia (SNHg) in the maintenance period, and to confirm superiority with respect to the proportion of patients with severe or symptomatic hypoglycaemia episodes in the maintenance period. If non-inferiority was confirmed then superiority was assessed based on the upper limit of the 95% CI.

Methods

- This was a 2 × 32-week randomised, double-blind, two-period, crossover, multicentre, treat-to-target phase 3b clinical trial conducted with T1D (Figure 1).

Results

- Baseline characteristics are shown in Table 1.
- Mean HbA1c at the end of treatment period 1 was 6.92% (0.56 mmol/L) for IDeg vs 7.05% (0.64 mmol/L) for IGlar, and at the end of treatment period 2 was 6.96% (0.54 mmol/L) for IDeg versus 6.97% (0.52 mmol/L) for IGlar (Figure 2).

Table 1. Baseline characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>IDeg</th>
<th>IGlar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full analysis set (n), n (%)</td>
<td>501</td>
<td>246</td>
<td>255</td>
</tr>
<tr>
<td>Male, %</td>
<td>53.7</td>
<td>54.5</td>
<td>53.0</td>
</tr>
<tr>
<td>White, Black/Asian/Other, n (%)</td>
<td>92.2/6.4/0.4/1.0</td>
<td>92.1/6.6/0.3/1.0</td>
<td>92.3/6.3/0.8/0.0</td>
</tr>
<tr>
<td>Race, White/Black/Asian/Other, n (%)</td>
<td>92.2/6.4/0.4/1.0</td>
<td>92.1/6.6/0.3/1.0</td>
<td>92.3/6.3/0.8/0.0</td>
</tr>
</tbody>
</table>

Figure 3 Forest plot showing the rates of the respective hypoglycaemia endpoints in both the maintenance and overall treatment periods.

Conclusions

- In this double-blind crossover trial in patients with T1D, IDeg was non-inferior in terms of a reduction in HbA1c at 24 weeks, and achieved a lower rate of severe or BG-confirmed symptomatic nocturnal hypoglycaemia endpoints compared with IGlar.
- For the maintenance period, results show:
  - 11% lower rate of severe or BG-confirmed symptomatic hypoglycaemia
  - 36% lower rate of severe or BG-confirmed symptomatic nocturnal hypoglycaemia
  - 35% lower rate of severe hypoglycaemia.

References


Figure 2 Mean number Hba1c, over time in treatment periods 1 and 2.

Figure 4 Flowchart showing study design and patient disposition.