Insulin icodec-abae is approved by the US FDA for the treatment of T2D. It is not currently approved for the treatment of T1D, and its safety and efficacy have not been established for the treatment of T1D. There is no guarantee that insulin icodec-abae will be commercially available for the use(s) under investigation.

ONWARDS 2

Switching from Previous Basal Insulin Therapy in Adults with Type 2 Diabetes

Insulin Icodec-abae vs **Insulin Degludec Injection**

Study Design

ONWARDS 2 was a Phase 3a, randomized, treat-to-target, open label trial comparing safety and efficacy of once-weekly insulin icodec-abae to insulin degludec injection in adult patients (≥18 years old) with type 2 diabetes inadequately controlled on previous once or twice-daily basal insulin therapy with or without non-insulin glucose-lowering drugs.[1]

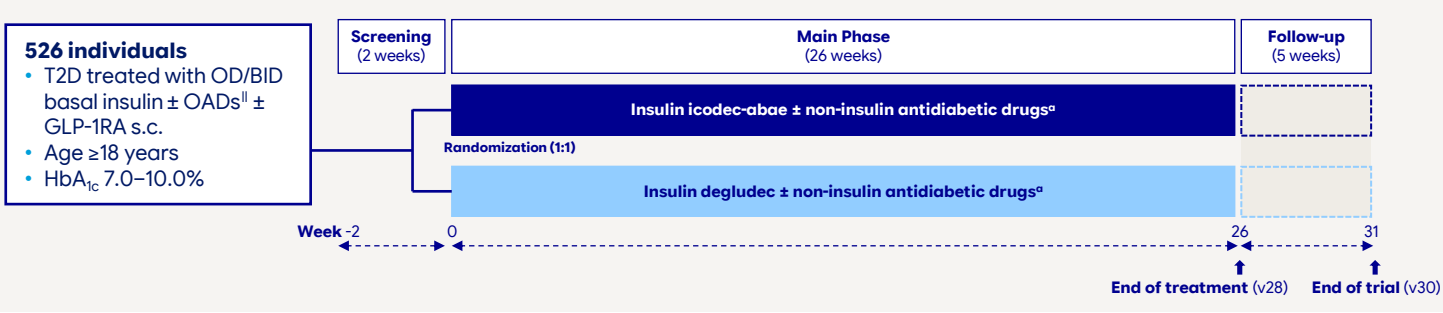
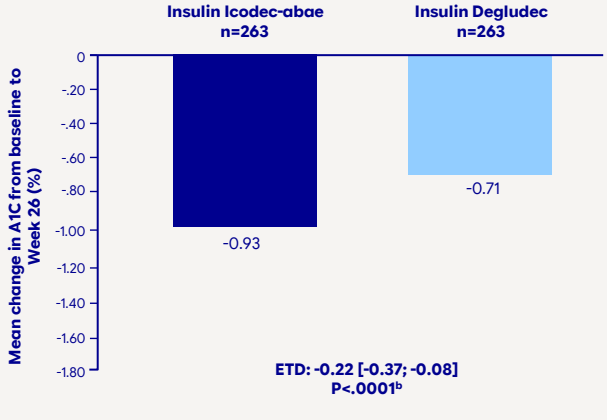


Figure 1. ONWARDS 2 Trial Design[1]

Primary Efficacy Endpoint

The primary endpoint was change in glycosylated hemoglobin (A1C) from baseline to Week 26.[1]



Secondary Efficacy Endpoints and Additional Assessments

Mean change in FPG from baseline to Week 26 (mg/dL)

-28.47 Insulin Icodec-abae — **-29.18** Insulin Degludec

ETD: 0.71 mg/dL [-5.12; 6.54]
P=.81

Patients achieving A1C <7% at Week 26 (%)c

40% Insulin Icodec-abae — **26%** Insulin Degludec

EOR: 1.88 [1.26; 2.79]
P=.0019

Proportion of Time in Range (TIR) (%) from Week 22 to 26c,d

63.1% Insulin Icodec-abae — **59.5%** Insulin Degludec

ETD: 2.41 [-0.84; 5.65]
P=.15

DTSQ score change from baseline (points)

4.22 Insulin Icodec-abae — **2.96** Insulin Degludec

ETD: 1.25 [0.41; 2.10]
P=.0035

Patients achieving A1C <7% at Week 26 without level 2 or 3 hypoglycemia (%)

37% Insulin Icodec-abae — **27%** Insulin Degludec

1.59 [1.07; 2.36]
P=.022*

Safety

Combined level 2 or level 3 hypoglycemia from baseline to Week 26

	n (%)	E (rate per PYE)
Insulin Icodec-abae	**37 (14)**	**113 (0.73)**
Insulin Degludec	19 (7)	42 (0.27)

ERR: 1.93 [0.93; 4.02]
P=.078

Body weight change from baseline to Week 26

1.4 Insulin Icodec-abae — **-0.3** Insulin Degludec

ETD: 1.70 kg [0.76; 2.63]
P<0.0004**

Proportion of Time Below Range (TBR) (%) from Week 22 to 26c,d,‡

0.3% Insulin Icodec-abae — **0.2%** Insulin Degludec

ETD: 1.37 [0.92; 2.04]
P=.12

a. Most common background non-insulin glucose-lowering drugs included metformin, sodium-glucose cotransporter-2 (SGLT-2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, and dipeptidyl peptidase-4 (DPP-4) inhibitors.
b. P-value for non-inferiority. Based on achievement of non-inferiority, superiority was then evaluated and confirmed (P=.0028).
c. Evaluated as an additional assessment.
d. Measurements were conducted via double-blinded continuous glucose monitoring (CGM) using the Dexcom G6 system during Weeks 0 to 4 (after randomization) and from Weeks 22 to 26.
*A1C <7% without level 2 or 3 hypoglycemia in prior 12 weeks. **Statistically significant difference in favor of degludec. ‡The percentage of time spent with glucose levels in the very low range (<54 mg/dL).
‖Pre-trial all OADs including oral GLP-1RAs are allowed but SU and glinides are to be discontinued at randomization
Abbreviations: A1C: glycosylated hemoglobin; E: episodes; EOR: estimated odds ratio; ERR: estimated rate ratio; ETD: estimated treatment difference; FPG: fasting plasma glucose; n: number of patients; PYE: Patient Year of Exposure.

Philis-Tsimikas A, et al. Lancet Diabetes Endocrinol. 2023;11(6):414-425.