A phase 1, randomized, double-blind, placebo-controlled, single-dose escalation, multiple-dose escalation, and food effect study of RPT193 in healthy subjects and patients with moderate to severe atopic dermatitis

Published: 27-06-2019
Last updated: 17-01-2025

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON49945

Source
ToetsingOnline

Brief title
RPT193 SAD, MAD and FE Study

Condition

- Other condition

Synonym
asthma, Atopic dermitis

Health condition

atopische dermatitis

Research involving
Human

Sponsors and support

Primary sponsor: RAPT Therapeutics, Inc.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: FE, MAD, RPT193, SAD

Outcome measures

Primary outcome

Part A

- To evaluate the safety and tolerability of single oral ascending doses of

RPT193 administered to healthy male and female subjects.

Part B

- To evaluate safety and tolerability of multiple oral ascending doses of

RPT193 administered for 7 days to healthy male and female subjects.

Part C

- To evaluate the safety and tolerability of RPT193 administered orally for 28

days to patients with moderate to severe AD.

Secondary outcome

Part A

* To evaluate the PK of RPT193 following administration of single oral

ascending doses of

RPT193 administered to healthy male and female subjects.

* To assess the FE on the PK of RPT193 following administration of a single

oral dose of

RPT193 administered to healthy male and female subjects.

* Part B

* To evaluate the PK of RPT193 following administration of multiple oral

ascending doses of

RPT193 administered for 7 days to healthy male and female subjects.

* Part C

* To evaluate the PK of RPT193 following administration of multiple oral doses

of RPT193

administered orally for 28 days to patients with moderate to severe AD.

Study description

Background summary

RPT193 is a new compound that may eventually be used for the treatment of allergic inflammatory diseases such as atopic dermatitis or asthma. RPT193 may stop certain immune cells that maintain and worsen the inflammation from moving into the area of inflammation. This may reduce the inflammation and its symptoms (eg, itching [dermatitis] or wheezing [asthma]), and may prevent the worsening of inflammation.

Study objective

The purpose of this study is to investigate how safe the new compound RPT193 is when it is administered to healthy subjects. RPT193 has not been administered to humans before. It has been previously tested in the laboratory and on animals. RPT193 will be tested at various dose levels.

It will also be investigated how quickly and to what extent RPT193 is absorbed and eliminated from the body. This is called pharmacokinetics. The effect of

food will also be examined. In addition, the effect of RPT193 on the body will be investigated (this is called pharmacodynamics).

This study will be performed in up to 72 healthy male or female volunteers, divided over 2 parts (Part A and Part B). Part C will be conducted in patients with atopic dermatitis, and will not be further discussed in this document. The remainder of this document concerns Part A only.

Part A has been performed in 32 healthy volunteers divided over 4 groups of 8 healthy volunteers each. In addition, there will be 2 additional groups of 4 healthy volunteers each. You can participate in one of these 2 additional groups. In Groups A1 to A4, single doses of RPT193 or placebo have been investigated at increasing dose levels. Also, the effect of giving RPT193 shortly after breakfast on the pharmacokinetics of RPT193 has been investigated in Group A3. In Groups A1 to A4, the effects of RPT193 were compared to the effects of a matching placebo

Part B will be performed in up to 32 healthy volunteers divided over 4 groups of 8 volunteers each. In addition, up to 16 volunteers divided over up to 2 additional groups may be added later. The volunteer can participate in one of these groups. In Part B, increasing doses of RPT193 will be tested when RPT193 or placebo is administered once daily for 7 days.

The effects of RPT193 will be compared to the effects of a matching placebo.

Part C will be conducted in patients with atopic dermatitis. Approximately 10 patients are expected to participate in the Netherlands. One Singel dose of RPT193 will be tested when RPT193 or placebo is administered once daily for 28 days.

Study design

Part A:

For Groups A1, A2 and A4:
The actual study will consist of 1 period during which the volunteer will stay in the research center for 5 days (4 nights). Day 1 is the day of administration of the study compound.

For Group A3:
Th actual study will consist of 2 periods. Each period, the volunteer will stay in the research center for 5 days (4 nights). Day 1 is the (first) day of administration of the study compound.

RPT193 or placebo will be taken once (in each period for Group A3) as oral capsules with 240 mL of (tap) water, without chewing on the capsules. The hands and mouth will be checked after the study compound intake.

