A two-part, multi-centre, randomized, placebo-controlled, double-blind study, of TRK-170 for the treatment of Crohn's disease.

Published: 05-07-2011
Last updated: 29-04-2024

The purpose of the collected study information is research, development and safety analysis of TRK-170.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON36043

Source
ToetsingOnline

Brief title
170CDT01

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Toray Industries, Inc. Europe Office
Source(s) of monetary or material Support: Toray Industries;Inc.

Intervention

Keyword: Crohn's disease, phase II trial

Outcome measures

Primary outcome

Primary endpoint:

Part A

Change in CDEIS score from baseline to end of treatment (week 8)

Part B

The proportion of patients in remission as defined by a CDAI score of <150 at

end of treatment (week 8)

Secondary outcome

Secondary endpoints:

Part A

* The proportion of patients in remission as defined by a CDAI score of <150 at

end of treatment (week 8)

Part A and Part B

* Proportion of responders as defined by a reduction in CDAI score by at least

70 at week 8 compared to baseline

* Safety and tolerability of TRK-170 in patients with active CD as assessed by

adverse events (AEs), vital signs and laboratory parameters

* PK characteristics of TRK-170

* Changes in faecal calprotectin concentration from baseline to week 8

* Changes in plasma CRP levels from baseline to week 8

* Changes in IBDQ score from baseline to week 8

Study description

Background summary

Crohn's Disease (CD) is a chronically inflammatory disease of the gastro-intestinal system and is part of a group of diseases known as inflammatory bowel diseases. Characteristic symptoms of CD are chronic diarrhoea, abdominal pain, weight loss, fever, and rectal bleeding reflecting the underlying inflammatory process.

Drugs used in the treatment of CD may either reduce active inflammation and symptoms of CD, or prevent a new active episode of the disease from developing. TRK-170 will be evaluated primarily for the induction of remission.

Study objective

The purpose of the collected study information is research, development and safety analysis of TRK-170.

Study design

The study will be conducted as a multi-centre, randomized, placebo-controlled, double-blind, parallel group study (consisting of Part A and Part B) with TRK-170.

Part A
Patients will be enrolled and randomized into one of 4 treatment cohorts to receive total daily doses of 12 mg, 60 mg, 120 mg of TRK-170 or placebo, administered twice daily over an 8 week period. Patients will thereafter be followed for an additional 4 weeks. Ileocolonoscopy including video recording will be performed before the start of treatment (Visit 2) and at 8 weeks (Visit 6) to assess the disease activity as measured by CDEIS score. When possible the ileocolonoscopy should be conducted by the same endoscopist at Visit 2 and Visit 6. Readings of the video recordings will be performed by an Independent Panel of Experts. CDAI score measurements will be performed at each clinic visit to assess the disease activity primarily associated with patient symptoms.
Additional assessments of disease activity based on symptoms and laboratory parameters will be performed.
After completion of Part A, an interim analysis of data reflecting disease

activity and safety will be performed to identify one or, at maximum, two dose levels of TRK-170 to be evaluated in Part B.

Part B
Patients will be enrolled and randomized to receive active treatment or placebo administered twice daily, approximately every 12 hours, over an 8 week period (patients that participated in Part A and received TRK-170 will not be eligible for Part B of the study). Patients will thereafter be followed for an additional 4 weeks. Based on the results of Part A, active treatment will be given at one or two dose levels within the range of 12 mg to 120 mg daily. Disease activity will be followed using CDAI and laboratory parameters, but not ileocolonoscopy.

Primary endpoint:
Part A
Change in CDEIS score from baseline to end of treatment (week 8)
Part B
The proportion of patients in remission as defined by a CDAI score of <150 at end of treatment (week 8)

Secondary endpoints:
Part A
* The proportion of patients in remission as defined by a CDAI score of <150 at end of treatment (week 8)
Part A and Part B
* Proportion of responders as defined by a reduction in CDAI score by at least 70 at week 8 compared to baseline
* Safety and tolerability of TRK-170 in patients with active CD as assessed by adverse events (AEs), vital signs and laboratory parameters
* PK characteristics of TRK-170
* Changes in faecal calprotectin concentration from baseline to week 8
* Changes in plasma CRP levels from baseline to week 8
* Changes in IBDQ score from baseline to week 8

Intervention

Part A
Patients will be enrolled and randomized into one of 4 treatment cohorts to receive total daily doses of 12 mg, 60 mg, 120 mg of TRK-170 or placebo, administered twice daily over an 8 week period.

Part B
Patients will be enrolled and randomized to receive active treatment or placebo administered twice daily, approximately every 12 hours, over an 8 week period. Based on the results of Part A, active treatment will be given at one or two

dose levels within the range of 12 mg to 120 mg daily.

Study burden and risks

Part A
- 56x 2 times a day, two pills of study medication, from visit 2 to visit 6.
- 1x Chest X-ray on visit 1
- 10x 12-lead ECG during a visit to 7 (including 4x at visit 3)
- 20x blood sampling from visit 1 to 7 (of which 9 samples at visit 3)
- 2x colonsccopy during a visit 2 and 6
- 2x preparation for colonoscopy (colonclensing) starting one day before visit 2 and 6.
- 4x the CDAI diary card filled out, during the 7 days prior to the visits 2, 4, 6 and 7. Furthermore, the CDAI will be filled in retrospectively during visit 1.
- 4x the IBDQ questionnaire completed, during visit 2, 4,6 and 7.

Part B
- 56x 2 times a day, two pills of study medication, from visit 2 to visit 6.
- 7x 12-lead ECG during a visit to 7 (including 4x at visit 3)
- 12x blood sampling from visit 1 to 7
- 4x the CDAI diary card filled out, during the 7 days prior to the visits 2, 4, 6 and 7. Furthermore, the CDAI will be filled in retrospectively during visit 1.
- 4x the IBDQ questionnaire completed, during visit 2, 4,6 and 7.

