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Patient experience of transitioning between two brands of adalimumab (Humira and a biosimilar – Imraldi) in the treatment of adults with Crohn's disease

Submission date
08/07/2019

Recruitment status
No longer recruiting

Registration date
24/07/2019

Overall study status
Completed

Last Edited
10/01/2020

Condition category
Digestive System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
This study is using both a reference product (Humira-adalimumab) and a biosimilar product (Imraldi-adalimumab). Biosimilars are biological medicines that were developed to be highly similar to the originator or reference medicines (in this case Humira) in terms of both efficacy (how well it works) and side effects, but offer the potential of lower treatment cost as compared to the originator medicine. As far as possible the study will mimic what would happen during a real-world cross over between reference product Humira and biosimilar Imraldi, and vice versa. A study of this nature is required because physicians and health authorities are interested in real-world data on effectiveness, safety and other outcomes, based on subject experience in the routine clinical setting. In particular, in a cost-constrained environment where non-medical transition between biosimilars and originators becomes an increasingly likely scenario, it is important to evaluate the transition process for outcome and safety measures. The aim of this study is to compare biosimilar Imraldi with Humira as assessed by the maintenance of baseline clinical status at both 24 and 48 weeks after initiation of study treatment.

Who can participate?
Patients aged 18 and over with Crohn's disease who are currently being treated with Humira

What does the study involve?
Participants attend five hospital visits at University Hospital Southampton NHS Trust (UHS) for assessments which as far as possible mirror exactly normal clinical care. At the first visit participants are randomly allocated to either continue on Humira for 24 weeks and then transition to receive Imraldi for a further 24 weeks, or transition to Imraldi for 24 weeks and transition back to Humira for a further 24 weeks. Participants are re-trained on how to self-inject the study drug and administer this themselves at home, as they have been doing with Humira.

What are the possible benefits and risks of participating?
There is no added benefit from taking part in the study. Most of the treatments and

assessments will be standard of care (i.e. participants will have received this anyway even if they weren't in the study). Both Humira and Imraldi are being currently prescribed in the NHS as treatments for CD. The risks associated with Humira are identical to those associated with Imraldi – as the active ingredient is the same - and are described in detail in the patient information leaflet provided with the current prescription. The most common risks include viral infections (such as flu or cold sores), headache, upper-respiratory-tract infection (colds), sinusitis (inflammation of the sinuses), nausea (feeling sick), abdominal pain (stomach ache), injection site-related reactions and pain. With any biologic medication, there is a risk of developing an allergic reaction. If a serious allergic reaction occurs, treatment will be given to alleviate the symptoms and further treatments with either Humira or Imraldi will be reviewed. In previous clinical trials, delayed hypersensitivity reactions (unwanted reactions produced by the normal immune system) have been reported so participants will be advised to seek immediate medical advice if they experience any delayed unwanted reactions noted above. If participants become pregnant whilst on the trial, then their baby should not have any 'live' vaccinations until they are at least six months old. This is because some of the adalimumab may pass across the placenta into the baby that could cause an abnormal response to a live vaccine, leading to an active infection rather than vaccination.

Where is the study run from?
University Hospital Southampton NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2019 to March 2021

Who is funding the study?
Biogen Idec

Who is the main contact?
Mr David Young
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2018-004967-30

Protocol serial number
CPMS: 40987

Study information

Scientific Title
IBD Reference and Biosimilar adalimumab CroSS over Study

Acronym
iBaSS

Study objectives
The primary objective is:
To compare biosimilar Imraldi with Humira as assessed by maintenance of baseline clinical status at both 24 and 48 weeks after initiation of study therapy.

The study will also explore:
1. Subject clinical characteristics and disease status over time
2. Adalimumab and relevant concomitant medication use over time
3. Immunogenicity to adalimumab
4. The presence of inflammatory markers over time
5. Subject experience and treatment satisfaction over time

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/04/2019, London – Chelsea Research Ethics Committee (Skipton House, 80 London Road, London, SE1 6LH; Tel: +44 (0)207 104 8241; Email: nrescommittee.london-chelsea@nhs.net), ref: 19/LO/0167

Primary study design
Interventional

Study design
Phase IV single-centre prospective randomised single-blind cross-over study

Study type(s)
Treatment

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

Interventions

This is a single-centre, prospective, randomised, single-blind, cross-over study in subjects with Crohn's Disease (CD). As far as possible the study will mimic what would happen during a real-world cross over between reference product Humira and biosimilar Imraldi, and vice versa.

Potential participants will be sent the patient information sheet by post, email or at other contacts with the clinical or research team up to 24 hours prior to enrolment. The patients will be given adequate time to consider the trial information before being asked to sign the informed consent form. This study will enrol subjects with Crohn's Disease
who are currently being treated with Humira. At the baseline visit subjects will be randomized to either continue on Humira for 24 weeks (treatment period 1) and then transition to receive Imraldi for a further 24 weeks (treatment period 2) i.e. Treatment sequence 1 below or transition to Imraldi for 24 weeks (treatment period 1) and transition back to
Humira for a further 24 weeks (treatment period 2) i.e. Treatment sequence 2 below.

Treatment sequence 1 -Humira-Imraldi
Treatment sequence 2 -Imraldi-Humira

After the Week 48 visit, or prior to this if a subject discontinues study treatment prematurely, subjects will receive standard therapy, according to physician decision. An End of Study (EoS) visit will be conducted for subjects discontinuing the study prior to Week 48. There will be no washout period.

