A double-blind, placebo-controlled, randomized clinical pharmacology study to evaluate the prevention effect and the recovery-promoting effect of a single subcutaneous administration of GYM329 on disuse muscle atrophy in healthy male volunteers.

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The primary objectives for this study are:To evaluate the preventive effect of GYM329 on disuse muscle atrophy in healthy male volunteers through changes in muscle strength following a single subcutaneous administration prior to unilateral thigh and...

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

Summary

ID

NL-OMON54969

Source
ToetsingOnline

Brief title
CS0355-200321

Condition

- Muscle disorders

Synonym
Muscular Atrophy

Research involving
Human

Sponsors and support

Primary sponsor: Chugai Pharmaceutical Co., Ltd.
Source(s) of monetary or material Support: Chugai Pharmaceuticals Co.;Ltd.

Intervention

Keyword: prevention effect, recovery-promoting effect, subcutaneous administration

Outcome measures

Primary outcome

Pharmacodynamic Endpoints

Percent change in thigh muscle strength score from Day 1 to Day 15

Percent change in thigh muscle strength score from Day 15 to Day 29

(Thigh muscle strength score: peak isometric knee extension torque and peak

isokinetic knee extension torque at 90°/s and 180°/s)

Secondary outcome

Safety Endpoints:

Adverse events

Laboratory tests

Vital signs

Electrocardiogram (ECG)

Pharmacokinetic Endpoints:

Serum GYM329 concentrations and PK parameters

Immunogenicity Endpoint:

Incidence of serum anti-GYM329 antibodies

Pharmacodynamic Endpoints:

Changes in thigh muscle volume over time

Thigh muscle volume: MRI-derived thigh muscle cross-sectional area [CSA])

Serum PD biomarkers (total and free latent myostatin, mature myostatin)

Study description

Background summary

Muscular atrophies and muscular dystrophies (e.g., spinal muscular atrophy [SMA], Duchenne muscular dystrophy [DMD], Becker muscular dystrophy [BMD], facial scapulohumeral muscular dystrophy [FSHD]) are a heterogeneous group of inherited disorders characterized by markedly reduced muscle strength and muscle function accompanied by muscle tissue changes, including degeneration, fibrosis, and muscle fiber size variation. Although of various etiologies and severities (SMA and DMD lead to premature death), all of the conditions cause significant physical disability, resulting in a lifelong need for physical rehabilitation and reduced quality of life. In most cases, the major pathologies cannot be adequately managed due to a lack of effective treatments. GYM329 is a humanized monoclonal antibody discovered by Chugai Pharmaceutical Co., Ltd. that binds to human latent myostatin to block its conversion to mature myostatin. The development of GYM329 is intended as a treatment for patients with muscle wasting diseases such as SMA, DMD, BMD and FSHD. GYM329 was engineered to have antibody-recycling and antigen-sweeping capabilities. GYM329 was developed using a novel technology called Sequential Monoclonal Antibody Recycling Technology (SMART-Ig) that combines four different innovative antibody engineering technologies. The four antibody engineering technologies consist of pH-dependent antigen binding, antibody charged engineering technology-Fc domain (ACT-Fc) technology (binding to neonatal Fc receptor at neutral pH), isoelectric point Fc domain (pI-Fc) technology (modification of the isoelectric point of the Fc region), and selective binding technology-Immunoglobulin (TwoB-Ig) technology (binding to Fcγ receptor IIb). The combination of these engineering technologies functions to prolong elimination half-life (antibody recycling) and accelerate antigen clearance through enhanced uptake of drug-target complex (antigen sweeping) [1]. GYM329 is therefore expected to promote effective clearance of antigens, allowing for lower and less frequent doses than similar antibodies produced without the use

of this technology. GYM329 is a subcutaneous formulation that is currently being evaluated in an ongoing Phase I clinical trial (Study BP40484) in healthy volunteers, including Japanese volunteers. Refer to the Investigator's Brochure for details on nonclinical and clinical studies.

Study objective

The primary objectives for this study are:
To evaluate the preventive effect of GYM329 on disuse muscle atrophy in healthy male volunteers through changes in muscle strength following a single subcutaneous administration prior to unilateral thigh and lower leg immobilization
To evaluate the recovery-promoting effect of GYM329 from disuse muscle atrophy in healthy male volunteers through changes in muscle strength following a single subcutaneous administration after unilateral thigh and lower leg immobilization

The secondary objectives for this study are:
To evaluate the safety, tolerability, PK, and immunogenicity of GYM329 in healthy male volunteers following a single subcutaneous administration prior to or after unilateral thigh and lower leg immobilization
To evaluate changes in thigh muscle volume in healthy male volunteers following a single subcutaneous administration of GYM329 prior to or after unilateral thigh and lower leg immobilization
To evaluate serum PD biomarkers in healthy male volunteers following a single subcutaneous administration of GYM329 prior to or after unilateral thigh and lower leg immobilization

Study design

In this study, healthy male volunteers will receive either GYM329 or placebo by subcutaneous injection at two time points, before and after 2 weeks of unilateral thigh and lower leg immobilization, in an investigator- and subject-blinded, randomized, placebo-controlled, parallel-group design.

Intervention

96 mg GYM329 or placebo by subcutaneous injection

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP. Please see the IB for further information.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Able and willing to provide written informed consent and to comply with the study protocol.
Healthy men aged from 18 to less than 40 years at the time of consent.
Right leg dominant.
Agreement to limit physical activity as directed by study site staff from the time of informed consent until the end of the muscle strength evaluation period (completion of Day 43).
Body mass index (BMI; weight in kg divided by height in meters squared) is between 18.5 and less than 25.0 at screening.

Exclusion criteria

Current cardiovascular disorder, renal disorder, hepatic disorder, gastrointestinal disorder, hematologic disorder, immune disorder, neurologic disorder, endocrine disorder, metabolic disorder, or pulmonary disorder or a history of clinical significance for any of these disorders and impaired renal, hepatic, or
cardiopulmonary function, as judged by the investigator.
History of congenital myopathy.
Congenital thrombophilia.
Previous or current VTE.
History of hip or limb surgery, spine or spinal cord surgery, or laparotomy (excluding laparotomy for appendicitis or inguinal hernia), or laparoscopic surgery (e.g. cholecystectomy).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-02-2021
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nap
Generic name:	Nap

Ethics review

Approved WMO Date:	05-10-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-10-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	23-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2020-003954-56-NL
CCMO	NL75182.056.20

Study results

Results posted: 23-01-2024

Summary results

Trial ended prematurely

First publication
12-01-2024