A randomized parallel-group, placebo-controlled, double-blind, multi-center dose finding phase II trial exploring the pharmacodynamic effects, safety and tolerability, and pharmacokinetics of four dose regimens of the oral sGC stimulator BAY 1021189 over 12 weeks in patients with worsening heart failure and preserved ejection fraction.

Published: 31-10-2013
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To characterize safety, tolerability, pharmacodynamic effects, and pharmacokinetics of the oral sGC stimulator BAY 1021189 in addition to standard diuretic and comorbidity treatment over 12 weeks in patients with worsening chronic heart failure with...

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

Summary

ID

NL-OMON40178

Source
ToetsingOnline

Brief title
SOCRATES-PRESERVED, 15829

Condition

- Heart failures

Synonym
Heart failure

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Heart Failure with Preserved Ejection Fraction, Worsening Heart Failure

Outcome measures

Primary outcome

Two split * primary endpoints are

* Change from baseline to week 12 in left atrial volume (LAV)

* Change from baseline to week 12 in log-transformed NT-proBNP

Secondary outcome

* ECHO parameters

* Change in composite endpoint

* Change in health-related QOL

* Change in vital signs (blood pressure and heart rate)

* Nr of participants with adverse events

Study description

Background summary

HF is associated with a wide spectrum of left ventricular (LV) functional abnormalities, ranging from patients with normal LV size and preserved ejection fraction (EF) to those with severe dilatation and/or markedly reduced EF (Hunt SA et al., J Am Coll Cardiol 53:e1*e90). It is important to differentiate those with HFrEF from those with HFpEF because these represent groups with different underlying pathophysiological, haemodynamic, and neurohormonal abnormalities and distinctly different clinical characteristics, varying risks for adverse outcomes, and dissimilar efficacy of existing therapies.
The nitric oxide (NO)*soluble guanylate cyclase (sGC)*cyclic guanosine monophosphate (cGMP) pathway is a relevant mechanism in HF that remains unaffected by neurohumoral antagonists. cGMP deficiency causes two important pathophysiologies in HF: Myocardial and endothelial dysfunction. Restoration of sufficient sGC*cGMP signaling appears to be an important pathophysiological target in HF. Previous attempts to increase cGMP remain limited.
A novel class of sGC stimulators directly stimulates the NO receptor sGC with a dual mode of action. They sensitize sGC to endogenous NO by stabilizing the NO-sGC binding and also directly stimulate sGC via a different binding site, independently of NO. The 3 times daily administered oral sGC stimulator BAY 63-2521 (riociguat) is currently developed in PH, including patients with HF and secondary PH. In the Phase IIb LEPHT study (IMP14308, NCT01065454) in patients with systolic HF and secondary PH, riociguat was well tolerated in these patients, and improved cardiac index, pulmonary vascular resistance (PVR), systemic vascular resistance (SVR), and quality of life in addition to standard HF treatment over 16 weeks without significantly changing systemic blood pressure or mPAP as primary endpoint (Circulation. 2012; 126: 2776-2799).

Study objective

To characterize safety, tolerability, pharmacodynamic effects, and pharmacokinetics of the oral sGC stimulator BAY 1021189 in addition to standard diuretic and comorbidity treatment over 12 weeks in patients with worsening chronic heart failure with preserved EF (HFpEF) in 4 dose arms and to find the optimal target dose

Study design

Randomized parallel-group, placebo-controlled, multi-center dose finding phase II trial exploring the pharmacodynamic effects, safety and tolerability, and pharmacokinetics of four dose regimens of the oral sGC stimulator BAY 1021189 over 12 weeks in patients with heart failure and preserved ejection fraction (HFpEF) suffering from worsening signs and symptoms of Heart Failure (HF) - SOluble Guanylate Cyclase stimulatoR in heArT failurE patientS with PRESERVED EF (SOCRATES-PRESERVED)

Intervention

12 weeks treatment with study medication

Study burden and risks

* As with any drug, side effects may occur with the study drug (see ABR section E9)
* Up to five study visits in 90 days
* Blood samples at every visit
* Physical examination at every visit
* ECG at every visit
* QOL questionnaire (KCCQ, EQ-5D-3L) at 4 visits
* ECHO cardiography at 2 visits

Contacts

Public
Bayer

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Mijdrecht 3641 RT
NL
Scientific
Bayer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Worsening chronic heart failure (WCHF) requiring hospitalization (or intravenous diuretic treatment for HF without hospitalization) with initiation of study treatment after clinical stabilization
- Left ventricular ejection fraction (LVEF) ><= 45% by echocardiography at randomization
For additional inclusion criteria see protocol section 5.1.1 page 26

Exclusion criteria

Intravenous inotropes at any time after hospitalization
For additional exclusion criteria see protocol section 5.1.2 page 27

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):	06-11-2013
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BAY 102 1189

Generic name:	BAY 102 1189

Ethics review

Approved WMO Date:	31-10-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-01-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-02-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-07-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-08-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-08-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-08-2014
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-08-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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

Other	Een beschrijving van dit onderzoek zal vermeld worden op websites: www.clinicaltrials.gov en op www.ccmo.nl. Identificatie nummer op dit moment nog onbekend
EudraCT	EUCTR2013-002288-25-NL
CCMO	NL45848.060.13