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A study to evaluate the safety and efficacy of tocilizumab in patients with severe COVID-19 pneumonia

Submission date
12/11/2020

Recruitment status
No longer recruiting

Registration date
21/01/2021

Overall study status
Completed

Last Edited
17/03/2021

Condition category
Infections and Infestations

[_] Prospectively registered
[_] 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.
The aim of this study is to assess the effectiveness and safety of tocilizumab in combination with standard of care compared with matching placebo (dummy drug) in combination with standard of care in hospitalized adult patients with severe COVID-19 pneumonia.

Who can participate?
Adult patients with severe COVID-19 pneumonia who meet the entry criteria

What does the study involve?
Patients will be randomly allocated to receive treatment with either tocilizumab or a matching placebo. Study treatment must be given in combination with standard of care. For both arms, if the clinical signs or symptoms worsen or do not improve, one additional infusion of blinded treatment of tocilizumab or placebo can be given, 8–24 hours after the initial infusion. The study

assessments to be conducted include the following: physical examination, vital signs, oxygen saturation, assessment of consciousness, presence and absence of breathing support, adverse events, other treatments, clinical laboratory tests, and nasopharyngeal swabs.

What are the possible benefits and risks of participating?
At the time of the study design, there were no drugs licensed for the treatment of patients with COVID-19. Given the results of previous studies, tocilizumab along with standard of care could be effective at treating COVID-19 in hospitalized populations more effectively than the current standard of care alone. Extensive safety data have previously been generated on the use of tocilizumab in other indications. Therefore, a placebo-controlled study in combination with SOC to assess safety and efficacy of TCZ in hospitalized patients with severe COVID-19 pneumonia is justified to address the high unmet need and burden of disease in this severely ill population.

Where is the study run from?
Genentech (USA)

When is the study starting and how long is it expected to run for?
March 2020 to July 2020

Who is funding the study?
1. Genentech (USA)
2. Biomedical Advanced Research and Development Authority (USA)

Who is the main contact?
global-roche-genentech-trials@gene.com, reference study ID WA42380

Contact information

Type(s)
Public

Contact name
Dr Clinical Trials

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Additional identifiers

EudraCT/CTIS number
2020-001154-22

IRAS number
282099

ClinicalTrials.gov number
NCT04320615

Secondary identifying numbers
WA42380, IRAS 282099

Study information

Scientific Title
A randomized, double-blind, placebo-controlled, multicenter study to evaluate the safety and efficacy of tocilizumab in patients with severe COVID-19 pneumonia

Acronym
COVACTA

Study objectives
To evaluate the efficacy, safety, pharmacodynamics, and pharmacokinetics of tocilizumab (TCZ) compared with a matching placebo in combination with standard of care (SOC) in hospitalized patients with severe COVID-19 pneumonia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/03/2020, Advarra (6940 Columbia Gateway Drive, Columbia, MD, 21046, USA; +1 4108842900; no email provided), ref: none provided

Study design
Randomized double-blind placebo-controlled multicenter study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection) pneumonia

Interventions

Patients will be randomized as soon as possible after screening at a 2:1 ratio to receive blinded treatment of either TCZ or a matching placebo, respectively. Study treatment must be given in combination with standard of care (SOC). The randomization will be stratified by geographic region (North America and Europe) and mechanical ventilation (yes, no). The proportion of patients who are on a mechanical ventilator at the time of randomization will be capped at no more than 50% of the overall study population.

Experimental arm:
Participants will receive one intravenous (IV) infusion of tocilizumab (TCZ), dosed at 8 mg/kg, up to a maximum dose of 800 mg. Up to one additional dose may be given if clinical symptoms worsen or show no improvement within 8-24 hours after the initial dose.

