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Efficacy and safety of oral BT-11 in mild to moderate ulcerative colitis

Submission date
11/03/2019

Recruitment status
No longer recruiting

Registration date
20/03/2019

Overall study status
Completed

Last Edited
10/01/2022

Condition category
Digestive System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Ulcerative colitis (UC) is an inflammatory disorder of the intestines that mainly affects the colon. As a result of genetic and environmental factors, the cells lining the intestine can become disrupted, causing the immune system to react and damage the tissue. Unlike with normal immune responses, immune responses in UC do not resolve naturally. Therefore, UC patients are treated with steroids, immunosuppressants and biologics that dampen the immune system. However, these treatments do not just affect the digestive system but also cause many side effects including increased risk of infections and cancers. In addition, current treatments do little to restore the balance in the immune system through regulatory responses, which can naturally counteract damaging inflammatory responses. The main aim of this study is to assess the effectiveness and safety of a new oral treatment BT-11 in mild to moderate UC.

Who can participate?
Patients aged 18 to 75 with a diagnosis of mild to moderate UC for at least 3 months

What does the study involve?
Participants are randomly allocated to one of three treatment groups (low-dose BT-11, high-dose BT-11, or placebo [dummy drug]). After informed consent, all participants undergo an endoscopy, blood tests and other measurements to determine characteristics and severity of disease. If eligible, participants begin 12 weeks of treatment according to the assigned treatment group. They attend visits at weeks 2 and 6 of the study to track concentrations of study drugs and measure biomarkers and patient-reported outcomes. At the end of the 12 weeks, participants undergo an endoscopy to observe changes in the health of the colon in addition to changes in biomarkers, histopathology, and patient-reported outcomes, such as stool frequency and rectal bleeding.

What are the possible benefits and risks of participating?
Potential benefits of participation include contributing to the development process in an area of unmet therapeutic need. BT-11 has no known dose-limiting side effects. It may offer an alternative for future patients with UC. BT-11 may decrease the production of inflammatory mediators and increase anti-inflammatory molecules in the digestive tract. Participants in both BT-11 and placebo groups may experience benefit from more frequent assessments by clinical

experts for management of UC. To minimize risk, women planning to become pregnant are not eligible for the study and pregnancy tests are performed throughout the study. Endoscopy with biopsy is generally well tolerated as in standard clinical care. However, risks include discomfort, bleeding, or in rare cases perforation.

Where is the study run from?
About 45 sites will participate in Europe and in North America in the following countries: Belarus, Poland, Bosnia and Herzegovina, Russian Federation, Croatia, Serbia, Georgia, Ukraine, Hungary, United States of America, Moldova

When is the study starting and how long is it expected to run for?
March 2019 to June 2025

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

Who is the primary contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2018-005086-39

IRAS number

ClinicalTrials.gov number
NCT03861143

Secondary identifying numbers
BT-11-201

Study information

Scientific Title
A randomized, placebo-controlled, double-blind, multi-center study to evaluate efficacy and safety of oral BT-11 in mild to moderate ulcerative colitis

Study objectives
This phase 2 study addresses the proof-of-concept therapeutic efficacy of BT-11 in mild to moderate UC patients. 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. The purpose of this study is to evaluate the efficacy and safety of oral BT-11 induction compared to placebo in subjects with mild to moderate active UC.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved by Advarra, 372 Hollandview Trail, Suite 300, Aurora, ON L4G OA5 Canada, Tel: +1 (0) 905 727 7989, Email: stacey.neshevich@advarra.com, 19/02/2019, ref: Pro00032343

Study design
Phase 2 randomized placebo-controlled double-blind parallel-group multicenter induction study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Ulcerative colitis

Interventions
A total of 195 subjects with mild to moderate UC (total Mayo Score 4-10; MES 2:2) are planned to be enrolled into this study from approximately 46 centers in Europe and the United States. Eligible subjects will be randomized in a 1:1:1 ratio to receive BT-11 low- dose (500 mg), BT-11 high-dose (1,000 mg) or placebo orally, once daily. Each of the treatment arms will comprise 65 subjects. The randomization will be stratified by prior exposure to biologic therapy for UC (yes /no) and corticosteroid use at baseline (yes/no). The study consists of a 28-day screening period,

a 12-week induction phase, and a 2-week post-treatment safety follow-up period. Upon completion of the study, subjects will be eligible to receive ongoing therapy as part of longer-term studies.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
Clinical remission rate at Week 12 as defined by total Mayo score less than or equal to 2 with all sub-scores less than or equal to 1

Secondary outcome measures
1. Endoscopic remission rate at Week 12 (Mayo endoscopic sub-score [MES] of 0 or 1)
2. Mucosal healing rate at Week 12 as defined by an MES of 0 or 1 and a Geboes Histologic Index score of less than 3
3. Mean change in fecal calprotectin measured by enzyme-linked immunosorbent assay (ELISA) from baseline to Weeks 2, 6, and 12
4. Concentration of BT-11 in feces measured by high-performance liquid chromatography (HPLC) assay at Weeks 2, 6, and 12
5. Number of participants with treatment-related adverse events at Week 12

