A PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER STUDY TO EVALUATE EFFICACY, SAFETY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF SATRALIZUMAB IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

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Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON54231

Source
ToetsingOnline

Brief title
WN42636 - Luminesce

Condition

- Autoimmune disorders
- Neuromuscular disorders

Synonym

Auto-immuunziekte, Myasthenia Gravis

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: Roche Nederland B.V.

Intervention

Keyword: Myesthenia Gravis, Open-label extension, Placebo controlled, Satralizumab

Outcome measures

Primary outcome

To evaluate the efficacy of satralizumab versus placebo on function in daily

life in the AChR + population.

Secondary outcome

The secondary objectives in this study are focused on: efficacy, safety,

pharmacokinetics, and pharmacodynamics.

for a detailed overview I would like to refer to the section 'objectives and

endpoints', section 2. of the WN42636 (LUMINESENCE) Protocol

Study description

Background summary

Myasthenia gravis (MG) is a rare chronic autoimmune disease that affects the postsynaptic membrane at the neuromuscular junction (NMJ).
It is caused by autoantibodies that bind to acetylcholine receptors (AChRs) or to other functionally related molecules in the postsynaptic membrane at the NMJ, such as muscle-specific kinase (MuSK) or low-density lipoprotein receptor-related protein 4 (LRP4).

Satralizumab is being developed for treatment of gMG, which is a chronic autoimmune condition that has substantial impact on day-to-day functioning of

patients. This monoclonal antibody, is a humanized anti-interleukin-6 receptor (IL-6R) IgG. Given the pathological relevance of autoantibodies, pro-inflammatory T-cell activity, and complement activation in gMG, IL-6 inhibition through satralizumab is expected to dampen immune mechanisms that underlie the clinical phenotype of gMG.

For a detail overview see section 1.1 of the protocol.

Study objective

This study will evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of satralizumab compared with placebo in patients with gMG on stable background therapy. In addition, the study will assess the long-term safety and efficacy of satralizumab during the open-label extension (OLE) period.

Study design

This Phase III, randomized, DB, placebo-controlled, multicenter study is designed to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of satralizumab compared with placebo as add-on therapy to standard of care (SOC) for the treatment of gMG. The study will include a 28-day screening period, a 24-week DB treatment period, and approximately 2-year OLE period after the last patient initiates open-label treatment.

Intervention

The treatment regards: Satralizumab (RO5333787)
This is a humanized anti-interleukin-6 receptor (IL-6R) IgG2 monoclonal antibody that was constructed by modifying the amino acid sequence of tocilizumab to prolong its plasma drug-elimination half-life.

Double-blind period:

- Group 1, Patients in this group receive an injection of satralizumab every 4 weeks (plus an additional dose at week 2) in addition to the background medication for gMG.
- Group 2. Patients in this group receive an injection of placebo every 4 weeks (plus an extra dose in week 2) in addition to the background medication for gMG.

In the open-label period:
During this period, the patient will receive satralizumab every 4 weeks for approximately 2 years (and up to 3.5 years), with an additional dose of satralizumab (group 2 in the double-blind period) or placebo (group 1 in the double-blind period) during week 2

Study burden and risks

For a detailed scheme regarding Satralizumab, I would like to refer to the investigators brochure(s) (IB) of Satralizumab - F. Hoffmann - La Roche Ltd.

Contacts

Public
Roche Nederland B.V.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age >= 12 years at time of signing Informed Consent Form
- Confirmed diagnosis of gMG
- MGFA class II, III or IV at screening

• A total MG-ADL score of >= 5 points at screening with more than 50% of this score attributed to non-ocular items
• Ongoing gMG treatment at a stable dose and not exceeding the maximum protocol allowed doses
• For female patients of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use adequate contraception during the treatment period and for at least 3 months after the final dose of satralizumab

Exclusion criteria

Exclusion Criteria Related to Myasthenia Gravis (MG):
• History of thymic cysts, thymoma, thymic carcinoma or other neoplasm of the thymus as defined by the 2015 WHO classification of tumors of the thymus unless deemed cured by adequate treatment with no evidence of recurrence for >= 5 years before screening
• History of thymectomy within 6 months prior to screening
• Ocular MG (Myasthenia Gravis Foundation of America [MGFA] Class I)
• Myasthenic crisis within the last 3 months prior to screening (MGFA Class V)
• Known disease other than gMG that would interfere with the course and conduct of the study

