A Randomized, Double-Blind, Placebo-Controlled Phase II Study to Investigate the Efficacy and Safety of Riociguat in Patients With Diffuse Cutaneous Systemic Sclerosis (dcSSc)

Published: 20-10-2014
Last updated: 21-04-2024

The purpose of this study is to investigate the effectiveness and safety of riociguat (BAY 63-2521) in patients with diffuse cutaneous systemic sclerosis.

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

Summary

ID

NL-OMON44560

Source
ToetsingOnline

Brief title
Riociguat in Diffuse Cutaneous Systemic Sclerosis (dcSSc)

Condition

- Autoimmune disorders
- Connective tissue disorders (excl congenital)
- Epidermal and dermal conditions

Synonym
Diffuse Cutaneous Systemic Sclerosis (dcSSc);a systemic autoimmune disease that result in abnormal blood vessel development and skin hardening.

Research involving

Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Bayer Healthcare AG

Intervention

Keyword: Diffuse Cutaneous Systemic Sclerosis

Outcome measures

Primary outcome

Primary: Change in mRSS from baseline to week 52

Secondary outcome

N/A

Study description

Background summary

Diffuse cutaneous SSc is one of the most severely incapacitating and life-threatening rheumatic diseases. Based on preclinical in vitro and in vivo data demonstrating that riociguat was safe and efficacious in different models of fibrotic diseases including scleroderma, the hypothesis is that riociguat may bring significant clinical benefit to patients with scleroderma. This study aims to recruit patients with dcSSc. The rationale is: a) there is a better understanding of the natural history of dcSSc than lcSSc, and b) dcSSc is a subset of SSc in which more rapid progression in disease occurs with worse prognosis, and where there is a high unmet need for effective treatment.

Study objective

The purpose of this study is to investigate the effectiveness and safety of riociguat (BAY 63-2521) in patients with diffuse cutaneous systemic sclerosis.

Study design

Randomized (1:1), double-blind, placebo-controlled, parallel-group,

multicenter, multinational study

Intervention

The optimal dose should be determined during the initial 10-week dose titration period based on monitoring of the patient*s SBP and well-being. The recommended starting dose is 0.5 mg TID. The intervals between drug intake should be 6 - 8 hours. The dosage should be increased by 0.5 mg increments no sooner than 2 weeks apart to 1 mg, 1.5 mg, 2 mg, and 2.5 mg TID, resulting in a maximum total daily dose of 7.5 mg. Patients should be maintained on lower doses if higher doses are not tolerated (minimum dose of 0.5 mg TID, see Section 5.2.1). After the dose titration period, riociguat should be continued at the optimal dose for the duration of the maintenance period.

Study burden and risks

Because riociguat has not been studied in patients with diffuse cutaneous systemic sclerosis it can`t even say at this point whether you can may benefit from this treatment.

A disadvantage may be that you have to come more often than you are used to the hospital and additional blood samples and skin biopsies can be taken. Furthermore, with placebo you can`t expect the potential effects of the treatment of riociguat. Potential adverse effects on Riociguat..

The knowledge produced by this drug, could contribute to improved future treatment of patients with diffuse systemic sclerodemie.

Contacts

Public
Bayer

Energieweg 1
Mijdrecht 3641 RT
NL
Scientific
Bayer

Energieweg 1
Mijdrecht 3641 RT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Men or women aged 18 years and older
- Systemic sclerosis, as defined by ACR/EULAR (American College of Rheumatology/European League Against Rheumatism) 2013 criteria
- dcSSc (diffuse cutaneous systemic sclerosis) according to the LeRoy criteria, i.e., skin fibrosis proximal to the elbows and knees in addition to acral fibrosis.
- Disease duration of * 18 months (defined as time from the first non*Raynaud*s phenomenon manifestation)
- * 10 and * 22 mRSS (modified Rodnan skin score) units at the screening visit
- FVC (forced vital capacity) * 45% of predicted at screening
- DLCO (diffusion capacity of the lung for carbon monoxide) * 40% of predicted (hemoglobin-corrected) at screening
-Negative serum pregnancy test in a woman of childbearing potential at the screening

Exclusion criteria

- Limited cutaneous SSc (systemic sclerosis) at screening
- Major surgery within 8 weeks prior to screening
- Hepatic insufficiency classified as Child-Pugh C. Patients with isolated AST or ALT >3xULN or bilirubin >2xULN can be included in the trial under the condition of additional monitoring during
the trial
- Estimated glomerular filtration rate (eGFR) < 15 mL/min/1.73m2 or on dialysis at the screening visit. Patients entering the trial with eGFR 15-29mL/min/1.73m2 will be undergo additional monitoring of renal function
- Any prior history of renal crisis
- Sitting SBP (systolic blood pressure) < 95 mmHg at the screening visit
- Sitting heart rate < 50 beats per minute (BPM) at the screening visit

- Left ventricular ejection fraction < 40% prior to screening
- Any form of pulmonary hypertension as determined by right heart catheterization
- Active state of hemoptysis or pulmonary hemorrhage, including those events managed by bronchial artery embolization
- Not permitted prior and concomitant medication (updated)
- Pregnant or breast feeding women
- Women of childbearing potential not willing to use adequate contraception and not willing to agree to 4-weekly pregnancy testing from Visit 1 (first administration of study drug) onwards until 30 (+5) days after last study drug intake.

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):	12-02-2015
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Adempas
Generic name:	riociguat
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	20-10-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-12-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-03-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-03-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-03-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-11-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-11-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-04-2016

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-05-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-10-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-11-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-06-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-06-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2014-001353-16-NL
ClinicalTrials.gov	NCT02283762
CCMO	NL50735.091.14