A PHASE II OPEN LABEL EXTENSION STUDY TO EVALUATE THE LONG TERM SAFETY AND TOLERABILITY OF UTTR1147A IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS OR CROHN'S DISEASE

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Safety objective: To evaluate the safety and tolerability of UTTR1147AExploratory Efficacy Objective: To evaluate the efficacy of UTTR1147AExploratory Pharmacokinetic Objective: To evaluate potential relationships between long-term drug exposure and...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON46443

Source
ToetsingOnline

Brief title
GA40209

Condition

- Gastrointestinal inflammatory conditions

Synonym
a type of Inflamatory bowel disease that may affect any part of the gastrointestinal tract from mouth to anus, chronic inflammation of the mucosa of the colon and rectum/ Crohn's Disease, Ulcerative Colitis

Research involving
Human

Sponsors and support

Primary sponsor: Genentech, Inc.
Source(s) of monetary or material Support: pharmaceutical company

Intervention

Keyword: CROHN'S DISEASE, Phase II, ULCERATIVE COLITIS, UTTR1147A

Outcome measures

Primary outcome

Safety objective:

* Occurrence and severity of adverse events, with severity determined according

to NCI CTCAE scale

* Change in targeted vital signs, physical findings, and clinical laboratory

test results during and following UTTR1147A administration

Secondary outcome

Exploratory Efficacy Objective:

* Clinical response at Weeks 28 and 52

* Clinical remission at Weeks 28 and 52

* Durability of clinical remission, defined as time from achieving clinical

remission to loss of clinical remission

* Change from baseline (i.e., either the baseline score in the parent study or

the last score prior to initiation of the most recent course of UTTR1147A

during the extension study, whichever score is the most recent) in PRO2 in

patients with Crohn's disease

Exploratory Pharmacokinetic Objective:

* Relationship between serum concentration or PK parameters for UTTR1147A and exploratory efficacy endpoints

* Relationship between serum concentration or PK parameters for UTTR1147A and safety endpoints

Exploratory Immunogenicity Objective:

* Presence of ADAs to UTTR1147A during the study relative to the presence of ADAs at baseline (Study Week 0)

Exploratory Biomarker Objective:

* Relationship between biomarkers in stool and colonic tissue and efficacy, safety, or immunogenicity endpoints

Study description

Background summary

While effective therapeutic options, including anti-integrin agents and TNF inhibitors, are available to reduce the acute symptomatic flares in disease activity in patients with moderate to severe IBD, no currently available therapy achieves sustained remission in more than 10%-30% of patients with chronic IBD. Furthermore, anti integrin agents and TNF inhibitors are associated with severe adverse events, including hypersensitivity reactions and increased risk of infections (including serious infections such as tuberculosis). Consequently, patients and physicians must carefully weigh the benefit-risk ratio both before starting and while managing long-term treatment with anti-integrin agents or TNF inhibitors.

IL-22 stimulates mucin and anti-microbial peptide production in the intestine, which can modulate bacterial growth and protect the intestinal epithelium. Changes in bacterial flora have been associated with a variety of

immunologically mediated diseases and, along with altered epithelial barrier function, are thought to be key drivers in the inflammatory process of IBD. UTTR1147A, an IL-22 fusion protein, is a novel therapeutic agent being developed to promote mucosal healing and achieve sustained clinical remission while potentially allowing reduction or elimination of the immunosuppression associated with current therapies for IBD.

The safety profile of UTTR1147A, as demonstrated in the Phase I studies, supports further investigation of UTTR1147A in the induction and maintenance of clinical remission for patients who have failed conventional therapy. The safety risks identified to date for UTTR1147A from the Phase I studies have been well characterized in HVs and consist of dermatologic adverse events that have been readily monitored, manageable, and reversible. As UTTR1147A is an investigational medicinal product with limited Phase I patient data, the full safety profile will be further characterized as Phase I and II clinical development progresses.

Study objective

Safety objective: To evaluate the safety and tolerability of UTTR1147A

Exploratory Efficacy Objective: To evaluate the efficacy of UTTR1147A

Exploratory Pharmacokinetic Objective: To evaluate potential relationships between long-term drug exposure and the safety and efficacy of UTTR1147A

Exploratory Immunogenicity Objective: To evaluate the immune response to UTTR1147A

Exploratory Biomarker Objective: To identify biomarkers that can increase the knowledge and understanding of disease biology

Study design

Open-label extension study

Intervention

Treatment with UTTR1147A will be determined on the basis of the patient's disease status. Upon entry into the extension study, patients will receive UTTR1147A 60 µg/kg IV Q4W or undergo observation, depending on their disease status at the time of their last endoscopy in the parent study.

