A phase II, randomised, double blind, placebo-controlled study of the pharmacokinetics, pharmacodynamic effects, and safety, of oral FT011 in participants with diffuse systemic sclerosis

Published: 22-06-2021
Last updated: 05-04-2024

Primary objective: To assess the PK of oral FT011 in participants with diffuse SSc.Secondary objectives: • To assess the safety and tolerability of oral FT011 compared to placebo in participants with diffuse SSc.• To evaluate the short-term efficacy...

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

Summary

ID

NL-OMON51103

Source
ToetsingOnline

Brief title
CER-FT011-SSc01

Condition

- Other condition

Synonym
Scleroderma, Systemic sclerosis (SSc)

Health condition

Diffuse systemic sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Certa Therapeutics Pty Ltd
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: diffuse systemic sclerosis, FT011, Phase 2, placebo-controlled

Outcome measures

Primary outcome

Primary Outcome Measures

• FT011 maximum concentration (cmax), time to maximum concentration (tmax), and area under the curve (AUC) in plasma after a single dose and after 12-weeks of treatment.

• Measurement of steady state FT011 levels in plasma.

Secondary outcome

Secondary Outcome Measures

Safety will be assessed by:

• Treatment emergent adverse events from first dose of study drug to End of Study

• Physical examination

• Vital signs (blood pressure, heart rate, respiratory rate, and temperature)

• 12-lead electrocardiograms (ECG)

• Safety laboratory results (haematology, biochemistry, coagulation, and urinalysis)

• Use of concomitant medications

Efficacy will be measured by:

Change in mRSS from Baseline at each visit.

• Change in percent predicted FVC from Baseline to Week 4, Week 8, and Week 12.

• Change in SHAQ-DI Score from Baseline to Week 4, Week 8, and Week 12.

• Change in Patient Global Assessment Score from Baseline to Week 4, Week 8, and Week 12.

• Change in Physician Global Assessment Score from Baseline to Week 4, Week 8, and Week 12.

• The proportion of patients showing an improvement (defined as ACR Composite Response Index in Diffuse Cutaneous Systemic Sclerosis (CRISS) score predicted probability of >=0.60) at Week 12.

• Change in the Scleroderma Clinical Trials Consortium Damage Index (SCTC-DI) score from Baseline to Week 12.

• Change in the 5-D Itch Scale from Baseline to Week 12.

Exploratory

• A histological analysis of skin biopsy samples before and after 12 weeks of treatment, looking at cellular markers of inflammation and fibrosis, and target localisation.

• Measurement, by computational biology, of the molecular markers of inflammatory and fibrotic signalling pathways in skin biopsy samples before and after 12 weeks of treatment, using techniques of whole tissue or single cell sorting and subsequent ribonucleic acid (RNA) analysis (scRNA-seq).

• Measurement of plasma and serum cytokines and chemokines before and after 12 weeks of treatment, and investigation of how the participant*s peripheral immune system responds to specific stimulus by measurement of immune cell activation markers

Study description

Background summary

Systemic sclerosis (SSc) is a rare and complex autoimmune disease, characterised by vascular damage, chronic inflammation, and fibrosis of the skin and internal organs. The current treatment recommendations include the use of immunosuppressants, such as methotrexate, mycophenolate mofetil, and cyclophosphamide, for managing the symptoms and preventing complications in SSc patients1. However, these treatments have poor efficacy and are associated with significant side effects, such as organ toxicities and serious infections. Nintedanib, a multiple tyrosine kinase inhibitor recently approved for the treatment of systemic sclerosis-associated interstitial lung disease (SSc-ILD), slowed the rate of decline in lung function in SSc-ILD2. Since no clinical benefit of nintedanib was observed for other manifestations of the disease, there remains an unmet need for safe and effective treatments in early diffuse SSc patients.

Study objective

Primary objective: To assess the PK of oral FT011 in participants with diffuse SSc.
Secondary objectives:
• To assess the safety and tolerability of oral FT011 compared to placebo in participants with diffuse SSc.
• To evaluate the short-term efficacy of oral FT011 compared to placebo in improving disease activity in participants with diffuse SSc.

Study design

This is a multi-centre, randomised, double blind, placebo-controlled study to assess the pharmacokinetic pharmacodynamic effects and safety of FT011 in participants with diffuse systemic sclerosis.

Intervention

Patients meeting all eligibility criteria will have a baseline skin biopsy (2 x 3mm punch biopsies) taken before being randomised 1:1:1 to FT011 200mg, FT011 400mg, or placebo.
Participants will take their investigational medicinal product (IMP) once a day for 3 months (12 weeks), in addition to their standard-of-care scleroderma medications.

