A Double Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy and Safety of MK-7240/ PRA023 in Subjects with Systemic Sclerosis Associated with Interstitial Lung Disease (SSc-ILD)

Published: 16-03-2022
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This study has been transitioned to CTIS with ID 2023-509743-27-00 check the CTIS register for the current data. x To assess the safety and tolerability of MK-7240/PRA023 in SSc-ILD x To compare the annual rate of change from Baseline in forced...

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

Summary

ID

NL-OMON53698

Source
ToetsingOnline

Brief title
The ATHENA-SSc-ILD Study

Condition

- Autoimmune disorders

Synonym
Systemic Sclerosis en Interstitial Lung Disease

Research involving

Human

Sponsors and support

Primary sponsor: Prometheus Biosciences, Inc, a subsidiary of Merck & Co.,Inc.(Rahway,NJ,USA)
Source(s) of monetary or material Support: Prometheus Biosciences;Inc;a subsidiary of Merck & Co.;Inc.(Rahway;NJ;USA)

Intervention

Keyword: Systemic Sclerosis Associated with Interstitial Lung Disease (SSc-ILD)

Outcome measures

Primary outcome

x The proportion of subjects reporting adverse events (AEs), serious adverse

events

(SAEs), AEs leading to discontinuation, and markedly abnormal laboratory

values

x To compare the annual rate of change from Baseline in FVC, in mL, of

MK-7240/PRA023 vs. placebo over 50 weeks

Secondary outcome

• To compare the change from Baseline in FVC in mL of MK7240/PRA023 vs. placebo

at Week 50

• To compare the change from Baseline in high-resolution computer tomography

(HRCT) quantitative interstitial lung disease - whole lung

(QILD-WL) of MK-7240/PRA023 vs. placebo at Week 50

• To compare proportion of subjects with an improvement in the revised

Composite Response Index in Systemic Sclerosis (CRISS) score of

MK7240/PRA023 vs. placebo at Week 50

• To assess the change from Baseline in Health Assessment Questionnaire

Disability Index (HAQ-DI) of MK-7240/PRA023 vs. placebo at Week 50

• To assess the change from Baseline in Living with Pulmonary Fibrosis (L-PF)

patient-reported quality of life (QoL) outcome of MK7240/PRA023

vs. placebo at Week 50

x To assess the change in histology in skin biopsy in subjects who consented to

the skin biopsy sub study

For more information please refer to study endpoints page 35 of the protocol

Study description

Background summary

Prometheus Biosciences a subsidiary of Merck & Co.,Inc. has developed MK-7240/ PRA023, a humanized IgG1 kappa (IgG1N) monoclonal antibody that binds human tumor necrosis factor-like cytokine 1A (TL1A) with high affinity and specificity. PRA023 binds to both membrane-bound and soluble forms of TL1A and blocks the binding of TL1A to its functional death receptor 3 (DR3).
TL1A is a cytokine which is part of the tumor necrosis factor (TNF) superfamily protein and is secreted by both innate and adaptive immune cells as well as by endothelial cells. TL1A occurs as both membrane-bound and soluble forms (Ferdinand 2018).
TL1A binds to DR3 that is found primarily on T cells, natural killer (NK) and NK-T cells, innate lymphoid cells (ILC), and epithelial cells (Valatas 2019).
TL1A potently drives inflammation through Th1, Th2, Th9, and Th17 responses (Prehn 2007).
Systemic Sclerosis with Diffuse Cutaneous Scleroderma and Interstitial Lung Disease (SSc-ILD) is characterized by fibrosis and a broad inflammatory profile (Mirsaeidi 2019). This profile is consistent with a role for the TL1A and its receptor DR3, which contribute to inflammation and fibrosis in inflammatory bowel disease (IBD) (Takedatsu 2008; Hsu 2011). The pleiotropic effects of TL1A include many effects directly implicated in the pathogenesis of SSc from direct effects on fibroblasts to Th2 and Th17 immune responses. In addition to their

roles in driving inflammation, TL1A and DR3 have been implicated in driving fibrosis independent of inflammatory mechanisms by direct stimulation of fibroblasts (Jacob 2020). TL1A also drives fibrosis by directly activating fibroblasts as well as up-regulating cytokines, such as transforming growth factor-beta (TGF-E), leading to collagen disposition and fibrosis. In fibrotic skin and lungs of patients with SSc, expression of TGF-*-regulated genes correlates with disease activity, which points to this cytokine as a mediator of pathogenesis (Lafyatis 2014). Higher serum values of TGF-* were also observed in SSc patients compared to those in healthy subjects with a positive correlation with the disease severity (e.g., digital ulcers, more extensive skin fibrosis)

For more information please refer to background page 27 of the protocol

Study objective

This study has been transitioned to CTIS with ID 2023-509743-27-00 check the CTIS register for the current data.

