A Two-Part, Open-Label, Single-Dose Relative Bioavailability and Food Effect Study of THB001 in Healthy Adults

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Part 1:Primary objective:• To estimate the relative bioavailability of two THB001 formulations in healthy adults.Secondary objectives:• To determine the single-dose pharmacokinetics (PK) of THB001•HCl salt and THB001 free base formulations in...

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

Summary

ID

NL-OMON50446

Source
ToetsingOnline

Brief title
CS0375-210372

Condition

- Other condition

Synonym
allergic asthma, and food allergy, chronic idiopathic and inducible urticaria, chronic rhinosinusitis

Health condition

allergic mediated diseases

Research involving
Human

Sponsors and support

Primary sponsor: Third Harmonic Bio
Source(s) of monetary or material Support: Third Hamonic Bio

Intervention

Keyword: Food effect, Open-Label, Relative bioavailability

Outcome measures

Primary outcome

PK parameters including but not limited to: Cmax, tmax, t1/2, AUC0-t, and

AUC0-inf, dose normalized Cmax.

Secondary outcome

Safety and tolerability parameters including: physical examination, AEs,

clinical laboratory values, vital signs and 12-lead ECGs.

Study description

Background summary

Mast cells play a central role in the pathology of allergic-mediated diseases, providing a strong rationale that depletion of mast cells can benefit patients diagnosed with allergic mucosal and cutaneous disorders in which mast cell degranulation plays a role in onset and progression. As a novel therapeutic approach, mast cell depletion should inhibit multiple mediators of symptoms of allergic diseases that have inadequate responses to single agents that target only individual mediators of mast cells or whose off-target toxicity profiles limit their use.

Mast cell activation, proliferation, and survival depend on the receptor tyrosine kinase. Studies have shown that KIT mutations and kinase inhibition of mutant KIT have profound effects on mast cells. Therefore, KIT is a pharmacologically and genetically validated target to drive mast cell depletion.

THB001 is highly selective for KIT and, therefore, mast cell proliferation and survival. The exquisite selectivity of THB001 was demonstrated in animals by limited-to-no off-target toxicity and a defined on-target toxicity with a

reasonable therapeutic window. THB001 is expected to have robust mast cell depletion and a favorable safety profile that supports clinical investigation.

Study objective

Part 1:
Primary objective:
• To estimate the relative bioavailability of two THB001 formulations in healthy adults.

Secondary objectives:
• To determine the single-dose pharmacokinetics (PK) of THB001•HCl salt and THB001 free base formulations in healthy adults.
• To assess the safety and tolerability of each treatment.

Part 2:
Primary objective:
• To assess the effect of dose and a high-fat meal on the bioavailability of THB001•HCl salt.

Secondary objective:
• To characterize the plasma PK profile of a single oral dose of THB001•HCl salt formulation in fasted and fed state in healthy adults.
• To assess the safety and tolerability of each treatment.

Study design

This is a single site, single dose, randomized, cross-over, 2-week, 2-arm, 2-part relative bioavailability (BA) study in healthy subjects.

Intervention

THB001 micronized blend free base as capsules.
Micronized THB001 HCl salt as capsules.

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP. Please see the IB for further information.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Subjects must understand the nature of the study and must provide signed and dated written informed consent in accordance with local regulations before the conduct of any study-related procedures.
2. Healthy as determined by the Investigator, based on a medical evaluation including medical history, physical examination, laboratory tests and ECG recording. A subject with a clinical abnormality or laboratory parameters outside the reference range for the population being studied may be included only if, in the opinion of the Investigator, the finding is (a) unlikely to introduce additional risk to the subject, (b) will not interfere with study procedures or confound study results, and (c) is not otherwise exclusionary (see Exclusion Criteria).
3. Men and women, age 18-65 years inclusive at Screening will be enrolled.
4. Women of child-bearing potential must agree not to attempt to become pregnant and to use a highly effective form of hormonal (excluding oral contraceptives) or non-hormonal birth control, which entails the use of a non-hormonal intra-uterine device/system in combination with a barrier method (e.g. condom, diaphragm, cervical cap with spermicide) or abstinence during the study and for 90 days after the last study drug administration. Postmenopausal

women must have had >=12 months of spontaneous amenorrhea (with documented follicle-stimulating hormone (FSH) >=30 mIU/mL). Surgically sterile women are defined as those who have had a hysterectomy, bilateral ovariectomy, or bilateral tubal ligation. Women who are surgically sterile must provide documentation of the procedure by a letter from their GP. All women must have a negative pregnancy test result at Screening and on Day -1 before first administration of study medication.
5. It is important that male subjects not impregnate others while in the study. Therefore, male subjects who are biologically capable of having children must:
- Remain sexually abstinent, when this is in line with his preferred and usual lifestyle.
OR
- Engage exclusively in same-sex relationships.
OR
- Agree to avoid impregnating his partner during the study (including washout periods) and for at least 90 days after the last dose of study medication.
AND
- Must use a combination of two methods of contraception during the study (including washout periods) and for at least 90 days after the last dose of study medication. One of the contraceptive methods must be a condom with spermicide (this is considered a single method). The second contraceptive method must include one of the following: diaphragm in combination with a spermicide; intrauterine device (IUD); contraception implant; progesterone-only pills (POPs); injectable progestogen (Depo-Provera®); combination hormonal contraceptive method (tablets, patches, or vaginal ring with both oestrogen and progestogen), OR have a partner who had her last natural menstruation >=24 months prior to the Screening Visit, OR have a partner who was surgically sterilized prior to the Screening Visit.
AND
- Not donate sperm during the study (including washout periods) and for at least 90 days after the last dose of study drug.
OR
- Male subjects who have had a vasectomy at least 4 months prior to the Screening Visit and must have completed post-surgical follow up to confirm success of the vasectomy. Furthermore, they must agree to use a condom from Day 1 of the first treatment period until 90 days after the last dose of study drug
6. Subjects must be, in the opinion of the Investigator, able to participate in all scheduled evaluations, likely to complete all required tests, and likely to be compliant.
...
8. Subjects participating in Part 2 must be willing and able to consume the entire high-fat, high-calorie breakfast meal in the designated timeframe.

Exclusion criteria

1. A positive urine drug screen/alcohol breath test at Screening or Day -1 of the first treatment period.
2. A positive Hepatitis B surface antigen or positive Hepatitis C antibody result at Screening.
3. A positive test for human immunodeficiency virus (HIV) antibody at Screening.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	24-03-2022
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nap.
Generic name:	Nap.

Ethics review

Approved WMO

Date:	23-12-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	11-02-2022
Application type:	First submission
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	EUCTR2021-006627-18-NL
CCMO	NL80045.056.21

Study results

Date completed:	06-08-2022
Results posted:	13-02-2023

First publication
19-01-2023