Overview of the ONWARDS phase 3 clinical development program for investigational once-weekly insulin icodec

The ONWARDS clinical development program comprises six phase 3a global clinical trials investigating once-weekly insulin icodec in more than 4,000 adults with type 1 or type 2 diabetes, including a trial with real-world elements[1].

ONWARDS 1

Once-weekly insulin icodec vs once-daily insulin glargine U100 in people with type 2 diabetes who have not previously been treated with insulin

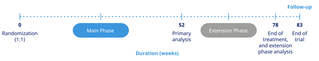
Trial design[1]

984 patients[2]
- Insulin-naive T2D* treated with OADs** ± GLP-1 RA s.c.
- Age ≥18 years
- HbA_{1c} 7.0–11.0%

Once-weekly insulin icodec + non-insulin glucose-lowering agents

Once-daily insulin glargine U100 + non-insulin glucose-lowering agents

- Open-label, treat-to-target
- Double-blinded CGM



*Short term insulin treatment for a maximum of 14 days prior to the day of screening was allowed, as was prior insulin treatment for gestational diabetes.
**Sulfonylureas and glinides were discontinued at randomization.

Endpoints[2]

Primary:
The primary endpoint was change in HbA_{1c} from baseline to week 52.

Secondary:
Secondary endpoints include time in target blood glucose range (70-180 mg/dL) from week 48-52, change in fasting plasma glucose (FPG) from baseline to week 52 and number of clinically significant (level 2) or severe (level 3) hypoglycemia episodes.

ONWARDS 2

Once-weekly insulin icodec vs once-daily insulin degludec in people with type 2 diabetes who have previously been treated with basal insulin

Trial design[1]

526 patients[3]
- T2D treated with OD/BID basal insulin ± OADs** ± GLP-1 RA s.c.
- Age ≥18 years
- HbA_{1c} 7.0–10.0%

Once-weekly insulin icodec ± non-insulin glucose-lowering agents

Once-daily insulin degludec ± non-insulin glucose-lowering agents

- Open-label, treat-to-target
- Double-blinded CGM

**Sulfonylureas and glinides were discontinued at randomization.

Endpoints[3]

Primary:
The primary endpoint was change in HbA_{1c} from baseline to week 26.

Secondary:
Secondary endpoints included change in fasting plasma glucose (FPG) from baseline to week 26, time in target blood glucose range (70-180 mg/dL) from week 22 to week 26.

ONWARDS 3

Once-weekly insulin icodec vs once-daily insulin degludec in people with type 2 diabetes who have not previously been treated with insulin

Trial design[1]

588 patients[4]
- Insulin-naive T2D* treated with OADs*** ± GLP-1 RA s.c.
- Age ≥18 years
- HbA_{1c} 7.0–11.0%

Once-weekly insulin icodec + non-insulin glucose-lowering agents + once-daily placebo

Once-daily insulin degludec + non-insulin glucose-lowering agents + once-weekly placebo

- Multinational (includes China)
- Double-blind, double-dummy, treat-to-target

*Short term insulin treatment for a maximum of 14 days prior to the day of screening was allowed, as was prior insulin treatment for gestational diabetes.
***Sulfonylureas or glinides were administered at a reduced (50%) dose at the discretion of the investigator.

Endpoints[4]

Primary:
The primary endpoint was change in HbA_{1c} from baseline to week 26.

Secondary:
Secondary endpoints included change in fasting plasma glucose (FPG) from baseline to week 26 and number of clinically significant (level 2) or severe (level 3) hypoglycemia episodes.

ONWARDS 4

Once-weekly insulin icodec vs once-daily insulin glargine U100 in people with type 2 diabetes who have previously been treated with basal/bolus insulin

Trial design[1]

582 patients[5]
- T2D treated with basal-bolus insulin ± OADs** ± GLP-1 RA s.c.
- Age ≥18 years
- HbA_{1c} 7.0–10.0%

Once-weekly insulin icodec + insulin aspart ≥ 2 times daily ± non-insulin glucose-lowering agents

Once-daily insulin glargine U100 + insulin aspart ≥ 2 times daily ± non-insulin glucose-lowering agents

- Open-label, treat-to-target
- Double-blinded CGM

**Sulfonylureas and glinides were discontinued at randomization.

Endpoints[5]

Primary:
The primary endpoint was change in HbA_{1c} from baseline to week 26.

Secondary:
Secondary endpoints included change in fasting plasma glucose (FPG) from baseline to week 26, time in target blood glucose range (70-180 mg/dL) from week 22 to week 26 and number of clinically significant (level 2) or severe (level 3) hypoglycemia episodes from baseline to week 31.

ONWARDS 5

Once-weekly insulin icodec with dosing guide app vs once-daily basal insulin analogs in people with type 2 diabetes who have not previously been treated with insulin

Trial design[1]

1,085 patients[6]
- Insulin-naive T2D* treated with OADs ± GLP-1 RA s.c.
- HbA_{1c} > 7.0%

Once-weekly insulin icodec with dosing guide app ± non-insulin glucose-lowering agents

Once-daily basal insulin analogs**** ± non-insulin glucose-lowering agents

- Open-label trial with real-world elements
- Insulin icodec was supported by a digital app to guide titration

*Short term insulin treatment for a maximum of 14 days prior to the day of screening was allowed, as was prior insulin treatment for gestational diabetes.
****Insulin glargine U100, insulin degludec, insulin glargine U300.

Endpoints[6]

Primary:
The primary endpoint was change in HbA_{1c} from baseline to week 52.

Secondary:
Secondary endpoints included time from baseline to treatment discontinuation or intensification and number of clinically significant (level 2) or severe (level 3) hypoglycemia episodes.

ONWARDS 6

Once-weekly insulin icodec vs once-daily insulin degludec in combination with insulin aspart in people with type 1 diabetes

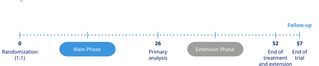
Trial design[1]

582 patients[7]
- T1D treated with basal-bolus insulin
- MDI ≥ 1 year prior to screening
- Age ≥18 years
- HbA_{1c} < 10.0%

Once-weekly insulin icodec + insulin aspart ≥ 2 times daily

Once-daily degludec + insulin aspart ≥ 2 times daily

- Open-label, treat-to-target
- Unblinded CGM



Endpoints[7]

Primary:
The primary endpoint was change in HbA_{1c} from baseline to week 26.

Secondary:
Secondary endpoints included change in fasting plasma glucose (FPG) from baseline to week 26, time in range blood glucose 70-180 mg/dL from week 22 to week 26.

Abbreviations

BID, twice-a-day; CGM, continuous glucose monitoring; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated hemoglobin; OAD, oral antidiabetic medicine; OD, once daily; s.c., subcutaneous; T1D, type 1 diabetes; T2D, type 2 diabetes; U100, 100 units per milliliter; MDI, multiple daily injections.

Glossary

Clinically significant hypoglycemia: Defined as blood glucose measured at <54 mg/dL.

Severe hypoglycemia: No specific glucose threshold but defined when hypoglycemia is associated with severe cognitive impairment and requires external assistance in recovery.

Insulin-naïve: People with type 2 diabetes who have not previously been treated with insulin.

Real-world elements: Data or assessments that include what is happening in routine everyday clinical practice, outside of a clinical trial setting.

References

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