Potential of FX06 to prevent disease progression in hospitalised nonintubated COVID-19 patients (Ixion)

Published: 23-07-2022
Last updated: 06-04-2024

The primary objective is to demonstrate a difference in the proportion of patients with progressed/worsened disease state in patients receiving FX06 compared to patients receiving placebo until day 28.Assessment and treatment comparison of the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON53826

Source
ToetsingOnline

Brief title
IXION

Condition

- Respiratory tract infections

Synonym
SARS-CoV-2 (Severe Acute Respiratory Syndrome)

Research involving
Human

Sponsors and support

Primary sponsor: F4Pharma GmbH i.G.
Source(s) of monetary or material Support: F4Pharma GmbH i.G.

Intervention

Keyword: COVID-19, SARS-CoV-2

Outcome measures

Primary outcome

The primary objective is to demonstrate a difference in the proportion of patients with progressed/worsened disease state in patients receiving FX06 compared to patients receiving placebo until day 28.

Secondary outcome

The secondary objectives and endpoints: Assessment and treatment comparison of the following objectives at all available visits and time points between the FX06 and placebo group.

Study description

Background summary

The emergence of a novel coronavirus, officially known as Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2), has presented an unprecedented challenge for the healthcare community across the world. High infectivity, ability to get transmitted even during the asymptomatic phase and relatively low virulence have resulted in a rapid transmission of SARS-CoV-2 beyond geographic regions, leading to a pandemic. The first case of this diseases, known as coronavirus disease 2019 (COVID-19), occurred on December 8,2019 in the Hubei province of China. Since then, the infection has spread worldwide, with nearly 194 million confirmed cases and over 4 million deaths (World Health organization situation report from July 27th, 2021). Respiratory involvement, presenting with mild flulike illness to potentially lethal acute respiratory distress syndrome or fulminant pneumonia, are the dominant clinical manifestations of COVID-19. Like other coronavirus, SARS-CoV-2 is characterized by a spherical morphology with spike projections on the surface. It was demonstrated that SARS-CoV-2 shared high sequence identity with that of SARS-CoV and SARS-like coronavirus (SL-CoV). Notably, SARS-CoV-2 has lower pathogenicity but higher transmissibility from human to human compared with SARS-CoV. Cell entry is the first step of cross-species transmission.

SARS-CoV-2 is more likely to infect lung type II alveolar cells, which may explain the severe alveolar damage after infection.

FX06 is a naturally occurring peptide, Bβ15-42, derived from the E1 fragment of fibrin. The mechanism of action of FX06 is an important new discovery in understanding acute inflammation and edema formation. FX06 competes with E1 fragments of fibrin for binding to an endothelial specific molecule, VE-cadherin, thereby acting as an anti-inflammatory, and it signals through VE-cadherin, thereby reducing plasma leakage into tissues. Based on animal models of vascular leakage and systemic inflammation, FX06 has considerable therapeutic potential for all diseases and pathological conditions associated with increased vascular permeability. FX06 binds to vascular endothelial (VE)-cadherin, preventing VE-cadherindependent transmigration of leukocytes. Besides many different animal models of shock (septic, hemorrhagic, hypovolemic), FX06 was also tested in acute and chronic models of myocardial ischemia and reperfusion in rats, mice and pigs. FX06 reduced relative infarct size by more than 40%; this effect size is comparable to ischemic preconditioning. The peptide is synthetically produced for exogenous human administration.

FX06 was found to have a benign safety profile in safety pharmacology and toxicology studies. The only findings representing potential risks to humans were mild platelet activation in response to shear stress in an in vitro study and mild transient hypotension observed in telemetered dogs. Preliminary data suggest that initial clearance of FX06 is mainly via the kidneys. FX06 is also partially degraded by plasma carboxypeptidases.

Escalating doses of FX06 were evaluated in a single Phase I study in 30 healthy volunteers using a pioneer dose design. PK analysis demonstrated a broadly linear relationship between dose and AUC. Clearance was independent of dose. The calculated plasma elimination half-life was between 11 and 17 minutes. FX06 was well tolerated in the Phase I study.