Exclusion Criteria Related to Previous or Concomitant Therapy:
• Use of IVIg or subcutaneous immunoglobulin (SCIg) within 6 weeks prior to randomization (Day 1)
• Use of PE within 8 weeks prior to randomization (Day 1)
• Treatment with IL-6 inhibitory therapy (e.g., tocilizumab) at any time,
• Treatment with total body irradiation, or bone marrow transplantation at any time
• Treatment with B and/or T cell-depleting agents
• Treatment with anti-CD20 ,within 6 months prior to screening, unless CD19 counts are within normal range, as assessed by the central laboratory at screening
• For patients with prior exposure to anti-CD20 agents, CD19 counts below the normal range, as assessed by the central laboratory at screening, or <6 months since last anti-CD20 treatment till screening
• Treatment with C5 complement inhibitors (e.g., eculizumab orravulizumab) within 6 months prior to screening
• Treatment with neonatal Fc receptor antagonist, within 6 months prior to screening
• Treatment with or anti-B-lymphocyte stimulator monoclonal antibody at any time
• Treatment with cyclophosphamide IV within 6 months prior to screening
• Treatment with oral cyclophosphamide at any time
• Treatment with methotrexate within 8 weeks prior to screening
• Treatment with any investigational agent within 24 weeks prior to screening

or 5 drug-elimination half-lives of the investigational drug (whichever is longer)
• Use of more than one IST as background therapy except for the combination of an oral corticosteroids (OCS) with another permitted IST drug

General Safety Exclusion Criteria:
• Any surgical procedure (except for minor non-ophthalmic surgeries) within 4 weeks prior to screening
• Planned surgical procedure (except minor non-ophthalmic surgeries) during the study
• Evidence of progressive multifocal leukoencephalopathy
• Evidence of serious uncontrolled concomitant diseases that may preclude patient participation
• Congenital or acquired immunodeficiency, including human immunodeficiency virus (HIV) infection
• Active or presence of recurrent bacterial, viral, fungal, mycobacterial infection, or other infection, excluding fungal infection of nail beds or dental caries
• Infection requiring hospitalization or treatment with IV anti-infective agents within 4 weeks prior to baseline visit or oral anti-infective agents within 2 weeks prior to baseline visit
• Positive screening tests for hepatitis B and C
• History of drug or alcohol abuse within 1 year prior to baseline
• History of diverticulitis or concurrent severe gastrointestinal (GI) disorders that, in the investigator*s opinion, may lead to increased risk of complications such as GI perforation
• Evidence of latent or active tuberculosis
• Receipt of live or live attenuated vaccine within 6 weeks prior to baseline
• History of blood donation (one unit or more), plasma donation or platelet donation within 90 days prior to screening and Day 1
• History of malignancy within the last 5 years, including solid tumors, hematologic malignancies and in situ carcinoma
• History of severe allergic reaction to a biologic agent
• Active suicidal ideation within 6 months prior to screening or history of suicide attempt within 3 years prior to screening
• Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the patient's safe participation in and completion of the study
• Pregnant or breastfeeding, or intending to become pregnant during the study or within 3 months after the final dose of satralizumab

Laboratory Exclusion Criteria (at Screening):
• White blood cells (WBC) < 3.0*10^3/microliter
• Absolute neutrophil count (ANC) < 2.0*10^3/microliter
• Absolute lymphocyte count < 0.5*10^3/microliter
• Platelet count < 10*10^4/microliter
• Aspartate aminotransferase (AST) or alanine transaminase (ALT) >1.5*upper

limit of normal (ULN)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2022
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	ENSPRYNG®
Generic name:	Satralizumab

Ethics review

Approved WMO

Date:	06-04-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 05-08-2021

Application type: First submission

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 20-12-2021

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 07-03-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 07-04-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 20-06-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 25-03-2023

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	13-04-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2020-004436-21-NL
CCMO	NL76930.058.21