A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER STUDY OF THE SAFETY AND EFFICACY OF 3-MONTH SUBCUTANEOUS REGN1033 TREATMENT IN PATIENTS WITH SARCOPENIA

Published: 14-01-2013
Last updated: 23-04-2024

Please refer to protocol, section 1.2 "Rationale"

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

Summary

ID

NL-OMON40282

Source
ToetsingOnline

Brief title
R1033-SRC-1239

Condition

- Other condition
- Muscle disorders

Synonym
loss of muscle mass, Sarcopenia

Health condition

spieraandoening (verlies van spiermassa)

Research involving
Human

Sponsors and support

Primary sponsor: Regeneron Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Vergoeding door sponsor

Intervention

Keyword: Phase 2, Placebo, Sarcopenia, Subcutaneous

Outcome measures

Primary outcome

The primary endpoint in the study is the percent change in total lean body mass

measured by DEXA from baseline to week 12.

Secondary outcome

The secondary endpoints are:

• TEAEs from baseline to the end of the study

• Changes from baseline in:

o Appendicular lean mass by DEXA

o Maximal leg press strength, 1-repetition max (1-RM)

o Maximal chest press strength (1-RM)

o 4M gait speed

o SPPB and SPPB subscores

o Distance walked in the 6MWT

o Regional and total fat mass by DEXA

o Hand grip strength by handheld dynamometer

Study description

Background summary

Please refer to protocol, section 1.1 "Introduction"

Study objective

Please refer to protocol, section 1.2 "Rationale"

Study design

Study Design:
This is a randomized, double-blind, placebo-controlled, multicenter phase 2 study of the safety and efficacy of 3-month SC REGN1033 treatment in patients with sarcopenia. Approximately 240 patients will be randomized in a 1:1:1:1 ratio to receive placebo SC every 2 weeks (Q2W) for a total of 6 treatments, REGN1033 at 300 mg SC Q2W for a total of 6 treatments,
REGN1033 at 300 mg SC every 4 weeks (Q4W) for a total of 3 treatments (with placebo on alternating weeks), and REGN1033 at 100 mg SC Q4W for a total of 3 treatments (with placebo on alternating weeks). The study has a screening/pretreatment period (day -28 to day -1), a 12-week treatment period (day 1 to day 85), and an 8-week follow-up period (through
day 141).

Screening and Pretreatment Procedures (Day -28 to Day -1):
There will be a sequential screening process across 3 visits, with initial eligibility determined at visit 1, and pretreatment procedures performed at visit 2 and visit 3. If feasible at the sites, visit 1 and visit 2 may be conducted at the same time - if so, the visit 2 procedures should still be performed within 21 days of the first dose of study drug. Initial eligibility will be determined at visit 1 by standard screening procedures, as well as 4-meter [4M] gait speed and the Mini-Mental State Examination (MMSE) score. Patients who meet the initial eligibility criteria will return to the clinic at visit 2 and visit 3 for pretreatment baseline procedures and measurements. The procedures consist of standard safety and laboratory assessments,
DEXA scans, echocardiograms, strength measures (leg press, chest press, and handgrip strength), and function measures (stair climb, Short Physical Performance Battery [SPPB], 4M gait speed, and 6-Minute Walk Test [6MWT]).

Treatment Period and Study Drug Administration (Day 1 to Day 85):
Starting on day 1, patients will be randomized to receive either REGN1033 or matching placebo. The injections will be administered in the abdomen. Patients will be observed for 30 minutes for vital signs and collection of adverse events (AEs), including occurrence of injection site reactions. Efficacy and

safety procedures will be performed, as well as patient-reported outcomes (PROs). Blood samples will be collected for pharmacokinetics (PK), anti-drug antibodies (ADAs), and research. All blood samples should be collected after an overnight fast and before dosing.

Follow-Up (Day 86 to Day 141):
The follow-up visit will be on day 141, 8 weeks after the end of treatment visit on day 85.

Study Duration:
The total expected duration of the study is up to 24 weeks (including the screening period of up to 4 weeks).

Intervention

Study Group 1 receives 300 mg study drug (injection) every two weeks for a total of 6 treatments.

Study Group 2 receives 300 mg study drug (injection) every four weeks for a total of 3 treatments and placebo (injection) doses on alternating weeks.

Study Group 3 receives 100 mg study drug (injection) every four weeks for a total of 3 treatments and placebo (injection) doses on alternating weeks.

Study Group 4 receives matching placebo (injection) every two weeks for a total of 6 treatments.

In order to monitor for any possible cardiac changes, the patient will have 4 electrocardiograms (ECGs) and 2 echocardiograms (ECHO, also known as a cardiac ultrasound) during the trial. Depending on the results of these examinations, the study doctor may decide to stop treatment with the study drug and refer the patient to an appropriate specialist.
Several questionnaires, DEXA scans (a special x-ray to measure fat and muscle in your body), strength and function tests will be required to monitor the effect of the study drug on the muscle mass. In order to achieve accurate study results, a whole body DEXA as well as strength and function tests will be done about 6 times at various time points during the study.

Study burden and risks

Please refer to IMPD, page 737 "Risk Benefit Assessment".

Contacts

Public
Regeneron Pharmaceuticals, Inc.