Study Assessments:
Baseline visit 0
Baseline assessments will be performed:
- Provide Informed Consent
- Medical history, including concomitant medication
- SOC clinical review, including Tuberculosis and Hepatitis B, C virus and Varicella tests (if previous test results not available) using locally defined procedures; These will be carried out as part of routine clinical care and do not form part of study-specific assessments
- A pregnancy test for women of childbearing potential
- Laboratory tests including haemoglobin, platelets, albumin and CRP (as per SOC)
- Anti-drug antibody and drug trough level measurements
- A stool sample will also be collected at this visit for a faecal calprotectin.
- Collecting modified Harvey Bradshaw Index (for CD)
- Health Related Quality of Life measures (IBD CTRL, PRO-2)
- Train subject on injection administration and the subject feedback app
- Confirm Inclusion/Exclusion Criteria
- Allocation of subject study ID number
randomized to either of the following arms;
Treatment sequence 1- Humira-Imraldi
Treatment sequence 2- Imraldi-Humira
Subjects will collect their study medication from pharmacy (to maintain the single blind) to self-administer every 2 weeks, or at a frequency determined by their treating physician (treatment period 1). The first administration of study medication for treatment period 1 must commence within 7 days following the baseline visit. Patient will be given a paper diary to record a visual analogue score to record their experience of the injection.

Week 12
At this visit subjects will have;
- SOC clinical review and documentation of concomitant medication
- SOC laboratory tests

- SOC Anti-drug antibody and drug trough level measurements
- SOC stool sample will also be collected at this visit for faecal calprotectin measurement
- Completion of modified Harvey Bradshaw Index
- Completion of IBD-Ctrl and PRO-2
- Completion of TSQM
- Adverse event recording

Week 24- Cross-over Visit
At this visit subjects will have;
- SOC clinical review and documentation of concomitant medication
- Protocol-specified laboratory tests
- Anti-drug antibody and drug trough level measurements
- A stool sample will also be collected at this visit for faecal calprotectin measurement
- Completion of modified Harvey Bradshaw Index
- Completion of IBD-Ctrl and PRO-2
- Completion of TSQM
- Adverse event recording
- Re-train subjects on medication administration
- Cross over to medication as per treatment sequence assigned by randomisation

Week 36
At this visit subjects will have;
- SOC clinical review and documentation of concomitant medication
- Routine laboratory tests
- Anti-drug antibody and drug trough level measurements
- A stool sample will also be collected at this visit for a faecal calprotectin
- Completion of modified Harvey Bradshaw Index
- Completion of IBD-Ctrl and PRO-2
- Completion of TSQM
- Adverse event recording

Week 48 - End of Study
At this visit subjects will have;
- SOC clinical review and documentation of concomitant medication
- Study-specific laboratory tests
- Anti-drug antibody and drug trough level measurements
- A stool sample will also be collected at this visit fora faecal calprotectin
- Completion of modified Harvey Bradshaw Index
- Completion of IBD-Ctrl and PRO-2
- Completion of TSQM
- Adverse event recording

The researchers will conduct semi-structured interviews on a purposive sample of subjects in a setting of their choice, either at home or on the hospital site. Interviews will take place at times convenient to the interviewees (likely to be at a study visit) and will last no longer than one hour. An interview guide will be constructed based on key issues identified from the literature and drawing on our combined clinical experience. This guide will be piloted with a small sample of subjects and revised if necessary. Subject interviews will also draw on individual subject responses in the outcome measures completed at regular time points throughout the period of the study. Interviews will be audio-recorded using a digital recorder and fully transcribed. Interview data will be analysed using thematic analysis to identify key themes and issues which characterise the subject and clinical staff experience. The researchers will use Braun and Clarke’s

(2006) six steps of data familiarisation, generating initial codes, themes searching, reviewing themes, defining and naming the themes and producing the report. The end of trial will be defined as the last subject's last visit at week 48.

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome(s)
The proportion of subjects maintaining baseline clinical status at week 24 and week 48. Modified Harvey-Bradshaw Index (mHBI) for Crohn's Disease and IBD Control (IBD-CTRL) Patient Reported Outcome Measure (PROM). increase in mHBI score of ≥3 and/or a decline in IBD-CTRL score of ≥4 points at any time during the respective study period will be classified as failure to maintain baseline clinical status.

Key secondary outcome(s)
1. Safety blood monitoring at baseline, weeks 12, 24, 36, and 48
2. Therapeutic drug monitoring (trough level and immunogenicity) at baseline, weeks 12, 24, 36, and 48
3. Disease activity measured using modified Harvey Bradshaw Index, PRO-2, CRP, faecal calprotectin, at baseline, weeks 12, 24, 36, and 48
4. Health-related quality of life measured using IBD-Control score roughly every 2 weeks
5. Treatment satisfaction measured using Treatment Satisfaction Questionnaire for Medication roughly every 4 weeks
6. Adverse effects measured throughout the study
7. Injection site pain measured using a VAS at each administration

Completion date
04/03/2021

Eligibility

Key inclusion criteria
1. 18 years and over with a confirmed diagnosis of Crohn's Disease
2. Stable dose of Humira over the 12 weeks prior to enrolment
3. mHBI < 8 at baseline
4. Anticipated to remain on the same adalimumab administration frequency for the duration of the study
5. Able to comply with study requirements
6. Able to provide informed consent

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Less than 18 years of age at enrolment
2. Not anticipated to remain on adalimumab therapy for more than 3 months after randomisation
3. Allergic to any of the known excipients of Humira or Imraldi
4. Scheduled for a surgical procedure or planned hospitalisation within 12 months of randomisation
5. Unable to comply with study requirements
6. Inability to provide consent
7. Pregnant or lactating women

Date of first enrolment
12/07/2019

Date of final enrolment
28/02/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospital Southampton NHS Foundation Trust
Mailpoint 18
Southampton General Hospital
Tremona Road
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SO16 6YD

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Industry

Funder Name
Biogen Idec

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Mr David Young (david.young@uhs.nhs.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No