# DUAL™ I Study Backgrounder

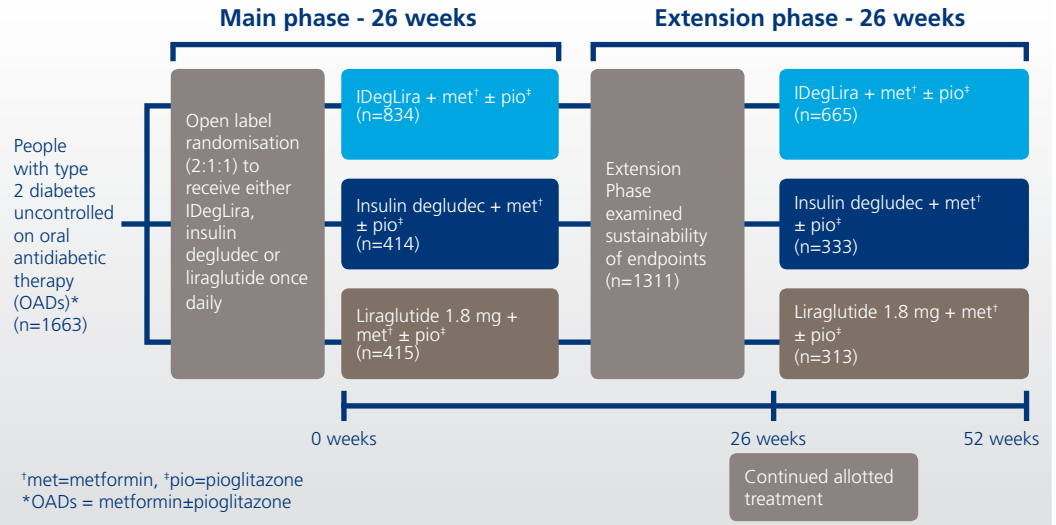
**IDegLira is a novel combination of basal insulin (Tresiba® / insulin degludec) and GLP-1 analogue (Victoza® / liraglutide), in one pen that has been investigated in two Phase 3a trials DUAL™ I and DUAL™ II (Dual Action of Liraglutide and Insulin Degludec). DUAL™ I is a 26-week randomised, parallel- three-arm, open-label, multicentre, multinational trial conducted at 271 sites across 19 countries. The trial compared the efficacy and safety of IDegLira with insulin degludec and liraglutide alone in insulin-naive adults with type 2 diabetes treated with metformin ± pioglitazone. A 26-week extension phase of the main trial was conducted to generate longer-term safety data and to assess the sustainability of the response to treatment.**

## Primary Endpoint

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

## Secondary Endpoints

- Confirmatory: daily insulin dose, body weight, hypoglycaemia and glucose concentration profile during meal test
- Supportive: proportion of participants achieving pre-defined $HbA_{1c}$* targets (<7% and ≤6.5%), laboratory-measured fasting plasma glucose and mean 9-point self-monitoring blood glucose (SMBG) profiles




## Inclusion Criteria

- Adults ≥18 years with type 2 diabetes ($HbA_{1c}$* of 7–10% inclusive)
- Body mass index of ≤40 kg/$m^2$
- Treated for ≥90 days prior to screening with metformin ± pioglitazone
- Not treated with GLP-1 receptor agonists, dipeptidyl peptidase-4 inhibitors or sulphonylureas within 90 days of screening

## Dosing

*Participants on metformin and pioglitazone continued at pre-trial doses*

Initiation dose for IDegLira was 10 dose steps (10 units insulin degludec /0.36 mg liraglutide). Maximum dose of 50 dose steps (50 units insulin degludec + 1.8 mg liraglutide).

Initiation dose of insulin degludec was 10 units; no maximum dose.

Liraglutide treatment was initiated at 0.6 mg/day for the first week of treatment, followed by weekly dose escalation steps of 0.6 mg for the following two weeks, reaching the maximum daily dose of 1.8 mg by the third week.

### 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 Evaluations

- Analysis of exposure
- Adverse events
- Hypoglycaemic 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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