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Before joining a study, talk to your health care professional about possible risks and benefits. To learn more about taking part in studies, read Learn About Studies (https://clinicaltrials.gov/study-basics/learn-about-studies).

Completed

A Research Study to See How Semaglutide Works Compared to Placebo in People With Type 2 Diabetes and Chronic Kidney Disease (FLOW)

ClinicalTrials.gov ID NCT03819153

Sponsor Novo Nordisk A/S

Information provided by Novo Nordisk A/S (Responsible Party)

Last Update Posted 2024-08-02

Study Details Tab

Study Overview

Brief Summary

The researchers are doing this study to see if semaglutide can slow down the growth and worsening of chronic kidney disease in people with type 2 diabetes. Participants will get semaglutide (active medicine) or placebo ('dummy medicine'). This is known as participants' study medicine - which treatment participants get is decided by chance. Semaglutide is a medicine, doctors can prescribe in some countries for the treatment of type 2 diabetes. Participants will get the study medicine in a pen. Participants will use the pen to inject the medicine in a skin fold once a week. The study will close when there is enough information collected to show clear result of the study. The total time participants will be in this study is about 3 to 5 years, but it could be longer.

Official Title

Effect of Semaglutide Versus Placebo on the Progression of Renal Impairment in Subjects With Type 2 Diabetes and Chronic Kidney Disease

Conditions

Diabetes Mellitus, Type 2

Intervention / Treatment

- Drug: Semaglutide
- Drug: Placebo (semaglutide)

Other Study ID Numbers

- NN9535-4321
- U1111-1217-6259 (Other Identifier) (OTHER: World Health Organization (WHO))

Study Start (Actual)

2019-06-17

Primary Completion (Actual)

2024-01-09

Study Completion (Actual)

2024-01-09

Enrollment (Actual)

3508

Study Type

Interventional

Phase

Phase 3

Resource links provided by the National Library of Medicine

MedlinePlus Genetics (https://medlineplus.gov/genetics/) related topics: Type 2 diabetes (https://medlineplus.gov/genetics/condition/type-2-diabetes)

MedlinePlus (https://medlineplus.gov/) related topics: Kidney Diseases (https://medlineplus.gov/kidneydiseases.html)

Genetic and Rare Diseases Information Center (https://rarediseases.info.nih.gov/gard) resources: Chronic Graft Versus Host Disease (https://rarediseases.info.nih.gov/diseases/10964/chronic-graft-versus-host-disease)

Drug Information (https://dailymed.nlm.nih.gov/dailymed/) available for: Semaglutide (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Semaglutide)

FDA Drug and Device Resources (https://clinicaltrials.gov/fda-links)

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the Contacts and Locations section in How to Read a Study Record (https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations).

Chiang Mai, Mueang Chiang Mai District, Thailand, 50200
Maharaj Nakorn Chiang Mai Hospital

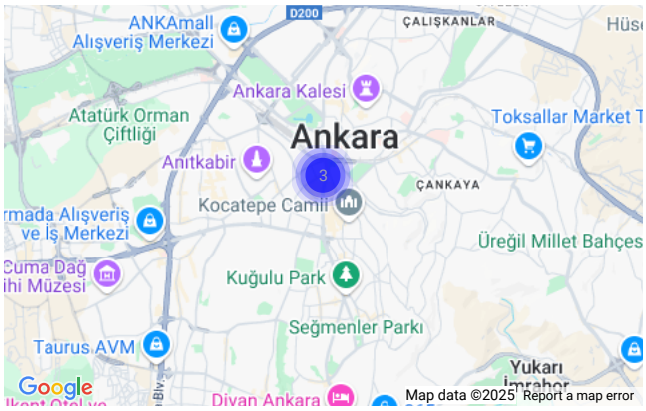
Turkey

Ankara, Turkey, 06100
Ankara Universitesi Ibni Sina Hastanesi

Ankara, Turkey, 06230
Hacettepe Universitesi Tip Fakultesi Nefroloji Bilim Dali

Ankara, Turkey, 06500
Gazi University Medical Faculty- Nephrology

Antalya, Turkey, 07058
Akdeniz Universitesi Hastanesi Nefroloji Bilim Dali



Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read Learn About Studies (https://clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Inclusion Criteria:

- Male or female, age above or equal to 18 years at the time of signing informed consent. Japan: Male or female, age above or equal to 20 years at the time of signing informed consent
- Diagnosed with type 2 diabetes mellitus
- HbA1c less than or equal to 10% (less than or equal to 86 mmol/mol)
- Renal impairment defined either by:
    1. serum creatinine-based eGFR greater than or equal to 50 and less than or equal to 75 mL/min/1.73 m^2 (CKD-EPI) and UACR greater than 300 and less than 5000 mg/g or
    2. serum creatinine-based eGFR greater than or equal to 25 and less than 50 mL/min/1.73 m^2 (CKD-EPI) and UACR greater than 100 and less than 5000 mg/g
- Treatment with maximum labelled or tolerated dose of a renin-angiotensin-aldosterone system (RAAS) blocking agent including an angiotensin converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB), unless such treatment is contraindicated or not tolerated. Treatment dose must be stable for at least 4 weeks prior to the date of the laboratory assessments used for determination of the inclusion criteria for renal impairment and kept stable until screening

Exclusion Criteria:

- Congenital or hereditary kidney diseases including polycystic kidney disease, autoimmune kidney diseases including glomerulonephritis or congenital urinary tract malformations
- Use of any glucagon-like peptide-1 (GLP-1) receptor agonist within 30 days prior to screening
- Myocardial infarction, stroke, hospitalisation for unstable angina pectoris or transient ischaemic attack within 60 days prior to the day of screening
- Presently classified as being in New York Heart Association (NYHA) Class IV heart failure
- Planned coronary, carotid or peripheral artery revascularisation
- Current (or within 90 days) chronic or intermittent haemodialysis or peritoneal dialysis
- Uncontrolled and potentially unstable diabetic retinopathy or maculopathy. Verified by a fundus examination performed within the past 90 days prior to screening or in the period between screening and randomisation. Pharmacological pupil-dilation is a requirement unless using a digital fundus photography camera specified for non-dilated examination

Ages Eligible for Study

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study

All

Accepts Healthy Volunteers

No

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose : Treatment
Allocation : Randomized
Interventional Model : Parallel Assignment
Masking : Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Masking Description: Sponsor staff involved in the clinical trial is masked according to company standard procedures

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Semaglutide Participants are to receive semglutide for up to 5 years or more (event driven). The trial is event driven with a pre-defined minimum number of renal endpoint events for the primary endpoint.	Drug: Semaglutide • Participants are to inject semaglutide with a needle in the stomach, thigh or upper arm. Participants will use a pen to inject semaglutide under their skin. Participants will inject semaglutide 1 time a week on the same day of the week. Participants' dose of semaglutide will be changed over time. Participants start by taking a smaller amount (0.25 mg). After 4 weeks the dose will be increased to 0.5 mg. It will be increased more (to 1 mg) at 8 weeks. Participants will then stay on the same dose for the rest of the study.
Placebo Comparator: Placebo Participants are to receive placebo (semglutide) for up to 5 years or more (event driven). The trial is event driven with a pre-defined minimum number of renal endpoint events for the primary endpoint.	Drug: Placebo (semaglutide) • Participants are to inject placebo (semaglutide) with a needle in the stomach, thigh or upper arm. Participants will use a pen to inject placebo (semaglutide) under their skin. Participants will inject placebo (semaglutide) 1 time a week on the same day of the week. Participants' dose of placebo (semaglutide) will be changed over time. Participants start by taking a smaller amount (0.25 mg). After 4 weeks the dose will be increased to 0.5 mg. It will be increased more (to 1 mg) at 8 weeks. Participants will then stay on the same dose for the rest of the study.

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Time to first occurrence of a composite primary outcome event defined as persistent eGFR decline of greater than or equal to 50 percentage from trial start, reaching ESRD, death from kidney disease or death from cardiovascular disease	Measured in month(s). End Stage Renal Disease (ESRD) is defined as the following individual components: Persistent estimated glomerular filtration rate (eGFR) less than 15 mL/min/1.73m^2 or, Chronic dialysis treatment or receiving a kidney transplantation.	Week 0 to month 61

