TBAJ-587-CL-001, Phase 1, Partially Blinded, Placebo-Controlled, Randomized, Combined Single Ascending Dose with Food Effect Cohort Trial (Part 1) and Multiple Ascending Dose Trial (Part 2) to Evaluate the Safety, Tolerability, and Pharmacokinetics of TBAJ-587 in Healthy Adult Participants.

Published: 14-07-2020
Last updated: 09-04-2024

PrimaryTo evaluate the safety and tolerability of single and multiple doses of TBAJ-587 in healthy participants.SecondaryTo determine the pharmacokinetics (PK) of single and multiple doses of TBAJ-587 and metabolites M2, M3 and M12. To compare the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mycobacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON54986

Source
ToetsingOnline

Brief title
CS0345-190557 TB Alliance

Condition

- Mycobacterial infectious disorders

Synonym
Tuberculosis

Research involving
Human

Sponsors and support

Primary sponsor: Global Alliance for TB Drug Development (TB Alliance)
Source(s) of monetary or material Support: The trial is being sponsored by the TB Alliance in the framework of the ERA4TB Project. This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under Grant Agreement No 853989. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA and Global Alliance for TB Drug Development Non-Profit Organisation;Bill & Melinda Gates Foundation;University of Dundee.

Intervention

Keyword: Food effect, Pharmacokinetics, Safety, Tolerability

Outcome measures

Primary outcome

PK

Part 1: Single Ascending Dose

Noncompartmental PK parameters of AUClast, AUCinf, Cmax, tmax, CL/F, Vz/F, *z,

and t1/2 will be calculated from plasma concentrations of TBAJ-587, M2, M3 and

M12. Additional PK parameters may be calculated if deemed appropriate.

All clinical safety data will be listed by participant. Continuous variables

will be summarized using sample size (N), mean, standard deviation, median,

minimum, and maximum.

Part 2: Multiple Ascending Dose

Multiple ascending dose cohort PK parameters using noncompartmental analysis,

calculated from plasma concentrations of TBAJ-587, M2, M3 and M12 following

doses on Days 1, 14 and 28, will include:

Day 1: AUCtau, Cmax, Tmax. Clast, Tmax. Parameters such as CL/F, Vz/F, *z, and t1/2 which require extrapolations of the concentration profile to infinity, may be calculated of PK results from the SAD indicate the feasibility based on 24 hours of sampling; otherwise not. If so, if for any individual participant AUCtau < 80% of AUCinf, CLss/F, Vz/F, *z, and t1/2 will be flagged as unreliable in listings and will not be included in summary statistics.

Day 14 and 28 : AUCtau, Cmax, Cmin, Tmax, Ctrough, Cavg, RAUC, RCmax. Parameters such as CLss/F, Vz/F, *z, and t1/2 may be calculated if feasible.

All clinical safety data will be listed by participant. Continuous variables will be summarized using sample size (N), mean, standard deviation, median, minimum, and maximum.

Secondary outcome

Nap.

Study description

Background summary

Tuberculosis (TB) is an infectious disease that continues to present a significant public health problem world-wide. Without treatment TB can be fatal, while those who survive without treatment can experience long-term health problems and remain infectious so put others at risk thorough on-going community transmission.
Current TB treatment regimens are lengthy in duration and involve multi-drug therapy. High rates of noncompliance are common, which often result in increased mortality and chronic, infectious, drug-resistant cases. The present TB epidemic and treatment conditions demonstrate the clear need for new TB drugs and drug regimens for patients with drug-sensitive or drug-resistant TB that are safe and well tolerated and will shorten the overall treatment duration required for cure. In addition, new TB drugs and regimens should be

affordable, easy to adopt and implement, suitable for pediatric use and for co administration with antiretroviral therapy in individuals co-infected with Mycobacterium tuberculosis and HIV.
This study is the first time into human study (FTIH) for TBAJ-587. The study will evaluate the safety, tolerability, and pharmacokinetics (PK) of single ascending and repeat oral doses of TBAJ-587 in healthy adult volunteers. The results of this study are intended to be used to identify appropriate and well tolerated doses of TBAJ-587 to be used in further studies. A food effect assessment will also be undertaken to investigate the influence of food on the pharmacokinetics of TBAJ-587.

Study objective

Primary
To evaluate the safety and tolerability of single and multiple doses of TBAJ-587 in healthy participants.

