A Randomized, Double-Masked, Sponsor-Unmasked, Ascending Multiple Dose Study of the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of PRM-151 Administered Intravenously to Patients with Idiopathic Pulmonary Fibrosis

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PRM-151 is being developed for potential therapeutic use to prevent, treat and reduce fibrosis. This study will provide an assessment of the safety, tolerability, pharmacokinetics and pharmacodynamics of PRM-151 after administration of ascending...

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

Summary

ID

NL-OMON36629

Source
ToetsingOnline

Brief title
PRM-151 and IPF patients

Condition

- Other condition
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym

Disturbed wound healing, excessive scar formation

Health condition

fibrose (idiopathische longfibrose)

Research involving
Human

Sponsors and support

Primary sponsor: Promedior Inc
Source(s) of monetary or material Support: Producent van het geneesmiddel

Intervention

Keyword: fibrosis, IPF, patients, serum amyloid P

Outcome measures

Primary outcome

Safety will be evaluated from reported adverse events, scheduled physical examinations, PFTs, vital signs, 12-lead ECGs, and clinical laboratory test results.

Secondary outcome

Pharmacokinetics

Venous blood samples will be obtained to determine the pharmacokinetics (PK) of endogenous levels of PTX-2 and PRM-151. Blood samples for PK (4 mL) will be obtained on day 1, 2, 3, 5, 8, 15, 16, 17, 18, 19, 22, 29 and 57 at different timepoints.

Pharmacodynamics

Pharmacodynamic (PD) blood samples (4mL) will be collected for the purpose of exploratory analysis related to the effects, mechanism, dynamics and/or adverse

events of PRM-151. Fibrocytes, monocyte subsets, MMP-1, MMP-7, MMP-9, MCP1, IP10, MDC, IL-6, IL-7, IL-8, IL-10, IL-1RA, TNFRSF1a, CCL18, and CCL-2 are examples of biomarkers that may be examined based on the information gained during the study and the biomarker strategy. Additional assays may be performed that contribute to the objectives of the trial. Pharmacodynamic samples will be collected on study days 1, 3, 5, 8, and 15 before test article administration (predose, time 0) and on days 2, 16, 22, 29, 36, 43, and at final study evaluation on day 57 (or upon early termination from the study) at different timepoints.

Fibrocyte analysis

Blood samples (10 mL) will be collected for exploratory fibrocyte analysis on study days 1, 3, 8, and 15 before test article administration (predose, time 0), and on days 22, 29, 36, 43, and at final study evaluation on day 57 (or upon early termination from the study). Samples will also be collected during the screening period; one sample to be collected between day -35 and day -28, and a second sample between day -21 and day -14.

Immune response analysis

Immune response samples (4 mL) for antibody to PTX-2 will be collected on days 1 (predose), 29, and 57 (or upon early termination from the study).

Study description

Background summary

During a previous study, the safety of a new drug, known as PRM-151, has been investigated in healthy volunteers and a small group of patients with idiopathic fibrosis (IPF). This study is designed to investigate the effect of PRM-151 in more detail in a larger group of IPF patients.

PRM-151 is a recombinant human Serum Amyloid P (rhSAP). SAP is a naturally occurring protein that circulates in the bloodstream and plays a crucial role in regulating wound healing. SAP's role is to regulate the activity of innate immune cells including monocyte-derived cells (fibrocytes, macrophages, dendritic cells) and myofibroblasts. The innate responses to injury can result in excess collagen production and scarring. This excess collagen production is an unwanted effect at surgical sites or in response to injury in a solid organ. Studies show that maintaining an elevated level of SAP in the blood or locally at the site of injury can prevent production of excess scarring and the progression of fibrosis.

Study objective

PRM-151 is being developed for potential therapeutic use to prevent, treat and reduce fibrosis. This study will provide an assessment of the safety, tolerability, pharmacokinetics and pharmacodynamics of PRM-151 after administration of ascending multiple intravenous (IV) doses to IPF patients.

Primary: To assess the safety and tolerability of ascending multiple IV doses of PRM-151 in patients with IPF.
Secondary: To provide the PK and PD profile of ascending multiple IV doses of PRM-151 in patients with IPF.

Study design

This is a randomized, double-masked, sponsor-unmasked, inpatient/outpatient, sequential-group study of ascending multiple doses of PRM-151 administered intravenously to patients with IPF.

Intervention

Multiple doses of PRM-151 (1mg/kg, 5mg/kg or 10mg/kg) will be evaluated in IPF patients. The doses will be administered as an intravenous infusion over a time period of 30 minutes. Each subject will participate in one cohort and will receive either multiple doses of PRM-151 or placebo (0.9% saline), administered in a randomized fashion.

Study burden and risks

Unexpected adverse events / Hypersensitivity reactions
Allergic reactions
Clinical significant findings during screening
Hematoma following venapunctures

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

IPF patients
Age: 40 - 80 yrs (limits included)
BMI: 16-33 kg/m2
Body weight: >= 50 kg and <= 75 kg (The upper weight limit of <= 75 kg may be increased or decreased depending upon the availability of test article.)
FVC >= 45%, corrected for age

DLCO: 35 to 80%

Exclusion criteria

History of amyloidosis, tuberculosis, cystic fibrosis, sarcoidosis or any other pulmonary disease other than IPF.
History of connective tissue disorder, severe pulmonary hypertension or COPD with an extent of emphysema
greater than the fibrosis.
Acute disease state.

Study design

Design

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):	02-05-2011
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	Recombinant human serum amyloid P

Ethics review

Approved WMO Date:	06-01-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-03-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-11-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2010-024508-89-NL
ClinicalTrials.gov	NCT01254409
CCMO	NL35135.078.10