A three-part, phase 1, randomized, controlled, dose-escalation study of INT-787 following single or multiple dose administration in healthy subjects.

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In this study we will investigate how safe the new compound INT-787 is and how well it is tolerated when it is used by healthy participants.We also investigate how quickly and to what extent multiple doses of INT-787 are absorbed, transported,...

Ethical review	Approved WMO
Status	Completed
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON52038

Source
ToetsingOnline

Brief title
SAD/MAD/FE Dose-Escalation Study of INT-787 in healthy subjects

Condition

- Hepatic and hepatobiliary disorders

Synonym
liver diseases

Research involving
Human

Sponsors and support

Primary sponsor: Intercept Pharmaceuticals, Inc.

Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: FE, INT-787, MAD, SAD

Outcome measures

Primary outcome

Part A:

To evaluate the safety and tolerability of single ascending doses of INT-787 capsule(s) administered orally to healthy male and female subjects

Part B:

To evaluate the safety and tolerability of multiple ascending doses of INT-787 capsule(s) administered orally for 14 days to healthy male subjects

Part C:

To assess the food effect on the PK of INT-787, and its tauro- and glyco-conjugates (and other metabolites as applicable) following administration of a single dose of INT-787 capsule(s) administered orally to healthy male subjects

Secondary outcome

Part A:

To evaluate the pharmacokinetics (PK) of INT-787, and its tauro- and glycoconjugates (and other metabolites as applicable) following administration of single ascending doses of INT-787 capsule(s) administered orally to healthy subjects

To assess the gender effect on the PK of INT-787, and its tauro-and glyco-conjugates (and other metabolites as applicable) following administration of a single dose of INT-787 capsule(s) administered orally to healthy subjects.
To explore the possible relationships between dose, exposure, and FXR activation biomarker responses as well as biomarkers of kidney function after single ascending doses of INT-787.

Part B:
To evaluate the PK of INT-787, and its tauro- and glyco- conjugates (and other metabolites as applicable) following administration of multiple ascending doses of INT-787 capsule(s) administered orally to healthy male subjects

Part C:
To evaluate the safety and tolerability of a single dose of INT-787 capsule(s) administered orally to healthy male subjects in fasted and fed conditions

Study description

Background summary

INT-787 is a new compound that may potentially be used for the treatment of chronic (long lasting) liver diseases. Some of these diseases can be caused by excessive alcohol consumption, but there may also be other causes. They are often accompanied with inflammation of the liver. The inflammation leads to damage and scar tissue (fibrosis) in the liver, which can lead to liver cirrhosis, cancer, and eventually liver failure. INT-787 works by activating a protein (FXR) that results, among other things, in a reduced inflammatory response.

Study objective

In this study we will investigate how safe the new compound INT-787 is and how well it is tolerated when it is used by healthy participants.

We also investigate how quickly and to what extent multiple doses of INT-787 are absorbed, transported, metabolized (broken down), and eliminated from the body (this is called pharmacokinetics). Additionally, we will investigate if and how INT 787 influences the composition and activity of the microbiota (microorganisms) in the gastrointestinal tract. We will collect stool samples for this.

We also look at the effect of your genetic information on your body*s response to INT-787. This part of the study is optional.

We compare the effects of INT-787 with the effects of a placebo. A placebo is a compound without any active ingredient (also called a *dummy pill*). Please note that when the term *study compound* is used in this document, we mean INT-787, placebo, or both.

INT-787 has not been used by humans before. It has been extensively tested in the laboratory and on animals. INT-787 will be tested at various dose levels. When Part B starts, INT-787 will have been administered to healthy participants in Part A.

When Part C starts, INT-787 will have been administered to healthy participants in Part A.

Study design

Part A:
For the research it is necessary to stay in the research center for 1 period of 6 days (5 nights). After this there is 1 short visit to the research center and a follow-up check. The short visit is on Day 8 and the follow-up is on Day 15. Day 1 is the day on which you receive the research drug. The volunteer is expected on the day prior to administration of the study drug at the study center. One must then report at approximately 2:00 pm. The research center is left on Day 5 of the examination.

INT-787 or placebo is given as capsules by mouth with 240 milliliters (ml) of water. Prior to administration, a fast is required for at least 10 hours and the fast continues until 4 hours after administration. From 1 hour before to 1 hour after dosing, do not drink anything except the 240 mL of water that must be taken with the dose.

Part B:
For the research it is necessary to stay in the research center for 1 period of 19 days (18 nights). After this there is 1 short visit to the research center and a follow-up check. This short visit is on Day 21 and the follow-up is on

Day 28.
Day 1 is the first day on which the research drug is given. We expect volunteers on the day prior to the first study drug administration at the study center. They must then report at approximately 2 p.m. They leave the research center on Day 18 of the examination. For the visits on Days 21 and 28 the volunteer is expected to arrive at the research center at approximately 10:00 AM. INT-787 or placebo is given as capsules by mouth with 240 milliliters (ml) of water. Whether the study drug is given after fasting or after eating will be decided based on the results of Part C of this study. You may need to fast for at least 10 hours before dosing.

