press release

Switching to investigational once-weekly insulin icodec from other basal insulins demonstrated to be efficacious and well-tolerated for people with type 2 diabetes in phase 2 trial

Bagsværd, **Denmark**, **22 September 2020** – Today, Novo Nordisk announced results from three phase 2 clinical trials for insulin icodec, an investigational once-weekly basal insulin analogue, which were presented during the 56th European Association for the Study of Diabetes (EASD) Annual Meeting 2020.

The first showed that switching to insulin icodec from other basal insulins using two different switch approaches was efficacious and well-tolerated compared to once-daily insulin glargine U100 and the switching approaches were without an increased risk of clinically significant or severe hypoglycaemic episodes compared to once-daily insulin glargine U100.[1] This 16-week phase 2 clinical trial involved 154 adults with type 2 diabetes inadequately controlled with oral antidiabetic drugs and once/twice-daily basal insulin randomised to once-weekly insulin icodec with or without a loading dose or insulin glargine U100.[1,2] The primary endpoint of the trial, the blood sugar 'time in range' 3.9–10.0 mmol/L during weeks 15 and 16, showed that people receiving insulin icodec with a loading dose demonstrated a significantly greater 'time in range' compared to insulin glargine U100 (73% vs 65%, respectively). People who received insulin icodec without a loading dose demonstrated similar blood sugar 'time in range' compared to insulin glargine U100 (66% vs 65%, respectively).[1]

"We know that many people with type 2 diabetes prefer simplicity, meaning fewer injections and more convenience than what is currently provided with once- or twice-daily basal insulin treatment regimens," said Dr Harpreet Bajaj, lead trial investigator and endocrinologist, LMC Diabetes & Endocrinology, Ontario, Canada. "This phase 2 trial demonstrates the potential benefit insulin icodec could offer to people with type 2 diabetes in need of insulin therapy, aiding easy transition onto a new treatment option without the daily burden and complexity that is associated with current therapies and potentially even experience more time in good glycaemic control with low risk of hypoglycaemia."

Key secondary endpoints included changes from baseline in HbA_{1c}, which were not statistically significantly different for icodec with and without a loading dose compared to insulin glargine U100 (–0.77, –0.47 and –0.54 % points, respectively). Rates of clinically significant or severe hypoglycaemic episodes, also known as a hypo or low blood sugar, were similar between insulin icodec with a

Novo Nordisk A/S
Corporate Communication

Novo Allé
2880 Bagsværd
Denmark

Tel: +45 4444 8888
www.novonordisk.com

CVR no:
24 25 67 90

VEEVA#: HQ20ICD00001 Date of approval: September 2020

loading dose and insulin glargine U100 (observed rates of level 2 [<3 mmol/L] and 3 [severe] hypoglycaemia were 0.78 and 0.79 events per patient year of exposure for insulin icodec and insulin glargine U100, respectively), and numerically lower for insulin icodec without a loading dose (0.15 events per patient year of exposure). No new safety issues were identified in relation to once-weekly insulin icodec and no severe episodes occurred in this trial.[1]

Data comparing the effect of different titration algorithms of insulin icodec with insulin glargine U100 to better understand the optimal titration for a once-weekly basal insulin in people with type 2 diabetes who were inadequately controlled with oral antidiabetics were also presented at the meeting. In this 16-week trial, all three once-weekly titration algorithms for insulin icodec investigated were shown to be well-tolerated and efficacious, and demonstrated an improved or similar 'time in range' versus once-daily insulin glargine U100, depending on the titration algorithm applied.[3,4]

Results from the 26-week phase 2 clinical trial in insulin-naïve adults with type 2 diabetes where insulin icodec demonstrated comparable blood sugar lowering and a similar safety profile to once-daily insulin glargine U100 were also presented at the EASD Annual Meeting and simultaneously published in the *New England Journal of Medicine*.[5,6] The data were previously presented at the 80th Scientific Sessions of the American Diabetes Association in June 2020.[7]

"As a leader in diabetes innovation, Novo Nordisk understands that there is a need to continue to offer innovative treatment options to support people living with diabetes and improve outcomes," said Mads Krogsgaard Thomsen, executive vice president and chief scientific officer of Novo Nordisk. "We are excited by the phase 2 data that have been presented at EASD 2020 and ADA 2020 for insulin icodec, which demonstrated its efficacy and tolerability, and has the potential to offer a simplified treatment option for people with type 2 diabetes initiating insulin treatment, as well as the option for those to switch."

The phase 2 trials will inform the trial designs for the phase 3 clinical development programme for once-weekly insulin icodec, which Novo Nordisk will initiate later in 2020.

For more news and media materials from Novo Nordisk at EASD 2020, please visit:
https://www.epresspack.net/novonordiskEASD2020/phase-2-once-weekly-insulin

About the phase 2 switching trial
This 16-week, randomised, open label, treat-to-target, phase 2 trial compared the efficacy and safety of once-weekly insulin icodec with and without a loading dose versus once-daily insulin glargine U100* in 154 people with type 2 diabetes inadequately controlled (HbA_{1c} 7.0–10.0%) with oral antidiabetic drugs and once/twice-daily insulin. A unit to unit switch (or a 20% reduction for those receiving twice-daily basal insulin or insulin glargine U300 prior to randomisation) with and without an initial 100% loading dose of insulin icodec was investigated compared to insulin glargine U100.

