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A clinical trial of antibody GSK1070806 in the treatment of patients with moderate to severe Crohn's disease

Submission date
22/07/2019

Recruitment status
No longer recruiting

Registration date
28/10/2019

Overall study status
Completed

Last Edited
15/01/2025

Condition category
Digestive System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The aim of this study is to assess whether a treatment called GSK1070806 can be delivered safely by intravenous infusion (into a vein) in patients with moderate to severe Crohn's disease. Crohn's disease is a disorder that causes inflammation of the gastrointestinal tract from mouth to anus. Crohn's disease is a type of inflammatory bowel disease and can present with a range of symptoms including diarrhoea, abdominal pain, tiredness and fatigue. The treatment of inflammatory bowel disease, both ulcerative colitis and Crohn's disease, is rapidly changing. Current treatments aim to control inflammation in the gut rather than simply control symptoms. Therefore, accurate assessment of the presence or absence of inflammation of the lining of the gut and healing of ulcers in ulcerative colitis and Crohn's disease is important. Currently the treatment for Crohn's disease can be medicinal, surgical or a combination of both. IL-18 is a key cytokine involved in inflammation resulting in Crohn's disease. Researchers are testing an antibody to this key cytokine in moderate to severe Crohn's disease where there is a large unmet need.

Who can participate?
Patients aged 16 to 80 years with moderate to severe Crohn's disease

What does the study involve?
Participants are randomly allocated to receive one dose of the active GSK1070806 drug or a placebo
(dummy) drug delivered into a vein over about 1 hour. Adverse effects, clinical laboratory tests, electrocardiograms, vital signs, and infections are assessed.

What are the possible benefits and risks of participating?
It is hoped that the combination of GSK1070806 will be of benefit to patients, but there is no guarantee. The information gained from this study may help improve the treatment of people who suffer from Crohn's disease in the future. Patients may have to come into clinic more often over the 6 months when taking part in the study. On most visits patients will have to provide a blood sample and on some visits a stool sample. In standard of care too, blood sampling and

stool testing may be ordered by the physician at a frequency determined by the disease severity. All patients will have two colonoscopies (examination of the lower bowel) and up to 12 biopsies per colonoscopy. The first will take place during the screening period and the second during the follow up period. In standard of care patients would normally have one colonoscopy. A colonoscopy is usually safe but in rare cases it can cause harm to the bowel. About 1 person in every 400 has bleeding after their colonoscopy but it is usually easy to stop. Bleeding is more common if a polyp is removed, but rare if biopsies are taken. Rarely, the bleeding is more difficult to stop and means that the person needs to be admitted to hospital. This happens to about 1 in every 2000 people having a colonoscopy. Even more rarely, colonoscopy can cause a small tear (perforation) in the bowel. This happens to about 1 in every 2500 people having a colonoscopy. If a patient receives sedation for colonoscopy, hypoxia (lack of oxygen reaching the tissues) may occur rarely, but patients are constantly under monitoring. Routine blood samples will be taken at every visit to monitor safety. Additional blood samples will be taken during the treatment visits to monitor what effect the drug is having on the body and to establish what the body is doing to the drug. Blood samples are usually taken from a vein in the arm, either from the inside of the elbow or the wrist. When blood samples are taken from a vein, there may be a slight pricking sensation, some temporary discomfort, minor pain, additional bleeding and risk of bruising at the site. Sometimes a person may become dizzy or faint when blood is drawn and there is a rare possibility of infection. A TB test will be carried out during the screening process of the trial. If the TB blood test indicates the patient may have TB, a chest x-ray may be arranged to further evaluate the blood test result. This will involve exposing the patient to a very small dose of x-rays equivalent to a few days of background radiation in the UK. The risk from this dose is negligible. The results of this chest x-ray along with other tests will be used to assess the patient's current medical condition in relation to the TB test results. If there is concern that the patient has TB, they will be excluded from the study. At this present time there is very limited research data on the use of GSK1070806 in pregnancy and therefore the risk of harm to an unborn child is unknown. For this reason patients will be excluded from the trial if they are pregnant, breastfeeding or if the patient or patient's partner may become pregnant during the trial period.

Where is the study run from?
University Hospitals Birmingham NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
November 2017 to September 2020

Who is funding the study?
GlaxoSmithKline (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2018-002001-65

Integrated Research Application System (IRAS)
251945

ClinicalTrials.gov (NCT)
NCT03681067

Protocol serial number
CPMS 40162

Study information

Scientific Title
A Phase Ib/IIb, randomised, double-blind, placebo-controlled trial to investigate the safety, tolerability and clinical activity of humanised antibody GSK1070806 in the treatment of patients with moderate-to-severe Crohn's disease

