Summary

EudraCT Number: 2009-012201-19

Sponsor's Protocol Code Number: EX2211-3748

National Competent Authority: Spain - AEMPS

Clinical Trial Type: EEA CTA

Trial Status: Completed

Date on which this record was first entered in the EudraCT database: 2010-07-21

Link: https://www.clinicaltrialsregister.eu/ctr-search/trial/2009-012201-19/ES/

A. Protocol Information

A.1 Member State Concerned: Spain - AEMPS

A.2 EudraCT number: 2009-012201-19

A.3 Full title of the trial: LEADER

(ES): Efecto y acción de laliraglutida en la diabetes: evaluación de los resultados de criterios de valoración cardiovasculares. Estudio a largo plazo, multicéntrico, internacional, aleatorizado, doble ciego y controlado con placebo para determinar los efectos de la liraglutida sobre los episodios cardiovasculares.

(EN): Liraglutide Effect and Action in Diabetes:

Evaluation of cardiovascular outcome Results

A Long-term, Multi-centre, International, Randomised Double-blind, Placebo-controlled Trial to Determine Liraglutide Effects on Cardiovascular Events

A.3.2 Name or abbreviated title of the trial where available: LEADER

A.4.1 Sponsor's protocol code number: EX2211-3748

A.7 Trial is part of a Paediatric Investigation Plan: Information not present in EudraCT

A.8 EMA Decision number of Paediatric Investigation Plan:

B. Sponsor Information

Sponsor 1

B.1.1 Name of Sponsor: Novo Nordisk A/S

B.1.3.4 Country: Denmark

B.3.1 and B.3.2 Status of the sponsor: Commercial

B.4 Source(s) of Monetary or Material Support for the clinical trial:

B.4.1 Name of organisation providing support:

B.4.2 Country:

B.5 Contact point designated by the sponsor for further information on the trial

B.5.1 Name of organisation:

B.5.2 Functional name of contact point:

D. IMP Identification

D.IMP: 1

D.1.2 and D.1.3 IMP Role: Test

D.2 Status of the IMP to be used in the clinical trial

D.2.1 IMP to be used in the trial has a marketing authorisation: Yes

D.2.1.1.1 Trade name: VICTOZA 6 mg/ml solución inyectable en pluma precargada

D.2.1.1.2 Name of the Marketing Authorisation holder: NOVO NORDISK A/S

D.2.1.2 Country which granted the Marketing Authorisation: Spain

D.2.5 The IMP has been designated in this indication as an orphan drug in the Community: No

D.2.5.1 Orphan drug designation number:

D.3 Description of the IMP

D.3.4 Pharmaceutical form: Solution for injection

D.3.4.1 Specific paediatric formulation: Information not present in EudraCT

D.3.7 Routes of administration for this IMP:

Subcutaneous use

D.3.8 to D.3.10 IMP Identification Details (Active Substances)

D.3.8 INN - Proposed INN: LIRAGLUTIDA

D.3.9.3 Other descriptive name: LIRAGLUTIDA

D.3.10 Strength

D.3.10.1 Concentration unit: mg/ml milligram(s)/millilitre

D.3.10.2 Concentration type: equal

D.3.10.3 Concentration number: 6.0

D.3.11 The IMP contains an

D.3.11.1 Active substance of chemical origin: No

D.3.11.2 Active substance of biological/ biotechnological origin (other than Advanced Therapy IMP (ATIMP): Yes

D.3.11.3 Advanced Therapy IMP (ATIMP): Information not present in EudraCT

D.3.11.3.1 Somatic cell therapy medicinal product: No

D.3.11.3.2 Gene therapy medical product: No

D.3.11.3.3 Tissue Engineered Product: Information not present in EudraCT

D.3.11.3.4 Combination ATIMP (i.e. one involving a medical device): Information not present in EudraCT

D.3.11.3.5 Committee on Advanced therapies (CAT) has issued a classification for this product: Information not present in EudraCT

D.3.11.4 Combination product that includes a device, but does not involve an Advanced Therapy: Information not present in EudraCT