Old Saw Mill River Road 777
Tarrytown NY 10591
US
Scientific
Regeneron Pharmaceuticals, Inc.

Old Saw Mill River Road 777
Tarrytown NY 10591
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Men and women aged 70 years and older;2. Are capable, in the investigator's opinion, to complete the study per protocol and have no significant health issues or conditions (including but not limited to severe arthritis of the major lower extremity joints and symptom-limited ambulation) that would impact the capability to get an accurate measurement of study endpoints;3. Appendicular lean mass relative to height squared: <=7.23 kg/m² (men); <=5.67 kg/m² (women);4. 4M gait speed <1.0 m/s (>4s to travel 4 meters at normal walking pace);5. BMI between 18.5 kg/m² and 37 kg/m², inclusive;6. Ability to follow a physical activity and walking program (involving activity such as walking starting with 5 to 10 minutes on most days of the week, and progressing to 30 minutes on most days of the week).;7. Willing and able to comply with clinic visits and study-related procedures;8. Provide signed informed consent;9. Able to understand and complete study-related questionnaires

Exclusion criteria

1. Hospitalization or immobilization with a duration of >48 hours within the month prior to screening;2. Having had a surgical procedure within 1 month prior to screening that required general anesthesia and was associated with loss of ambulation for at least 3 days, or a planned surgical procedure requiring general anesthesia within the next 6 months.;3. Participate in muscle strengthening training involving major muscle groups of arms and legs for at least 20 minutes 3 times per week AND regular exercise consisting of an average of 30 minutes per day or more of at least moderate physical activity which increases heart rate and breathing rate. ;4. Chronic medications introduced within 2 weeks prior to screening;5. Weight loss of >10% body weight within 6 months prior to screening;6. Respiratory disease (eg, severe chronic obstructive pulmonary disease) that requires oxygen treatment;7. Cancer requiring treatment currently or in the past 3 years (except primary nonmelanoma skin cancer or in situ cervical cancer), or any weight loss attributed to cancer within the last year (per the investigator's assessment);8. Neurological conditions that are causing impaired muscle function or mobility (may include stroke with residual paresis, paralysis, neuropathy, Parkinson disease, or multiple sclerosis);9. MMSE score of <24;10. Active or inadequately treated Major Depressive Disorder within 3 months prior to screening;11. Cardiovascular conditions such as New York Heart Association class III or IV heart failure, cardiomyopathy, intermittent claudication, myocardial infarction, or acute coronary syndrome within 6 months prior to screening; symptomatic ventricular cardiac arrhythmia (note: sinus dysrhythmia, asymptomatic block or well controlled atrial fibrillation with normal resting ventricular rate are not exclusion criteria);12. Abnormal echocardiogram findings at screening that are clinically significant, which may include but are not limited to:;- Cardiomyopathy;- Left ventricular ejection fraction <50%;- Moderate or severe diastolic dysfunction, grade II/III;- Aortic stenosis;- Valvular disease with hemodynamic significance;- Left ventricular wall thickness >=1.4 cm (men) and >=1.3 cm (women);13. Uncontrolled diabetes defined as hemoglobin A1C (HbA1C) >10% at screening (1 retest allowed);14. Diastolic blood pressure >100 mm Hg or systolic blood pressure >180 mm Hg (average of 2 readings);15. Alanine aminotransferase (ALT) >3x the upper limit of normal (1 retest allowed);16. Reduced renal function defined as estimated glomerular filtration rate <30 mL/min/1.73 m^2 (1 retest allowed);17. Creatine phosphokinase >5 x the upper limit of normal (1 repeat lab is allowed);18. Use of any prescription or over-the-counter agents known to influence muscle mass or performance within 1 year prior to screening. These may include but are not limited to;anabolic steroids, insulin-like growth factor-1 (IGF-1), growth hormone (GH), replacement androgen therapy, and anti-androgen therapy.;19. Participation in any clinical trial of small molecule drugs within 30 days prior to screening or biologics within 3 months prior to screening;20. Participation within 6 months prior to screening in clinical trials of interventions that are intended to influence muscle mass or performance;21. History of human immunodeficiency virus infection;22. Positive test for hepatitis B surface antigen and/or hepatitis C antibody at the screening visit;23. Pregnant or breastfeeding women;24. Sexually active men* or women of childbearing potential** who are unwilling to practice adequate contraception during the study (adequate contraceptive measures include stable use of oral contraceptives or other prescription pharmaceutical contraceptives for 2 or more menstrual cycles prior to screening; intrauterine device; bilateral tubal ligation; vasectomy; condom plus contraceptive sponge, foam, or jelly, or diaphragm plus contraceptive sponge, foam, or

jelly);*Contraception is not required for men with documented vasectomy.;**Postmenopausal women must be amenorrheic for at least 12 months in order not to be considered of childbearing potential. Pregnancy testing and contraception are not required for women with documented hysterectomy or tubal ligation.

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):	30-07-2014
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	REGN1033
Generic name:	REGN1033

Ethics review

Approved WMO

Date:	14-01-2013
Application type:	First submission

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-12-2013
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-02-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	21-05-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	29-08-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	30-09-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)

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	EUCTR2013-003134-33-NL
CCMO	NL46547.028.13