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Annual rate of change in eGFR (chronic kidney disease - epidemiology collaboration (CKD-EPI)) (total eGFR slope)	Measured in (mL/min/1.73 m^2)/year.	Week 0 to month 61
Time to first occurrence of a composite cardiovascular major adverse cardiovascular event (MACE) endpoint consisting of: Non-fatal myocardial infarction, non-	Measured in month(s).	Week 0 to month 61

fatal stroke, and cardiovascular (CV) death		
Time to occurrence of all-cause death	Measured in month(s).	Week 0 to month 61
Time to occurrence of each of the individual components of the primary composite endpoint and of the confirmatory secondary MACE endpoint	Measured in month(s).	Week 0 to month 61
Time to first occurrence of major adverse limb events (MALE), a composite endpoint consisting of: Acute limb ischemia hospitalisation and chronic limb ischemia hospitalisation	Measured in month(s).	Week 0 to month 61
Annual rate of change in eGFR (CKD-EPI) (chronic eGFR slope)	Measured in (mL/min/1.73 m^2)/year.	Week 12 to month 61
Change in eGFR (CKD-EPI)	Measured in mL/min/1.73 m^2.	Week 0, Week 12
Change in eGFR (cystatin C CKD-EPI)	Measured in mL/min/1.73 m^2.	Week 0, Year 3
Relative change in urinary albumin-to-creatinine ratio (UACR)	Measured in percentage.	Week 0, Year 3
Change in body weight	Measured in kilogram.	Week 0, Year 3
Change in glycosylated haemoglobin (HbA1c)	Measured in percentage point.	Week 0, Year 3
Change in systolic blood pressure	Measured in mmHg.	Week 0, Year 3
Change in diastolic blood pressure	Measured in mmHg.	Week 0, Year 3
Number of severe hypoglycaemic episodes	Number of events.	Week 0 to month 61

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Novo Nordisk A/S

Investigators

- Study Director: Clinical Transparency (dept. 1452), Novo Nordisk A/S

Publications

General

These publications are provided voluntarily by the person who enters information about the study and may be about anything related to the study.

- Rossing P, Baeres FMM, Bakris G, Bosch-Traberg H, Gislum M, Gough SCL, Idorn T, Lawson J, Mahaffey KW, Mann JFE, Mersebach H, Perkovic V, Tuttle K, Pratley R. The rationale, design and baseline data of FLOW, a kidney outcomes trial with once-weekly semaglutide in people with type 2 diabetes and chronic kidney disease. Nephrol Dial Transplant. 2023 Aug 31;38(9):2041-2051. doi: 10.1093/ndt/gfad009. Erratum In: Nephrol Dial Transplant. 2024 Mar 27;39(4):724. doi: 10.1093/ndt/gfad252. (https://pubmed.ncbi.nlm.nih.gov/36651820)

From PubMed

These publications come from PubMed, a public database of scientific and medical articles. This list is automatically created by ClinicalTrials.gov Identifier (NCT Number), and these articles may or may not be about the study.

- Cohen S, Sternlicht H, Bakris GL. Mineralocorticoid Receptor Antagonists in the Treatment of Diabetic Kidney Disease: Their Application in the Era of SGLT2 Inhibitors and GLP-1 Receptor Agonists. Curr Diab Rep. 2022 May;22(5):213-218. doi: 10.1007/s11892-022-01461-4. Epub 2022 Apr 20. (https://pubmed.ncbi.nlm.nih.gov/35441935)

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted
2019-01-18

First Submitted that Met QC Criteria
2019-01-25

First Posted
2019-01-28

Study Record Updates

Last Update Submitted that met QC Criteria
2024-08-01

Last Update Posted
2024-08-02

Last Verified
2024-08

More Information

Terms related to this study

Additional Relevant MeSH Terms

Glucose Metabolism Disorders
Metabolic Diseases
Endocrine System Diseases
Urologic Diseases
Female Urogenital Diseases
Female Urogenital Diseases and Pregnancy Complications
Urogenital Diseases

Male Urogenital Diseases
Renal Insufficiency
Chronic Disease
Disease Attributes
Pathologic Processes
Kidney Diseases
Renal Insufficiency, Chronic
Diabetes Mellitus
Diabetes Mellitus, Type 2
Glucagon-Like Peptide-1 Receptor Agonists
Hypoglycemic Agents
Physiological Effects of Drugs
Semaglutide

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)?

Yes

IPD Plan Description

According to the Novo Nordisk disclosure commitment on novonordisk-trials.com

IPD Sharing Url

https://www.novonordisk-trials.com (https://www.novonordisk-trials.com)

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

Yes

Studies a U.S. FDA-Regulated Device Product

No