Study burden and risks

Participating in the study can have advantages and disadvantages. The study drug may cause a reduction in some of the scleroderma symptoms, but this is not certain. It is also possible that patient's/ participant's condition could get worse at any time during this study.
Participating in the study can have the following disadvantages:
- Patient/ Participant may experience side effects or adverse effects of the study drug.
- Patient/ Participant may suffer from the measurements during the study. For example: a blood draw can be painful. Or patient/ participant could get bruising as a result.
- Participating in the study costs you extra time.
- Patient/ Participant must be admitted to the hospital. Or longer than usual.
- Patient/ Participant must adhere to the agreements associated with the study.
- The questionnaires can be confronting.
- Patient/ Participant must adhere to strict rules about taking drugs.
- There could be disadvantages for the patient's/ participant's partner or housemate.

Contacts

Public
Certa Therapeutics Pty Ltd

Level 9, 31 Queen Street Level 9, 31 Queen Street
Melbourne VIC 3000
AU
Scientific
Certa Therapeutics Pty Ltd

Level 9, 31 Queen Street Level 9, 31 Queen Street
Melbourne VIC 3000
AU

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Participants must meet all the following criteria:
• Provide written informed consent prior to any study procedures and who agree to adhere to all protocol requirements.
• Aged 18 to 75 years inclusive at the time of consent.
• Have a classification of systemic sclerosis, as defined by American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) criteria with disease duration <=5 years from first non-Raynaud phenomenon manifestation.
• Have a diagnosis of diffuse cutaneous SSc defined as systemic sclerosis with skin thickening on the upper arms proximal to the elbows, on the upper legs proximal to the knees, or on the trunk.
• Have skin thickening in a body area suitable for repeat biopsy.
• Have a mRSS at Screening of >=15 to <=40.
• FVC >=50% of predicted at Screening.
• If on azathioprine, mycophenolate mofetil, or hydroxychloroquine, have been on a stable dose for at least 2 months prior to baseline.
• Participants must agree to use contraception according to protocol section 5.4.4.

Exclusion criteria

Participants must not meet any of the following criteria:
• Pregnant or breast-feeding, or plan to become pregnant during the study.
• Have received any IMP within 30 days or 5 half-lives prior to randomisation (4 months if the previous drug was a new chemical entity), whichever is longer.
• Have known or suspected contraindications to the IMP.
• Have severe or unstable SSc or end-stage organ involvement as evidenced by:
o On an organ transplantation list or has received an organ transplant

including autologous stem cell transplant.
o Renal crisis within 1 year prior to Baseline.
• Interstitial lung disease or pulmonary hypertension requiring constant oxygen therapy. This excludes oxygen used to aid sleep or exercise.
• Gastrointestinal dysmotility requiring total parenteral nutrition or requiring hospitalisation within the 6 months prior to Baseline.
• Concomitant inflammatory myositis, rheumatoid arthritis, or systemic lupus erythematosus when definite classification criteria for those diseases are met (Bohan and Peter criteria for polymyositis and dermatomyositis)
• SSc-like illnesses related to exposures or ingestions
• The use of the following drugs within the specified periods:
o Methotrexate in the 2 weeks prior to Day 1
o Other anti-fibrotic agents including D-penicillamine or tyrosine kinase inhibitors (nilotinib, imatinib, dasatinib) in the month prior to Screening.
o Biologic drugs such as tumour necrosing factor (TNF) inhibitors, tocilizumab, or Janus kinase (JAK) inhibitors, in the 3 months prior to Screening.
o Rituximab in the 6 months prior to Screening.
o Cyclophosphamide oral or intravenous (IV) in the 3 months prior to Screening.
o Oral prednisolone >10 mg per day or IV steroids in the month prior to Screening.
• Have any malignancy not considered cured (except basal cell or squamous cell carcinoma of the skin, or carcinoma in situ of the cervix); a subject is considered cured if there has been no evidence of cancer recurrence for the 6 years prior to randomisation.
• Have aspartate transaminase (AST), alanine transaminase (ALT), gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH), or bilirubin values above the upper limit of normal (ULN) at Screening or Baseline, or evidence of hepatic disease as determined by any one of the following: history of hepatic encephalopathy, history of oesophageal varices, or history of portacaval shunt.
• Estimated glomerular filtration rate (eGFR) <60mL/min, urinary albumin/creatinine ratio <30mg/g.
• Haemoglobin < 80 g/L, platelets < 90 x 109/L, or neutrophil count < 1.4 x 109/L
• Other than SSc, have any other medical condition or significant co-morbidities, clinically relevant social or psychiatric conditions, or any finding during Screening, which in the investigator*s opinion may put the subject at risk or interfere with the study objectives.

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):	23-11-2021
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	FT011 100 mg
Product type:	Medicine
Brand name:	N/A
Generic name:	FT011 200 mg

Ethics review

Approved WMO Date:	22-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-08-2021
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-01-2022
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	EUCTR2020-005116-21-NL
ClinicalTrials.gov	NCT04647890
CCMO	NL77724.056.21