Acronym
CDAID GSK1070806

Study objectives
The aim of this study is to assess the safety and tolerability of an antibody treatment GSK1070806 in patients with moderate to severe Crohn’s disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/12/2018, East Midlands – Derby REC (Riverside Centre (Derwent Room) Pride Park, Derby Riverside Court, Pride Park, Derby, DE24 8HY, UK; Tel: +44 (0)207 104 8109, +44 (0)207 104 8036; Email: NRESCommittee.eastmidlands-derby@nhs.net), REC ref: 18/EM/0320

Study design
Randomized; Interventional; Design type: Treatment, Drug

Primary study design

Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Crohn's disease

Interventions
The proposed study will be a randomised, double-blind, placebo-controlled trial to investigate the safety, tolerability, clinical activity, pharmacokinetics and pharmacodynamics of single intravenous infusion (one dose on Day 1) of GSK1070806 or placebo, in patients with active, moderate to severe CD. The primary objective of the study is to assess the safety and tolerability of a single-dose IV administration of GSK1070806.

A placebo-controlled design is chosen as the most sensitive for determining effect size and benefit: risk profile of GSK1070806. Since subjects are allowed to continue with certain protocol-defined CD maintenance medications in stable doses, many will, in fact, be receiving some treatment over and above placebo making this more acceptable to both physicians and patients.

30 patients will be recruited with randomisation of 2:1 active drug to placebo. Recruitment will be in three stages with interim analysis taking place after the initial 6 patients have been treated, then a further 12 have been treated. A further 12 patients will be treated to reach the target of 30. After 30 patients have been recruited into the study the sample size will be reassessed and up to an additional 6 patients could be recruited (i.e. up to 36 patients). These additional patients will also be recruited with randomisation of 2:1 active drug to placebo. The sample size has been chosen based on feasibility and practical constraints. The maximum potential sample size, 36, has been calculated to cover patient withdrawals.

The first five patients randomised into the trial will be dosed at least 3 days apart. At the interim analysis time points, the Data Monitoring Committee (DMC) will convene and a safety decision will be taken on the subsequent recruitment and patient spacing out strategy.

Each patient will be on trial for 24 weeks (excluding 4 week screening period). Patients with CD suitable for the trial will receive details of what to expect during the trial in the form of the Patient Information Sheet (PIS). This will include a Schedule of Events.

An initial screening shall take place to identify patients diagnosed with CD for at least 3 months prior to screening, active disease based on CDAI score of 220-450 points and colonoscopic confirmation of inflammation.

The screening period will take place over two visits. Eligibility for the trial will be assessed over Screening Visits 1 & 2. Patients will be asked to sign a consent form to say they agree to take part. Checks will then be made to see if they are eligible to take part. These include laboratory assessments of disease activity, as well as careful review of the inclusion and exclusion criteria. Eligible patients will be randomised onto the trial if they consent to do so. Treatment will take place at Visit 3 with an optional visit, Visit 3a, the day after. Patients will be given an infusion of either active GSK1070806 or the placebo. Patients can arrange to have Visit 3a as a telephone appointment if they wish to do so.

Follow Up visits will take place at Weeks 1, 2, 4, 8, 12, 16 and 24. These visits will be to check for safety and general health. It is possible that patients would need to attend unscheduled visits between the visits detailed above, and these would be arranged as needed on safety grounds.

The trial lasts approximately 24 weeks from the first day of treatment through to the last follow up visit.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
GSK1070806

Primary outcome(s)
Safety and tolerability parameters including:
1. Adverse events and serious adverse events assessed using NCI-CTCAE criterion Version 4 at screening, week 1, 2, 4, 8, 12, 16, 24
2. Clinical laboratory tests (haematology panel: haemoglobin (g/L), Platelets (10*9/L), White Blood Cells (10*9/L), International normalized ratio, Neutrophils (10*9/L) at screening, week 1, 2, 4, 8, 12, 16, 24
3. Clinical laboratory tests (biochemistry panel: Creatinine (umol/L), Sodium (mmol/L), Potassium (mmol/l), Bilirubin (umol/L), Alanine Transferase (u/L) Aspartate Transaminase (U/L), Albumin (g /L), eGFR ml/min/1.7, C-Reactive Protein (CRP)) at screening, week 1, 2, 4, 8, 12, 16, 24
4. Electrocardiogram review for any abnormalities i.e. QT interval etc at screening, week 1, 2, 24
5. Frequency, type and severity of infections assessed using NCI-CTCAE criterion Version 4 - grading system at screening, week 1, 2, 4, 8, 12, 16, 24
6. Heart rate (vital signs) at screening, week 1, 2, 4, 8, 12, 16, 24
7. Blood pressure (vital signs) at screening, week 1, 2, 4, 8, 12, 16, 24
8. Oral body temperature (vital signs) at screening, week 1, 2, 4, 8, 12, 16, 24
9. Respiratory rate (vital signs) at screening, week 1, 2, 4, 8, 12, 16, 24

Key secondary outcome(s))
Symptoms of Crohn’s disease measured using Crohn’s disease activity index (CDAI) score (pre-treatment, post treatment) at screening, week 1, 2, 4, 8, 12, 16, 24