For Group A5 and A6:
The actual study will consist of 1 period during which the volunteer will stay in the research center for 4 days (3 nights). Day 1 is the day of administration of the study compound.

For Group A1:
For safety reasons, initially 2 volunteers will receive the study compound in Group A1. One volunteer will receive RPT193, and one will receive placebo. After administration, the safety and tolerability of the study compound in these 2 volunteers will be closely monitored. If there are no concerns about the safety and tolerability 48 hours after administration, then the remaining 6 volunteers (5 will receive RPT193 and 1 will receive placebo) in Group A1 will be dosed.

If the volunteer will participate in Groups A1, A2, A4, A5 and A6: the volunteer will need to fast for at least 10 hours before RPT193 or placebo is administered.

For Group A3:
Volunteers in Group A3 will receive the study compound in 2 periods. In Period 1, you will receive RPT193 or placebo after fasting for at least 10 hours. In Period 2, you will receive RPT193 or placebo after a standardized high-fat breakfast (see Section 5 for more information and Appendix C for the composition of this breakfast).

For all groups:
Please refer to the table below to see the planned dose levels for each group. The doses of Groups A2 to A4 can be adjusted based on the results of the previous group(s). However, the dose will not be lower than 50 mg and not higher than 400 mg. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and in case of no objection by the Medical Research Ethics Committee. Also, a safety review committee, will evaluate the safety and tolerability of the study compound prior to dose escalation in a next group. The investigation will be discontinued if, in the opinion of the investigators, unacceptable adverse effects appear.

Group Day Treatment* Condition How often
A1 Day 1 RPT193 50 mg or placebo fasted once
A2 Day 1 RPT193 100 mg or placebo fasted once
A3 Day 1 of Period 1 RPT193 200 mg or placebo fasted once
Day 1 of Period 2 RPT193 200 mg or placebo fed once
A4 Day 1 RPT193 400 mg or placebo fasted once
A5 Day 1 RPT193 5 mg fasted once
A6 Day 1 RPT193 20 mg fasted once

* In case the dose level will be lower or higher than planned, the volunteer

will be informed verbally.

Part B:
The actual study will consist of 1 period during which the volunteer will stay in the research center for 11 days (10 nights). Day 1 is the first day of administration of the study compound.

RPT193 or placebo will be taken once daily for 7 days as oral capsules with 240 mL of (tap) water, without chewing on the capsules. Your hands and mouth will be checked after the study compound intake.

Before RPT193 or placebo is administered, the volunteer should have fasted for at least 10 hours. Based on the outcome of Part A of this study, it may be decided to administer the study compound with a breakfast. Furthermore, based on the results in previous groups in Part A or B, it may be decided to administer RPT193 or placebo twice daily instead of once daily. The volunteer will be informed in case of such changes.

Please refer to the table below to see the planned dose levels for each group. The doses of Groups B2 to B4 can be adjusted based on the results of the previous group(s). However, the dose will not be lower than 50 mg and not higher than 400 mg. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and in case of no objection by the Medical Research Ethics Committee. Also, a safety review committee, will evaluate the safety and tolerability of the study compound prior to dose escalation in a next group. The investigation will be discontinued if, in the opinion of the investigators, unacceptable adverse effects appear.

Group Day Treatment* How often#
B1 Days 1-7 RPT193 50 mg or placebo once daily
B2 Days 1-7 RPT193 100 mg or placebo once daily
B3 Days 1-7 RPT193 200 mg or placebo once daily
B4 Days 1-7 RPT193 400 mg or placebo once daily
* In case the dose level will be lower or higher than planned, the volunteer will be informed verbally.
# In case the treatment will be given twice daily, the volunteer will be informed verbally.

Part C
This part of the trial consists of a screening, treatmentperiod and a follow-up visit. From screening until the follow-up visit, this trial will last about 79 days in total. The patient will visit the hospital 7 times in total, Screening, Day 1, Day 8, Day 15, Day 28, Day 29, and Day 43/Early Termination visit.

RPT193 or placebo will be taken once daily for 28 days as oral capsules with approximately 240 mL of (tap) water, without chewing on the capsules. The

dosage to be used in this part of the study will be 400mg RPT193 or placebo. The patient will take the study drug by themselves, at home or at the hospital during study visits.

The patient will receive either RPT193 or placebo at randomization at a 2:1 ratio. Neither the patient nor the study doctor will know if the patient will receive RPT193 or placebo.

