Phase 2, randomized, controlled, open label multi-center study to assess efficacy and safety of DFV890 for the treatment of SARS-CoV-2 infected patients with COVID-19 pneumonia and impaired respiratory function

Published: 13-05-2020
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON49323

Source
ToetsingOnline

Brief title
CDFV890D12201

Condition

- Respiratory disorders NEC

Synonym
COVID-19 pneumonia

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: COVID-19, DFV890, pneumonia

Outcome measures

Primary outcome

APACHE II severity of disease score on Day 15 or on day of discharge (whichever

is earlier)

Secondary outcome

Serum C-reactive protein (CRP) levels

Study description

Background summary

As of 22-Apr-2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been confirmed in over 2.5 million people worldwide, with over 179,000 deaths to date due to coronavirus disease 2019 (COVID-19). The mortality rate of approximately 4-5% is significantly higher than that seen with seasonal influenza (less than 1%).
Between 5-10% of COVID-19 patients develop lung injury, respiratory distress progressing to acute respiratory distress syndrome (ARDS) requiring prolonged ventilator support over weeks that results in intensive care units, hospitals and health care systems becoming overwhelmed.

ARDS is characterized by pro-inflammatory cytokine release, inflammatory cellular infiltrate and cell death resulting in severe pulmonary damage and the development of respiratory failure that requires mechanical ventilation with high positive end-expiratory pressures (PEEP) to maintain life.
There is at present no health authority (HA) approved treatments for COVID-19 or its sequelae, including the cytokine storm which develops in those most

severely affected. Current SoC in the European Union (EU) and United States of America (US) includes a variety of supportive therapies, ranging from the administration of supplementary oxygen to full intensive care support, alongside the use of antiviral agents and intravenous corticosteroids, though there is considerable inter-center variability regarding the use of these. Local SoC is permitted in all participants of the study, though every effort will be made by investigators to standardize this within individual centers.

Study objective

The purpose of this study is to evaluate the efficacy and safety of DFV890 in addition to current standard of care (SoC) compared with SoC alone in controlling the inflammatory syndrome and resultant acute respiratory distress syndrome (ARDS) in hospitalized patients presenting with COVID-19 pneumonia and impaired respiratory function

Study design

A Phase 2, randomized, controlled, open label multi-center study
The study consists of four parts:

Screening / Baseline visit (Day -1 to 1): lasts up to a maximum of 24 hours to confirm that the study inclusion and exclusion criteria are met and serves as baseline assessment prior to randomization.

Treatment period (Day 1-15): Participants in the investigational treatment arm will receive DFV890 50 mg b.i.d. orally or via a nasogastric feeding tube administered for a total of 14 days (28 doses) in addition to SoC. Study assessments will be conducted every 2 days for hospitalized participants. The End of Treatment (EOT) visit will take place on Day 15.

Follow-up (Day 16-29): After completion of the 14 day- treatment period, participants will be observed until Day 29 or discharged from hospital, whichever is sooner. Study assessments to be conducted every 2 days for hospitalized participants.

30-day safety follow-up assessment (Day 45): A follow-up visit for safety will be conducted by telephone.

Intervention

DFV890 50 mg: administered orally twice per day approximately 12 hours apart (morning and evening) 14 days

Study burden and risks

Known side effects of the investigational drug DFV890

Very common side effects
- Skin rash (more common in women) -
- Infections
- Headache

Common side effects
- Vomiting

Uncommon side effects
- Changes in kidney function

Risks and inconveniences related to assessments
- Blooddraw (vene or artery)
- COVID-19 testing by using via a nasal swab
- Imaging (X-Ray and CT-scan)
- Urine collection

Contacts

Public
Novartis

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NL
Scientific
Novartis

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Clinically diagnosed with the SARS-CoV-2 virus
* Hospitalized with COVID-19-induced pneumonia evidenced by chest Xray, CT scan, MR scan taken within 5 days prior to randomization (within 24 hours in patients in the Netherlands)
* Impaired respiratory function, defined as peripheral oxygen saturation (SpO2) *93% on room air or partial pressure of oxygen (PaO2) / fraction of inspired oxygen (FiO2) <300 millimeter of mercury (mmHg)
* APACHE II score of *10 at time of randomization
* C-reactive protein (CRP) *20 mg/L and/or ferritin level *600 *g/L
* Body weight mass index of *18 to <40kg/m2

Exclusion criteria

* Suspected active or chronic bacterial (including Mycobacterium tuberculosis), fungal, viral, or other infection (besides SARS-CoV-2)
* In the opinion of the investigator, progression to death is imminent and inevitable within the next 24 hours, irrespective of the provision of treatment
* Intubated prior to randomization
* Have received either oral anti-rejection, or immunomodulatory drugs within the past 2 weeks, or immunomodulatory therapeutic antibodies within the 5 half-lives or 30 days from randomization (whichever is longer), with the exception of hydroxychloroquine, chloroquine or corticosteroids at doses up to and including prednisolone 10mg daily or equivalent. In patients in the Netherlands only, the use of hydroxychloroquine and/or chloroquine in the past 2 weeks are exclusionary
*ALT or AST >5 x ULN (upper limit of normal) detected within 24 hours at screening or at baseline or other evidence of severe hepatic impairment (Child-Pugh Class C)
* Absolute peripheral blood neutrophil count of *1000/mm3
* Estimated glomerular filtration rate (eGFR) *30 mL/min/1.73m2

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-09-2020
Enrollment:	4
Type:	Actual

Ethics review

Approved WMO Date:	13-05-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-05-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2020

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-09-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-09-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2020-001870-32-NL
CCMO	NL73972.056.20