Overall study start date
15/03/2019

Completion date
15/06/2025

Eligibility

Key inclusion criteria
1. Male and female subjects aged 18 to 65 years, inclusive
2. Diagnosis of UC for at least 3 months before screening
3. Mild to moderate UC, as defined by a total Mayo Score of 4 to 10 inclusive at baseline with an MES 2 (confirmed by the central reader)
4. If subjects have previously received biologic therapy for UC (i.e., tumor necrosis factor [TNF] antagonists, vedolizumab or ustekinumab), they must have a washout period of 8 weeks before randomization
5. If subjects are receiving the following UC treatments, they must be on a stable dose for at least I month before randomization: 5- aminosalicylates (5-ASAs), oral corticosteroids
6. If subjects are receiving bile-salt sequestrant, they must be on a stable dose for at least 3 months before randomization
7. If subjects are receiving any non-prohibited medications, they must agree to maintain stable doses of concomitant medication s for UC for the duration of the trial
8. Unlikely to conceive, as defined by 1 of the following: (a) subject is surgically sterilized female,

(b) subject is postmenopausal female 2: 45 years of age with clinical documentation of menopause (i.e., 12 months without menses), or c) matter is male or subject is woman of childbearing potential (WOCBP), and agrees to abstain from heterosexual activity, use adequate hormonal contraception, or use double barrier contraception
9. For WOCBP, the subject must have a negative pregnancy test at screening and within 24 hours before the first dose of study drug.
10. Able to participate fully in all aspects of this clinical trial
11. Written informed consent must be obtained and documented

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
195

Key exclusion criteria
1. A diagnosis of CD, indeterminate colitis, or presence or history of the fistula with CD
2. Severe UC as per modified Truelove and Witts criteria
3. Disease activity limited to the distal 15 cm (proctitis)
4. Treatment with an immunosuppressant (azathioprine, 6- mercaptopurine [6-MP]) within 25 days before randomization
5. History of toxic megacolon, abdominal abscess, symptomatic colonic stricture, or stoma; history or is at imminent risk of colectomy
6. History or current evidence of colonic dysplasia or adenomatous colonic polyps
7. Current bacterial or parasitic pathogenic enteric infection, including Clostridium difficile, known infection with hepatitis B or C virus, known infection with human immunodeficiency virus, infection requiring hospitalization or intravenous s antimicrobial therapy, or opportunistic infection within 6 months prior to screening, any infection requiring antimicrobial therapy within 2 weeks prior to screening, history of more than 1 episode of herpes zoster or any episode of disseminated zoster
8. Live virus vaccination within 1 month prior to screening
9. Treatment with cyclosporine, mycophenolate, tacrolimus, or tofacitinib within 4 weeks prior to randomization
10. Treatment with intravenous corticosteroids, rectal corticosteroids, or rectal 5-ASA within 2 weeks before randomization
11. Fecal microbiota transplantation within 1 month prior to screening
12. A concurrent clinically significant, unstable, or uncontrolled cardiovascular, pulmonary, hepatic, renal, Gl, genitourinary, hematological, coagulation, immunological, endocrine /metabolic, or other medical disorder that, in the opinion of the investigator, might confound the study results or poses additional risk to the subject
13. Known primary or secondary immunodeficiency
14. History of myocardial infarction, unstable angina, transient ischemic attack, decompensated

heart failure requiring hospitalization, congestive heart failure (New York Health Association [NYHA] Class 3 or 4), uncontrolled arrhythmias, cardiac revascularization, stroke, uncontrolled hypertension, or uncontrolled diabetes within 6 months of screening
15. Laboratory abnormalities at screening, as determined and documented by the investigator
16. Pregnant or lactating females
17. Any surgical procedure anesthesia within I month prior to screening, or planned elective surgery during the study
18. History of malignant neoplasms or carcinoma in situ within 5 years prior to screening
19. Current or recent history of alcohol dependence or illicit drug use that in the opinion of the investigator may interfere with the subject's ability to comply with the study procedures
20. Mental or legal incapacitation at the time of screening visit or a history of clinically significant psychiatric disorders that would impact the ability to participate in the trial according to the investigator
21. Unable to attend study visits or comply with procedures
22. Concurrent participation in any other interventional study
23. Received any investigational therapy within 30 days of initiation of study drug
24. Underlying severe disease other than UC that in the opinion of the investigator may interfere with the subject's ability to participate fully in the study
25. Previous exposure to BT-11
26. Prior enrollment in the current study and had received study treatment

Date of first enrolment
21/03/2019

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
Belarus

Bosnia and Herzegovina

Croatia

Georgia

Hungary

Moldova

Poland

Russian Federation

Serbia

Ukraine

United States of America

Study participating centre
University Clinical Hospital Mostar
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Sponsor information

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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
Landos Biopharma Inc.

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal around June 2021. Additional documents will be made available upon request.

Intention to publish date
01/06/2021

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other