A Phase II/III seamless, randomised, double-blind, placebo-controlled, parallel-group, group-sequential study to evaluate efficacy, safety and tolerability of BI 767551 for the treatment of symptomatic, non-hospitalized adults with mild to moderate COVID-19.

Published: 30-03-2021
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Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON51124

Source
ToetsingOnline

Brief title
A study to test BI 767551 in people with mild to moderate COVID-19 symptoms

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
Coronavirus Disease 2019 (COVID-19), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim

Intervention

Keyword: COVID-19, Efficacy and safety, Neutralizing antibodies, Pharmacological activity

Outcome measures

Primary outcome

The primary endpoint in Phase II is the time-weighted change from baseline in

viral shedding over 8 days (in site collected) nasopharyngeal swabs by RT-qPCR,

defined as a change from baseline in log10 viral load. Refer to Section 7.2.3

of the protocol for further details.

The primary endpoint in Phase III is hospitalization or death from any cause by

Day 29.

Secondary outcome

The secondary endpoints in Phase II are:

* Time-weighted change from baseline in viral shedding over 29 days in site

collected NP

swabs by RT-qPCR, defined as a change from baseline in log10 viral load.

* Loss of detection of SARS-CoV-2 RNA by site collected NP swab at Day 4, 8,

15, 22

and 29.

2.1.3.2 Secondary endpoints in Phase III

The secondary endpoints in the Phase III are:

* Time to death over 29 days

* Hospitalization by Day 29

* Hypoxia or hospitalization or death from any cause by Day 29

* Hypoxia by Day 29

* Time to clinical improvement over 29 days, defined as the time to either an

improvement

of two points on the 11-point WHO Clinical Progression Scale or a score of 0 on

the

Clinical Progression Scale, whichever comes first.

* Time to loss of detection of SARS-CoV-2 RNA by site collected NP swabs over

29 days

Study description

Background summary

People with mild to moderate COVID-19 symptoms may benefit from treatment with BI 767551 by reducing the risk of worsening the condition, reducing hospitalization or death.
We think that BI 767551 can help the body prevent further virus uptake and break down the virus more quickly.

Study objective

The overall objective of this trial is to evaluate the concept of pharmacological activity of BI 767551 in non-hospitalized patients with mild to moderate COVID-19 symptoms and to identify a potentially efficacious and safe dose regimen from Phase II part to take into the Phase III part.

The Phase II part of the trial will aim to prove the concept of pharmacological activity of different dose levels of BI 767551 i.v. in comparison to placebo and to identify efficacious and safe dose regimens in non-hospitalized patients with mild to moderate COVID-19 symptoms.

The Phase II part of the trial will support the decision on whether to move to Phase III and which i.v. dose to take to the Phase III part of the study. The lowest efficacious dose showing adequate viral clearance with an acceptable safety profile will be taken into Phase III. The inhaled route administration is further evaluated in a different confirmatory trial conducted by NIAID (ACTIV-2).

The Phase III part of the trial will aim to confirm efficacy, safety and tolerability of the dose regimen of BI 767551 selected from the Phase II part in comparison to placebo in non-hospitalized patients with mild to moderate COVID-19 symptoms.

Study design

This is a Phase II/III seamless, randomised, double-blind, placebo controlled, parallel group, group-sequential study

Intervention

In the Phase II part, the study medication.is administered via an infusion (i.v.) or by inhalation.
The i.v. dose is dependent on the weight of the patient, and the dose for inhalation (nebulized) is fixed with the following treatment arms:
* Placebo i.v. + Placebo inhaled
* BI 767551 i.v. 10 mg/kg + Placebo inhaled
* BI 767551 i.v. 40 mg/kg + Placebo inhaled
* Placebo i.v. + BI 767551 250 mg inhaled

In Phase III, the medication will be administered via i.v as a fixed dose with the following
potential treatment arms:
* BI 767551 i.v. 700 mg or 2800 mg
* Placebo

Study burden and risks

Burden:
Patients eligible for this study are not admitted to the hospital for their COVID-19 infection. So if a patient chooses to participate in this study, they will have to come to the hospital for study visits which are all extra. Of the 10 visits 2 may be done remotely. Additionally, extra assessments will be done:

- 11-point WHO Clinical Progression Scale 9x
- Physical examination: 6x
- COVID-19 test at site: nasofarynx (nose)swab 6x
- COVID-19 test at site: orofarynx (throat)swab 6x
- COVID-19 test at home nasofarynx (nose)swab 11x
- Vital functions (blood pressure, heart rate, temperature, respiratory rate): 7x
- Blood draws: 7x
- Urine collection 5x
- Pregnancy test (if applicable): 6x

The patients are also asked to maintain a diary to document the symptoms they are experiencing from day 2-29. They also will document their temperature and oxygen saturation values in this diary.

