A randomized, double-blind, placebo-controlled, two parallel groups, international multicenter trial to evaluate the effect of Plerixafor in acute respiratory failure related to COVID-19 (LEONARDO)

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To demonstrate that Plerixafor is able to reduce the need for invasive mechanical ventilation or death in severe COVID-19 patients admitted in Intensive Care Unit (ICU)

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51400

Source
ToetsingOnline

Brief title
LEONARDO

Condition

- Other condition

Synonym
acute respiratory failure

Health condition

acute respiratory failure related to COVID-19

Research involving
Human

Sponsors and support

Primary sponsor: 4Living Biotech SAS
Source(s) of monetary or material Support: Pharma/Biotech industry

Intervention

Keyword: acute respiratory failure, COVID-19, international, Plerixafor

Outcome measures

Primary outcome

Proportion of patients with need for invasive mechanical ventilation or death

between randomization and D28

Secondary outcome

• Percentage of death (all-cause mortality)

• Number of Ventilator-free days

• Duration of invasive mechanical ventilation in survivors

• Number of ICU stay days

• Respiratory function at 3 months (FEV-1, FVC, PaO2, TLCO, 6-minute walk test)

• Ordinal Scale for Clinical Improvement (7 point-WHO scale)

• Level of consciousness (Alert, Voice, Pain, Unresponsive scale)

• SpO2 measured via pulse oxymetry and arterial blood gas: Partial pressure of

oxygen (PaO2), Partial pressure of carbon dioxide (PaCO2), Bicarbonate (HCO3),

Oxygen saturation (O2 Sat), pH, Base excess (when performed before intubation)

• Blood CRP, fibrinogen, D-dimers levels

• Incidence of treatment-emergent AEs (TEAEs), serious AEs (SAEs), and AEs of

special interest (AESIs),

• Incidence of Plerixafor discontinua-tion and withdrawals due to TEAEs

• WBC count and differential, RBC count, hemoglobin level, MCV, Reticulocyte

and Platelet counts

• Blood Chemistry (Creatinine, AST, ALT, total bilirubin, K, total Ca)

Study description

Background summary

Plerixafor is a chemical compound approved in Europe since 2009 and commercialized under the tradename Mozobil® by Sanofi-Genzyme. It is indicated in lymphoma and multiple myeloma (both types of blood cancer) to help collect blood stem cells from the patient for storage and reintroduction (transplantation). Plerixafor is considered an investigational drug in this study because it has not been approved for marketing by any health authority for the condition being studied (severe COVID-19 infection).
Plerixafor reduces migration of immature and inefficient white blood cells and consequently the damages done by these cells. As observed in mice, plerixafor is also expected to ameliorate the aspect of the lungs after a respiratory viral infection.
Since severity of COVID-19 is associated with elevated blood and lung levels of those type of white blood cells, plerixafor is considered as a promising candidate to treat severe COVID-19 infection.

Study objective

To demonstrate that Plerixafor is able to reduce the need for invasive mechanical ventilation or death in severe COVID-19 patients admitted in Intensive Care Unit (ICU)

Study design

A randomized, double-blind, placebo-controlled, two parallel groups, international multicenter trial to evaluate the effect of Plerixafor in acute respiratory failure related to COVID-19.

Participants will be randomized in a 2:1 ratio to receive either Plerixafor (n=100) or placebo (n=50) as a continuous IV infusion for 7 days (from D1 to D8), in addition to standard of care (e.g. glucocorticoids*). Intervention randomization will be stratified per investigational site.

Intervention

Plerixafor (Mozobil®) 30 microgrammes/kg/hour continuous intravenous infusion for 7 days or Placebo similar modalities for infusion.

Study burden and risks

Preclinical data previously described suggest that plerixafor could reduce the severity of COVID-19 lung injury in patients with acute respiratory failure.

See protocol 2.3 Benefit/Risk assessment

Contacts

Public
4Living Biotech SAS

Campus de l'Institut Pasteur de Lille 1 rue du Professeur Calmette
Lille 59 000
FR
Scientific
4Living Biotech SAS

Campus de l'Institut Pasteur de Lille 1 rue du Professeur Calmette
Lille 59 000
FR

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• I1 Male or female >= 18 years of age,
• I2 Using contraceptive consistent with local regulations regarding the methods of contraception for those participating in clinical studies,
• I3 Willing and able to provide written informed consent (or provided by legally acceptable representative if he/she is present and if in line with local regulations),
• I4 Admitted in ICU within 48 hours before randomization for COVID-19 related respiratory failure.
* ICU or equivalent medical structure according to country specificities e.g., Acute Respiratory Care Unit, High Dependency Care Unit if they can provide:
* continuous IV infusion,
* continuous ECG, respiratory rate, percutaneous oxygen saturation screen monitoring
* high flow nasal oxygen
• I5 Not requiring immediate (within 24-36 hours) invasive mechanical ventilation according to investigator's judgment,
• I6 Confirmed pneumoniae due to SARS-CoV-2 with Laboratoryconfirmed SARS-CoV-2 infection as determined by RT-PCR (in nasopharynx or throat samples) or other commercial or public health assay in any specimen, performed within 2 weeks prior to randomization,
• I7 Acute respiratory failure requiring oxygen support (>= 5L/min) to achieve a transcutaneous oxygen saturation > 94%,
• I8 Estimated glomerular filtration rate (eGFR) > 50 mL/min/1.73m² by the CKD-EPI (Chronic Kidney Disease - Epidemiology Collaboration) equation.

Patients vaccinated against SARS-CoV-2 can be included in the study.
Before or during the whole study, patients may have or will receive standard of care i.e.,
routinely administered in such patients in the country study site as per current health
authorities* recommendations (e.g., glucocorticoids, tocilizumab, remdesivir *.).

Exclusion criteria

• E1 Pregnancy or breast feeding,
• E2 Anticipated transfer to another hospital, which is not a study site within 72 hours of randomisation,
• E3 Need for Invasive mechanical ventilation at time of inclusion,
• E4 Evidence of uncontrolled bacterial pneumopathy or active infection other than SARS-Cov-2 (laboratory confirmation),
• E5 Primitive pulmonary arterial hypertension,

• E6 Cardio-vascular co-morbidity:
o History of vascular ischemic events (myocardial infarction or stroke) or congestive heart failure or peripheral arterial disease,
o History or current significant cardiac rhythm disorders (e.g., ventricular tachycardia),
o Known medical history of proven symptomatic postural hypotension,
• E7 Known cancer (solid or blood) in the last 5 previous years or previous haematological disorders
(malignancies and other chronic conditions) or having received bone marrow transplant,
• E8 Inadequate haematological function defined by:
o Neutrophil count < 1.0 x 109/L,
o Haemoglobin < 9.0 g/dL (90 g/L),
o Platelets < 100 x 109/L,
• E9 Kaliemia < 3.5 mmol/L and/or total Calcemia < 2.2 mmol/L,
• E10 Inadequate hepatic function defined by Aspartate aminotransferase (AST) and/or Alanine Aminotransferase (ALT) > 3 x upper limit of normal (ULN) and/or Total bilirubin > 2 x ULN,
• E11 Patients with known allergy to Plerixafor or its excipients.
• E12 Previous (within 4 weeks) or current participation in another clinical study other than an observational study.
• E13 Patients with auto immune disease treated or not,

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:	25

Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Mozobil
Generic name:	Plerixafor
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-01-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-07-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2021-001245-13-NL
CCMO	NL79887.091.22