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Best available treatment study for inflammatory conditions associated with COVID-19

Submission date
31/05/2020

Recruitment status
No longer recruiting

Registration date
02/06/2020

Overall study status
Completed

Last Edited
01/11/2023

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Paediatricians worldwide are seeing rapidly increasing numbers of children with a wide spectrum of inflammatory syndromes temporally associated with the SARS-CoV-2 (COVID-19) pandemic. These emerging disorders appear to represent unusual responses to COVID-19 driven by children's immune systems, with overlapping features with Kawasaki Disease (KD), a rare paediatric inflammatory disorder.
Currently, paediatricians around the world are managing these patients with treatments that they judge to be best for their patients with the resources they have available; these include a range of anti-inflammatory and immunomodulatory treatments. Furthermore, many centres will not have certain treatments available due to a worldwide shortage of many agents as a result of their use in COVID-19 patients. This has raised urgent questions for children, families and their clinicians, including: are there clinical or blood markers which predict disease severity? Do the available anti-inflammatory and immunomodulatory treatments improve the outcomes including reducing the risk of coronary artery aneurysms? What are the risks and benefits of these treatments? What is the risk of long-term complications, e.g. coronary artery aneurysm, and how does this relate to syndrome and severity?
The aim of this study is to collect anonymised data on all patients with this emerging condition using an online case report form. Capturing the patient's clinical findings, inflammatory markers, treatments and outcomes will allow a careful analysis of these data to advance the understanding of these disorders and their complications and rapidly provide answers on the questions as to which patients to treat, which treatments work and which may be harmful.

Who can participate?
Clinicians from across the world are welcome to join the study and enrol any patient with a suspected inflammatory condition associated with SARS-CoV-2 onto the online database. Detailed inclusion criteria will be sent to prospective project partners.

What does the study involve?
The study involves the collection of non-identifiable routinely collected clinical data on confirmed or suspected cases of a new inflammatory syndrome associated with COVID-19 from

across the UK and globally. A secure online database system (REDCap) will be used for data collection. If a centre wants to take part in the study, they will nominate a lead for their institution, who will be provided with an individual REDCap account and a user guide for entering data onto the REDCap database. Doctors caring for patients in emergency departments, wards or intensive care units will identify patients meeting the study criteria. The relevant patients can then be enrolled onto the REDCap database and data entered retrospectively. Data will then be analysed by the study management team to address the primary and secondary objectives.

What are the possible benefits and risks of participating?
Each clinical site that joins the study will become part of an international “BATS consortium” and the data submitted to the online database will be used to address essential questions regarding a new inflammatory syndrome associated with COVID-19. Project partners will have access to records entered from their site only. There are no risks involved with participating.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
May 2020 to November 2024

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Prof. Michael Levin
Unfortunately, this study is not recruiting public volunteers at this time. This is because the research isn’t ready for volunteers yet or 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.

Contact information

Type(s)
Scientific

Contact name
Prof Michael Levin

Contact details
Imperial College London
London
United Kingdom
W2 1PG
+44 (0)20 7594 3760
m.levin@imperial.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)
284825

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 284825

Study information

Scientific Title
Best available treatment study for inflammatory syndromes associated with SARS-CoV-2

Acronym
BATS

Study objectives
Administration of drugs to regulate or suppress the immune system (immunomodulators, e.g. immunoglobulin, steroids, anti-TNF, IL1-inhibitors, IL6- inhibitors, ciclosporin) will result in more rapid resolution of fever and inflammation, prevent disease progression, reduce the need for intensive care or organ support and reduce the risk of children developing coronary artery aneurysms and other long-term complications.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/06/2020, London - Camden & Kings Cross Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 104 8068, +44 (0)207 104 8222; camdenandkingscross.rec@hra.nhs.uk), REC ref: 20/HRA/2957

Study design
Observational cohort study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
A spectrum of new inflammatory syndromes associated with COVID-19 (SARS-CoV-2 infection)

Interventions
The researchers will study routinely collected non-identifiable data from patients presenting to hospitals worldwide with clearly defined clinical phenotypes.

Study size:
The researchers anticipate recruitment of at least 1800 in total (150 cases from the UK, 50 from the host site). In the last month, since the establishment of a case definition in the UK (RCPCH 1 May 2020), over 100 cases have been reported across the UK and numbers are continuing to rise.

Recruitment process:
Study information including clear guidance on which patients to enrol on the database and how to use the database will be disseminated across UK NHS hospital and internationally, through existing consortia and collaborations as well as international societies. If a centre wants to take part in the study, they will nominate a lead for their institution, who will be provided with user log-in details and a user guide for entering data onto the REDCap database. Paediatric doctors caring for children in emergency departments, wards or intensive care units will identify patients meeting the study criteria. The relevant patients can then be enrolled onto the REDCap database and data entered retrospectively.

