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Impact of biologic therapy on SARS-CoV-2 infection and immunity in patients with inflammatory bowel disease

Submission date
14/09/2020

Recruitment status
No longer recruiting

Registration date
21/09/2020

Overall study status
Completed

Last Edited
03/12/2024

Condition category
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe.
In 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of April 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.
Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.
Inflammatory bowel disease (IBD) affects about 1% of the UK population and is usually treated with immunosuppressive and/or biologic drugs (e.g. inflixamab or vedolimumab). By inhibiting the immune system, these drugs increase the risk of serious infections and may prevent vaccines from working fully. Because COVID-19 is caused by a new virus, it is not yet known whether these drugs increase the risk of infection or life-threatening illness or reduce the immunity that usually follows infection or vaccination. As a precaution, the UK Government advised patients treated with these medicines to follow strict social distancing measures, known as shielding, during the 12-week lockdown. The aim of this study is to measure the impact of biologic therapy on COVID-19 and immunity in patients with IBD.

Who can participate?
IBD patients who are receiving inflixamab or vedolimumab infusions

What does the study involve?
This study will use a COVID-19 antibody test to look for past infection in blood samples from patients with IBD stored since the start of the pandemic. At the same time, the researchers will follow for 40 weeks a further 6970 UK patients treated with one of two biologic drugs, infliximab and vedolizumab. Patients will be asked to complete a questionnaire every 8 weeks and donate a blood sample at infusion visits.

What are the possible benefits and risks of participating?
There are no benefits of participating, although antibody test results will be returned to participants. The only risks are bruising at the blood test site. The results from both parts of the study will allow the researchers to determine the impact of specific drugs and shielding on COVID-19 infection and subsequent immunity.

Where is the study run from?
Exeter IBD Research (UK)

When is the study starting and how long is it expected to run for?
May 2020 to October 2021

Who is funding the study?
Roche (Switzerland)

Who is the main contact?
Unfortunately, this study is not recruiting public volunteers at this time. This is because the researchers are directly identifying volunteers in certain areas or hospitals. Please do not contact the research team as they will not be able to respond. For more information about COVID-19 research, visit the Be Part of Research homepage.

Study website
https://www.clarityibd.org/

Contact information

Type(s)
Public

Contact name
Ms Claire Bewshea

ORCID ID
http://orcid.org/0000-0002-0965-9587

Contact details
Exeter IBD Research Group
RILD
Royal Devon and Exeter NHS Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Type(s)
Scientific

Contact name
Prof Tariq Ahmad

ORCID ID
http://orcid.org/0000-0002-6058-5528

Contact details
Exeter IBD Research Group
RILD
Royal Devon and Exeter NHS Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
283251

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
RDE CLARITY 2102102, IRAS 283251, CPMS 46188

Study information

Scientific Title
Impact of biologic and immunomodulatory therapy on SARS-CoV-2 infection and immunity in patients with inflammatory bowel disease

Acronym
CLARITY IBD

Study objectives
Inflammatory bowel disease (IBD) affects about 1% of the UK population and is usually treated with immunosuppressive drugs. Side effects include an increased risk of serious infection, most notably pneumonia. Vaccination studies also show these drugs impair protective antibody responses. The impact of immunosuppressive treatment on SARS-CoV-2 infection and disease severity is unknown but is a major concern for patients and clinicians. As a precaution, the UK Government advised prolonged shielding for many patients treated with these drugs.

Using the Roche Elecsys immunoassay to test serum samples from >7500 IBD patients stored since the start of the pandemic, the researchers will report the SARS-CoV-2 emerging seroprevalence. They will simultaneously conduct a 40-week prospective study of an additional 6970 patients treated with infliximab (anti-TNF) versus vedolizumab (anti-integrin) using our established clinical network of UK IBD centres. Data from both cohorts will be used to define the impact of immunosuppressive drug therapy and physical distancing strategies on SARS-CoV-2 seroprevalence. Serial testing in the prospective cohort will define the durability and magnitude of protective immune responses.

This study will provide an evidence base for safer prescribing of immunomodulator and biologic drugs in the COVID-19 era and inform public health policy regarding physical distancing measures, and future vaccination strategies. Although this study will define risk in IBD patients, there are potentially important lessons to be learned for millions of patients across the UK with other immune-mediated diseases treated with similar therapies.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 01/07/2020, London -Surrey Borders Research Ethics Committee (REC) (London Centre, Ground Floor, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0)207 972 2568; surreyborders.rec@hra.nhs.uk), REC ref: 20/HRA/3114

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Available at https://www.clarityibd.org/

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection), inflammatory bowel disease

Interventions
Workflow 1: Retrospective study of SARS-CoV-2 seroprevalence across the UK using surplus serum samples.

