A Multicenter, Randomized, Subject-Blind, Investigator-Blind, Placebo-Controlled, Parallel-Group Study Evaluating the Efficacy, Safety, and Tolerability of Rozanolixizumab in Subjects with Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)

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The primary objective of the study is:• To evaluate the clinical efficacy of rozanolixizumab as a treatment for subjects with CIDPThe secondary objectives of the study are:• To evaluate the safety and tolerability of rozanolixizumab sc infusion in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Demyelinating disorders
Study type	Interventional

Summary

ID

NL-OMON48909

Source
ToetsingOnline

Brief title
CIDP01

Condition

- Demyelinating disorders

Synonym
Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)

Research involving
Human

Sponsors and support

Primary sponsor: UCB Biopharma SPRL
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: CIDP, Efficacy safety, randomized, Rozanolixizumab

Outcome measures

Primary outcome

The primary efficacy variable is the change from Baseline to Week 13 (Day 85) in iRODS score.

Further variables include values and change from Baseline in maximum grip strength score recorded by site personnel at each scheduled assessment during the Treatment and Observation Periods; values and change from Baseline in daily maximum grip strength score recorded by the subject each day during the Treatment and Observation Periods; additional patient-reported outcomes (PROs); values and change from Baseline in Rasch-built, modified interval Medical Research Council scale (RT-MRC) sum score at each scheduled assessment during the Treatment and Observation Periods; and subjects receiving rescue medication and time to rescue medication administration.

Secondary outcome

• Subject experienced CIDP relapse (iRODS) up to Week 13 (Day 85) after first

treatment and time to CIDP relapse (iRODS) at each scheduled assessment during the Treatment Period, where CIDP relapse (iRODS) is defined as a clinically important deterioration from Baseline in iRODS score, ie, a minimum clinically important differences-standard error (MCID-SE) of <= 1.96. Values and change from Baseline in iRODS scores at each scheduled assessment during the Treatment and Observation Periods will be assessed.

• Subject experienced CIDP relapse up to Week 13 (Day 85) after first treatment and time to CIDP relapse during the Treatment Period will be determined using the adjusted INCAT disability score where CIDP relapse is defined as an increase from Baseline of at least 1 point in the adjusted INCAT score. Values and change from Baseline in adjusted INCAT score at each scheduled assessment during the Treatment and Observation Periods will be assessed.

• Subject experienced CIDP relapse up to Week 13 (Day 85) after first treatment and time to CIDP relapse during the Treatment Period will be determined using maximum grip strength assessed by the site personnel, where CIDP relapse is defined as a clinically important deterioration from Baseline in grip strength, ie, a decline of >14kPa.

Other and exploratory variables include: safety and tolerability variables, pharmacokinetic (PK), pharmacodynamic (PD), immunologic variables, exploratory pharmacogenetics variables, and exploratory ribonucleic acid (RNA), proteins, and metabolites biomarkers. Plasma concentration of rozanolixizumab over time will be assessed as the PK variable. The PD variables are minimum and maximum decrease from Baseline in total IgG concentration during the study; value and

change from Baseline in IgG concentrations at each scheduled assessment during Treatment and Observation Periods; value and change from Baseline in IgG subclass concentrations at each scheduled assessment during Treatment and Observation Periods; and value and change from Baseline in neurofilament light chain (NF-L) levels at each scheduled assessment during Treatment and Observation Periods. Immunological variables will also be assessed.
Safety and tolerability variables will include occurrence of treatment-emergent adverse events (TEAEs); TEAEs leading to withdrawal of IMP; vital sign values and changes from Baseline (systolic and diastolic blood pressure [BP], temperature, pulse rate, and body weight) at each scheduled assessment during Treatment and Observation Periods; 12 lead electrocardiogram (ECG) parameters and change from Baseline at each scheduled assessment during Treatment and Observation Periods; laboratory values and changes from Baseline at each scheduled assessment during Treatment and Observation Periods (hematology, clinical chemistry, and urinalysis); tuberculosis (TB) evaluation; and values and change from Baseline in concentrations of total protein, albumin, α and β globulins at each scheduled assessment during the Treatment and Observation Periods.