Insulin doses were titrated weekly based on the lowest (if below target) or the mean of 3 pre-breakfast self-measured blood glucose values to a target of 4.4–7.2 mmol/L. The primary endpoint was 'time in range' 3.9–10.0 mmol/L (70–180 mg/dL) based on continuous glucose monitoring (Dexcom G6®, Dexcom Inc, CA, USA) during weeks 15 and 16. Secondary endpoints included HbA_{1c} and body weight changes from baseline to week 16, weekly insulin dose during weeks 15 and 16, and hypoglycaemic episodes.[1,2]

About insulin icodec

Insulin icodec is an investigational, long-acting basal insulin analogue with a half-life of approximately one week.[8] Once injected, insulin icodec binds strongly but reversibly to albumin. This results in a continuous, slow and steady release of active icodec to achieve effective lowering of blood sugar throughout the week. The injection volume of once-weekly insulin icodec is equivalent to daily insulin glargine U100 due to the concentrated formulation.[9]

About Novo Nordisk

Novo Nordisk is a leading global healthcare company, founded in 1923 and headquartered in Denmark. Our purpose is to drive change to defeat diabetes and other serious chronic diseases such as obesity and rare blood and endocrine disorders. We do so by pioneering scientific breakthroughs, expanding access to our medicines and working to prevent and ultimately cure disease. Novo Nordisk employs about 43,500 people in 80 countries and markets its products in around 170 countries. For more information, visit novonordisk.com, Facebook, Twitter, LinkedIn, YouTube.

Further information

Media:		
Mette Kruse Danielsen	+45 3079 3883	mkd@novonordisk.com
Investors:		
Daniel Muusmann Bohsen	+45 3075 2175	dabo@novonordisk.com
Valdemar Borum Svarrer	+45 3079 0301	jvls@novonordisk.com
Ann Søndermølle Rendbæk	+45 3075 2253	arnd@novonordisk.com
Mark Joseph Root	+45 3079 4211	mjhr@novonordisk.com

---

*NCT03922750: A Research Study in People With Type 2 Diabetes to Compare Two Types of Insulin: Insulin 287 and Insulin Glargine

References

1. Bajaj HS, Isendahl J, Gowda A, *et al*. Efficacy and Safety of Switching to Insulin Icodec, a Once-Weekly Basal Insulin, vs Insulin Glargine U100 in Patients with T2D Inadequately Controlled on OADs and Basal Insulin. Abstract 657. Presented at the 56th European Association for the Study of Diabetes (EASD) Annual Meeting 2020, The impact of new basal insulins, 12:00-13:00 CEST on 22 September 2020.
2. ClinicalTrials.gov. A Research Study in People With Type 2 Diabetes to Compare Two Types of Insulin: Insulin 287 and Insulin Glargine. Available at: https://clinicaltrials.gov/ct2/show/NCT03922750. Last accessed: September 2020.
3. Lingvay I, Koefoed MM, Stachlewska K, *et al.* Effect of Three Different Titration Algorithms of Insulin Icodec vs Insulin Glargine U100 on Time in Range in Patients with T2D Inadequately Controlled on OADs. Abstract 658. Presented at the virtual 56th European Association for the Study of Diabetes (EASD) Annual Meeting 2020, The impact of new basal insulins, 12:00-13:00 CEST on 22 September 2020.
4. ClinicalTrials.gov. A Research Study to Compare Two Types of Insulin: Insulin 287 and Insulin Glargine in People With Type 2 Diabetes Who Have Not Used Insulin Before. Available at: https://clinicaltrials.gov/ct2/show/NCT03951805. Last accessed: September 2020.
5. Rosenstock J, Kjærsgaard MIS, Møller DV, *et al.* Once-Weekly Basal Insulin Icodec Offers Comparable Efficacy and Safety vs Once-Daily Insulin Glargine U100 in Insulin Naïve Patients with T2D Inadequately Controlled on OADs. Abstract 56. Presented at the virtual 56th European Association for the Study of Diabetes Annual Meeting 2020, Developing better insulins, 14:45-15:00 CEST on 22 September 2020.
6. Rosenstock J, Bajaj HS, Janez A, *et al*. Once-Weekly Insulin for Type 2 Diabetes Without Previous Insulin Treatment. *New England Journal of Medicine*. 2020; Published online ahead of print; DOI: 10.1056/NEJMoa2022474. Available at: https://www.nejm.org/doi/full/10.1056/NEJMoa2022474.
7. Rosenstock J, Kjærsgaard MIS, Møller DV, *et al*. Once-Weekly Basal Insulin Icodec Offers Comparable Efficacy and Safety vs Once-Daily Insulin Glargine U100 in Insulin Naïve Patients with T2D Inadequately Controlled on OADs. Abstract 238-OR. Presented at the 80th Scientific Sessions of the Virtual American Diabetes Association Annual Meeting, Insulin Therapies, 18:15-18:30 CDT on 14 June 2020.
8. Hövelmann U, Brøndsted L, Kristensen NR. *et al.* Insulin Icodec: An Insulin Analog Suited for Once-Weekly Dosing in Type 2 Diabetes. Abstract 237-OR. Presented at the 80th Scientific Sessions of the American Diabetes Association, Insulin Therapies, 18:00-18:15 CDT on 14 June 2020.
9. Nishimura E, Kjeldsen T, Hubálek F, *et al*. Molecular and Biological Properties of Insulin Icodec, a New Insulin Analog Designed to Give a Long Half-Life Suitable for Once-Weekly Dosing. Abstract 236-OR. 80th Scientific Sessions of the American Diabetes Association; Insulin Therapies, 17:45-18:00 CDT on 14 June 2020.

Novo Nordisk A/S
Corporate Communication

Novo Allé
2880 Bagsværd
Denmark

Tel: +45 4444 8888
www.novonordisk.com

CVR no:
24 25 67 90