Placebo arm:
Participants will receive one IV infusion of placebo matched to TCZ. Up to one additional dose may be given if clinical symptoms worsen or show no improvement within 8-24 hours after the initial dose.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Clinical status assessed using a 7-category ordinal scale on day 28

Secondary outcome measures
Measured using patient records (unless otherwise noted):
1. Time to clinical improvement (TTCI), defined as a National Early Warning Score 2 (NEWS2) of < /= 2 maintained for 24 hours, up to 60 days
2. Time to improvement of at least two categories relative to baseline on a 7-category ordinal scale of clinical status, up to 60 days
3. Incidence of mechanical ventilation, up to 60 days
4. Ventilator-free days up to Day 28
5. Incidence of intensive care unit (ICU) stay up to 60 days
6. Duration of ICU stay up to 60 days
7. Time to clinical failure, from first dose to time of death, mechanical ventilation, ICU admission, or study withdrawal (whichever occurs first, for up to 60 days). If already in ICU on ventilation, failure = a one-category worsening on the ordinal scale, withdrawal, or death
8. Mortality rate on days 7, 14, 21, 28, and 60
9. Time to hospital discharge up to 60 days
10. Time to recovery, defined as discharged or “ready for discharge” (as evidenced by normal body temperature and respiratory rate, and stable oxygen saturation on ambient air or 2L supplemental oxygen); OR, in a non-ICU hospital ward (or “ready for hospital ward”) not requiring supplemental oxygen, up to 60 days
11. Duration of time on supplemental oxygen up to 60 days
12. Percentage of participants with adverse events up to 60 days
13. COVID-19 (SARS-CoV-2) viral load over time, up to 60 days measured using RT-PCR

14. Time to reverse-transcriptase polymerase chain reaction (RT-PCR) virus negativity, up to 60 days measured using RT-PCR
15. Proportion of participants with post-treatment infection, up to 60 days measured using AE summary
16. Serum concentration of IL-6, up to 60 days measured using ELISA
17. Serum concentration of sIL-6R, up to 60 days measured using ELISA
18. Serum concentration of Ferritin, up to 60 days measured using ELISA
19. Serum concentration of C-reactive protein (CRP), up to 60 days measured using ELISA
20. Serum concentration of TCZ, up to 60 days measured using ELISA

Overall study start date
10/03/2020

Completion date
28/07/2020

Eligibility

Key inclusion criteria
1. Hospitalized with COVID-19 pneumonia confirmed per a positive PCR of any specimen (e.g., respiratory, blood, urine, stool, other bodily fluid) and evidenced by chest X-ray or CT scan
2. SPO_2 </=93% or PaO_2/FiO_2 <300 mmHg

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
450

Total final enrolment
452

Key exclusion criteria
1. Known severe allergic reactions to TCZ or other monoclonal antibodies
2. Active tuberculosis (TB) infection
3. Suspected active bacterial, fungal, viral, or other infection (besides COVID-19)
4. In the opinion of the investigator, progression to death is imminent and inevitable within the next 24 hours, irrespective of the provision of treatments
5. Have received oral anti-rejection or immunomodulatory drugs (including TCZ) with the past 3 months
6. Participating in other drug clinical trials (participation in COVID-19 antiviral trials may be permitted if approved by Medical Monitor)
7. Pregnant or breastfeeding, or positive pregnancy test in a pre-dose examination
8. Treatment with an investigational drug within 5 half-lives or 30 days (whichever is longer) of

randomization (investigational COVID-19 antivirals may be permitted if approved by Medial Monitor)
9. Any serious medical condition or abnormality of clinical laboratory tests that, in the investigator's judgment, precludes the patient's safe participation in and completion of the study
10. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >10 x upper limit of normal (ULN) detected within 24 hours at screening (per local lab)
11. Absolute neutrophil count (ANC) < 1000/ml at screening (per local lab)
12. Platelet count < 50,000/mL at screening (per local lab)

Date of first enrolment
03/04/2020

Date of final enrolment
28/05/2020

Locations

Countries of recruitment
Canada

Denmark

France

Germany

Italy

Netherlands

Spain

United Kingdom

United States of America

Study participating centre
Baylor College of Medicine
1 Baylor Plaza
Houston
United States of America
TX 77030

Study participating centre
61 other centers globally
United States of America
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Sponsor information

Organisation
Genentech

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Sponsor type
Industry

Website
https://www.roche.com/about_roche/roche_worldwide.htm

Funder(s)

Funder type
Industry

Funder Name
Genentech

Alternative Name(s)
Genentech, Inc., Genentech USA, Inc., Genentech USA

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
Biomedical Advanced Research and Development Authority

Alternative Name(s)
BARDA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/07/2021

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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?
Preprint results	non-peer-reviewed results in preprint	12/09/2020	21/01/2021	No	No
Results article	results	25/02/2021	17/03/2021	Yes	No