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 3

Insulin-Naïve Adults with Type 2 Diabetes

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

Study Design

ONWARDS 3 was a Phase 3a, randomized, double-blind, double-dummy, treat-to-target trial comparing the safety and efficacy of once-weekly insulin icodec-abae to insulin degludec injection in insulin-naïve adult patients (≥ 18 years old) with type 2 diabetes.[1]

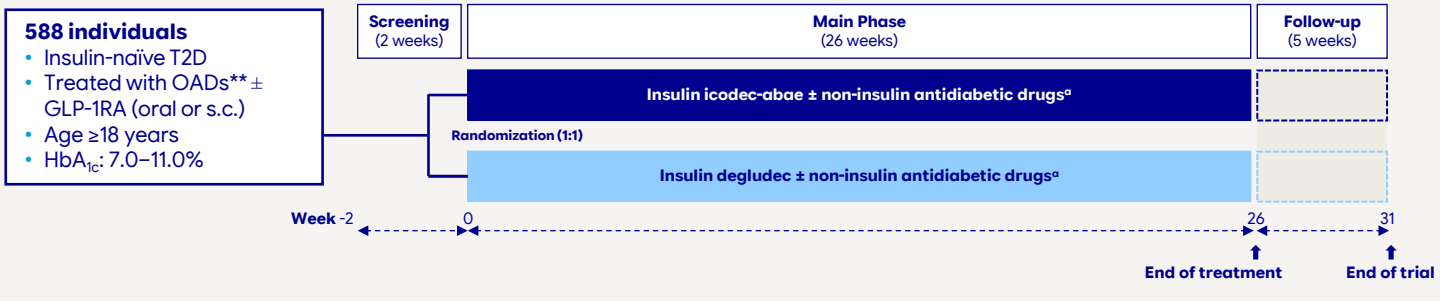
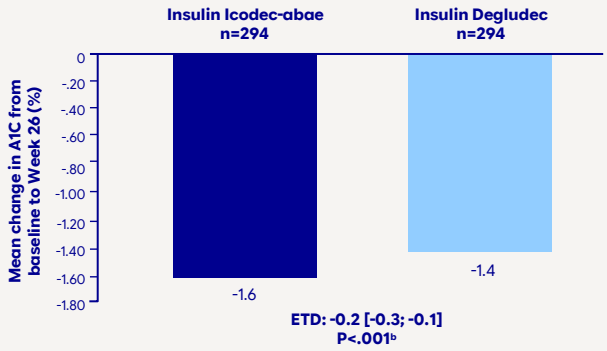


Figure 1. ONWARDS 3 Trial Design[1]

Primary Efficacy Endpoint

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



Secondary Efficacy Endpoints

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

- 54 Insulin Icodec-abae | **- 54** Insulin Degludec

ETD: 0 [-6.0; 5.0]
P=.90

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

52.1% Insulin Icodec-abae | **39.9%** Insulin Degludec

EOR: 1.64 [1.16; 2.33]
P=.005*

Additional Assessments

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

56.8% Insulin Icodec-abae | **41.6%** Insulin Degludec

Safety

Combined level 2 or level 3 hypoglycemia from baseline to Week 31

	n (%)	E (rate per PYE)
Insulin Icodec-abae	**26 (8.9)**	**53 (0.31)**
Insulin Degludec	18 (6.1)	25 (0.15)

ERR: 1.82 [0.87; 3.80]
P=.11

Body weight change from baseline to Week 26

2.8 Insulin Icodec-abae | **2.3** Insulin Degludec

ETD: 0.46 kg [-0.19; 1.10]
P=0.17

a. Most common background non-insulin glucose-lowering drugs at screening included metformin, sodium-glucose cotransporter-2 (SGLT-2) inhibitors, sulfonylureas, dipeptidyl peptidase-4 (DPP-4) inhibitors, and glucagon-like peptide-1 (GLP-1) receptor agonists.
b. P-value for non-inferiority. Based on achievement of non-inferiority, superiority was then evaluated and confirmed _P<.002).
c. Measurements were conducted via double-blinded continuous glucose monitoring (CGM) using the Dexcom G6 system.
*Patients achieving A1C <7% without level 2 or 3 hypoglycemia during the prior 12 weeks. **Sulfonylureas and glinides, if used were reduced by 50% at randomization at the investigator's discretion
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.

1. Lingvay I, et al. JAMA. 2023;330(3):228-237.