A multicentre, randomised, double-blind (sponsor-unblinded), placebo-controlled study with open label extension to investigate the safety and tolerability, pharmacokinetics, pharmacodynamics, and efficacy of GSK2982772 in subjects with active ulcerative colitis (study 202152)

Published: 23-01-2017
Last updated: 12-04-2024

Primary:To investigate the safety and tolerability of 60 mg 3 times daily doses of GSK2982772 in subjects with moderate to severe ulcerative colitis.Secondary:To assess the preliminary efficacy, biomarkers, histological disease activity, response…

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

Summary

ID

NL-OMON45582

Source
ToetsingOnline

Brief title
study 202152

Condition

- Gastrointestinal inflammatory conditions

Synonym
ulcerative colitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: colitis ulcerosa, GSK2982772

Outcome measures

Primary outcome

Adverse effects.

Secondary outcome

Mayo score, UCEIS, change from baseline of markers (incl. CRP and FCP),

Modified Riley Score and Geboes Index, plasma concentrations.

Study description

Background summary

This study is the first experience with GSK2982772, a receptor-interacting protein-1 (RIP1) kinase inhibitor, in subjects with active ulcerative colitis (UC) who are currently being treated with standard of care therapy. All subjects will be allowed to continue standard of care therapy during the study, provided that the medication type and dose is stable throughout the study.
RIP1 is a key signalling node which plays an essential role in inflammation and cell death. Recent work has demonstrated that RIP1 catalytic kinase activity can regulate TNF-mediated necroptosis and apoptosis. In addition, the production of certain inflammatory cytokines can be regulated by RIP1 kinase activity.
With the inhibition of RIP1 kinase activity with GSK2982772 may fill a unique niche in the treatment of inflammatory conditions through multiple mechanisms, including inhibition of inflammation-induced cell death (necroptosis and

apoptosis) and inhibition of the production of certain pro-inflammatory cytokines.

Study objective

Primary:
To investigate the safety and tolerability of 60 mg 3 times daily doses of GSK2982772 in subjects with moderate to severe ulcerative colitis.
Secondary:
To assess the preliminary efficacy, biomarkers, histological disease activity, response and remission, pharmacokinetics.

Study design

Double blind multicenter placebo controlled parallel group study. Randomization (1:1) to 3 times daily
• GSK2982772 60 mg
• Placebo.
Screening 30 days, treatment phase part A (double blind) 42 days, treatment phase part B (open label GSK2982772 only) 42 days, follow-up 28 days.
Approx. 36 subjects. Should the dropout rate in Part A be higher than anticipated, or the sample size review warrants an increase in randomized subjects, additional subjects may be randomized (up to a maximum of 48).

Intervention

Treatment with GSK2982772 (treatment phase part A and B) or placebo (part A only) on top of standard therapy.

Study burden and risks

Risk: Adverse events of the study medication and the sigmoidoscopy.
Burden:
9 visits and 6 telephone calls in 20 weeks. At the end of the double blind period, one day may not be enough to perform all tests. An extra day may be added.
Physical examination: 9 times.
Blood draws: 9 times (200-225 ml blood in total).
Faecal examination: 8 times.
Pregnancy test: 9 times.
ECG: 9 times.
Sigmoidoscopy plus biopsy: 3 times.
Diary entire study period: Medication intake and adverse events.
Questionnaires (Columbia Suicide Severity Rating Scale, IBDQ) 4 times.
Optional: blood sample for pharmacogenetics.

Contacts

Public
GlaxoSmithKline

Huis ter Heideweg 62
Zeist 3705 LZ
NL
Scientific
GlaxoSmithKline

Huis ter Heideweg 62
Zeist 3705 LZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Between 18 and 75 years of age inclusive.
• Confirmed diagnosis of active UC, as documented by complete diagnostic colonoscopy to the terminal ileum with biopsy at least 3 months prior to screening.
• Complete Mayo Score of >=3 points and endoscopy sub score of 2 to 3 at screening, despite concurrent treatment with at least oral corticosteroids or 5-ASA or purine analogues or all. See protocol page 28 for details.
• Naive to any biological therapies for UC or previous exposure to a single anti-TNF biologic agent which was discontinued for reasons other than primary non-response more than 8 weeks (or 5 half lives whichever is longer) prior to first dose or previous exposure to a single anti-TNF biologic agent in the context of a clinical trial which was discontinued more than 8 weeks (or 5 half lives whichever is longer) prior to first dose.
• BMI 18.5 - 35 kg/m2 (inclusive).

• Females must not be pregnant of lactating.
• Females of childbearing potential and males must comply with the contraception requirements outlined on page 29 of the protocol.

Exclusion criteria

• Indeterminate colitis, Crohn*s Disease, infectious colitis, or ischemic colitis.
• Fulminant UC, or UC limited to the rectum (disease extent <15 cm from the anal verge).
• Previous small bowel or colonic surgery, histological evidence of colonic dysplasia or bowel stricture.
• Colostomy, fistulae or known symptomatic stenosis of the intestine.
• Clostridium difficile toxin test or active/previous colonic CMV infection.
• Suicidal ideation behaviour as measures using the Columbia Suicide Severity Rating Scale or history of attempted suicide.
• Active infection, or a history of infections. See protocol page 30-31 for details.
• Treatment with the therapies listed in Section 6.11.2, or changes to those treatments, within the prescribed timeframe.
• Received a live or attenuated vaccine within 30 days of randomization or plan to receive a vaccination during the study until 5 half-lives (or 2 days) plus 30 days after receiving GSK2982772.
• Presence of HBsAg, positive hepatitis C antibody test result. Positive serology for HIV.
• Exposure to more than 4 investigational medicinal products within 12 months prior to the first dose.

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):	22-01-2018
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK2982772
Generic name:	GSK2982772

Ethics review

Approved WMO Date:	23-01-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-08-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2018
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	EUCTR2016-001833-29-NL
CCMO	NL58479.018.17
Other	www.gskclinicalstudyregister.com, nummer 202152