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Study to evaluate the safety, tolerability, and pharmacokinetics of oral BT-11 in healthy adult male and female volunteers

Submission date 05/01/2019	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 06/02/2019	**Overall study status** Completed	
Last Edited 09/01/2020	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Inflammatory Bowel Disease (IBD) is an autoimmune disease of the digestive system with unknown causes that has two main types: Ulcerative Colitis (UC) and Crohn's Disease (CD). CD and UC are not well managed with current drugs either because of limited effectiveness or significant side effects. BT-11 is a new drug targeting UC and CD. Its effectiveness has been demonstrated in mouse models of IBD. The aim of this study is to assess the safety, tolerability and pharmacokinetic profile of BT-11 (movement of drug through the body) after single and multiple increasing oral doses in healthy volunteers.

Who can participate?
Healthy male and female volunteers aged 18 to 65 years, inclusive

What does the study involve?
Participants are randomly allocated to receive either BT-11 or a placebo (dummy drug) as a single ascending dose (SAD) or multiple ascending dose (MAD) to measure the safety of the drug. The total maximum duration on study for SAD participants is about 35 days (up to 28-day screening period, 3-day treatment/confinement period, and 4-day follow-up). The total maximum duration on study for MAD participants is about 44 days (up to 28 days screening, 8 days treatment/confinement, and 8 days follow-up).

What are the possible benefits and risks of participating?
The patients were not expected to receive any direct medical benefits from the study. The information developed in this study may help people with Inflammatory Bowel Disease. As this drug is new, it was not known what all the possible side effects may be and there may be unknown risks. However, based on animal data, no specific safety concerns have been identified.

Where is the study run from?
CMAX Clinical Research (Australia)

When is the study starting and how long is it expected to run for?
June 2018 to October 2018

Who is funding the study?
Landos Biopharma Inc. (USA)

Who is the main contact?
Josep Bassaganya-Riera

Contact information

Type(s)
Scientific

Contact name
Dr Josep Bassaganya-Riera

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
BT-11-1a; ACTRN12618001210268

Study information

Scientific Title
A randomized, placebo-controlled, sequential single and multiple dose-escalation study to evaluate the safety, tolerability, and pharmacokinetics of oral BT-11 in healthy adult male and female volunteers

Study objectives
BT-11 is a first-in-class modulator of LANCL2 signaling. Through its action on LANCL2, BT-11 intervention will suppress the pathology of IBD patients at 2 levels: by decreasing the production of inflammatory mediators and increasing anti-inflammatory molecules in the GI tract.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Bellberry Human Research Ethics Committee, 129 Glen Osmond Rd, Eastwood SA 5063, Tel: +61 (0)8 8361 3222, 06/07/2018

Study design
Randomized placebo-controlled sequential single and multiple dose-escalation study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Ulcerative colitis and Crohn's disease

Interventions
This is a two-stage, single-center, double-blinded, randomized, placebo-controlled study of BT-11 in healthy male and female volunteers. The two stages are a single ascending dose (SAD), and multiple ascending dose (MAD).

All participants who were dosed were assigned a randomization number in accordance with the randomization schedule after confirmation of eligibility on Day 1.

The single ascending dose (SAD) cohorts consist of five groups of eight healthy male and female participants per cohort, each receiving a single oral dose of BT-11 or placebo in a 6-hour fasted state for a total n = 8, with n= 6 receiving active and n=2 receiving placebo. Five different doses were used for SAD (7.7 mg/kg, 25 mg/kg, 50 mg/kg, 75 mg/kg, and 100 mg/kg).

The multiple ascending dose (MAD) cohorts will consist of three cohorts of ten healthy male and female participants, each receiving an oral dose of BT-11 or placebo once daily for seven days, with n = 8 receiving active and n = 2 receiving placebo. For MAD three different doses were used (7.7 mg/kg, 50 mg/kg, and 100 mg/kg).

SAD Follow up: Total maximum duration on study for SAD participants will be approximately 35 days (up to 28-day screening period, 3-day treatment/confinement period, and 4- day follow-up period).

MAD Follow up: Total maximum duration on study for MAD participants will be approximately 44 days (up to 28 days screening, 8 days treatment/confinement, and 8 days follow-up).