Part C:
For the research it is necessary to stay in the research center for 2 periods of 6 days (5 nights). In each period they also come for 1 short visit to the research center. These short visit is on Day 8 of each period. There will be approximately 4 weeks between doses, but this may change based on the results of Part A of the study. The follow-up takes place between Day 15 of each period. In both periods, Day 1 is the day on which the study drug is received. We expect volunteers on the day prior to administration of the study drug at the study center. One must then report at approximately 2:00 pm. The research center is left on Day 5 of each period. For the visits on Days 8, 15 and 22, you are expected to arrive at the research center at approximately 10:00 AM. INT-787 is given as capsules by mouth with 240 milliliters (ml) of water. Prior to administration, one must fast for at least 10 hours. All participants will receive the study drug once with and once without breakfast. The order in which this is done will be determined by drawing lots. Breakfast is a high-fat breakfast with a fixed composition that must be started right on time and eaten completely within 20 minutes. Eating is not allowed until 4 hours after taking the study drug. From 1 hour before to 1 hour after dosing, you should not drink anything except the drink that accompanies the high-fat breakfast and the 240 mL of water that must be taken with the dose

Intervention

Part A:
Group 1 Day 1 once INT-787 2.5 mg or placebo
Group 1 Day 1 once INT-787 5 mg or placebo
Group 3 Day 1 once INT-787 10 mg or placebo
Group 4 Day 1 once INT-787 25 mg or placebo
Group 5 Day 1 once INT-787 50 mg or placebo
Group 6 Day 1 once INT-787 100 mg or placebo
Group 7 Day 1 once INT-787 200 mg or placebo
Group 8 Day 1 once INT-787 300 mg or placebo
Group 9 Day 1 once INT-787 450 mg or placebo

Part B:
Group 1 day 1-14 INT-787 5 mg or placebo once daily

Group 2 day 1-14 INT-787 15 mg or placebo once daily
Group 3 day 1-14 INT-787 45 mg or placebo once daily
Group 4 days 1-14 INT-787 100 mg or placebo once daily
Group 5 days 1-14 INT-787 200 mg or placebo once daily

Part C:
INT-787 once per period, 2 times in total.

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 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.

In total, about 450 milliliters (mL) of blood is taken. This amount does not cause any problems in adults.

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

Meals/Fasting
If the volunteers have to fast for a prolonged time during the study, this may lead to symptoms such as dizziness, headache, stomach upset, or fainting.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the 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 the throat may cause them to gag. When the sample is taken from the back of the nose, they may experience a stinging sensation and the eyes may become watery.

Contacts

Public
Intercept Pharmaceuticals, Inc.

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Morristown NJ07960

US
Scientific
Intercept Pharmaceuticals, Inc.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Subject must be male (18 to 55 years of age, inclusive) or female (gender effect cohort only; 18 to 55 years of age, inclusive).
2. Female subjects (included in the gender effect cohort only) must be of non-childbearing potential, who have undergone a sterilization procedure at least 6 months prior to dosing with official documentation (e.g., hysteroscopic sterilization, bilateral tubal ligation or bilateral salpingectomy, hysterectomy, or bilateral oophorectomy), or are postmenopausal with amenorrhea for at least 1 year prior to dosing and folliclestimulating hormone (FSH) serum levels consistent with postmenopausal status and serum pregnancy test at screening and upon admission with a negative result as per Investigator*s judgment.
3.Male subjects who are sexually active with a woman of childbearing potential and have not had a vasectomy must agree to use a barrier method of birth control (e.g., either condom or partner with occlusive cap [diaphragm or cervical/vault caps]). Male subjects must also agree to not donate sperm for the duration of the study and for at least 90 days after study discharge.
4. Body mass index (BMI) between 18.0 and 30.0 kg/m2 (inclusive) at screening.
5. Judged to be in good health on the basis of medical history, physical examination, and routine laboratory measurements (i.e., without clinically

relevant pathology).

Exclusion criteria

1.History of any illness or condition that, in the opinion of the Investigator, might confound the results of the study or pose an additional risk in administering investigational product to the subjects.
2. Smokers (subjects who have smoked within 3 months of screening or those with positive results from the cotinine urine test).
3. Inflammatory bowel disease, cholecystectomy or surgery of the gastrointestinal tract that could interfere with pharmacokinetics of the study medication (except appendectomy and simple hernia repair).
4. Routine treatment with prescription medications. Subjects should have stopped taking any prescription and nonprescription medications at least 14 days before the first dosing of investigational product. Potential subjects should only stop taking any prescription and nonprescription medications at the direction of a
physician.
5. Consumption of herbal medications, dietary supplements, and specific fruit products. Subjects should have stopped consumption of herbal medications or dietary supplements (e.g., St. John*s Wort, ginkgo biloba, and garlic supplements), vitamins, grapefruit, grapefruit hybrids or grapefruit juice, Seville oranges,
pomelos, cranberries, pomegranates, star fruit, apples, vegetables from the mustard green family (e.g., kale, broccoli, watercress, collard greens, Brussels sprouts, and mustard) and charbroiled meats for 7 days prior to Day 1, on any dosing day, and through the completion of the last PK sampling.1.

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):	11-06-2021
Enrollment:	96
Type:	Actual

Ethics review

Approved WMO Date:	18-05-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-04-2022

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-12-2022
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	EUCTR2021-001025-43-NL
CCMO	NL77625.056.21

Study results

Date completed: 07-02-2023

Results posted: 05-02-2024

First publication
26-01-2024

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

Internal documents
File