Completion date
01/06/2020

Eligibility

Key inclusion criteria
A patient will be eligible for inclusion in this study only if all of the following criteria apply:
1. Written informed consent prior to any of the screening procedures including discontinuation of prohibited medications. (see Section 7.11 for additional information)
2. Patients that have been diagnosed with moderate to severe Crohn’s disease for at least 3 months prior to Screening Visit 1 defined by CDAI score between 220-450
3. Patients are required to have endoscopic evidence of active Crohn’s disease at Baseline (screening visit 1) defined by endoscopic appearance: SES-CD excluding the narrowed

component of > = 6 (or > = 4 for patients with isolated ileal disease).
4. AST and ALT < = 2xULN; alkaline phosphatase and bilirubin < = 1.5xULN (isolated bilirubin > 1.5 xULN is acceptable if bilirubin is fractionated and direct bilirubin < 35%)
5. Male or female participants aged > = 16 years (up to 80 years)

Male participants:
6. A male participant must agree to use contraception as detailed in Appendix 5 of this protocol for at least 180 days post-dose of study medication and refrain from donating sperm during this period.

Female participants:
7. A female participant is eligible to participate if she is not pregnant or breastfeeding and not a woman of childbearing potential (WOCBP) defined as at least one of the following conditions:
7.1. Premenopausal female with documented hysterectomy
7.2. Premenopausal female with documented bilateral salpingectomy or oophorectomy
7.3. Postmenopausal female defined as no menses for 12 months without an alternative medical cause. A high follicle stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT). However, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient.
7.4. Females on HRT and whose menopausal status is in doubt will be required to use one of the non-hormonal highly effective contraception methods if they wish to continue their HRT during the trial. Otherwise, they must discontinue HRT to allow confirmation of postmenopausal status before trial enrolment.
7.5. A WOCBP who agrees to follow the contraceptive guidance in Appendix 5 for at least 180 days post-dose of trial medication. If a hormonal method of birth control is selected from the list in Appendix 1 then participants must have been using these methods at least 28 days prior to GSK1070806 administration, or be abstinent, or utilise a condom as a method of contraception until the selected hormonal method has been in place for the 28 day period.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
5

Key exclusion criteria
A participant will not be eligible for inclusion in this trial if any of the following criteria apply:
1. Diagnosis of ulcerative or indeterminate colitis

Crohn's Disease complications:
2. Evidence of an infected abscess by MRI or other examinations
3. Bowel surgery other than appendectomy within 12 weeks prior to screen and/or has planned surgery or deemed likely to need surgery for CD during the trial period
4. Participants with ileostomies, colostomies or rectal pouches
5. Participants with a bowel stricture that is fixed
6. Participants with evidence of short bowel syndrome
7. Participants requiring enteral or parenteral feeding
8. Deep penetrating ulcers at endoscopy thought to be at risk for perforation

Viral and bacterial infections:
9. Presence of Hepatitis B surface antigen (HBsAg), (confirmed by Hepatitis B surface antigen test – within 12 months of randomisation) core antigen (HBcAg) or surface antibody (HBsAb), positive Hepatitis C (qualitative enzyme immunoassay) test result
10. Known varicella, herpes zoster, or other severe viral infection within 6 weeks of randomisation
11. The participant has a history of tuberculosis (TB) disease or latent TB infection, in the absence of documented adequate therapy for same.
12. Positive screening test for TB (including T-SPOT.TB TB test), unless respiratory review confirms false positive test results
13. History of uncontrolled bacterial or fungal infection requiring intravenous antibiotics
14. Positive immunoassay for Clostridium difficile toxin and other enteric pathogens

Other exclusion criteria:
15. Cardiology assessment/co-morbidity defined as:
15.1. QTc > 450 msec (480msec for those with Bundle Branch Block) and/or
15.2. Either QTcb or QTcf, machine or manual overread, males or females. The QT correction formula used to determine exclusion and discontinuation should be the same throughout the trial and/or
15.3. Based on single QTc value (average of triplicate readings) of ECG obtained over a brief recording period

16. The participant has congenital or acquired immunodeficiency, or a history of chronic or recurrent opportunistic infections
17. The participant has 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 cancer in situ that has been resected)
18. Use of any investigational drug within 30 days prior to screening, 5 half-lives or twice the duration of the biological effect of the investigational product (whichever is longer)
19. Participant has received live, attenuated or recombinant vaccine(s) within 2 months of randomisation or will require vaccination within 3 months of trial drug infusion
20. Any patients that are receiving medication(s) detailed in Section 7.11.2 of the trial protocol, will not be eligible for randomisation into the trial

Date of first enrolment
20/02/2019

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Trust HQ, PO Box 9551
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B15 2TH

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 1.0	10/10/2024	10/10/2024	No	No
HRA research summary			28/06/2023	No	No
Protocol file	version 6.0	07/08/2019	15/01/2025	No	No