The efficacy and safety of liraglutide as adjunct therapy to insulin in the treatment of type 1 diabetes

This trial is conducted globally. The aim of the trial is to confirm the efficacy and safety of liraglutide as adjunct therapy to insulin in the treatment of type 1 diabetes. The total trial duration per subject is approximately 58 weeks.

**Scientific Title**
The efficacy and safety of liraglutide as adjunct therapy to insulin in the treatment of type 1 diabetes. A 52-week randomised, treat-to-target, placebo-controlled, double blinded, parallel group, multinational, multi-centre trial

<table>
<thead>
<tr>
<th>Trial IDs and acronym(s)</th>
<th>Condition</th>
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<tbody>
<tr>
<td>Novo Nordisk Trial ID</td>
<td>Diabetes</td>
</tr>
<tr>
<td>NN9211-3919</td>
<td>Diabetes Mellitus, Type 1</td>
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<td>Clinical Trials.gov Registration</td>
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<td>Other Identifier(s)</td>
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<td>Other Identifier: U1111-1133-0590</td>
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<tr>
<td>ADJUNCT ONE™</td>
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<table>
<thead>
<tr>
<th>Trial dates</th>
<th>Trial phase</th>
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<tbody>
<tr>
<td>Start date: 30.Nov.2013</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Primary completion date: 30.Jun.2015</td>
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<td>Completion date: 30.Jun.2015</td>
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<th>Treatment</th>
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<tbody>
<tr>
<td>• liraglutide</td>
</tr>
<tr>
<td>• placebo</td>
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</tbody>
</table>

**Arm Information with Assigned Treatment**
No. of arms: 6

- Liraglutide 0.6 mg + insulin (Experimental):
  - Arm description:
  - Drug: liraglutide
  - Subjects randomised to 0.6 mg liraglutide treatment or liraglutide placebo as an add-on to their pre-trial insulin treatment will remain on this dose throughout the study (52 weeks).
  - Administered subcutaneously (s.c., under the skin) once daily.
- Liraglutide 1.2 mg + insulin (Experimental):

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http://www.novonordisk-trials.com
Arm description:
Drug: liraglutide
Subjects randomised to 0.6 mg liraglutide treatment or liraglutide placebo as an add-on to their pre-trial insulin treatment will remain on this dose throughout the study (52 weeks). Administered subcutaneously (s.c., under the skin) once daily.

- Liraglutide 1.8 mg + insulin (Experimental):
  Arm description:
  Drug: liraglutide
  Subjects randomised to 0.6 mg liraglutide treatment or liraglutide placebo as an add-on to their pre-trial insulin treatment will remain on this dose throughout the study (52 weeks). Administered subcutaneously (s.c., under the skin) once daily.

- Liraglutide placebo 0.6 mg + insulin (Placebo Comparator):
  Arm description:
  Drug: placebo
  Subjects randomised to 0.6 mg liraglutide treatment or liraglutide placebo as an add-on to their pre-trial insulin treatment will remain on this dose throughout the study (52 weeks). Administered subcutaneously (s.c., under the skin) once daily.

- Liraglutide placebo 1.2 mg + insulin (Placebo Comparator):
  Arm description:
  Drug: placebo
  Subjects randomised to 0.6 mg liraglutide treatment or liraglutide placebo as an add-on to their pre-trial insulin treatment will remain on this dose throughout the study (52 weeks). Administered subcutaneously (s.c., under the skin) once daily.

- Liraglutide placebo 1.8 mg + insulin (Placebo Comparator):
  Arm description:
  Drug: placebo
  Subjects randomised to 0.6 mg liraglutide treatment or liraglutide placebo as an add-on to their pre-trial insulin treatment will remain on this dose throughout the study (52 weeks). Administered subcutaneously (s.c., under the skin) once daily.

<table>
<thead>
<tr>
<th>Trial status</th>
<th>No. of trial participants</th>
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<tbody>
<tr>
<td>Completed</td>
<td>1398</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>18 years to 75 years</td>
<td>Both</td>
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<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>- Informed consent obtained</td>
<td>- Prior use of glucagon-like peptide-1 (GLP-1) receptor agonist or dipeptidyl peptidase IV (DPP-4) inhibitors</td>
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<tr>
<td>- Type 1 diabetes mellitus for 12 months or longer</td>
<td>- Use of any medication, which is in the</td>
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<tr>
<td>- Basal bolus or CSII (Continuous</td>
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http://www.novonordisk-trials.com
Subcutaneous Insulin Infusion, insulin pump) treatment for 6 months or longer
- Stable insulin treatment for the last 3 months prior to Screening, as judged and documented by the investigator
- HbA1c 7.0-10% (Diabetes Control and Complications Trial (DCCT)), both inclusive, (corresponding to 53-86 mmol/mol (International Federation of Clinical Chemistry (IFCC))
- Ability and willingness to comply with all protocol procedures e.g. correct handling of trial product, complete trial related questionnaires, diaries, self-monitoring of plasma glucose, self titration of insulin and attend all scheduled visits
- investigator’s opinion could interfere with the glycaemic control or affect the subject’s safety.Premix insulin is not allowed
- Known proliferative retinopathy or maculopathy requiring acute treatment
- Severe neuropathy, in particular autonomic neuropathy, i.e. gastroparesis, as judged by the investigator
- Uncontrolled/ untreated blood pressure at screening above 160 mmHg for systolic or above 100 mmHg for diastolic
- History of acute or chronic pancreatitis
- Screening calcitonin value equal to or above 50 ng/L
- Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia type 2 (MEN2)
- Diagnosis of malignant neoplasm in the previous 5 years (except basal cell skin cancer or squamous cell skin cancer)

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<tr>
<th>Trial type</th>
<th>Interventional</th>
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| Trial design | Purpose: Treatment  
Allocation: Randomized  
Masking: Double Blind  
Control: Placebo Control  
Assignment: Parallel Assignment |

| Primary outcome |  
• Change from baseline in HbA1c (glycosylated haemoglobin)  
Time frame: Week 0, week 52  
• Change from baseline in body weight  
Time frame: Week 0, week 52  
• Change from baseline in total daily insulin dose  
Time frame: Week 0, week 52 |
| Secondary outcome(s) |  
• Number of treatment-emergent symptomatic hypoglycaemic episodes  
Time frame: Weeks 0-52 |

| Participating countries |  
Argentina: Completed  
Australia: Completed  
Belgium: Completed  
Canada: Completed/Suspended  
Finland: Completed/Suspended  
France: Completed  
Germany: Completed/Suspended |
Ireland: Completed
Israel: Completed
Netherlands: Completed/Suspended
Norway: Completed
Poland: Completed
Russian Federation: Completed
Sweden: Completed
Ukraine: Completed
United Kingdom: Completed
United States: Completed/Suspended

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
• EU:

Information provided by Novo Nordisk A/S
PDF generation date: 27.Oct.2017

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