An open-label extension trial to assess the long term safety of nintedanib in patients with *Systemic Sclerosis associated Interstitial Lung Disease* (SSc-ILD)

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This clinical trial is an open-label extension trial of the main study SENSCISTM (1199.214) and 1199-0340 to further evaluate the safety of long term treatment with nintedanib in patients with scleroderma related lung fibrosis.Also, in this trial,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON53112

Source
ToetsingOnline

Brief title
SENSCIS (TM) Extension

Condition

- Lower respiratory tract disorders (excl obstruction and infection)
- Cornification and dystrophic skin disorders

Synonym
Systemic sclerosis associated lung fibrosis. Scar formation in the lungs caused by systemic sclerosis.

Research involving

Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: De opdrachtgever van dit onderzoek;Boehringer Ingelheim BV

Intervention

Keyword: Nintedanib, Safety, Sclerosis

Outcome measures

Primary outcome

The primary endpoint is the incidence (number and % of patients) of overall

adverse events over the course of this extension trial.

Secondary outcome

Not applicable.

Study description

Background summary

Systemic Sclerosis (SSc) is an orphan, devastating disease of unknown etiology. Patients suffer from multiple organ fibrosis, leading to abnormalities of the skin, lungs, vascular abnormalities, kidney disease, oesophageal and gastrointestinal involvement (hypomotility), cardiac disorders and muscle disease.

No approved SSc treatment is available, and no treatment is considered to be the gold standard for chronic treatment of SSc-ILD.

The rationale for development of nintedanib in SSc-ILD is based on the pre-clinical evidence of potential effects in SSc and clinical evidence of antifibrotic activity of nintedanib in Idiopathic Pulmonary Fibrosis (IPF) along with an acceptable safety profile.

This clinical trial is planned as an open label extension trial following the parent trial SENSCISTM (1199.214) and 1199-0340, the latter investigating the

safety and efficacy of nintedanib in Systemic Sclerosis interstitial lung disease.

Study objective

This clinical trial is an open-label extension trial of the main study SENSCISTM (1199.214) and 1199-0340 to further evaluate the safety of long term treatment with nintedanib in patients with scleroderma related lung fibrosis. Also, in this trial, patients who experienced benefits on using nintedanib in the SENSCISTM (1199.214) or 1199-0340 study, get the oppertunity to keep using nintedanib until it becomes availble in a different way for this group of patients.

Study design

This is a multi-centre, multi-national, prospective, open label extension clinical trial. It is anticipated that approximately 400 patients with SSc-ILD will complete the parent trial SENSCISTM or 1199-0340 as planned. These patients will be eligible for enrolment in this extension trial.

After signing Informed Consent and if all eligibility criteria are met, patients will initiate treatment with nintedanib (Visit 2).

The trial is estimated to last a total of approximately 3 years. The trial will end either when nintedanib is available on the market or will be made otherwise available to the patient, it is not expected that this will be a lot sooner than 3 years after the start of this study. If after 3 years, nintedanib is still not available on the market, this trial will continue or nintedanib will be made otherwise available for the patient so that it certain that the patients can be treated with nintedanib anyhow.

During this trial, treatment will be stopped if a reason for withdrawal is met.

See protocol section 3.1.

Intervention

All patients will be treated with nintedanib in this trial; there is no active comparator or placebo.

See also protocol section 4.1.1 - 4.1.3.

Study burden and risks

Duration: this trial ends when the medication becomes available (on the marktet) for these patients, it is expected that this study will last three

years. Six to seven visits will take place within the first year. In the next two years, there will be full visits every 16 weeks and visits for only blood drawing every 16 weeks. That means that a patient needs to visit the hospital every 8 weeks. In total (expecting that this study will last for three years) 26 visits will take place.

Burden: During the 'a' vists, only bloodsamples will be taken: 5x during the first year, then once after 8 weeks and then every 16 weeks.
Completing questionnaires: 3x during the first year, then every 16 weeks and during the end of treatment visit.
Physical examination and vital signs (blood pressure and pulse): every visit except for the 'a' visits.
Digital Ulcers assesment: 6x during the first year and then every 16 weeks.
Pregnancy testing (if applicable): every 4-6 weeks.
Blood- and urine tests: 12x during the first year and then every 8 weeks (every visit)
Lungfunction testing (FVC): 7x during the first year and then every 16 weeks
ECG: 3x during the entire study.

Risks: Known dide effects of the use of nintedanib are mostly gastrointestinal relates (diarrhea, nausea, abdominal pain, vomiting) and liverfunction disorders. Liverfunction will be check every visit. Side effects can be treated symptomatic in most cases. Blood drawing can be painful and can cause bruisings. Lungfunction tests are standard for this disease but can be exhausting. The stickers used for making the ECG's can cause minor skin irritations.

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

1. Patients who completed the SENSCISTM trial or 1199-0340 per protocol and did not permanently discontinue blinded treatment, 2. Signed and dated written informed consent in accordance with ICH-GCP and local legislation prior to admission to the trial, 3. Women of childbearing potential1 must be ready and able to use highly effective methods of birth control for 28 days prior to and 3 months after nintedanib administration. , See protocol section 3.3.2

Exclusion criteria

1. AST, ALT > 3 x ULN, 2. Bilirubin > 2 x ULN, 3. Creatinine clearance < 30 mL/min, 4. Clinically relevant anaemia , 5. Bleeding risk, any of the following:
a. Known genetic predisposition to bleeding
b. Patients who require:
i. Fibrinolysis, full-dose therapeutic anticoagulation (e.g. vitamin K antagonists, direct thrombin inhibitors, heparin, hirudin)
ii. High dose antiplatelet therapy.
c. Hemorrhagic central nervous system (CNS) event after completion of the parent trial SENSCISTM
d. Any of the following after last treatment of SENSCISTM:
i. Haemoptysis or haematuria
ii. Active gastro-intestinal bleeding or GI - ulcers
iii. Gastric antral vascular ectasia (GAVE)
iv. Major injury or surgery.
e. Coagulation parameters: International normalised ratio (INR) > 2, prolongation of prothrombin time (PT) and partial thromboplastin time (PTT) by > 1.5 x ULN at Visit 1., 6. New major thrombo-embolic events developed after completion of the parent trial SENSCISTM:

a. Stroke;
b. Deep vein thrombosis;
c. Pulmonary embolism;
d. Myocardial infarction., 7. Major surgery performed within the next 3 months,
8. Time period > 12 weeks between last drug intake in SENSCISTM and Visit 2 of this trial., Further criteria apply, see protocol section 3.3.3.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-12-2017
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ofev or Vargatef
Generic name:	Nintedanib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	27-09-2017
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-11-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-02-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-03-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-10-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	17-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-03-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-03-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-07-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-01-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	25-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-02-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-12-2022

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	EUCTR2016-003403-66-NL
ClinicalTrials.gov	NCT03313180
CCMO	NL62488.056.17