Risks:
Risks of adverse reactions or allergic reaction to study medication.
Risks of adverse reactions to study procedures, such as bruising after venapunction.

Contacts

Public
Boehringer Ingelheim

Comeniusstraat 6
Alkmaar 1817MS
NL
Scientific
Boehringer Ingelheim

Comeniusstraat 6
Alkmaar 1817MS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. * 18 years old, males and females.
2. Signed and dated written informed consent in accordance with ICH-GCP and local legislation prior to admission to the trial.
3. Documentation of laboratory-confirmed SARS-CoV-2 infection, as determined by a molecular test (antigen or nucleic acid) from any respiratory tract specimen (NP or nasal swab or saliva) collected no more than 72 hours prior to start of treatment.
4. Patients experienced mild to moderate COVID-19-related symptoms or measured fever for no more than 5 days prior to start of treatment where symptoms are defined by fever, feeling feverish, fatigue, cough, shortness of breath at rest or during activity, sore throat, body pain or muscle pain/ aches, chills, headache, nasal obstruction or congestion, loss of smell or taste, nausea, diarrhea, vomiting, or dysgeusia.
5. One or more of the following signs/symptoms present on day of start of treatment: fever, feeling feverish, fatigue, cough, shortness of breath at rest or during activity, sore throat, body pain or muscle pain/ aches, chills, headache, nasal obstruction or congestion, loss of smell or taste, nausea, diarrhea, vomiting, or dysgeusia.
6. Women of childbearing potential (WOCBP) and men able to father a child must be ready and able to use highly effective methods of birth control per ICH M3 (R2) that result in a low failure rate of less than 1% per year when used consistently and correctly.

Exclusion criteria

1. Body weight of less than 40 kg.
2. Severe or critical COVID-19 including at least one of:

o Oxygen saturation (SpO2) * 93 % on room air or on their usual level of oxygen supplementation in case of chronic oxygen use
o Ratio of arterial oxygen partial pressure (PaO2 in millimeters of mercury) to fractional inspired oxygen (FiO2) < 300 (in case arterial blood sample was taken)
o Respiratory rate * 30/min or heart rate * 125/min. Measure should be obtained at rest by study staff within 24 hours of start of treatment.
o History of hospitalization for COVID-19
o Current or imminent need for hospitalization or immediate medical attention in the clinical opinion of the site investigator. Does not include patients hospitalized for isolation only.
3. Receipt of intraveneous immunoglobulin within 12 weeks prior to Visit 2.
4. Receipt of COVID-19 convalescent plasma treatment at any time prior to Visit 2.
5. Receipt of any SARS-CoV-2 monoclonal antibody treatment at any time prior to Visit 2.
6. Receipt of SARS-CoV-2 vaccine at any time prior to Visit 2.
7. Receipt of an investigational product for COVID-19 within 5 half-lives prior to Visit 2.
8. Receipt of systemic steroids (e.g. prednisone, dexamethasone) within 4 weeks prior to Visit 2 unless used for chronic condition (see Section 4.2.2.1).
9. Patients who must or wish to continue the intake of restricted medications or any drug considered likely to interfere with the safe conduct of the trial.
10. Any co-morbidity requiring surgery within 7 days prior to study entry, or that is considered life threatening in the opinion of investigator within 30 days prior to study entry.
11. Have any serious concomitant systemic disease, condition or disorder that, in the opinion of the investigator, should preclude participation in this study.
12. Patients not expected to comply with the protocol requirements or not expected to complete the trial as scheduled (e.g. chronic alcohol or drug abuse or any other condition that, in the investigator*s opinion, makes the patient an unreliable trial participant).
13. Currently enrolled in any other type of medical research judged not to be compatible with this study.
14. Known allergy/sensitivity or any hypersensitivity to any of the components used in the formulation of the interventions.
15. Previous enrolment in this trial. Patients participating in Phase II are not eligible for Phase III. Re-screening is allowed once, for repeat of RT-qPCR or antigen SARS-CoV-2 test, if required. The test method used for initial screening (RT-qPCR or antigen) should be used for re-screening.
16. Women who are pregnant, nursing, or who plan to become pregnant while in the trial.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	EX 14870/ DZIF-10c
Generic name:	not assigned

Ethics review

Approved WMO Date:	30-03-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	18-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-005588-29-NL
ClinicalTrials.gov	NCTnummernognietbekend
CCMO	NL77209.078.21

Study results

Results posted: 05-09-2022

Summary results
Trial never started

First publication
01-07-2022