A Randomised, Double-blind, Active Treatment Study to Induce Clinical Response and/or Remission with GSK1605786A in Subjects with Moderately-to-Severely Active Crohn*s Disease

Published: 07-11-2012
Last updated: 26-04-2024

Primary Objective:To induce clinical response (CDAI decrease from baseline * 100 points) and/or remission(CDAI

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

Summary

ID

NL-OMON39870

Source
ToetsingOnline

Brief title
GSK CCX114643

Condition

- Gastrointestinal inflammatory conditions

Synonym
chronic inflammation of the digestive tract, Crohn's disease

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: chemokine antagonist, Crohn□s Disease, GSK CCX114643

Outcome measures

Primary outcome

Proportion of subjects achieving clinical response, defined by CDAI decrease

from baseline of *100 points, at Week 12.

Secondary outcome

1. Proportion of subjects in clinical remission, defined as a CDAI score of <150

points, at Week 12.

2. Proportion of subjects with a clinical response (CDAI decrease from baseline

of

*100 points) at both Week 8 and Week 12.

3. Proportion achieving clinical remission (CDAI <150 points) at both Week 8 and

Week 12.

4. Proportion of subjects with a clinical response (CDAI decrease from baseline

of

*100 points) at Week 8.

5. Proportion achieving clinical remission (CDAI <150 points) at Week 8.

Study description

Background summary

This study is being conducted as part of a Phase III program to support a registration package for GSK1605786A in the maintenance of remission in Crohn*s disease patients. The purpose of Study CCX114643 is to qualify subjects for the follow-on pivotal maintenance study CCX114157, through induction of clinical response and/or remission following treatment with GSK1605786A. Subjects with moderately-to-severely active Crohn*s disease (CDAI score *220**450 at baseline) who achieve clinical response (CDAI decrease from baseline * 100 points) and/or remission
(CDAI <150) following 12 weeks of treatment with one of two doses of GSK605786A (500 mg once daily, 500 mg twice daily) will be eligible for enrolment into CCX114157.

Study objective

Primary Objective:
To induce clinical response (CDAI decrease from baseline * 100 points) and/or remission
(CDAI <150) following 12 weeks of treatment with one of two active doses of GSK1605786A for qualification of subjects for enrolment into a follow-on 52-week maintenance study (CCX114157).
Secondary Objectives:
In subjects with moderately-to-severely active Crohn*s disease:
* To assess induction of response with two doses of GSK1605786A over 12 weeks.
* To assess induction of remission with two doses of GSK1605786A over 12 weeks.
* To evaluate the safety of GSK1605786A over a 12-week treatment period.
* To investigate the effect of GSK1605786A on biomarkers of inflammation [Creactive
protein (CRP) and faecal calprotectin].
* To explore the dose relationships between GSK1605786A plasma concentration and clinical response endpoints.
* To explore potential relationships between genetic variants and GSK1605786A efficacy and safety endpoints.

Study design

This is a multi-centre, double-blind, randomised, active treatment, parallel group study designed to induce clinical response and//or remission with two oral doses of GSK1605786A (500mg once daily, 500mg twice daily) over a 12-week treatment period in subjects with moderately-to-severely active Crohnn*s disease.

Intervention

Two oral doses of GSK1605786A (500mg once daily or 500mg twice daily).

Patients are blinded and will all take two tablets in the morning and two tablets in the evening.

Study burden and risks

GSK1605786A can have the following side-effects (occurring in more than 1 in 20 patients):
* stomach pain (14%)
* feeling poorly from Crohn*s disease (10%)
* feeling sick to the stomach (8%)
* diarrhoea (8%)
* vomiting (5%)
* joint pain (7%)
* headache (6%)

See for a complete overview the table study assessments and procedures in the protocol.
Patients have to swallow the study medication once or twice per day. Other procedures required per protocol:
- blood tests: in total at 9 visits
- physical examination: at screening, Week 12, end of study
- questionnaires (IBDQ, SF-36 v2, EQ-5D WPAI-CD) : baseline, Week 4, 8 and 12, end of study
- body weight, blood pressure, temperature, and heart rate: screening, Week 0, 4, 8 and 12, end of study
- ECG: screening, Week 12, and end of study
- stool sample: screening, Week 12 and end of study
- phone questionnaire: every day from screening until Week 0 and during the 8 days before visit Week 4, 8 and 12.

