A 4-part Phase 1/2 study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of M254 in healthy volunteers and in patients with immune thrombocytopenic purpura.

Published: 05-12-2018
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The purpose of this study is to investigate how safe the new compound M254 is and how well it is tolerated when it is administered to healthy volunteers and patients with immune thrombocytopenia (ITP). M254 has not been administered to humans before...

Ethical review	Approved WMO
Status	Completed
Health condition type	Platelet disorders
Study type	Interventional

Summary

ID

NL-OMON49624

Source
ToetsingOnline

Brief title
Safety and tolerability of M254 in HV and ITP patients.

Condition

- Platelet disorders

Synonym
immune thrombocytopenia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Healthy Volunteers, ITP Patients, M254

Outcome measures

Primary outcome

Part A: To assess the safety and tolerability of a single ascending dose of

intravenous administration of M254 in healthy volunteers.

Part B: To assess the safety and tolerability of a single intravenous

administration of M254 in immune thrombocytopenia

patients compared to 1000 mg/kg intravenous Privigen

Part C: To assess the safety of a single intravenous administration of M254

compared to 1000 mg/kg of Privigen

To characterize the PD of single intravenous administration of M254 compared to

1000 mg/kg Privigen

Part D: To assess the safety and tolerability of repeated intravenous

administration of M254 in ITP patients.

Secondary outcome

Part A: To characterize the pharmacokinetics (PK) of a single intravenous

administration of M254 at different doses in healthy volunteers

Part B: To characterize the PK of a single intravenous administration of M254

at different doses in ITP patients

Part C: To characterize the PK of a single intravenous administration of M254

at different doses.

Part D: To characterize the PK of repeated intravenous doses of M254 in ITP

patients and to assess PD of repeated intravenous doses of M254 in ITP patients

Study description

Background summary

M254 is a new compound that may eventually be used for the treatment of primary immune thrombocytopenia Purpura (ITP). ITP is an autoimmune disease characterized by decreased numbers of platelets in the blood. ITP affects both children and adults. Symptoms of ITP include petechia (very small red or purple spots on the skin), purpura (red or purple discolored spots on the skin caused by bleeding under the skin), bruising, and overt bleeding. To stop or prevent bleeding, ITP patients can be treated with intravenous antibodies, so called immunoglobulin G (IVIg). IVIg is a therapeutic blood product prepared from pooled blood plasma of 3,000 to 60,000 healthy donors. IVIg has been used for treatment of a variety of acute and chronic autoimmune and systemic inflammatory diseases for decades, including ITP.

Due to treatment with IVIg, the number of platelets in the blood will be increased. However, high doses and long infusion times are required for efficacy.

M254 is derived from commercially available IVIg. In M254, the level of sialylation of the IgG subtypes present has been increased via enzymatic reactions. Literature suggests that the anti-inflammatory properties of IVIg may be dependent on the level of sialic acid. Therefore, due to the higher level of sialylation of IgG antibodies in M254, it is expected that M254 has potentially greater effectiveness when compared to IVIg.

Study objective

The purpose of this study is to investigate how safe the new compound M254 is and how well it is tolerated when it is administered to healthy volunteers and patients with immune thrombocytopenia (ITP). M254 has not been administered to humans before. It has been previously tested in the laboratory and on animals.

It will also be investigated how quickly and to what extent M254 is eliminated from the body (this is called pharmacokinetics [PK]). In addition, the effect of M254 on the body will be investigated (this is called pharmacodynamics [PD]).

This study will be performed in approximately 25 healthy male or female volunteers and approximately 55 patients with ITP. The study will be performed in 4 parts, Part A, Part B, Part C and Part D.

Part A has been completed. Twenty five healthy male or female volunteers were enrolled.

In Part A of the study, the safety, tolerability and PK of a single dose of M254 will be compared to placebo. M254 will be tested at various dose levels. A placebo contains no active ingredient. The safety and tolerability of M254 can be studied better, when some subjects in the trial receive placebo in an identical situation for comparison.

Part B of the study will consist of 4 tot 6 groups, each with 2 patients with ITP. After completion of Part B, patients are also allowed to participate in Part D of the study.

In Part B, the safety, tolerability, PK and PD of M254 will be compared to that of a similar compound, IVIg. IVIg has been the standard treatment of ITP for decades. In addition, the PK and PD of different doses of M254 will be evaluated.

Part C of the study will consist of 2 groups, each with 10 patients with ITP. After completion of Part C, patients are also allowed to participate in Part D of this study.

In Part C of the study, the safety, tolerability, PK and PD of up to 2 dose levels of M254 will be compared to that of IVIg.

Part D includes 15 to 34 patients with ITP. Patients who have participated in Part B or Part C may be offered to participate in Part D

In Part D of the study the safety, tolerability, PK and PD of 3 to 4 doses of M254 will be evaluated.