Using the Roche Elecsys assay the researchers will test >7500 serum samples from IBD patients for SARS-CoV-2 antibodies. These include: i) surplus serum samples from UK therapeutic drug monitoring laboratories retained since 09/02/2020 and ii) serum samples from patients recruited

to the UK NIHR IBD Bioresource project from 01/12/2019 to 30/03/2020. For each sample the supplier of the sample (the therapeutic drug monitoring laboratory or the UK NIHR IBD Bioresource) will provide the age and sex of the patient, the date of the serum sample, the drug tested and the name of the referring hospital. No other patient identifiers will be provided to ensure these samples will be anonymous to the research team. Patient consent for SARS-CoV-2 antibody testing will not be sought and no study visits are required.

Workflow 2: 40-week prospective observational UK-wide study of SARS-CoV-2 seroprevalence in IBD patients receiving infliximab or vedolizumab.

In parallel the researchers will conduct a prospective observational study of 6970 patients receiving infliximab or vedolizumab in UK infusion units. This study is specifically designed to determine whether anti-TNF therapy (with or without an immunomodulator) impacts SARS-CoV-2 seroprevalence, the magnitude/durability of serological responses and the proportion of patients who acquire PCR positive COVID-19 after seroconversion. A comparator group will comprise patients receiving vedolizumab. Current data suggests that vedolizumab, a gut selective anti-integrin α4β7 monoclonal antibody, is not associated with an increased risk of systemic infection or pneumonia. Furthermore, it is administered in hospital at the same 8 weekly intervals as infliximab.

Study visits will occur at the same time as scheduled infusions/injections of infliximab or vedolizumab.

At visit 1 the study will be discussed and electronic informed consent obtained. Patients will complete an electronic questionnaire which will capture symptoms (aligned to the COVID symptoms study, Menni Nature Medicine 2020) tests and hospitalisations related to suspected, or confirmed, COVID-19 illness and details of isolating strategies adopted (see patient questionnaire). The research teams will complete an electronic case report form detailing IBD treatment at the time of the visit and confirm details of prior SARS-CoV-2 testing and/or hospitalisations. A blood sample will be collected immediately prior to biologic infusion or injection and sent to the central laboratory in Exeter for SARS-Cov-2 antibody testing. This result will be returned to the local research team.

Subsequent visits will depend on the SARS-CoV-2 antibody test result from study visit 1.

Patients with positive SARS-CoV-2 antibody test at visit 1:
Visits will occur at weeks 8, 16, 24, 32 and 40 and timed to coincide with biologic infusions or injections. At each visit patients will complete an electronic questionnaire and study teams will complete a CRF. A blood sample will be collected immediately prior to biologic infusion or injection and sent to the central laboratory in Exeter for SARS-Cov-2 antibody testing.

Patients with negative SARS-CoV-2 antibody test at visit 1:
Patients will be asked to complete the on-line questionnaire every 8 weeks (detailed above) and attend 1 further study visit at week 40 (as above).

Remote visits:
If a patient is receiving subcutaneous infliximab or vedolizumab and it is not feasible, or appropriate for them to attend hospital then the visit may occur by telephone or video call. Blood samples may be obtained using conventional venepuncture or using the Exeter home finger prick test kit.

Intervention Type

Other

Primary outcome measure
Workflow 1– retrospective study:
Cumulative seropositivity of anti-SARS-CoV-2 antibodies, measured using the Roche Elecsys assay between 01/01/2020 and 30/09/2020

Workflow 2:
Positive anti-SARS-CoV-2 antibody test, using the Roche Elecsys assay, at week 0 or week 40

Secondary outcome measures
Workflow 1:
In patients with more than one test, change in anti-SARS-CoV-2 antibody positivity and cut-off index (COI) measured using the Roche Elecsys assay between 01/01/2020 and 30/09/2020

