A randomised, investigator and subject blinded, placebo-controlled study to determine the safety, tolerability, and pharmacokinetics of INF904 in healthy subjects after single and multiple ascending doses

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We will investigate how safe the new compound INF904 is and how well it is tolerated when it is used by healthy subjects.We also investigate how quickly and to what extent INF904 is absorbed, transported, and eliminated from the body. In addition,...

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

Summary

ID

NL-OMON53655

Source
ToetsingOnline

Brief title
SAD and MAD to assess safety, tolerability and PK of INF904

Condition

- Other condition

Synonym
None

Health condition

healthy volunteers

Research involving
Human

Sponsors and support

Primary sponsor: InflaRx GmbH
Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: INF904, SAD/MAD, safety, tolerability

Outcome measures

Primary outcome

Part 1 and Part 3:

• Adverse events

• Physical examination

• ECG assessments

• 12-lead ECG continuous cardiac monitoring

• Vital signs

• Clinical safety laboratory assessments

Secondary outcome

Part 1:

• Maximum observed plasma concentrations (Cmax)

• Systemic exposure, defined as the AUCinf

• Time of occurrence of tmax

• Other derived pharmacokinetics parameters - AUClast, t*, Vz/F, Cl/F

• Intra-subject comparison of AUClast, AUCinf, and Cmax after dosing with

INF904 at various capsule strengths.

Part 3:

• Maximum observed plasma concentrations (Cmax)

• Systemic exposure, defined as the AUC0-12 and AUC0-24

• Time of occurrence of tmax

• Other derived pharmacokinetics parameters - t*, Vz/F, Cl/F, peak-trough ratio

(PTR)

• Maximum observed plasma concentrations (Cmax_ss)

• Systemic exposure, defined as the AUC

• Time of occurrence of tmax

• Other derived pharmacokinetics parameters - AUC0-t, t*, Vz/F, Cl/F,

accumulation ratios (RA_AUC, RA_Cmax), peak-trough ratio (PTR)

• Inter-subject comparison of AUClast, AUCinf, and Cmax after dosing with

INF904 in fasted states.

Study description

Background summary

INF904 is a new compound that may potentially be used for the treatment of inflammatory diseases. INF904 works by inhibiting the so called C5aR1 receptor, preventing C5a from binding. C5a is a highly inflammatory protein which activates multiple pathways of the innate and developed immune system. From research it is known that this protein is involved in a number of inflammatory diseases, including inflammatory bowel disease, rheumatoid arthritis and systemic lupus erythematosus. In the future INF904 can possible be used for the treatment of these inflammatory diseases.

Study objective

We will investigate how safe the new compound INF904 is and how well it is tolerated when it is used by healthy subjects.

We also investigate how quickly and to what extent INF904 is absorbed, transported, and eliminated from the body. In addition, we look at the effect of INF904 on CD11b.

We compare the effects of INF904 with the effects of a placebo.

INF904 has not been administered to humans before. It has been extensively tested in the laboratory and on animals.

Study design

Part 1:

In total the volunteer will visit the research center 3 times if he/she participates in Group 1, 2, 3, 5, 6 or an alternative Group:

- 1 day of screening
- Stay in the research center for 1 period of 8 days (7 nights)
- 1 follow-up visit

The volunteer will be given 3, 10, 30, 60, 90, 120, 180 or 240 mg INF904 or placebo as oral capsule(s) with 240 milliliters (mL) of (tap) water.

In total the volunteer will visit the research center 5 times if he/she participates in Group 4:

- 1 day of screening
- Stay in the research center for 3 periods of 8 days (7 nights)
- 1 follow-up visit

The volunteer will be given 60 mg INF904 or placebo in each of three periods as oral capsule(s) with 240 milliliters (mL) of (tap) water.

Part 3:

In total the volunteer will visit the research center 3 times:

- 1 day of screening
- Stay in the research center for 1 period of 22 days (21 nights)
- 1 follow-up visit

The volunteer will be given 30, 60, 90 or 120 mg INF904 or placebo once or twice daily as oral capsule(s) with 240 milliliters (mL) of (tap) water.

Intervention

Part 1:

Groups 1, 2, 3, 5, 6 or alternative group): The volunteer will be given 3, 10, 30, 60, 90, 120, 180 or 240 mg INF904 or placebo as oral capsule(s) with 240 milliliters (mL) of (tap) water.