Study design

Part A: Participation from screening until follow-up is in total about 8 weeks. M254 or placebo will be given as an intravenous infusion (solution of the compound that will be administered directly in a blood vessel). The infusion duration will depend on the dose to be administered. In general, the infusion duration will be between approximately 6 minutes and 3.5 hours, depending on the dose received
.
Part B: Participation from screening until follow-up is in total about 8 weeks. All patients receive a single dose of M254 which is followed 4 weeks later by a single dose with IVIg. No placebo will be administered in this part of the

study. M254 and IVIg will be given as an intravenous infusion (solution of the drug administered directly into a blood vessel). The infusion duration will depend on the amount of M254 to be administered (up to 4 hours for M254). The infusion of IVIg may take up to 5 hours and 30 minutes depending on the body weight.

Part C: Participation from screening until follow-up is in total about 12 to 20 weeks.
All patients receive a single dose of M254 and a single dose of IVIg. There is approximately 4 weeks between the administration of M254 and IVIg. The group in which the patients participate and thus in which order they receive M254 or IVIg is determined by chance. No placebo will be administered in this part of the study. M254 and IVIg will be given as an intravenous infusion (solution of the drug administered directly into a blood vessel). The infusion duration will depend on the amount of M254 to be administered (up to 4 hours for M254). The infusion of IVIg may take up to 5 hours and 30 minutes depending on the body weight.

Part D: Participation from screening until follow-up is in total about 12 to 14 weeks.

If one has not participated in Part B or C, the volunteer receives 4 times a dose of M254 (Group 1). If one has already participated in Part B or C, one receives 3 times a dose of M254 (Group 2). There is approximately 2 weeks between each dose with M254. No placebo will be administered in this part of the study. M254 will be given as an intravenous infusion (solution of the drug administered directly into a blood vessel). The infusion duration will depend on the amount of M254 to be administered. (up to 4 hours).

Intervention

Part A:
Group 1; Day 1; M254 3 mg / kg or placebo; once; Intravenous infusion
Group 2; Day 1; M254 10 mg / kg or placebo, once, intravenous infusion
Group 3; Day 1; M254 30 mg / kg or placebo, once, intravenous infusion
Group 4; Day 1; M254 60 mg / kg or placebo, once, intravenous infusion
Group 5; Day 1; M254 120 mg / kg or placebo, once; intravenous infusion
Group 6; Day 1; M254 250 mg / kg or placebo, once; intravenous infusion
Group 7c; Day 1; M254 NTB mg / kg or placebo, once; intravenous infusion
Group 8c; Day 1; M254 NTB mg / kg or placebo, once; Intravenous infusion

Part B:
Group 1; Day 1; M254 60 mg / kgb; once; intravenous infusion
Group 1; Day 29; Privigen 1000 mg / kg; once, intravenous infusion
Group 2; Day 1; M254 120 mg / kg; once; intravenous infusion
Group 2; Day 29; Privigen 1000 mg / kg; once; intravenous infusion
Group 3; Day 1 M254 250 mg / kg; once; intravenous infusion

Group 3; Day 29; Privigen 1000 mg / kg; once; intravenous infusion
Group 4; Day 1; M254 500 mg / kg; once; intravenous infusion
Group 4; Day 29; Privigen 1000 mg / kg; once; intravenous infusion
Group 5; Day 1; M254 TBD mg / kg; once; intravenous infusion
Group 5; Day 29; Privigen 1000 mg / kg; once; intravenous infusion
Group 6; Day 1; M254 TBD mg / kg; once; intravenous infusion
Group 6; Day 29; Privigen 1000 mg / kg; once; intravenous infusion

Part C:
Two different amounts of M254 will be used based on the results of Parts A and B of this study and will not exceed 500 mg/kg. Patients will receive either the low amount or the high amount of M254 depending on which amount is being tested when entering the study.

Part D:
Group 1 Day 1; M254 (NTB mg/kgb); once, Intravenous Infusion
Group 1 Day 15; M254 (NTB mg/kg); once, Intravenous Infusion
Group 1 Day 29; M254 (NTB mg/kg); once, Intravenous Infusion
Group 1 Day 43; M254 (NTB mg/kg); once, Intravenous Infusion

Group 2 Day 1; M254 (NTB mg/kg); once, Intravenous Infusion
Group 2 Day 15; M254 (NTB mg/kg); once, Intravenous Infusion
Group 2 Day 29; M254 (NTB mg/kg); once, Intravenous Infusion

Study burden and risks

Pain, minor bleedings, bruises and possibly an infection.

Contacts

Public
Momenta Pharmaceuticals, Inc.

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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
Weight: body weight must be within a range that allows for the planned M254 infusion time to be completed in * 4 hours.
BMI 18.5 - 30 kilograms/meter2
Patients:
male or female diagnosed with ITP for at least 3 months
18 years and older

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 30 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 phase:	2
Study type:	Interventional

Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	04-01-2019
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	05-12-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	25-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-06-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	24-06-2020
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	EUCTR2018-003534-32-NL
CCMO	NL68253.056.18

Study results

Date completed:	21-01-2021
Results posted:	28-06-2022

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File