Workflow 2:
1. Proportion of patients with symptomatic COVID-19 disease and a positive PCR test prior to week 0 and prior to week 40
2. Proportion of patients with symptomatic COVID-19 disease and a positive anti-SARS-CoV-2 antibody test measured using the Roche Elecsys assay prior to week 0 and prior to week 40
3. Anti-SARS-CoV-2 antibody COI measured using the Roche Elecsys assay at week 0 and 40
4. Proportion of patients with symptomatic COVID-19 disease, a positive PCR test, and hospitalisation or death, prior to week 0 and prior to week 40
5. In patients with detectable anti-SARS-CoV-2 antibodies at week 0, time in days to a reduction in antibody COI by at least 50% or undetectable anti-SARS-CoV-2 antibodies measured using the Roche Elecsys assay between week 0 and week 40
6. In patients with detectable anti-SARS-CoV-2 antibodies at week 0, time in days to a reduction in antibody COI by at least 75% or undetectable anti-SARS-CoV-2 antibodies measured using the Roche Elecsys assay between week 0 and week 40
7. Proportion of patients with detectable anti-SARS-CoV-2 antibodies measured using the Roche Elecsys assay at week 0 who acquire PCR-positive COVID-19 disease between week 0 and week 40

Overall study start date
30/05/2020

Completion date
08/10/2021

Eligibility

Key inclusion criteria
1. Age 5 years and over
2. Diagnosis of inflammatory bowel disease
3. Current treatment with infliximab or vedolizumab for 6 weeks or more
4. Written informed consent obtained from patient or parent/guardian

Participant type(s)
Patient

Age group

Mixed

Sex
Both

Target number of participants
6970

Total final enrolment
6935

Key exclusion criteria
Patients participating in a vaccine trial

Date of first enrolment
23/09/2020

Date of final enrolment
21/12/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Exeter IBD Research
RILD
Royal Devon and Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 9RY

Sponsor information

Organisation
Royal Devon & Exeter NHS Foundation Trust

Sponsor details
Barrack Road
Exeter
England

United Kingdom
EX2 5DW
+44 (0)1392 411611
alison.kerridge@nhs.net

Sponsor type
Hospital/treatment centre

Website
http://www.rdehospital.nhs.uk/

ROR
https://ror.org/03085z545

Funder(s)

Funder type
Industry

Funder Name
Roche

Alternative Name(s)
F. Hoffmann-La Roche Ltd, F. Hoffmann-La Roche & Co, F. Hoffmann-La Roche AG, Roche Holding AG, Roche Holding Ltd, Roche Holding, Roche Holding A.G., Roche Holding, Limited, F. Hoffmann-La Roche & Co.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Publication and dissemination plan
The patient information sheets and study protocol are available at https://www.clarityibd.org/

Findings will be written up and submitted to a peer-reviewed scientific journal. Findings will be presented by the study team at national and international conferences including the British

Society of Gastroenterology annual meeting and the European Crohn's and Colitis meeting. The study team will prepare a lay summary of the study findings for dissemination to the members of the national patient group, Crohn's and Colitis UK.

Intention to publish date
31/10/2021

Individual participant data (IPD) sharing plan
The CIs, SMC, sponsor, funders and research team members are committed to ensuring that the research findings and data relevant to the coronavirus pandemic are shared rapidly and openly to inform the public health response and help save lives. The data will be shared in line with the principles set out in the 2016 statements of data sharing in public health emergencies (https://wellcome.ac.uk/press-release/statement-data-sharing-public-health-emergencies). Please contact Professor Tariq Ahmad (tariq.ahmad1@nhs.net) for further information regarding data access.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version V3	16/09/2020	21/09/2020	No	No
Results article	SARS-CoV-2 vaccine immunogenicity results	26/04/2021	13/08/2021	Yes	No
Results article	anti-SARS-CoV-2 antibody response result	01/05/2021	13/08/2021	Yes	No
Results article	Vaccine escape, increased breakthrough and reinfection in infliximab-treated patients with IBD during the Omicron wave of the SARS-CoV-2 pandemic	28/07/2022	29/07/2022	Yes	No
Results article	Neutralising antibody potency against SARS-CoV-2 wt and omicron BA.1 and BA.4/5 variants in patients with IBD treated with infliximab and vedolizumab	05/12/2022	12/12/2022	Yes	No
Results article	Antibody decay, T cell immunity and breakthrough infections	16/03/2022	23/01/2023	Yes	No
HRA research summary			28/06/2023	No	No
Results article	Adalimumab and infliximab impair SARS-CoV-2 antibody responses	14/03/2022	03/12/2024	Yes	No