Study burden and risks

Side effects associated with UTTR1147A (in previous clinical studies these side

effects have not been serious and have been fully reversible):

Common (occurred in more than 10% of 44 healthy volunteers):
* Reddening of skin
* Dry/scaly skin
* Dry lips
* Increase in substance produced by the liver that increases in the presence of inflammation in the body (C-reactive protein), but without signs or symptoms to suggest inflammation (e.g., fevers, chills, or fatigue)

Less common (occurred in 1%-10% of 44 healthy volunteers)
* Itchy skin
* Painful skin
* Increase in protein that helps in the formation of blood clots, but without signs or symptoms of blood clots

The following are side effects that may be associated with UTTR1147A:
* Risk of growth of existing tumors (such as skin tumors or other tumors that you may already have in your body), because UTTR1147A may stimulate growth of certain tumors. To date, UTTR1147A has not increased the growth of any cancers in humans.
* Risk of having an infusion reaction or allergic reaction to UTTR1147A. Infusion reactions or allergic reactions may be mild, such as skin rash or hives, or severe, such as breathing difficulties. A severe infusion reaction or severe allergic reaction requires immediate medical treatment and could result in permanent disability or death.
* Risk that the immune system might develop special antibodies to the drug or to the body*s own IL-22. If this occurs, these antibodies could cause several different effects, such as an allergic reaction to UTTR1147A or a change in your body*s ability to respond to infections (including infections in your digestive system that may or may not be due to your ulcerative colitis) that could be long-lasting.

Possible Risks and Discomfort Associated With switching Treatment from vedolizumab to UTTR1147A
If patient participated in the parent study GA39925, there is a possibility that the treatment he/she receive will be switched from vedolizumab to UTTR1147A. If this happens, the disease might worsen and he/she might require rescue treatment. It is also possible that patient might develop special antibodies against vedolizumab if the vedolizumab treatment is stopped.

Possible Risks and Discomfort Associated with Drawing Blood
During this study, small amounts of blood will be drawn from a vein and used for tests that allow your study doctors to see how you are doing. Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising or infection at the place where the needle is inserted. Some people experience dizziness, upset stomach, or fainting when their blood is drawn.

Flexible Sigmoidoscopy, ileocolononscopy, and colonoscopy
Patient may experience some discomfort during the examination. Rare complications include bleeding (occurring less than 1%-2% of the time, complications relating to sedation, such as low blood pressure or heart rhythm problems (occurring less than 0.5% of the time), and bowel perforation (occurring less than 1% of the time), which could require surgery or could even be fatal.

Electrocardiogram
An ECG is painless. No electricity is sent through the body. In rare cases, some people may develop a rash or irritation where the patches were placed.

Possible Risks and Discomfort Associated with Biopsies
Risks associated with a colon biopsy sample collection include bleeding and infection. Rare complications include bowel perforation, which may require urgent surgery. A skin biopsy may be collected if you experience a skin reaction. Risks associated with skin biopsies include pain, redness, swelling, excessive bleeding, bruising, or draining at the needle site, abnormal wound healing, fever, infection, and allergic reaction to the medication used to numb the skin over the biopsy site.

Contacts

Public
Genentech, Inc.

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Scientific
Genentech, Inc.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Prior enrollment in Study GA29469 or Study GA39925 and meeting protocol defined entry criteria;- Ability to comply with requirements of the study, in the investigator's judgment;- Age 18-80 years;- For women and men: Use of highly effective contraception as defined by the protocol

Exclusion criteria

- Withdrawal of consent from parent study;- Discontinuation of study drug as required by the parent study protocol ;- Noncompliance in the parent study, specifically defined as missing scheduled visits or non-adherence with background medications and concomitant medications;- Pregnant or breastfeeding, or intending to become pregnant during the study or within 8 weeks after the final dose of study drug or within 18 weeks after the final dose of study drug from GA39925, whichever is longer;- Any new malignancy, significant uncontrolled comorbidity, such as cardiac, pulmonary, renal, hepatic, endocrine, or gastrointestinal disorders, or signs or symptoms of infection judged by the investigator to be clinically significant since enrolling in the parent study;- Use of prohibited therapies as defined in the parent study;- Abnormal laboratory value recorded at the last visit in the parent study

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	UTTR1147A
Generic name:	-

Ethics review

Approved WMO Date:	06-12-2018
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-01-2019
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

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	EUCTR2017-004997-32-NL
ClinicalTrials.gov	NCT03650413
CCMO	NL65388.028.18