Intervention

Part A:

RPT193 or placebo will be taken once (in each period for Group A3) as oral capsules with 240 mL of (tap) water, without chewing on the capsules. The hands and mouth will be checked after the study compound intake.

For Group A1:
For safety reasons, initially 2 volunteers will receive the study compound in Group A1. One volunteer will receive RPT193, and one will receive placebo. After administration, the safety and tolerability of the study compound in these 2 volunteers will be closely monitored. If there are no concerns about the safety and tolerability 48 hours after administration, then the remaining 6 volunteers (5 will receive RPT193 and 1 will receive placebo) in Group A1 will be dosed.

If the volunteer will participate in Groups A1, A2, A4, A5 and A6: the volunteer will need to fast for at least 10 hours before RPT193 or placebo is administered.

For Group A3:
Volunteers in Group A3 will receive the study compound in 2 periods. In Period 1, you will receive RPT193 or placebo after fasting for at least 10 hours. In Period 2, you will receive RPT193 or placebo after a standardized high-fat breakfast (see Section 5 for more information and Appendix C for the composition of this breakfast).

For all groups:
Please refer to the table below to see the planned dose levels for each group. The doses of Groups A2 to A4 can be adjusted based on the results of the previous group(s). However, the dose will not be lower than 50 mg and not higher than 400 mg. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and in case of no objection by the Medical Research Ethics Committee. Also, a safety review committee, will evaluate the safety and tolerability of the study compound prior to dose escalation in a next group. The investigation will be discontinued if, in the opinion of the investigators, unacceptable adverse effects appear.

Group Day Treatment* Condition How often
A1 Day 1 RPT193 50 mg or placebo fasted once
A2 Day 1 RPT193 100 mg or placebo fasted once
A3 Day 1 of Period 1 RPT193 200 mg or placebo fasted once
Day 1 of Period 2 RPT193 200 mg or placebo fed once
A4 Day 1 RPT193 400 mg or placebo fasted once
A5 Day 1 RPT193 5 mg fasted once
A6 Day 1 RPT193 20 mg fasted once

* In case the dose level will be lower or higher than planned, the volunteer will be informed verbally.

Part B:
RPT193 or placebo will be taken once daily for 7 days as oral capsules with 240 mL of (tap) water, without chewing on the capsules. Your hands and mouth will be checked after the study compound intake.

Before RPT193 or placebo is administered, the volunteer should have fasted for at least 10 hours. Based on the outcome of Part A of this study, it may be decided to administer the study compound with a breakfast. Furthermore, based on the results in previous groups in Part A or B, it may be decided to administer RPT193 or placebo twice daily instead of once daily. The volunteer will be informed in case of such changes.

Please refer to the table below to see the planned dose levels for each group. The doses of Groups B2 to B4 can be adjusted based on the results of the previous group(s). However, the dose will not be lower than 50 mg and not higher than 400 mg. The dose for the next group will only be increased if the lower dose of the previous group was found to be well tolerated and in case of no objection by the Medical Research Ethics Committee. Also, a safety review committee, will evaluate the safety and tolerability of the study compound prior to dose escalation in a next group. The investigation will be discontinued if, in the opinion of the investigators, unacceptable adverse effects appear.

Group Day Treatment* How often#
B1 Days 1-7 RPT193 50 mg or placebo once daily
B2 Days 1-7 RPT193 100 mg or placebo once daily
B3 Days 1-7 RPT193 200 mg or placebo once daily
B4 Days 1-7 RPT193 400 mg or placebo once daily
* In case the dose level will be lower or higher than planned, the volunteer will be informed verbally.
# In case the treatment will be given twice daily, the volunteer will be informed verbally.

Part C
This part of the trial consists of a screening, treatmentperiod and a follow-up

visit. From screening until the follow-up visit, this trial will last about 79 days in total. The patient will visit the hospital 7 times in total, Screening, Day 1, Day 8, Day 15, Day 28, Day 29, and Day 43/Early Termination visit.

RPT193 or placebo will be taken once daily for 28 days as oral capsules with approximately 240 mL of (tap) water, without chewing on the capsules. The dosage to be used in this part of the study will be 400mg RPT193 or placebo. The patient will take the study drug by themselves, at home or at the hospital during study visits.

The patient will receive either RPT193 or placebo at randomization at a 2:1 ratio. Neither the patient nor the study doctor will know if the patient will receive RPT193 or placebo.