Group 4: The volunteer will be given 60 mg INF904 or placebo in each of three periods as oral capsule(s) with 240 milliliters (mL) of (tap) water.

Part 3: The volunteer will be given 30, 60, 90 or 120 mg INF904 or placebo once or twice daily as oral capsule(s) with 240 milliliters (mL) of (tap) water.

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, sweating, low heart rate, or drop in blood pressure with dizziness or fainting. Also, in very rare cases, it can lead to an injury to a nerve with e.g. sensory deficits in certain areas of the skin through the puncture of the needle. Very rare motor complications (e.g. limited mobility of the arm) cannot be completely ruled out.

In total, we will take about 301 milliliters (mL) of blood from you from screening to follow-up. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time at once. If the investigator thinks it is necessary for the safety of a subject, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing/telemetry
To make a heart tracing, electrodes will be placed on your arms, chest and legs. To monitor the electrical activity of your heart over a longer period, electrodes will be placed on the chest and abdomen. Prolonged use of these electrodes can cause skin irritation.

Coronavirus test
Samples for the coronavirus test will be taken from the back of your nose and throat using swabs. 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 your throat may cause you to gag. When the sample is taken from the back of your nose, you may experience a stinging sensation and your eyes may become watery. Corona tests will be performed according to ICON policy

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Male or female participant must be 18 to 55 years of age inclusive, at the time of signing the informed consent.
2. Participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, and cardiac monitoring.
3. Body weight at least 50 kg and body mass index (BMI) within the range 18.0 and 30.5 kg/m2 (inclusive)
4. Contraceptive use by men and women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
Male participants:
Male subjects, if not surgically sterilised, must agree to use adequate contraception and not donate sperm from admission to the clinical research

centre until 90 days after the ESV. Adequate contraception for the male subject (and his female partner, if she is of childbearing potential) is defined as using hormonal contraceptives or an intrauterine device combined with at least 1 of the following forms of contraception: a diaphragm, a cervical cap, or a condom. Total abstinence from heterosexual intercourse, in accordance with the lifestyle of the subject, is also acceptable.
Female participants:
Female subject must be either:
• Post-menopausal (defined as at least 1 year without any menses) prior to screening; or
• Pre-menarchal prior to screening; or
• Documented surgically sterile or status post-hysterectomy (at least 1 month prior to screening); or
• If of childbearing potential, must have a negative urine pregnancy test at screening and admission and must be using highly effective contraception.
• Female subjects of childbearing potential who have a fertile male sexual partner must agree to use adequate contraception until 180 days after the ESV. Adequate contraception is defined as using hormonal contraceptives or an intrauterine device combined with at least 1 of the following forms of contraception: a diaphragm, a cervical cap, or a condom. True abstinence: When this is in line with the preferred and usual lifestyle of the subject.
(Periodic abstinence [e.g., calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable methods of contraception).
5. Capable of giving signed informed consent as described in Appendix 1 which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol.

Further criteria apply

Exclusion criteria

1. Female subject who has been pregnant within 6 months before screening assessment or breastfeeding or lactating within 3 months before screening.
2. Known or suspected hypersensitivity to INF904, or any components of the formulation used.
3. Any clinically significant history of allergic conditions (including drug allergies, asthma, eczema, or anaphylactic reactions, but excluding untreated, asymptomatic, seasonal allergies at time of dosing).
4. Any history or evidence of any clinically significant cardiovascular, gastrointestinal endocrinologic, hematologic, hepatic, immunologic, metabolic, urologic, pulmonary, neurologic, dermatologic, psychiatric, renal, and/or other major disease or malignancy, as judged by the Investigator.
5. The subject has/had febrile illness or symptomatic, viral, bacterial (including upper respiratory infection), or fungal (non-cutaneous) infection within 1 week prior to admission to the clinical unit.

Further criteria apply

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):	19-10-2022
Enrollment:	86
Type:	Actual

Ethics review

Approved WMO Date:	26-09-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-10-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-11-2022
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-04-2023
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	EUCTR2022-002765-14-NL
CCMO	NL82465.056.22

Study results

Date completed:	19-10-2023
Results posted:	08-05-2024

First publication
23-04-2024