DUAL™ II Study Backgrounder

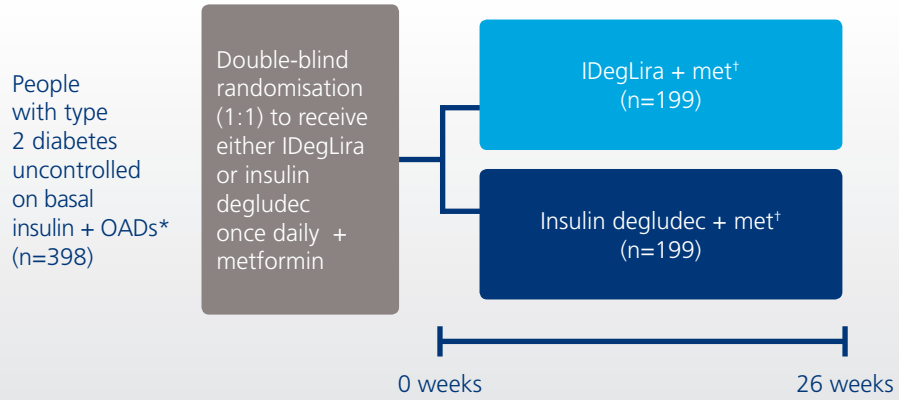
IDegLira is a novel combination of basal insulin (Tresiba®/insulin degludec) and GLP-1 analogue (Victoza®/liraglutide) in one pen, that has been investigated in two Phase 3a trials DUAL™ I and DUAL™ II (Dual Action of Liraglutide and Insulin Degludec). DUAL™ II is a 26-week, randomised, parallel-two-arm, double-blind, multicentre, multinational trial conducted at 75 sites across 7 countries comparing the efficacy and safety of IDegLira and insulin degludec once daily, both added on to metformin in adults with type 2 diabetes uncontrolled (HbA_{1c}* 7.5–10.0%) on basal insulin (20–40 units) in combination with 1–2 oral antidiabetic (OAD) therapies (metformin ± sulphonylurea/glinides).

Primary Endpoint

Change from baseline HbA_{1c}* after 26 weeks of treatment

Secondary Endpoints

- Proportion of participants achieving HbA_{1c}* targets <7% and ≤6.5% (with or without hypoglycemia and/or weight gain)
- Changes in laboratory-measured fasting plasma glucose, mean 9-point self-measured blood glucose (SMBG) profiles and body weight



†met=metformin
*OADs=metformin±sulphonylurea/glinides

Inclusion Criteria

- Adults ≥18 years with type 2 diabetes (HbA_{1c}* of 7.5-10% inclusive)
- Body mass index ≥27 kg/m²
- Treated for ≥90 days with basal insulin at a stable dose (20-40 units/day, ±10%) +metformin ±sulphonylurea/glinides

Dosing

At randomisation:
- Participants discontinued sulphonylurea/glinides
- Transferred from current basal insulin treatment to either IDegLira or insulin degludec once-daily
- Metformin was continued at pre-trial doses

Initiation dose for IDegLira was 16 dose steps of IDegLira (16 units insulin degludec and 0.6 mg liraglutide). Maximum dose of 50 dose steps (50 units insulin degludec + 1.8 mg liraglutide).

Initiation dose of insulin degludec was 16 units. Maximum dose of 50 units in order to evaluate the contribution of the liraglutide component in IDegLira at equivalent insulin doses.

Definition of an IDegLira dose step

1 dose step

1 U insulin degludec
+
0.036 mg liraglutide

50 dose steps

50 U insulin degludec
+
1.8 mg liraglutide

Titration algorithm for dose adjustments

Mean fasting plasma glucose (FPG) mmol/L (mg/dL)	Dose change (dose steps or units)
<4.0 (<72)	-2
4.0-5.0 (72-90)	0
>5.0 (>90)	+2

Titration algorithm for dose adjustment of IDegLira or insulin degludec in the DUAL™ phase 3a trials. Dose adjustments were made based on SMBG values with a target FPG (fasting plasma glucose) of 4.0-5.0 mmol/L (72-90 mg dL).

Safety Assessments

- Analysis of exposure
- Adverse events
- Hypoglycemic episodes
- Clinical laboratory evaluation
- Vital signs
- Physical findings

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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