Study burden and risks

The study compound may cause side effects.

As RPT193 will be administered to humans for the first time in this study, adverse events of RPT193 in humans have not been reported to date. However, RPT193 has been studied in animals. In mice, RPT193 was associated with a lower cholesterol level in the blood. In dogs, vomiting was observed at higher doses of RPT193. These symptoms disappeared after the treatment was stopped. Based on animal studies, the following potential side effects may occur:
- Low cholesterol
- Vomiting

Other side effects not observed in animal studies and not yet known, may also occur.

If during the study more information becomes available regarding side effects that may be related to the study compound, the responsible doctor will inform the volunteer about this.
Possible discomforts due to procedures
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

In total, we will take about 300 milliliters (mL) of blood from the volunteer.

To make a heart tracing, electrodes will be pasted at specific locations on the arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

Samples for the coronavirus test will be taken from the back of the nose and throat using a swab. Taking the samples only takes a few seconds but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause the volunteer to gag. When the sample is taken from the

back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

For Part C please also refer to appendix E of the patient information sheet.

Contacts

Public
RAPT Therapeutics, Inc.

Eccles Avenue 561
South San Francisco 94080
US
Scientific
RAPT Therapeutics, Inc.

Eccles Avenue 561
South San Francisco 94080
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Part A and B:
- Sex: male or female
- Age: 18-55 years, inclusive, at the time of consent.
- Body mass index (BMI): 18.0*30.0 kg/m2 at screening.
- Weight: *50 kg.
- Status: healthy subjects

(Note: For Groups A5 and A6, the age range will be 18-54 years, inclusive, at the time of consent to mitigate Coronavirus Disease 2019 [COVID-19] risks).

Part C:
- Male or female patient aged 18 to 65 years, inclusive, at the time of consent.
- Patient has a body mass index *18 and *35 kg/m2 at screening.
- Patient has at least a 12-month history of AD and had no significant flares in AD for at least 4 weeks before screening, as determined by the Investigator through patient interview at the screening visit or information obtained from medical chart or patient*s physician.
- Patient has clinically confirmed diagnosis of active AD, according to the revised Hanifin and
Rajka criteria

Exclusion criteria

Part A and B:
Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. Participation in a drug study within 60 days prior to (the first) drug administration in the current study. Participation in more than 4 other drug studies in the 12 months prior to (the first) drug administration in the current study.
Donation or loss of more than 100 mL of blood within 60 days prior to (the first) drug
administration. Donation or loss of more than 1.5 liters of blood (for male subjects) / more
than 1.0 liters of blood (for female subjects) in the 10 months prior to (the first) drug
administration in the current study.

Part C:
Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS.
- Patient has a history of skin disease or presence of skin condition that, in the opinion of the Investigator, would interfere with the study assessments. Note: Fungal infection of nail beds is allowed.
- Patient who is still participating in a clinical trial or who has participated in a clinical trial within 1 month prior to the Screening visit.
- Patient has used tanning beds or phototherapy (narrowband UVB [NBUVB], UV-B, ultraviolet A1 [UVA1], or psoralen-UV-A [PUVA]) within 4 weeks prior to the Baseline visit.
- Patient has received treatment with systemic immunosuppressive/ immunomodulating drugs (eg, methotrexate, cyclosporine A, or systemic Janus kinase [JAK] inhibitors), immunoglobulins, blood products and/or systemic corticosteroids (eg, oral, intravenous, intraarticular, rectal) within 4 weeks prior to the Baseline visit. Note: Intranasal corticosteroids and inhaled corticosteroids are allowed. Eye and ear drops containing corticosteroids are

also allowed.
- Patient has used any topical medicated treatment that could affect AD within 2 weeks prior to the Baseline visit, including, but not limited to, topical corticosteroids, crisaborole, calcineurin inhibitors, tars, antimicrobials, medical devices, and bleach baths.

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:	Completed
Start date (anticipated):	17-07-2019
Enrollment:	76
Type:	Actual

Ethics review

Approved WMO Date:	27-06-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-07-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	04-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-01-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-02-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-02-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-07-2020
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	EUCTR2019-002306-47-NL
CCMO	NL70619.056.19

Study results

Date completed: 08-09-2020

Results posted: 01-02-2024

First publication
27-10-2021

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek Article in place of Lay Person Summary
URL
Type
int
Naam
M2.2 Samenvatting voor de leek Article in place of Lay Person Summary
URL