Contacts

Public
GlaxoSmithKline

Great West Road 980
Brentford, Middlesex TW8 9GS
GB
Scientific
GlaxoSmithKline

Great West Road 980
Brentford, Middlesex TW8 9GS
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subjects eligible for enrolment in the study must meet all of the following criteria:
1. Male or female subjects aged *18 years
2. Written informed consent prior to any of the screening procedures including discontinuation of prohibited medications
3. Crohn*s disease for >4 months duration, which has been confirmed by diagnosis prior to study entry, with small bowel and/or colonic involvement
4. Current evidence of moderately-to-severely active disease defined by a CDAI score of *220**450 at baseline (Week 0)
5. Confirmation of active disease by
i. Elevated CRP (*3mg/L, the upper limit of normal (ULN) for the highly sensitive CRP test) at screening or
ii. Elevated levels of faecal calprotectin (>200*g/g stool) at Screening or
iii. Ileocolonscopy with documentation of a minimum of 3 nonanastomotic ulcerations(each > 5 mm in diameter) consistent with CD, within 3 months prior to Screening.
6. History of inadequate response and/or intolerance/adverse event leading to discontinuation of at least one of the following treatments for Crohn*s disease: corticosteroids or immunosuppressants
7. Stable doses of permitted concomitant medications or having previously received, but are not currently receiving, medications for Crohn*s disease. The number of subjects who have received treatment in the past with an anti-TNF for Crohn*s disease and discontinued due to loss or lack of efficacy will be limited to 50% of
those randomised.
8. Demonstrated ability to comply with Crohn*s disease symptom recording using the IVRS.

Exclusion criteria

Subjects meeting any of the following criteria must not be enrolled in the study:

1 Known coeliac disease, those who follow a gluten-free diet to manage symptoms of suspected coeliac disease and subjects with a positive screening test for coeliac disease (elevated anti-tissue transglutaminase antibodies)
2 Diagnosis of ulcerative or indeterminate colitis
3 Fistulae with abscesses, or fistulae likely to require surgery during the course of the study period
4 Bowel surgery, other than appendectomy, within 12 weeks prior to screening and/or has planned surgery or deemed likely to need surgery for CD during the study period
5 Extensive colonic resection, subtotal or total colectomy
6 Presence of ileostomies, colostomies or rectal pouches
7 Fixed symptomatic stenoses of small bowel or colon
8 Diagnosis of short bowel syndrome or chronic diarrhoea related to malabsorption and/or multiple bowel re-sections for Chron's disease
9 Chronic use of narcotics for chronic pain defined as daily use of one or more doses of narcotic containing medications
10 Use of prohibited medications, within their specified timeframes and throughout the study.
11 Positive immunoassay for C. difficile
12 Known HIV infection
13 Known varicella, herpes zoster, or other severe viral infection within 6 weeks of screening
14 Subjects who have received immunisation with a live vaccine e.g. measles, mumps, rubella (each as in MMR vaccine), oral polio, varicella, yellow fever, within 4 weeks of screening and throughout the study, with the exception of influenza vaccine
15 Confirmed positive hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (HBcAb) test or positive Hepatitis C test result
16 Confirmed positive result for QuantiFERON TB Gold test.
17 Current sepsis or infections requiring intravenous antibiotic therapy > 2 weeks
18 Previous infections characterised by opportunistic pathogens, and/or dissemination suggestive of clinically significant immunocompromise
19 The subject exhibits evidence of hepatic dysfunction, viral hepatitis, or exhibits serum ALT (SGPT) and/or AST (SGOT) values *2 times the upper limit of normal; has a total bilirubin value >1.5 times the upper limit of normal (isolated bilirubin >1.5xULN is acceptable if bilirubin is fractionated and direct bilirubin <35%); has alkaline phosphatase >1.5 times the upper limit of normal; has current or chronic history of liver disease including non-alcoholic steatohepatitis (NASH); has known hepatic or biliary abnormalities with the exception of Gilbert*s syndrome or asymptomatic gallstones
20 QTc *450 msec (*480msec for those with Bundle Branch Block)
21 Congenital or acquired immunodeficiency or has evidence of immunocompromise manifested by current opportunistic infection
22 Current evidence of, or has been treated for a malignancy within the past five years (other than localised basal cell, squamous cell skin cancer, cervical dysplasia, or any cancer in situ that has been resected)
23 History of evidence of adenomatous colonic polyps that have not been removed.
24 History of evidence of colonic mucosal dysplasia
25 If female, is pregnant, has a positive pregnancy test or is breast-feeding
26 Concurrent illness or disability that may affect the interpretation of clinical data, or otherwise contraindicates participation in this clinical study
27 Medical history of sensitivity to any of the components of GSK1605786A.

28 Use of any investigational product within 30 days prior to screening.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-07-2013
Enrollment:	56
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK1605786A
Generic name:	GSK1605786A

Ethics review

Approved WMO Date:	07-11-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-04-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	10-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2013
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	EUCTR2011-002817-12-NL
ClinicalTrials.gov	NCT01536418
CCMO	NL41913.018.12