D.3.11.5 Radiopharmaceutical medicinal product: No

D.3.11.6 Immunological medicinal product (such as vaccine, allergen, immune serum): No

D.3.11.7 Plasma derived medicinal product: No

D.3.11.8 Extractive medicinal product: No

D.3.11.9 Recombinant medicinal product: Information not present in EudraCT

D.3.11.10 Medicinal product containing genetically modified organisms: No

D.3.11.11 Herbal medicinal product: No

D.3.11.12 Homeopathic medicinal product: No

D.3.11.13 Another type of medicinal product: No

D.8 Information on Placebo

D.8 Placebo: 1

D.8.1 Is a Placebo used in this Trial? Yes

D.8.3 Pharmaceutical form of the placebo: Solution for injection

D.8.4 Route of administration of the placebo: Subcutaneous use

E. General Information on the Trial

E.1 Medical condition or disease under investigation

E.1.1 Medical condition(s) being investigated: (ES): Diabetes mellitus tipo 2

(EN): Type 2 diabetes mellitus

MedDRA Classification

E.1.2 Medical condition or disease under investigation:

E.1.2 Version: 12.1

E.1.2 Level: LLT

E.1.2 Classification code: 10067585

E.1.2 Term: Type 2 diabetes mellitus

E.1.3 Condition being studied is a rare disease: No

E.2 Objective of the trial

E.2.1 Main objective of the trial: (ES): Evaluar el efecto del tratamiento con liraglutida en comparación con un placebo durante un mínimo de 3,5 años y un máximo de 5 años sobre la incidencia de episodios cardiovasculares, según lo definido por los siguientes criterios de valoración principales y secundarios, en adultos con diabetes tipo 2 que tienen un riesgo elevado de sufrir episodios cardiovasculares.

(EN): To assess the effect of treatment with liraglutide compared to placebo for at least 3.5 year and up to 5 years on the incidence of cardiovascular events, as defined by the below primary and secondary endpoints, in adults with type 2 diabetes that are at high risk for cardiovascular events

E.2.2 Secondary objectives of the trial: (ES): Evaluar la eficacia y la seguridad con respecto a acontecimientos clínicamente importantes u otros parámetros sustitutivos del tratamiento con liraglutida en comparación con un placebo en adultos con diabetes tipo 2 que tienen un riesgo elevado de sufrir episodios cardiovasculares.

(EN): To assess the efficacy and safety with regard to clinically important events or other surrogate parameters of treatment with liraglutide compared to placebo in adults with type 2 diabetes that are at high risk for cardiovascular events

E.2.3 Trial contains a sub-study: No

E.3 Principal inclusion criteria: (ES):

 Varones o mujeres con diabetes de tipo 2.

 Edad mayor o igual a 50 años en el momento de la selección y enfermedad cardiovascular, enfermedad cerebrovascular, vasculopatía periférica, insuficiencia renal crónica o insuficiencia cardiaca crónica o edad mayor o igual a 60 años en el momento de la selección y otros factores de riesgo especificados de vasculopatía.

 HbA1c mayor o igual a 7,0% en el momento de la selección.

(EN):

- Men or women with type 2 diabetes

- Age major or equal to 50 years at screening and concomitant cardiovascular, cerebrovascular or peripheral vascular disease or chronic renal failure or chronic heart failure OR age major o equal to 60 years at screening and other specified risk factors of vascular disease

- HbA1c major or equal to 7.0% at screening

E.4 Principal exclusion criteria: (ES):

 Diabetes tipo 1.

 Uso de un agonista de los receptores del GLP-1 (exenatida, liraglutida u otro) o pramlintida o cualquier inhibidor de la dipeptidil-peptidasa 4 (DPP-4) en los 3 meses previos a la selección.

 Uso de insulina distinta de la insulina de tipo protamina neutra de Hagedorn (NPH) humana o de un análogo de la insulina de acción prolongada en los 3 meses previos a la selección. Se permite, a discreción del investigador, el uso a corto plazo durante ese periodo de otro tipo de insulina por una enfermedad intercurrente.

