A randomized, double blind, placebo controlled, multi-centre study to assess the pharmacodynamics, pharmacokinetics, safety and tolerability of BYM338 in chronic obstructive pulmonary disease patients with cachexia (CBYM338X2204)

Published: 12-02-2013
Last updated: 24-04-2024

Primary: Assess the effect of i.v. infusions of BYM338 on muscle volume of the thigh (assessed by MRI) at 4, 8, 16 and 24 weeks, compared to placebo, in COPD patients with pulmonary cachexia.Secondary: Effect on 6-minute walk test, safety and...

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

Summary

ID

NL-OMON39660

Source
ToetsingOnline

Brief title
CBYM338X2204

Condition

- Other condition
- Muscle disorders
- Respiratory disorders NEC

Synonym
COPD

Health condition

cachexie/spierverlies

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: BYM338, Cachexia, COPD, Muscle

Outcome measures

Primary outcome

Muscle volume of the thigh.

Secondary outcome

6 minute walk test, whole body muscle mass, adverse events, PK and

immunogenicity parameters.

Study description

Background summary

Muscle loss and dysfunction in COPD is linked to an increase in myostatin levels, poor physical performance, decreased sense of well being and increased mortality. The causes of muscle dysfunction in COPD are remain to be clearly established. Possibilities include physical inactivity, hypoxia, nutritional insufficiency, systemic inflammation and hormonal insufficiency.
Apart from pulmonary rehabilitation no pharmacologic or non-pharmacologic interventions have been shown to improve muscle dysfunction associated with COPD. Pulmonary rehabilitation increases muscle strength, physical performance and quality of life in COPD patients, without a concomitant improvement in

airflow obstruction, indicating that improvement in the muscle dysfunction per se can be clinically beneficial in these patients.
Imaging data demonstrate that the muscle loss in COPD particularly involves the thigh and calf. Studies have demonstrated an association between the loss of skeletal muscle in the lower limbs and symptoms and reduced function in COPD patients. The 25-30% loss of muscle mass observed in COPD patients can manifest as 20-30% lower quadriceps strength. Although muscle wasting can occur in all stages of COPD, it tends to be more marked with more severe disease.
Myostatin, a member of the TGF-* family, is a protein that negatively regulates skeletal muscle mass. Inhibition of myostatin increases muscle mass and strength. The absence of myostatin in developing animals results in a hypermuscular phenotype with an increased number and size of muscle fibers. In the adult, myostatin is produced in skeletal muscle and circulated in the blood in part as a latent inactive complex.
BYM338 is a fully human monoclonal antibody developed to bind competitively to activin receptor type II B with greater affinity than myostatin, its natural ligand.
The purpose of this study is to determine the effects of two doses of BYM338 (week 1 and 8) on skeletal muscle volume, mass, strength and physical function in COPD patients with associated muscle wasting (cachexia). In addition, this study will generate data on the pharmacokinetics, safety and tolerability of BYM338 in COPD patients with cachexia and its effect on pulmonary function measures in this population. The extended study duration will provide information on the duration of BYM-induced changes in skeletal muscle and patient function.

Study objective

Primary: Assess the effect of i.v. infusions of BYM338 on muscle volume of the thigh (assessed by MRI) at 4, 8, 16 and 24 weeks, compared to placebo, in COPD patients with pulmonary cachexia.
Secondary: Effect on 6-minute walk test, safety and tolerability, PK and immunogenicity.
Several exploratory objectives (see protocol page 29).

Study design

Randomized, double blind, placebo controlled, phase II study. First study in COPD patients.
Randomization (1:1) to
* two i.v. doses of BYM338 (week 1 and 8)
* Placebo.
60 patients.
Follow-up 24 weeks
Internal DMB.

Intervention

Treatment with BYM338 or placebo.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: Study duration approx. 6 months. 13 visits. Duration 2-4 h.
2 i.v. infusions (250 mL), duration 2 hours, 4 hours observation thereafter.
Physical examination 8x.
Blood draw during 13 visits, 10-60 ml per occasion and approx. 400 ml in total.
Optional pharmacogenetic blood testing (10 ml).
Urine tests 13x.
Pulmonary function 8x
ECG 10x.
Muscle strength: respiratory: 5x, grip/leg/quadriceps/6 minute walk test/timed up and go 6x.
Physical Monitoring device 6 x(24 h).
DXA whole body muscle mass 6x.
MRI thigh 5x.
Muscles biopsy (optional) 3x.
Questionnaires severity of symptoms, quality of life 6x.
Diary muscle symptoms.

Contacts

Public
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL
Scientific
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Male and female patients with COPD, 40 to 80 years of age.
* Smoking history of at least 10 pack-years.
* Post-bronchodilator FEV1 < 80% predicted and FEV1/FVC ratio < 0.70.
* BMI <20 kg/m2 or skeletal muscle mass index by DXA < 7.25 kg/m2 for men or <5.45 kg/m2 for women.

Exclusion criteria

* Patients with MRC dyspnoea grade 5 (i.e. patients too breathless to leave the house or breathless when dressing).
* Weight < 40 kg or * 120 kg.
* Participation in a formal pulmonary rehabilitation program within 3 months of dosing.
* Other diseases known to cause cachexia or muscle atrophy.
* Pregnant or lactating women.
* Women of child-bearing potential.

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):	07-06-2013
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BYM338
Generic name:	BYM338

Ethics review

Approved WMO

Date:	12-02-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	12-02-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	20-03-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	16-05-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	07-06-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	04-07-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	22-08-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	04-02-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	10-02-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	27-02-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	28-03-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	24-07-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	28-07-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	03-02-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	01-02-2016
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	EUCTR2011-000461-12-NL
ClinicalTrials.gov	NCT01669174
CCMO	NL42644.098.12