Study description

Background summary

Production of pathogenic auto-antibodies is a major feature of a number of autoimmune diseases
often associated with a specific pathomechanism. Cellular and humoral immune mechanisms are

thought to be involved in the pathogenesis of CIDP resulting in inflammatory lesions in the spinal roots, proximal nerve trunks, and along the peripheral nerves. The essential role of the autoimmune antibodies in mediating this pathology is supported by the improvement seen after PLEX and IA. Identification of the specific antigenic target(s) of the autoimmune antibodies in CIDP is expanding with recent immunological techniques. Treatments aimed at reducing the quantity of circulating IgG auto-antibodies are being used for primary and secondary therapy of autoimmune diseases, particularly where corticosteroid-based immune suppression is not or no longer effective. The therapeutic approach of these treatments is based on lowering levels of pathogenic auto-antibodies, which represents rational and effective treatment modalities of autoimmune diseases.

Rozanolixizumab is a humanized IgG4 monoclonal antibody that is being developed as an inhibitor of the activity of FcRn. The FcRn recycles IgG and albumin and transports it bidirectionally across epithelial barriers. Recent studies have shown that FcRn rescues both IgG and albumin from intracellular lysosomal degradation by recycling it from the sorting endosome to the cell surface (Anderson et al, 2006). Rozanolixizumab has been specifically designed to block IgG binding to FcRn without blocking the binding and recycling of albumin. By blocking the activity of FcRn, rozanolixizumab accelerates the catabolism of IgG antibodies, including IgG auto-antibodies. The aim is to reduce the concentration of pathogenic IgG in patients with autoimmune diseases mediated by the action of IgG auto-antibodies.

Study objective

The primary objective of the study is:
• To evaluate the clinical efficacy of rozanolixizumab as a treatment for subjects with CIDP
The secondary objectives of the study are:
• To evaluate the safety and tolerability of rozanolixizumab sc infusion in subjects with CIDP
• To assess the PD effect of rozanolixizumab as measured by the total IgG

concentrations in serum
Exploratory objectives are:
• To evaluate the effects of rozanolixizumab on the concentration of total protein, albumin, α and β globulins, IgG subclasses, IgM, IgA, and IgE, serum and plasma complement levels
• To evaluate the incidence and emergence of anti-drug antibody (ADA) with respect to immunogenicity and PK and PD
• To evaluate the effect of rozanolixizumab on complement and cytokines
• To assess the plasma concentrations of rozanolixizumab administered by sc infusion
• To assess the PD effect of rozanolixizumab as measured by NF-L in serum
• To assess the effect of rozanolixizumab on gene and protein expression, and explore the relationship between DNA, RNA, protein, and metabolite biomarkers and cause, progression, and appropriate treatment of CIDP
• To assess the effect of rozanolixizumab on CIDP-specific auto-antibody levels
• To assess the effect of rozanolixizumab on vaccine antibody levels (influenza A and tetanus)

Study design

CIDP01 is a Phase 2A, multicenter, randomized, subject-blind, investigator-blind, placebo controlled, parallel-group study with the primary objective of evaluating the clinical efficacy of rozanolixizumab (UCB7665) as a treatment for subjects with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Secondary objectives include evaluating the safety and tolerability of rozanolixizumab subcutaneous (sc) infusion in subjects with CIDP, and assessing the effect of rozanolixizumab as measured by the total immunoglobulin G (IgG) concentrations in serum.