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
BT-11

Primary outcome measure
The safety and tolerability of BT-11 after single and multiple ascending oral dose administration in healthy volunteers, measured during 4 days follow up (SAD), and 8 days follow up (MAD)

Secondary outcome measures
The pharmacokinetic profile of BT-11 after single and multiple ascending oral dose administration in healthy volunteers, measured using blood samples during 4 days follow up (SAD), and 8 days follow up (MAD)

Overall study start date
12/06/2018

Completion date
23/10/2018

Eligibility

Key inclusion criteria
1. Healthy male and female volunteers aged 18 to 65 years, inclusive
2. Body weight 65 - 85 kg
3. Body Mass Index (weight in kg divided by square of height in meters) 19-31 kg/m2, inclusive
4. Male volunteers must agree to abstain, between dosing and 30 days post-dosing, from sexual intercourse with pregnant or lactating women and, if sexually active with a female partner, to use a condom in addition to his female partner’s use of another form of contraception (e.g., IUD, diaphragm, oral contraceptive, injectable progesterone contraceptive, subdermal implant contraceptive, or tubal ligation). A male practicing abstinence is also acceptable
5. Female subjects of child-bearing potential, with a fertile male sexual partner, should be willing to use adequate contraception from Day 1 until 30 days after the follow-up visit. Adequate contraception is defined as a combination of two methods of contraception known to be

effective, such as an intrauterine device with a barrier method, or two different barrier methods.. Also, total abstinence, in accordance with the lifestyle of the subject, is acceptable
6. Volunteer agrees not to take any concomitant medications, including prescriptions or over-the-counter (OTC) medications during the interval from 3 days prior to dosing until after the last PK blood draw for the study
7. Volunteer agrees not to consume alcohol during the interval from 3 days prior to dosing until after the last PK blood draw for the study
8. Volunteer is able to communicate effectively with study personnel
9. Volunteer is able to understand and comply with protocol and investigative site requirements, instructions, and restrictions.
10. Volunteer has read, confirmed understanding of, and signed the written informed consent form after the nature of the study and all essential elements of the informed consent document have been fully explained and all of the Volunteer's questions have been answered to his or her satisfaction, prior to initiation of any study procedures

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
70

Total final enrolment
70

Key exclusion criteria
1. Any clinically significant abnormality identified in the screening history, physical examination (including Vital Signs), laboratory testing, or electrocardiographic testing. Repeat testing of vital signs to confirm the value is allowed. Up to two repeat tests are permitted to confirm eligibility
2. An excessive fall in blood pressure on orthostatic testing at screening or Day –1 (i.e., a fall in systolic blood pressure > 25 mmHg or in diastolic blood pressure > 15 mmHg)
3. Any 12-lead ECG finding at screening or on Day –1 that may, in the opinion of the Investigator, compromise interpretation of ECGs for cardiac safety assessment or complicate interpretation of events that may occur post-dose (e.g., QT not accurately measurable, conduction abnormalities)
4. Positive test for HIV, hepatitis B surface antigen, or hepatitis C antibody
5. Any clinically significant cardiac, pulmonary, renal, metabolic, neurologic, or other medical, behavioural, or genetic condition
6. Any condition that places the volunteer at significantly increased risk or may risk compromise of study objectives
7. Use of prescription or non-prescription drugs 3 days or 5 half-lives (whichever is longer) prior to dosing to after last PK draw
8. Use of herbal supplements within 3 days or 5 half-lives (whichever is longer) prior to the first

dose of study drug to after last PK draw
9. Use of alcohol within 72 hours prior to first dose of study drug
10. History of drug or alcohol abuse (by DSM-IV definition) within 3 months prior to screening
11. Positive urine drug screen (including cotinine, cannabis, cocaine, opiates, amphetamines, and other tests as determined by Investigator). Repeating analyses will be allowed if the PI suspects that there might be false positive results
12. Volunteer has a contraindication to blood sampling or is considered to have insufficient peripheral venous access
13. Volunteer has donated blood or blood products in volumes of 450 mL or more within 30 days prior to study enrollment
14. Volunteer has been previously exposed to BT-11
15. Volunteer has participated in a study of any investigational drug, device, biologic, or other agent within 30 days prior to study enrollment.
16. Volunteer has known hypersensitivity to BT-11 or any of its constituents
17. Volunteer has any disorder (e.g., psychiatric, addictive) that, in Investigator's judgement, may compromise his/her ability to provide legal written informed consent

Date of first enrolment
06/07/2018

Date of final enrolment
22/09/2018

Locations

Countries of recruitment
Australia

Study participating centre
CMAX Clinical Research
s: 5/18a North Terrace
Adelaide SA
Australia
5000

Sponsor information

Organisation
Landos Biopharma Inc.

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Sponsor type
Industry

Website
https://landosbiopharma.com/

Funder(s)

Funder type
Industry

Funder Name
Landos Biopharma Inc.

Results and Publications

Publication and dissemination plan
The protocol is not publicly available yet but high level results are publicly available on sponsor's website (www.landosbiopharma.com). Planned publication in a high-impact peer reviewed journal.

Intention to publish date
01/07/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Jyoti Chauhan and Josep Bassaganya-Riera.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	04/03/2020	09/01/2020	Yes	No