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

Patient has to meet all of the following criteria to be eligible to enter the study:
1) Male and female patients aged 18 to 50 years
2) Patient has a diagnosis of CD at least 4 months prior but not more than 10 years before screening. The diagnosis should have been confirmed by endoscopic findings including histological examination
3) Patient has had disease activity with lesions in the colon within the past 12 months before dosing, as confirmed by ileocolonoscopy
4) Patient with moderately active CD at time of screening defined as a CDAI score of between 220 and 450
5) Patient has stable disease activity (stable for * 2 weeks prior to screening) and not foreseen to require treatment with high dose steroids or other short term, potent treatments (e.g. tumour necrosis factor (TNF) * inhibitors) during the study period
6) Patient has an increased CRP level (> upper limit of normal) at screening, as a sign of active disease, as judged by the Investigator
7) Patient with a body weight of greater than 50 kg but less than 120 kg
8) Patient willing and able to participate in the study and provide signed informed consent
9) Patient agrees to use adequate contraceptive measures, in other words,
Female patient who has not been post-menopausal for more than 3 months or female patients of childbearing potential must use adequate contraception (i.e. a method with less than 1% failure rate [e.g. diaphragm or condom used in combination with spermicidal cream, sterilization, an intrauterine device, or a vasectomised partner]) during and for at least three months after the last dose of investigational product (IP). Females using hormonal contraception methods must also use an additional contraception method (as described above) during and for at least three months after the study has ended
or
Male patient who agrees to use condoms in combination with spermicidal cream during the study and for three months after the last dose of IP, or patients who have a female partner using adequate contraception as described above

Exclusion criteria

Patient meeting any of the following criteria will not be permitted to enter the study:
1) Increased risk of hypersensitivity or allergy to the IP or placebo product as judged by the Investigator
2) Patient has had a clinically significant illness within 4 weeks prior to screening, at the Investigator*s discretion, or history of any severe liver disease with cirrhosis, active hepatitis or chronic hepatitis
3) Patient with clinically significant deviations in laboratory values as determined by the Investigator, high level(s), e.g., 2X upper limit of normal of ALT, AST, ALP, GGT or total bilirubin at screening indicative of hepatic impairment. Laboratory values >3X upper limit of normal will be a strict criteria for exclusion
4) Patient who had a serious infection within 3 months, opportunistic infection within one month, or current signs or symptoms of severe, progressive or uncontrolled disease
5) Severe renal impairment defined as a predicted creatinine clearance of 30 mL/min or less, based on the Cockroft-Gault equation
6) Patient has a history of cancer or lymphoproliferative disease within the last 5 years
7) History of substance or alcohol abuse within the past one year prior to screening
8) Positive viral test result for hepatitis B or C or HIV 1 or 2 or positive pre-study testing for major drugs of abuse or excessive alcohol consumption
9) Chest X-ray positive or suspected positive for active tuberculosis
10) Female patient currently pregnant or breast-feeding or intending to become pregnant during the study or within three months after the last dose of IP
11) Female patient of childbearing age (unless surgically sterile) without a negative urine pregnancy test at screening and at enrolment
12) Patient currently has gastrointestinal disease (GI) other than CD (e.g., ulcerative colitis, short bowel syndrome, malabsorption, intestinal obstruction). This includes patients with an ostomy, ileal pouch, a previous ileo-rectal anastomosis, a history of procto-colectomy but not subtotal colectomy, draining fistula or abscess or are receiving enteral nutrition via a feeding tube or parenteral nutrition
13) Treatment with immunosuppressants or anti-cancer drugs (e.g., azathioprine, 6-MP, 6 thioguanin, methotrexate, mycophenolate mofetil, sirolimus (rapamycin), tacrolimus, thalidomide, cyclophosphamide, or cyclosporine) within the last 3 months prior to screening
14) Treatment with intravenous (IV)/rectal steroids for CD, antibiotics (e.g., metronidazole or ciprofloxacin) or continued repeated use of nonsteroidal anti inflammatory agents (NSAIDs) within 2 weeks prior to screening
15) Treatment with Tysabri® or inhibitors of TNF-* within 8 weeks prior to screening
16) Treatment with a 5-ASA formulation (oral mesalazine) at a fixed dose of 2.4 g/day or higher (not exceeding the approved dose) within 1 week prior to screening
17) Patient who changed the dose of oral corticosteroids within 2 weeks prior to screening or ongoing treatment with prednisolone exceeding 25 mg/day or corresponding doses of other corticosteroids
18) Patient who stopped using oral corticosteroids within 4 weeks prior to screening
19) Patient has previous treatment failure or had an inadequate response or intolerance to biologic drugs for CD (e.g., Tysabri® or inhibitors of TNF-*)
20) Patient who had a previous gastrointestinal surgical procedure (except appendectomy

and ileocecal resection) within 8 weeks of screening or foreseen to need GI surgery during the study
21) Patient has contributed blood (e.g., blood donation or clinical study participation) or suffered from blood loss, of at least 450 mL (1 unit of blood) within 90 days before screening or has donated plasma within 7 days prior to screening
22) Patient has participated in a clinical study in which he/she received an investigational drug within 3 months prior to dosing
23) Patient with unwillingness or inability to follow the procedures outlined in the study protocol.
24) Patient considered by the Investigator to be unsuitable to participate in the study for any other reason

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-10-2011
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	TRK-170
Generic name:	TRK-170

Ethics review

Approved WMO Date:	05-07-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-09-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-12-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2011-000854-44-NL
ClinicalTrials.gov	NCT01345799
CCMO	NL36737.018.11