Collection of clinical data:
Data will be collected systematically on any patients meeting the study criteria using an online case report form. Patients will be anonymised and identified only by the clinician reporting the case. The severity of each patient's clinical findings, inflammatory markers and organ dysfunction will be recorded on a daily basis before and after initiation of immunomodulating agents, or during observation (if no specific treatment given). Outcomes including, time in intensive care units, duration of organ support, or death along with the presence of coronary artery aneurysms and any other long term complications will be recorded.

Clinical data recorded for routine clinical care will be entered retrospectively onto the database. There will be no follow up. The database will be open for 2 years for data entry.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measures as of 08/04/2021:
1. Composite: Inotropic support or ventilation (invasive or non-invasive) at any time from the second day post-treatment or death at any time
2. Improvement on ordinal clinical severity scale at day 2 relative to day 0, comprising
2.1. Discharge on or before day 2 for any patient
2.2. Step down from ventilation/inotropic support/oxygen
2.3. Fall in CRP from >/= 50 to < 50 mg/l

Previous primary outcome measures:
1. Comparative effectiveness of different anti-inflammatory and immunomodulatory drugs in treating the inflammatory syndrome as measured by:
1.1. Fall in blood inflammatory markers (CRP, pro-calcitonin, ferritin)
1.2. Prevention of cardiac dysfunction (left ventricular function on echocardiogram) and coronary artery aneurysms (z-scores of coronary arteries on echocardiogram)
1.3. Other long-term complications (any long-term disability not present on admission)

Data collected using an online case report form. Clinical data entered onto the online database will span the duration of each patient's hospital stay for that episode of illness.

Key secondary outcome(s))

Current secondary outcome measures as of 08/04/2021:
1. Failure/escalation of primary treatment:
1.1. Addition of any immunomodulator from the first day after primary treatment
1.2. For patients receiving corticosteroids within primary treatment, an escalation of more than 5 mg/kg prednisolone equivalent in total daily dose
2. Time to one-level improvement in ordinal severity scale
3. Increase in level of support, based on death, or any commencement of:
3.1. ECMO for patients not on ECMO on day 0
3.2. Ventilation for patients not ventilated on day 0
3.3. Inotropic support for patients not ventilated on day 0
3.4. Oxygen for patients not on oxygen on day 0
4. Fever: presence of fever at any point from day 2
5. Persisting coronary artery dilatation: presence of a coronary artery with Lopez z-score ≥ 2.5 or a report of aneurysm without z-score on the final echocardiogram, undertaken on the second or subsequent days following treatment
6. Left ventricular dysfunction: presence of left ventricular dysfunction on any echocardiogram 24 hours after commencement of primary immunomodulatory treatment.
7. Complications of drug therapy: Complications deemed by the treating clinician to be the result of immunomodulatory treatment, including but not limited to: allergy/anaphylaxis, cataracts, gastric perforation, gastric ulceration, hip necrosis, hyperglycaemia, hyperlactataemia, opportunistic infection, profound bradycardia, psychosis and steroid-induced hypertension

Previous secondary outcome measures:
1. Proportion dying
2. Proportion requiring intensive/high dependency care
3. Total duration of fever
4. Risk of long-term complications (excluding CAA)
5. Proportion receiving any immunomodulator therapy
6. Proportion receiving individual immunomodulator classes
7. Total number of immunomodulators received per patient
8. Proportion with each organ system involved

Data collected using an online case report form. Clinical data entered onto the online database will span the duration of each patient's hospital stay for that episode of illness.

Completion date
30/11/2024

Eligibility

Key inclusion criteria
1. Any suspected case of inflammatory condition associated with SARS-CoV-2 in all ages
2. Data entry can be prospective or retrospective

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

All

Sex
All

Key exclusion criteria
There are no exclusion criteria

Date of first enrolment
08/06/2020

Date of final enrolment
31/05/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Imperial College Healthcare NHS Trust
St Mary's Hospital
Praed Street
London
United Kingdom
W2 1NY

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans and agreements are currently being finalised and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/07/2021	17/06/2021	Yes	No
Results article		14/02/2023	02/03/2023	Yes	No
HRA research summary			28/06/2023	No	No
Protocol file	version 1		08/04/2021	No	No
Statistical Analysis Plan			08/04/2021	No	No
Statistical Analysis Plan	version 2		25/04/2022	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes