Trial to evaluate cardiovascular and other long-term outcomes with semaglutide in subjects with type 2 diabetes

This trial is conducted globally.

The aim of the trial is to evaluate cardiovascular and other long-term outcomes with semaglutide in subjects with type 2 diabetes. The trial is event-driven, i.e. the maximum trial duration (up to max. 148 weeks) will depend on the accrual of major adverse cardiovascular events (MACE) in this trial and the remaining research programme. The incidence of MACE will be monitored throughout the trial which will be terminated according to plan when pre-specified stopping criteria are met.

Scientific Title
A long-term, randomised, double-blind, placebo-controlled, multinational, multi-centre trial to evaluate cardiovascular and other long-term outcomes with semaglutide in subjects with type 2 diabetes (SUSTAIN™ 6 – Long-term outcomes)

Trial IDs and acronym(s)
Novo Nordisk Trial ID
NN9535-3744

Clinical Trials.gov Registration
NCT01720446

Other Identifier(s)
EudraCT Number: 2012-002839-28
Other Identifier: U1111-1131-7227
SUSTAIN™ 6

Condition
Diabetes
Diabetes Mellitus, Type 2

Trial dates
Primary completion date: 15.Mar.2016
Completion date: 15.Mar.2016

Trial phase
Phase 3

Treatment
• semaglutide
• placebo

Arm Information with Assigned Treatment
No. of arms: 4
• Semaglutide 0.5 mg (Experimental):
  Arm description:
  Drug: semaglutide
  Once weekly doses of 0.5 mg semaglutide after an initial dose escalation step of 0.25 mg as
an add-on to the standard-of-care treatment. Administered subcutaneously (s.c., under the skin)

• Semaglutide 1.0 mg (Experimental):
  Arm description:
  Drug: semaglutide
  Once weekly doses of 1.0 mg semaglutide after an initial dose escalation step of 0.25 mg followed by 0.5 mg dose escalation as an add-on to the standard-of-care treatment. Administered subcutaneously (s.c., under the skin)

• Semaglutide placebo 0.5 mg (Placebo Comparator):
  Arm description:
  Drug: placebo
  Once weekly doses volume-matched placebo, as an add-on to the standard-of-care treatment. Administered subcutaneously (s.c., under the skin).

• Semaglutide placebo 1.0 mg (Placebo Comparator):
  Arm description:
  Drug: placebo
  Once weekly doses volume-matched placebo, as an add-on to the standard-of-care treatment. Administered subcutaneously (s.c., under the skin).

<table>
<thead>
<tr>
<th>Trial status</th>
<th>No. of trial participants</th>
</tr>
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<tbody>
<tr>
<td>Completed</td>
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<table>
<thead>
<tr>
<th>Age eligible for trial participation</th>
<th>Genders eligible for trial participation</th>
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<tbody>
<tr>
<td>50 years and above</td>
<td>Both</td>
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<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>Men and women with type 2 diabetes mellitus</td>
<td>Type 1 diabetes mellitus</td>
</tr>
<tr>
<td>Age above or equal to 50 years at screening and clinical evidence of cardiovascular disease or age above or equal to 60 years at screening and subclinical evidence of cardiovascular disease</td>
<td>Use of glucagon-like peptide-1 (GLP-1) receptor agonist (exenatide, liraglutide, or other) or pramlintide within 90 days prior to screening</td>
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<tr>
<td>Anti-diabetic drug naïve, or treated with one or two oral antidiabetic drug (OADs), or treated with human Neutral Protamin Hagedorn (NPH) insulin or long-acting insulin analogue or pre-mixed insulin, both types of insulin either alone or in combination with one or two OADs</td>
<td>Use of any dipeptidyl peptidase 4 (DPP-IV) inhibitor within 30 days prior to screening</td>
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<tr>
<td>Treatment with insulin other than basal and pre-mixed insulin within 90 days prior to screening - except for short-term use in connection with intercurrent illness</td>
<td>Acute decompensation of glycaemic control requiring immediate intensification of treatment to prevent acute complications of</td>
</tr>
</tbody>
</table>

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- HbA1c above or equal to 7.0% at screening
- diabetes (e.g., diabetes ketoacidosis) within 90 days prior to screening
- History of chronic pancreatitis or idiopathic acute pancreatitis
- Acute coronary or cerebro-vascular event within 90 days prior to randomisation
- Currently planned coronary, carotid or peripheral artery revascularisation
- Chronic heart failure New York Heart Association (NYHA) class IV
- Personal or family history of multiple endocrine neoplasia type 2 (MEN2) or familial medullary thyroid carcinoma
- Personal history of non-familial medullary thyroid carcinoma
- Screening calcitonin above or equal to 50 ng/L

**Trial type**
[Interventional]

**Trial design**
Purpose: Treatment
Allocation: Randomized
Masking: Double Blind
Control: Placebo Control
Assignment: Parallel Assignment

**Primary outcome**
- Time from randomisation to first occurrence of a MACE, defined as cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke
  Time frame: Time from randomisation up to end of follow up scheduled at week 109

**Secondary outcome(s)**
- Time from randomisation to first occurrence of an expanded composite cardiovascular outcome
  Time frame: Time from randomisation up to end of follow up scheduled at week 109
- Time from randomisation to each individual component of the expanded composite cardiovascular outcome
  Time frame: Time from randomisation up to end of follow up scheduled at week 109
- Time from randomisation to first occurrence of all-cause death, non-fatal MI, or non-fatal stroke
  Time frame: Time from randomisation up to end of follow up scheduled at week 109
- Change from baseline to last assessment during the treatment period in other treatment outcomes: glycosylated haemoglobin (HbA1c)
  Time frame: Week 0, up to week 104

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- Change from baseline to last assessment during the treatment period in other treatment outcomes: fasting plasma glucose
  Time frame: Week 0, up to week 104
- Change from baseline to last assessment during the treatment period in other treatment outcomes: body weight
  Time frame: Week 0, up to week 104
- Change from baseline to last assessment during the treatment period in other treatment outcomes: lipid profile
  Time frame: Week 0, up to week 104
- Change from baseline to last assessment during the treatment period in other treatment outcomes: urinary albumin to creatinine ratio
  Time frame: Week 0, up to week 104
- Change from baseline to last assessment during the treatment period in other treatment outcomes: vital signs
  Time frame: Week 0, up to week 104
- Incidence during the treatment period in other treatment outcomes: hypoglycaemic events
  Time frame: Weeks 0-109
- Incidence during the treatment period in other treatment outcomes: adverse events
  Time frame: Weeks 0-109
- Occurrence during the treatment period in other treatment outcomes: anti-semaglutide antibodies
  Time frame: Weeks 0-109
- Change from baseline to last assessment during the treatment period in other treatment outcomes: patient reported outcome (PRO)
  Time frame: Week 0, up to week 104

**Participating countries**
- Algeria: Completed
- Argentina: Completed
- Australia: Completed
- Brazil: Completed
- Bulgaria: Completed
- Canada: Completed/Suspended
- Denmark: Completed

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<table>
<thead>
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<td>United States</td>
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**Central contact information**

Trial sponsored by: Novo Nordisk A/S  
Contact: clinicaltrials@novonordisk.com  
For trials conducted in the US: (+1) 866-867-7178

**Labeling information**

N/A

Information provided by Novo Nordisk A/S  
PDF generation date: 10.Oct.2017

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