A phase 1, single center, randomized, double-blind, placebo-controlled, single (Part 1) and multiple (Part 2) ascending dose study to evaluate the safety,tolerability, pharmacokinetics and pharmacodynamics of M281 administered to healthy volunteers.

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

Summary

ID

NL-OMON43123

Source
ToetsingOnline

Brief title
M281 SAD/MAD study.

Condition

- Other condition

Synonym
autoimmune diseases and inflammatory diseases

Health condition

auto-immuunziekten en ontstekingsziekten.

Research involving
Human

Sponsors and support

Primary sponsor: Momenta Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Farmaceutische Industrie.

Intervention

Keyword: autoimmune diseases, inflammatory diseases, M281

Outcome measures

Primary outcome

To establish the safety and tolerability of ascending single (Part 1) and multiple doses (Part 2) of M281 relative to placebo, administered intravenously (IV) to healthy male and female volunteers at dose intensities that lead to progressively higher levels, and longer periods, of receptor occupancy (RO).

Secondary outcome

To evaluate the pharmacokinetics (PK) of M281 following single dose and multiple dose administration.

To evaluate target engagement by M281 following single and multiple dose administration, where target engagement is assessed as FcRn RO in circulating monocytes and granulocytes

To evaluate the pharmacodynamic (PD) effects of M281 when administered as ascending single or multiple doses, where the primary PD effect is assessed as circulating IgG level. Other exploratory PD effects to be assessed include the

level of antigen-specific IgG, and levels of total IgG1, IgG2, IgG3, IgG4, IgA, IgM, and IgE.

To evaluate the duration of target engagement and PD effects of M281.

To determine an optimal dose and dosing interval for further studies by examining receptor occupancy, PD, and tolerability data from the single and multiple ascending dose periods. Information from the single dose (Part 1) portion will be used to re-estimate the appropriate doses and dosing interval for the multiple dose (Part 2) portion.

Study description

Background summary

M281 is a new investigational compound that may eventually be used for the treatment of autoimmune and inflammatory diseases mediated by a specific kind of antibody, called IgG antibodies. M281 is an antibody that binds to a protein that is called the neonatal Fc receptor. This Fc receptor can be found on many cell types of the human body, such as white blood cells and cells in the kidney and the liver. The neonatal Fc receptor is involved in transport of IgG antibodies and inhibition of breakdown of these IgG antibodies. In autoimmune diseases there are *wrong* IgG antibodies that are involved in the disease process. The new investigational compound M281 is able to bind the neonatal Fc receptor. It is hoped that this binding will ultimately lead to less IgG antibodies, including the *wrong* IgG antibodies that are involved in autoimmune or inflammatory diseases. This is the first time that this study compound is being given to humans.

Study objective

The study will be performed in 2 parts, Parts 1 and 2. The purpose of the study is to investigate whether M281 is safe and to what extent M281 is tolerated. It will also be investigated how quickly and to what extent M281 is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, the effect of M281 on the antibodies and inflammatory markers in the blood will be studied (this is called pharmacodynamics).

In Part 1 the effect of one single dose on safety, pharmacokinetics and

pharmacodynamics will be investigated, whereas in Part 2, the effect of multiple doses on safety, pharmacokinetics and pharmacodynamics will be investigated.

Study design

Part 1:
The actual study will consist of 1 period during which the volunteers will stay in the clinical research center in Groningen for 9 days (8 nights) followed by 8 days (over a period of 7 weeks) during which they will visit the clinical research center in Groningen for a short visit. The follow-up period may be extended if deemed necessary by the responsible doctor.

Day 1 is the day of administration of the study compound. The volunteers are expected at the clinical research center at 14:00 h in the afternoon prior to the day of administration of the study compound. They will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water).

They will leave the clinical research center on Day 8. However, if the concentrations of IgG antibodies in the blood are too low on Day 8, they will need to remain in the clinical research center until the concentrations of IgG have increased again to a predetermined level.

The post-study screening will take place 7 weeks after the end of the participation in this study. The appointment for the post-study screening will be made with the volunteer during the study.

The participation to the entire study, from the pre-study screening until the post study screening, will be a maximum of 12 weeks.

Part 2:

The actual study will consist of 4 periods during which the volunteers will stay in the clinical research center in Groningen for 4 days (3 nights) each period. Between these 4 periods they will go home. The inclinic period will be followed by 15 days (over a period of approximately 11 weeks) during which they will visit the clinical research center in Groningen for a short visit. The follow-up period may be extended if deemed necessary by the responsible doctor.

Day 1 is the day of first administration of the study compound. For the first period, the volunteers are expected at the clinical research center at 14:00 h in the afternoon prior to the day of first administration of the study compound. They will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water).

They will leave the clinical research center on Day 3. For the periods thereafter they are expected at the clinical research center at 14:00 h in the afternoon on Days 7, 14 and 21, which are the days prior to the remaining dose administrations. They will leave the clinical research center 3 days thereafter, thus on Days 10, 17 and 24. However, if the concentrations of IgG antibodies in your blood are too low on the day they will leave, they will need to remain in the clinical research center until the concentrations of IgG have increased again to a predetermined level.

the volunteers will be asked to return to the clinical research center for a short visit on Days 29, 31, 36, 39, 43, 47, 50, 53, 57 and then once weekly in the 6 weeks thereafter. The post-study screening will take place 11 weeks after they have left the clinical research center on Day 24. The appointment for the post-study screening will be made with the volunteers during the study. The participation to the entire study, from the pre-study screening until the post-study screening, will be a maximum of 18 weeks.

Intervention

Part 1:
Group 1: 1 x 0.3 mg per kg bodyweight M281 or placebo
Group 2: 1 x 3 mg per kg bodyweight M281 or placebo
Group 3: 1 x 10 mg per kg bodyweight M281 or placebo
Group 4: 1 x 30 mg per kg bodyweight M281 or placebo
Group 5: 1x 100 mg per kg bodyweight M281 or placebo

Part 2:

Group 1: 4 x 30 mg per kg bodyweight M281 or placebo
Group 2: To be determined
Group 3: To be determined

Study burden and risks

Pain, minor bleeding, bruising, possibly an infection due too blood sampling.

Contacts

Public
Momenta Pharmaceuticals, Inc.

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US

Scientific
Momenta Pharmaceuticals, Inc.

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

healthy male or female subjects
18 - 55 years of age, inclusive
BMI 18 - 30 kilograms/meter2, inclusive
weight 50 -110 kg, inclusive
non smoking

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study

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):	09-05-2016
Enrollment:	74
Type:	Actual

Ethics review

Approved WMO Date:	14-04-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-04-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-01-2017
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-02-2017
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□000986□22-NL
CCMO	NL57461.056.16

Study results

Results posted: 06-06-2019

First publication
01-01-1900

URL result
Type
ext
Naam
ascpt.onlinelibrary.wiley.com
URL