Alkaline phosphatase for reducing systemic inflammatory response syndrome (SIRS) in patients with Sars-CoV-2 infection and acute respiratory insufficiency (COVID 19)

Published: 26-05-2020
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To assess the preliminary efficacy of AP in reducing the inflammatory reaction in COVID-19 patients and thereby shorten time on mechanical ventilation or prevent the need for mechanical ventilation in COVID-19 patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON54916

Source
ToetsingOnline

Brief title
COVID-RESCAP

Condition

- Viral infectious disorders
- Pulmonary vascular disorders

Synonym
COVID 19 and coronavirus

Research involving
Human

Sponsors and support

Primary sponsor: Rode Kruis Ziekenhuis
Source(s) of monetary or material Support: local university medical centres pays for physicians;research nurses and researchers ;while Alloksys Life Sciences provides study drug + pays for CRO

Intervention

Keyword: alkaline phosphatase, COVID 19, RESCAP, Sars-CoV-2

Outcome measures

Primary outcome

Duration of mechanical ventilation (days) and withholding of mechanical

ventilation (%)

Secondary outcome

- not applicable -

Study description

Background summary

Up to 15% of COVID-19 patients are admitted to the hospitals with signs of (near) respiratory failure. The CT of the chest shows extensive interstitial pneumonia in all these cases. In this acute setting however, PCR analyses of nasopharynx swabs are frequently negative for Sars-CoV-2. Our hypothesis is that these critical ill patients suffer more from their own immune response against the virus, than from the viral infection itself. Alkaline phosphatase (RESCAP®) has proven to reduce SIRS reactions by neutralizing the inflammatory response in various medical conditions, like sepsis induced acute kidney injury and ischemia-reperfusion reactions in cardiothoracic surgery. Furthermore, endogenous alkaline phosphatase (AP) is highly expressed on type II lung alveolar (surfactant producing) cells and is thought to stabilize the alveolar barrier. In acute inflammation, endogenous AP is lost from the cells after binding to its substrate. Replenishing AP might restore the alveolar barrier and combat subsequent SIRS and secondary organ failure.

Study objective

To assess the preliminary efficacy of AP in reducing the inflammatory reaction in COVID-19 patients and thereby shorten time on mechanical ventilation or prevent the need for mechanical ventilation in COVID-19 patients.

Study design

Multicentre prospective placebo-controlled interventional clinical trial.

Intervention

Bolus alkaline phosphatase of 1000iU; followed by 9000 iU the same day. For the 3 consecutive days 10.000iU/day on top of regular care (all patients)

Study burden and risks

Alkaline phosphatase (AP) is an endogenous protein/enzyme. RESCAP is AP derived from bovine intestinal cells and processed for clinical application. Critically ill patients with COVID-19 are treated with AP for 4 consecutive days in this study. In 3 other (Dutch) clinical trials, no treatment-related side effects were reported (see DSUR). RESCAP has the potential to reduce (pulmonary) complications in critically ill COVID-19 patients. In the current APhIRI clinical trial running in Amsterdam UMC (prevention of ischemia-reperfusion injury in renal transplantation), the intervention was considered as low-risk because of the small amount of protein that is infused (<10 mg/24 hours) and no observed IMP related side effects in other clinical trials.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Sars-CoV-2 infection based on: highly clinical suspicion on admission and/or positive PCR test on naso-pharynx swab or sputum and/or a CT imaging of the chest compatible with COVID-19 + type 1 or type 2 respiratory failure needing supplemental oxygen that indicates airway support or ICU admittance and meeting any of the following criteria: .
- SpO2 <90% or PaO2/FiO2 < 200 mmHg
- Clinical evidence of respiratory distress (RR > 25 breaths/minute)

Exclusion criteria

- Inclusion in another interventional clinical trial
- Age < 18
- Age > 80
- Patients who are pregnant or lactating
- Patients expected to have fatal disease within 24 hours
- Patients who are already on dialysis (Renal Replacement Therapy, RRT) or a decision has been made to initiate RRT within 24 hours after planned start of study drug administration
- Patients who have advanced chronic liver disease confirmed by a Child-Pugh C
- Patients who are having a known history of immune system that has been impaired by disease, such as patients with HIV and with a CD4 count of less than 200 cells/mm, neutropenic patients (<0.5 x 109/l) Patients who are receiving chronic high doses (equivalent to prednisone/prednisolone 0.5 mg/kg/day) steroids therapy immediately prior to recruitment exceeding 2 weeks of treatment. This means dexamethasone 6 mg once daily serving as treatment for severe COVID-19 is not an exclusion criterion.
- Patients with active haematological malignancy

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:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-12-2020
Enrollment:	106
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	alkaline phosphatase
Generic name:	alkaline phosphatase

Ethics review

Approved WMO Date:	26-05-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	04-03-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2020-001714-38-NL
CCMO	NL73891.029.20
Other	NL8578