IDegLira improves glycemic control in subjects with type 2 diabetes uncontrolled on basal insulin without deterioration pre-trial sulfonylurea

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Aim

- To investigate the efficacy and safety of IDegLira/degludec and SU (43) vs placebo in patients with T2D on basal insulin + metformin ± SU in combination with metformin, in patients with type 2 diabetes (T2D) uncontrolled on 20–40 U basal insulin + metformin ± sulfonylurea (SU)/metformin, in patients discontinuing pre-trial SU, compared with patients not previously treated with SU during the trial with IDegLira.

Methods

- **Trial design for DUAL II: a double-blind, randomised, multicentre, parallel-group, 26-week, phase III study**
  - Patients: randomised 1:1 to IDegLira + metformin or degludec + metformin
  - SU doses were either continued or discontinued based on the clinician's decision during the trial

Results

- **Inclusion criteria:**
  - BMI ≥27 kg/m²
  - Fasting plasma glucose (FPG) > 7.5 mmol/L
  - HbA1c > 7.5%
  - No history of hypoglycemia or severe hypoglycemia

- **Exclusion criteria:**
  - hsCRP > 3 mg/L
  - Liver enzymes > 2.5 x ULN
  - Creatinine clearance < 45 ml/min

- **Maximum doses were 50 U for both IDegLira and degludec. Metformin was continued at pre-trial doses.**

- **Figure 1: DUAL II trial design**
  - In the SU trial, patients were treated with SU at screening (SU group) and 200 patients were not treated with SU (non-SU group) at screening. Baseline characteristics were broadly similar across the two groups.
  - The mean duration of diabetes was 11.5 years in the SU group and 9.8 years in the non-SU group.
  - Daily insulin dose at screening was slightly lower in the SU group (16.5 U) than in the non-SU group (17.0 U).

- **Glycemic control**
  - Treatment with Degludec resulted in a mean decrease in self-monitored blood glucose (SMBG) after 26 weeks in both the SU and non-SU groups (Figure 2).
  - Mean SMBG was lower with Degludec compared with degludec for both treatment groups throughout the duration of the trial.
  - Change from baseline in HbA1c, fasting plasma glucose (FPG) and body weight, and end of trial (EOT) insulin dose were analyzed with an analysis of covariance (ANCOVA) model with region, pre-trial use of SU and body weight as fixed factors, and baseline value as co-variate.

- **Table 1: Outcomes in DUAL II by pre-trial SU use group**

<table>
<thead>
<tr>
<th>Category</th>
<th>SU group (N=100)</th>
<th>Non-SU group (N=100)</th>
<th>ETD/ERR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline weight, kg</td>
<td>93.2 (4.0)</td>
<td>96.5 (4.9)</td>
<td>–2.26</td>
<td>0.008</td>
</tr>
<tr>
<td>Δ Body weight, kg</td>
<td>–3.3 (1.0)</td>
<td>–2.7 (1.0)</td>
<td>–0.60</td>
<td>0.3828</td>
</tr>
<tr>
<td>Hypo events/PYE</td>
<td>1.0  (0.0)</td>
<td>1.0  (0.0)</td>
<td>–0.00</td>
<td>1.000</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.7  (0.7)</td>
<td>7.5  (0.5)</td>
<td>–1.23</td>
<td>0.2628</td>
</tr>
<tr>
<td>Δ HbA1c, %</td>
<td>–2.2  (0.8)</td>
<td>–1.5  (0.6)</td>
<td>–0.70</td>
<td>0.2628</td>
</tr>
<tr>
<td>Δ FPG, mmol/L</td>
<td>–1.2  (0.7)</td>
<td>–0.6  (0.5)</td>
<td>–0.60</td>
<td>0.3828</td>
</tr>
<tr>
<td>Δ FPG, mEq/L</td>
<td>–2.4  (1.0)</td>
<td>–2.4  (1.0)</td>
<td>0.00</td>
<td>1.000</td>
</tr>
<tr>
<td>Δ FPG, mg/dL</td>
<td>–3.3  (1.0)</td>
<td>–2.7  (1.0)</td>
<td>–0.60</td>
<td>0.3828</td>
</tr>
<tr>
<td>Δ FPG, mmol/L to HbA1c (%)</td>
<td>–1.2  (0.8)</td>
<td>–1.5  (0.6)</td>
<td>–0.70</td>
<td>0.2628</td>
</tr>
<tr>
<td>ADA/EASD HbA1c target &lt;7.0%</td>
<td>95.2 (4.9)</td>
<td>92.6 (4.5)</td>
<td>2.60</td>
<td>0.013</td>
</tr>
<tr>
<td>ADA/EASD HbA1c target &lt;7.5%</td>
<td>94.0 (4.7)</td>
<td>92.0 (4.8)</td>
<td>2.00</td>
<td>0.045</td>
</tr>
</tbody>
</table>

Discussion

- **IDegLira was more favorable compared with degludec in terms of change in HbA1c and FPG during the first 3 weeks of trial in the SU group, in both the IDegLira and degludec arms, with continued improvement in mean SMBG levels from baseline to 26 weeks.**

- **Conclusion:**
  - IDegLira improves glycemic control in subjects with type 2 diabetes uncontrolled on basal insulin without deterioration despite discontinuing pre-trial sulfonylurea.