Secondary
To determine the pharmacokinetics (PK) of single and multiple doses of TBAJ-587 and metabolites M2, M3 and M12.
To compare the rate and extent of absorption of a single oral dose of TBAJ-587 when administered after a high-calorie, high-fat meal versus when it is administered fasting in healthy adult participants.

Study design

This is a two-part, partially blinded, placebo-controlled, combined single ascending dose (SAD) trial with a food effect cohort (Part 1) and multiple ascending dose (MAD) trial (Part 2) to be conducted in one trial centre in Europe.

Part 1: Has a single ascending dose (SAD) design with up to 6 planned dose levels with a food effect cohort at one of the dose levels.
The first SAD cohort will be separated into 2 groups. A sentinel group of two participants (1 active and 1 placebo) will be dosed at least 72 hours before the remaining 6 participants (5 active and 1 placebo). The other cohorts will not be separated.
First cohort: current total duration and scheduling of safety and PK sampling is based on the assumption that the expected t1/2 will be 26 days which will ensure coverage for PK and safety out to approximately 5 half-lives. Refer to Section 1.2.1 Schedule of Assessments & Procedures for more details. However, the sampling schedule may change depending on the observed PK profile.
Other Dose Level cohorts: scheduling of safety and PK sample collection will be based on the PK data collected from previous cohorts and could require that the participants return to the clinic for up to 20 weeks or longer after dosing, depending on what is learned about the half-life of TBAJ-587.

Food Effect Cohort: Based on exposure levels from preceding SAD cohorts, one of the planned cohorts and the specific dose will be selected for the food effect (FE) cohort which will study the effect on PK after a high-calorie, high-fat meal. The food effect on the PK of TBAJ-587 will be studied in one of the previously completed cohorts using a parallel group design involving two groups, one group dosed fasted and the other group dosed after a meal. Additional participants will be recruited to reach a total of 9 active participants, inclusive of the previously dosed participants, in the fasted group, and 9 additional active participants will be recruited for the group dosed with food.

Part 2: Has a multiple ascending dose (MAD) design. Three cohorts are planned for Part 2 and will be determined based on model predictions of steady state AUC exposures and safety from Part 1.
In this MAD part, each participant, based on current assumptions, is expected to be administered TBAJ-587 or matching placebo daily for 28 days with corresponding PK and safety measurements.

Parts 1 and 2:
Additional cohorts: up to three additional cohorts in Part 1 and one additional cohort in Part 2 may be enrolled if deemed appropriate by the Sponsor to repeat a dose level or to study another dose level.

See CSP section 4 for further details.

Intervention

The test product is TBAJ-587 5 mg/mL and 20 mg/mL oral suspension formulation and TBAJ-587 matching placebo.

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

Public
Global Alliance for TB Drug Development (TB Alliance)

40 Wall Street 24th Floor
New York NY 10005
US

Scientific
Global Alliance for TB Drug Development (TB Alliance)

40 Wall Street 24th Floor
New York NY 10005
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Provide written, informed consent prior to all trial-related procedures.
Healthy adult male and females of non-childbearing potential, 18-64 years of age (inclusive) at the time of screening.
Body mass index (BMI) >= 18.5 and <= 32.0 (kg/m2) and a body weight of no less than 50.0 kg.
Medically healthy with no clinically significant screening results (e.g., laboratory profiles normal or up to Grade 1 per FDA Toxicity Tables), medical histories, vital signs, ECGs, physical examination findings, as deemed by the Investigator. Lab results within the testing facilities normal range will not be considered AEs when referenced to the FDA Toxicity Scales (Appendix 2) assessment/grading scale. If exclusionary lab criteria are met, values may be confirmed by repeat evaluation

Exclusion criteria

History or presence of significant cardiovascular abnormalities, Heart Murmur, pulmonary, hepatic, renal, haematological, gastrointestinal, endocrine, immunologic, dermatologic, neurological, or psychiatric disease as determined by the Investigator to be clinically relevant.
Any musculoskeletal toxicity (severe tenderness with marked impairment of

activity) or musculoskeletal toxicity (frank necrosis).
History of any illness that, in the opinion of the Investigator, might confound the results of the trial or poses an additional risk to the participant by their participation in the trial.
Surgery within the past 90 days prior to dosing or other previous surgery as determined by the Investigator to be clinically relevant.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2020
Enrollment:	133
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	14-07-2020
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-08-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-04-2022
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	EUCTR2020-001935-28-NL
CCMO	NL73973.056.20