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 5

Insulin-Naïve Adults with Type 2 Diabetes

Insulin Icodec-abae 700 units/mL injection with dosing guide vs **Once-daily Basal Insulin Analogs**

Study Design

ONWARDS 5 was a Phase 3a, randomized, open-label, parallel-group trial comparing safety and efficacy of once-weekly insulin icodec-abae titrated using a dosing guide app to once-daily basal insulins dosed and titrated according to standard clinical practice in insulin-naïve adults (≥ 18 years old) with type 2 diabetes (T2D).[1]

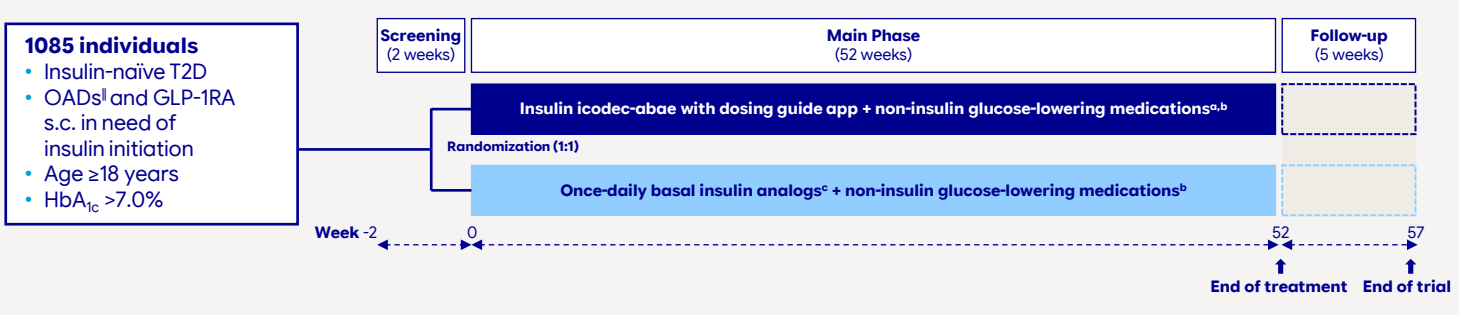
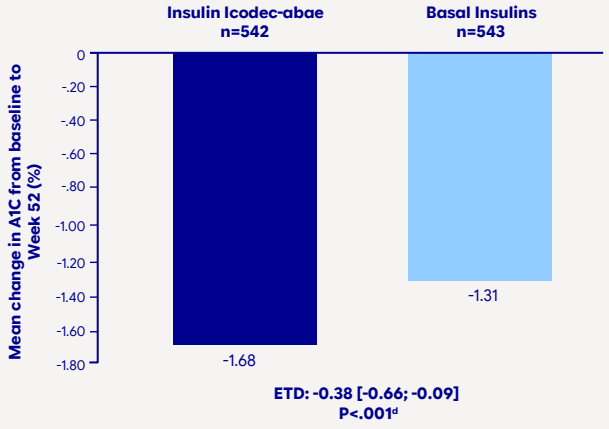


Figure 1. ONWARDS 5 Trial Design[1]

Primary Efficacy Endpoint

The primary endpoint was change in glycosylated hemoglobin (A1C) from baseline to Week 52.[1]



Secondary Efficacy Endpoints and Additional Assessments[1]

Change in DTSQ score from baseline to Week 52

4.68 Insulin Icodec-abae — **3.90** Basal Insulins

ETD: 0.78 [0.10; 1.47]
P=.02

TRIM-D compliance score at Week 52

90.42 Insulin Icodec-abae — **87.37** Basal Insulins

ETD: 3.04 [1.28; 4.81]
P=.0007

Patients achieving A1C <7% at Week 52 (%)

47% Insulin Icodec-abae — **35%** Basal Insulins

EOR: 1.66 [1.24; 2.21]

Patients achieving A1C <7% at Week 52 without level 2 or 3 hypoglycemia (%)**

41% Insulin Icodec-abae — **32%** Basal Insulins

EOR: 1.47 [1.13; 1.92]

Safety

Combined level 2 or level 3 hypoglycemia from baseline to Week 52[1]

	n (%)	E (rate per PYE)
Insulin Icodec-abae	**64 (11.8)**	**104 (0.19)**
Basal Insulins	45 (8.4)	81 (0.14)

ERR: 1.17 [0.73; 1.86]
P=.5153

a. The dosing guide app utilized an algorithm to provide automated weekly dose recommendations of insulin icodec-abae based on patient input of three pre-breakfast self-measured blood glucose (SMBG) values and injection data.[1]
b. 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.
c. Once-daily basal insulins Lantus ® (insulin glargine) injection, U-100, Sanofi-Aventis U.S. LLC, Toujeo® (insulin glargine) injection, U-300, Sanofi-Aventis U.S. LLC, and Tresiba® (insulin degludec) injection.
d. P-value for non-inferiority. Based on achievement of non-inferiority, superiority was then evaluated and confirmed _P<.009).
‖ All pre-trial OADs and s.c. GLP-1RAs are allowed but a 50% dose reduction of SU and glinides are recommended at the discretion of investigator.**Patients achieving A1C<7% without level 2 or 3 hypoglycemia during the previous 12 weeks.
Abbreviations: A1C: glycosylated hemoglobin; DTSQ: Diabetes Treatment Satisfaction Questionnaire; E: episodes; EOR: estimated odds ratio; ETD: estimated treatment difference); n: number of patients; PYE: Patient Year of Exposure; TRIM-D: Treatment Related Impact Measure for Diabetes

1. Bajaj HS, et al. Ann Intern Med. 2023;176(11):1478-1488.