**DUAL™ V Study Backgrounder**

**IDegLira (Xultophy®)** is a combination of basal insulin (Tresiba® (insulin degludec)) and GLP-1 analogue (Victoza® (liraglutide)), in one pen that has been investigated in the DUAL™ (Dual Action of Liraglutide and Insulin Degludec) clinical trial programme. DUAL™ V is a phase 3b, 26-week randomised, parallel- two-arm, open-label, treat-to-target, multicentre, multinational trial conducted across 10 countries comparing the efficacy and safety of IDegLira versus insulin glargine in adults with type 2 diabetes uncontrolled (HbA\(_1c\) * 7-10% or 53-86 mmol/mol) on insulin glargine in combination with metformin.

**Primary Endpoint**
Change in HbA\(_1c\) * from baseline after 26 weeks of treatment

**Secondary Endpoints**
- Confirmatory Secondary Endpoints: Change from baseline in body weight and number of treatment emergent hypoglycaemic episodes confirmed at 26 weeks of treatment
- Proportion of participants achieving predefined HbA\(_1c\) * targets of <7.0%, and ≤6.5% (<53 mmol/mol and ≤48 mmol/mol) after 26 weeks of treatment
- Supportive efficacy endpoints: change from baseline in fasting plasma glucose, waist circumference, blood pressure, mean 9-point plasma glucose profile, post prandial plasma glucose increments, fasting C-peptide, human insulin and glucagon, fasting lipid profile and end of trial insulin dose

**Dosing**
- **Initiation dose for IDegLira was 16 dose steps (16 units insulin degludec + 0.6 mg liraglutide). Maximum dose of 50 dose steps (50 units insulin degludec + 1.8 mg liraglutide)**
- **Initiation dose of insulin glargine was the pre-trial dose (mean 32 units; no maximum)**

**Definition of an IDegLira dose step**
- 1 dose step
  - 1 units insulin degludec + 0.036 mg liraglutide
- 50 dose steps
  - 50 units insulin degludec + 1.8 mg liraglutide

**Titration algorithm for dose adjustments**

<table>
<thead>
<tr>
<th>Mean fasting plasma glucose (FPG)</th>
<th>Dose change (dose steps or units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4.0 (&lt;72)</td>
<td>-2</td>
</tr>
<tr>
<td>4.0-5.0 (72-90)</td>
<td>0</td>
</tr>
<tr>
<td>&gt;5.0 (&gt;90)</td>
<td>+2</td>
</tr>
</tbody>
</table>

Dose adjustments were made based on the mean of three consecutive self-measured blood glucose values with a target FPG of 72-90 mg/dL for both arms.

**Inclusion Criteria**
- Adults ≥18 years of age with type 2 diabetes (HbA\(_1c\) * 7.0-10.0% or 53-86 mmol/mol both inclusive)
- Body mass index ≤40kg/m\(^2\)
- Treated with insulin glargine for ≥90 days at a stable daily dose (20 – 50 units/day) + metformin
- No treatment with the following antidiabetes medication: oral antidiabetic agents other than metformin; insulin regimen other than basal insulin (e.g. pre-mixed or rapid-acting insulin); GLP-1 receptor agonists

**Open label randomisation (1:1) to receive either IDegLira once-daily or continued insulin glargine up titration, both + metformin**

**Reference:** ClinicalTrials.gov. NCT01952145. A Trial Comparing the Efficacy and Safety of Insulin Degludec/Liraglutide Versus Insulin Glargine in Subjects With Type 2 Diabetes Mellitus (DUAL™ V).

Available at: https://www.clinicaltrials.gov/ct2/show/study/NCT01952145?show_locs=Y#locn Last accessed: 03.02.2015

*HbA\(_1c\) is a test that shows a person’s average level of blood glucose for the previous 2–3 months. It is a common test used to monitor long-term diabetes control.

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