 Descompensación aguda del control de la glucemia que requiere una intensificación inmediata del tratamiento para prevenir complicaciones agudas de la diabetes (por ejemplo, cetoacidosis diabética) en los 3 meses previos.

 Episodio coronario o cerebrovascular agudo en los 14 días previos.

 Terapia de reemplazo renal continuo

 Hepatopatía terminal.

 Insuficiencia cardiaca en clase funcional IV de la NYHA.

 Trasplante de órgano sólido previo o a la espera de un trasplante de órgano sólido.

 Familia o antecedentes personales de neoplasia endocrina múltiple de tipo 2 (MEN2) o carcinoma medular de tiroides familiar (CMTF).

 Antecedentes personales de carcinoma medular de tiroides no familiar.

 Neoplasia maligna que requería quimioterapia, cirugía, radioterapia o tratamiento paliativo en los 5 años anteriores. Se permitirá participar en el estudio a sujetos con carcinoma epidermoide intraepitelial de la piel (enfermedad de Bowen) tratados con 5-fluorouracilo (5FU) tópico y a sujetos con cáncer de piel basocelular.

(EN):

- Type 1 diabetes

- Use of a GLP-1 receptor agonist (exenatide, liraglutide or other) or pramlintide or any (dipeptidyl peptidase 4 (DPP-4) inhibitor within the 3 months prior to screening

- Use of insulin other than human neutral protamine hagedorn (NPH) insulin or long-acting insulin analogue within 3 months prior to screening. Short-term use of other insulin during this period in connection with intercurrent illness is allowed at Investigator's discretion

- Acute decompensation of glycaemic control requiring immediate intensification of treatment to prevent acute complications of diabetes (e.g., diabetic ketoacidosis) in the previous 3 months

- An acute coronary or cerebrovascular event in the previous 14 days

- Current continuous renal replacement therapy

- End-stage liver disease

- Chronic heart failure NYHA IV

- A prior solid organ transplant or awaiting solid organ transplant

- Family or personal history of multiple endocrine neoplasia type 2 (MEN2) or familial

medullary thyroid carcinoma (FMTC)

- Personal history of non-familial medullary thyroid carcinoma

- Malignant neoplasm requiring chemotherapy, surgery, radiation or palliative therapy in the previous 5 years. Subjects with intraepithelial squamous cell carcinoma of the skin (Bowen's disease) treated with topical 5-fluorouracil (5FU) and subjects with basal cell skin cancer are allowed to enter the trial

E.5 End points

E.5.1 Primary end point(s): (ES): Tiempo desde la aleatorización hasta la primera aparición de muerte de origen cardiovascular, infarto de miocardio no mortal o ictus no mortal (un criterio de valoración cardiovascular compuesto).

(EN): Time from randomisation to first occurrence of cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke (a composite cardiovascular outcome)

E.6 and E.7 Scope of the trial

E.6 Scope of the Trial

E.6.1 Diagnosis: No

E.6.2 Prophylaxis: No

E.6.3 Therapy: No

E.6.4 Safety: Yes

E.6.5 Efficacy: Yes

E.6.6 Pharmacokinetic: No

E.6.7 Pharmacodynamic: No

E.6.8 Bioequivalence: No

E.6.9 Dose response: No

E.6.10 Pharmacogenetic: No

E.6.11 Pharmacogenomic: No

E.6.12 Pharmacoeconomic: No

E.6.13 Others: No

E.7 Trial type and phase

E.7.1 Human pharmacology (Phase I): No

E.7.1.1 First administration to humans: Information not present in EudraCT

E.7.1.2 Bioequivalence study: Information not present in EudraCT

E.7.1.3 Other: Information not present in EudraCT

E.7.1.3.1 Other trial type description:

E.7.2 Therapeutic exploratory (Phase II): No

E.7.3 Therapeutic confirmatory (Phase III): Yes

E.7.4 Therapeutic use (Phase IV): No

E.8 Design of the trial

E.8.1 Controlled: Yes

E.8.1.1 Randomised: Yes

E.8.1.2 Open: No

E.8.1.3 Single blind: No

E.8.1.4 Double blind: Yes

E.8.1.5 Parallel group: Yes

E.8.1.6 Cross over: No

E.8.1.7 Other: Yes

E.8.1.7.1 Other trial design description: Run-in period is open label

E.8.2 Comparator of controlled trial

E.8.2.1 Other medicinal product(s): No

E.8.2.2 Placebo: Yes

E.8.2.3 Other: No

E.8.3 The trial involves single site in the Member State concerned: No

E.8.4 The trial involves multiple sites in the Member State concerned: Yes

E.8.4.1 Number of sites anticipated in Member State concerned: 9

E.8.5 The trial involves multiple Member States: Yes

E.8.5.1 Number of sites anticipated in the EEA: 133

E.8.6 Trial involving sites outside the EEA

E.8.6.1 Trial being conducted both within and outside the EEA: Yes

E.8.6.2 Trial being conducted completely outside of the EEA: Information not present in EudraCT

E.8.6.3 If E.8.6.1 or E.8.6.2 are Yes, specify the regions in which trial sites are planned:

E.8.7 Trial has a data monitoring committee: Yes

E.8.8 Definition of the end of the trial and justification where it is not the last visit of the last subject undergoing the trial: Not applicable

E.8.9 Initial estimate of the duration of the trial

E.8.9.1 In the Member State concerned years: 5

E.8.9.1 In the Member State concerned months: 4

E.8.9.1 In the Member State concerned days: 19

E.8.9.2 In all countries concerned by the trial years: 5

E.8.9.2 In all countries concerned by the trial months: 4

E.8.9.2 In all countries concerned by the trial days: 19

F. Population of Trial Subjects

F.1 Age Range

F.1.1 Trial has subjects under 18: No

F.1.1.1 In Utero: Information not present in EudraCT

F.1.1.2 Preterm newborn infants (up to gestational age < 37 weeks): Information not present in EudraCT

F.1.1.3 Newborns (0-27 days): Information not present in EudraCT

F.1.1.4 Infants and toddlers (28 days-23 months): Information not present in EudraCT

F.1.1.5 Children (2-11years): Information not present in EudraCT

F.1.1.6 Adolescents (12-17 years): Information not present in EudraCT

F.1.2 Adults (18-64 years): Yes

F.1.3 Elderly (>=65 years): Yes

F.2 Gender

F.2.1 Female: Yes

F.2.2 Male: Yes

F.3 Group of trial subjects

F.3.1 Healthy volunteers: No

F.3.2 Patients: Yes

F.3.3 Specific vulnerable populations: Yes

F.3.3.1 Women of childbearing potential not using contraception

(For clinical trials recorded in the database before the 10th March 2011 this question read: "Women of childbearing potential" and

did not include the words "not using contraception". An answer of yes could have included women of child bearing potential whether

or not they would be using contraception. The answer should therefore be understood in that context. This trial was recorded in the

database on 2010-07-21) : Yes

F.3.3.2 Women of child-bearing potential using contraception: Yes

F.3.3.3 Pregnant women: No

F.3.3.4 Nursing women: No

F.3.3.5 Emergency situation: No

F.3.3.6 Subjects incapable of giving consent personally: No

F.3.3.7 Others: No

F.4 Planned number of subjects to be included

F.4.1 In the member state: 180

F.4.2 For a multinational trial

F.4.2.1 In the EEA: 3000

F.4.2.2 In the whole clinical trial: 8754

F.5 Plans for treatment or care after the subject has ended the participation in the trial (if it is different from the expected normal treatment of that condition): Not applicable

G. Investigator Networks to be involved in the Trial

N. Review by the Competent Authority or Ethics Committee in the country concerned

N. Competent Authority Decision: Authorised

N. Date of Competent Authority Decision: 2010-09-16

N. Ethics Committee Opinion of the trial application: Favourable

N. Ethics Committee Opinion: Reason(s) for unfavourable opinion:

N. Date of Ethics Committee Opinion: 2010-09-07

P. End of Trial

P. End of Trial Status: Completed