x To assess the safety and tolerability of MK-7240/PRA023 in SSc-ILD
x To compare the annual rate of change from Baseline in forced vital capacity (FVC), in mL, of MK-7240/PRA023 vs. placebo over 50 weeks

For more information please refer to objectives page 35 of the protocol

Study design

This is a multi-center, double-blind, randomized, placebo-controlled study designed to assess the safety, tolerability, and efficacy of MK-7240/PRA023 in subjects with SSc with diffuse cutaneous disease and ILD. This study will be conducted under the aegis of a DMC.
The study has 4 periods (Screening Period, Treatment Period, Open-Label Extension [OLE] Period, and Follow-Up [FU] Period).
Following the Screening Period, approximately 100 eligible subjects will be randomized in a 1:1 fashion to receive 1000 mg of MK-7240/PRA023 or placebo via intravenous (IV) administration on Week
0/Day 1, followed by 500 mg or placebo IV on Week 2, then every 4 weeks (Q4W) until Week 46. Randomization on Week 0/Day 1 will be stratified by presence of anti-topoisomerase antibody (+/-) and CDx status (+/-).

For more information please refer to study design page 38 of the protocol

Intervention

A placebo arm is needed to allow for a true assessment of the effects of MK-7240/ PRA023 on the rate of decline in FVC. In this study, the placebo arm will be commercially available 0.9% normal saline solution which will be sourced locally by the study sites. To address current practice, patients without immunosuppressive background therapy as well as patients on a stable background therapy of mycophenolate mofetil (MMF), methotrexate (MTX), azathioprine, or corticosteroid will be eligible for the trial. Rescue treatment is allowed in case of clinical deterioration of SSC either in the lungs FVC decrease >= 10% compared to Baseline), in the skin (mRSS increase of > 25% and > 5 points compared to Baseline) or in any other organ system (Section 4.4.5). By implementing these measures, the inclusion of a placebo arm is considered to be ethically justifiable.

Patients with the rare condition of SSc-ILD with diffuse cutaneous disease will be included in this trial. Placebo-controlled randomized trials provide the most robust results and are thus considered the most appropriate design, especially in rare patient populations, where multiple trials are not possible due to lack of patients

Study burden and risks

establishing medical history, use of medication and side effects
-collect urine
- smoking history/behaviour
-physical examination
-blood pressure, height, weight and BMI
-ECG
-questionnaires QoL,SSPRO,L-PF,HAQ-DI,UCLA-SCTC

Infusion of MK-7240/PRA023 or placebo 13x outpatient in OLE every 4 weeks and every 12 weeks HH visit
lung function test (PFT)
blood samples
DCLO assessment
PK genetic testing (blood and saliva)

All drugs can cause unwanted effects. Pain at the injection site
and anaphylaxis, rash wheezing and difficulty breathing dizziness and fainting swelling around the mouth, throat, or eyes a fast heartbeat sweating

You may experience side effects or adverse effects
You may be bothered by the measurements during the examination. For example: blood draw may hurt a little. Or you could get a bruise as a result

Contacts

Public
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San Diego CA 92121
US
Scientific
Prometheus Biosciences, Inc, a subsidiary of Merck & Co.,Inc.(Rahway,NJ,USA)

3050 Science Park Road -
San Diego CA 92121
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Confirmed diagnosis of systemic sclerosis with onset of disease < or = 5 years ago 2. Diffuse cutaneous scleroderma 3. Systemic sclerosis related to interstitial lung disease confirmed by HRCT 4. FVC > or = 45% of predicted normal 5. Diffusing capacity of lung for carbon monoxide (DLCO) > or = 45% of predicted normal 6. Stable dosing of myocphenolate mofetil (MMF), methotrexate (MTX) or azathioprine, as well as corticosteroids 7. Able to provide written informed consent and understand and comply with the requirements of the study

Exclusion criteria

1. WOCBP and men with female partners of childbearing potential who are unwilling or unable to use tow highly effective methods of contraception to

avoid pregnancy for the entire study period and for up to 12 weeks after the last dose of study drug
2. Airway obstruction per pulmonary function test (PFT) or clinically significant pulmonary arterial hypertension
3. Current clinical diagnosis of another inflammatory connective tissue disease
4. Any active infections, a serious infection within the past 3 months, or chronic bacterial infection
5. Current smoker or smoking within 6 months of screening
6. Subjects in the opinion of the investigator that are at an unacceptable risk for participation in the study
7. Subjects who meet the protocol criteria for important laboratory exclusion criteria

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:	Pending
Start date (anticipated):	01-07-2022
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	MK-7240/PRA023 monoclonal antibody that binds to the TNF
Generic name:	NA

Ethics review

Approved WMO Date:	16-03-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-08-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-01-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-02-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-02-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-10-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-02-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-03-2024
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
EU-CTR	CTIS2023-509743-27-00
EudraCT	EUCTR2021-005206-10-NL
CCMO	NL80536.091.22