Intervention

Subjects will be randomized to 1 of 2 treatment arms: rozanolixizumab 10mg/kg sc or placebo sc in a ratio of 1:1. Subjects will receive 12 weekly doses of investigational medicinal product (IMP). The maximum duration of the study per subject is approximately 28 weeks (up to maximum 40 weeks), consisting of a Screening Period of between 2 and 5 weeks duration, an 11-week Treatment Period, and an Observation Period of 12 weeks (up to 24 weeks). The study is planned to be conducted in approximately 24 sites globally. Approximately 34 subjects will be randomized to ensure at least 30 subjects are evaluable for the primary efficacy analysis.
All subjects completing the Treatment Period (ie, all visits performed without relapse) will be offered the possibility to enter in the Open-Label Extension (OLE) study, CIDP04, and be treated with rozanolixizumab. If they enter in the OLE, Visit 17 will be the last study visit in CIDP01. If the subjects wish to test whether they still need treatment, they will continue the Observation Period without standard of care (SOC) treatment (ie, Ig treatment; subcutaneous

immunoglobulin [SCIg] and intravenous immunoglobulin [IVIg]). The subjects have also the opportunity to return immediately to SOC for the duration of the Observation Period.

Study burden and risks

The study load includes:
Visits to research doctor: 21 visits
Blood collection: 19 times
Urine sampling: 12 times
IMPD infusion (SC): 12 times
X-Thorax: 1 time
ECG: 11 times
Physical examination: 11 times
Questionnaires about the ability to perform daily and social activities, and about signs and symptoms of tuberculosis.

The subject may experience physical or psychological discomfort with the aforementioned tests, procedures and questionnaires.
The subject may get side effects from the study medication.

Contacts

Public
UCB Biopharma SPRL

Allée de la Recherche 60
Brussels 1070
BE
Scientific
UCB Biopharma SPRL

Allée de la Recherche 60
Brussels 1070
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Subject is >= 18 years of age at Visit 1 (Screening)
- Subject has a documented definite or probable diagnosis of Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) according to the European Federation of Neurological Societies (EFNS)/ Peripheral Nerve Society (PNS) criteria 2010
- Subject has an immunoglobulin-dependency confirmed by clinical examination during therapy or upon interruption or reduction of therapy within 18 months prior to Screening and documented in medical history
- Subject is on a stable dosage (not more than ±20% deviation) for subcutaneous immunoglobulin (SCIg) or intravenous immunoglobulin (IVIg) and a fixed interval for at least 4 months of either treatment
- Female subjects of childbearing potential must agree to use a highly effective method of birth control, during the study and for a period of 3 months after their final dose of IMP
- Male subjects with a partner of childbearing potential must be willing to use a condom when sexually active during the study and for 3 months after the final administration of IMP

Exclusion criteria

- Previously received treatment in this study or subject has previously been exposed to rozanolixizumab- Current diagnosis or has a history of Type 1 or Type 2 diabetes mellitus and/or hemoglobin A1c level >6.0%
- Known immunoglobulin M (IgM)
-mediated neuropathy
- Clinical or known evidence of associated systemic diseases that might cause neuropathy or treatment with agents that might lead to neuropathy
- History of clinically relevant ongoing chronic infections
- Family history of primary immunodeficiency
- Received a live vaccination within 8 weeks prior to the Baseline Visit; or intends to have a live vaccination during the course of the study or within 7 weeks following the final dose of IMP
- Received any experimental biological agent within or outside of a clinical study in the past 3 months or within 5 half-lives prior to Baseline
- Prior treatment with rituximab, ofatumumab, or ocrelizumab in the 6 months

prior to the Baseline Visit or subject has had prior treatment with rituximab, ofatumumab, or ocrelizumab in the 12 months prior to Baseline and B cells are not within the normal range
- Female subject who is pregnant or lactating

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-02-2020
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Rozanolixizumab
Generic name:	Rozanolixizumab

Ethics review

Approved WMO

Date:	02-04-2019
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-06-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-002411-17-NL
ClinicalTrials.gov	NCT03861481
CCMO	NL61913.018.19