FX06 has been evaluated in a Phase IIa clinical trial of first-time acute STEMI (ST-segment elevation myocardial infarction) patients undergoing primary percutaneous coronary intervention. In this proof-of concept trial, FX06 reduced the necrotic core zone as one measure of infarct size on magnetic resonance imaging and appeared safe and well tolerated.

Preliminary data from an investigator-initiated trial (IIT) in critically ill COVID-19 patients revealed a trend to improved survival in FX06-treated patients. However, no statistically significant difference could be observed in this 50-patient randomized, placebo-controlled study. Importantly, no safety concern was raised. Furthermore, FX06 has been applied in a severe case of an Ebola virus infected patient under compassionate use. The patient recovered after critical illness and no drug related safety

concerns were raised

Study objective

The primary objective is to demonstrate a difference in the proportion of patients with progressed/worsened disease state in patients receiving FX06 compared to patients receiving placebo until day 28.

Assessment and treatment comparison of the objectives at all available visits and time points between the FX06 and placebo group

Study design

This will be a multicentre, placebo-controlled, double-blinded, parallel, randomized (2:1), phase II clinical study to investigate the potential of FX06 to prevent disease progression in hospitalised non-intubated COVID-19 patients.

Patients fulfilling inclusion criteria will be stratified according their WHO severity group (moderate: score 4-5 or severe: score 6) and by country and randomized 2:1 to either one of the two treatment groups (FX06 or placebo).

Patients will be treated for 5 consecutive days and will be observed until day 28 and followed up at day 60. They will receive FX06 or placebo i.v. as a two-time (2x 200 mg) bolus injection per day. The interval between the two injections should be 10 ± 5 min. IMP administration will start at BL.

Patients will be assessed according to Table 1 until day 28 (and followed up until day 60). After BL, day 1-6, 10 and 28 are planned as personal visits (visit at the study centre or home visitation; the latter only if patients have been released from the hospital). If this will not be feasible (e.g., because patients have been released and are not able to come to the study centre and the study centre is not able to perform home visitations) visits can be performed remotely (at least the WHO score, concomitant medication and adverse events need to be assessed).

Once patients leave the hospital, the necessary information for days 7-9 and 11-27 can be retrieved remotely to assess safety and main efficacy endpoints (patients can be contacted every 2-3 days to retrieve the information retrospectively in order not to demotivate patients to participate). A follow-up visit will be performed as a telephone/video-call at day 60.

If patients leave the hospital before day 6 they will continue the study as planned (they will not be considered drop-outs as far as at least IMP dose was administered). Day 6 should still be performed as a personal visit (if feasible, see above); the days beforehand could be performed remotely for these patients if personal visits are not feasible. All other visits after day 6

should be performed as planned. If patients leave the hospital with a better WHO score than at BL before day 5, IMP/placebo administration will not be continued. IMP/placebo will only be given during their hospital stay. Number of IMP/placebo administrations will be documented.

Intervention

There will be 2 study treatments: 1 active FX06) and 1 placebo.

FX06/placebo will be administered over a 5-day period in two-bolus administration per day. The patients will then be further observed until day 28. The study duration for individual patients will be maximally 28 days (plus up to 5 days Screening period) for the main study period plus a FU telephone call at day 60).

Study burden and risks

The burden and risk mainly consist of extra time spent compared to standard treatment.

Contacts

Public
F4Pharma GmbH i.G.

Gersthofer Straße 103/23
Vienna 1180
CH
Scientific
F4Pharma GmbH i.G.

Gersthofer Straße 103/23
Vienna 1180
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. SARS-CoV-2 infection confirmed by PCR test
2. Hospitalised patients
3. WHO score 4-6
4. Oxygen saturation <= 92% under room air
5. Breathing frequency per minute >= 20
6. Patients >= 18 years
7. Written informed consent obtained prior to the initiation of any protocol-required procedures by the patient
8. Willingness to comply to study procedures and study protocol
9. Patients able to understand the requirements of the study and give written informed consent

Exclusion criteria

1. Significant underlying known co-morbidities or conditions, defined as:
o Other severe advanced or chronic lung diseases (e.g., COPD Gold >= III, severe silicosis)
o End-stage chronic kidney disease (stage 5)
o End-stage chronic heart failure (NYHA >= III)
o Dementia
o Baseline neurologic disease which would preclude rehabilitation potential
o Disseminated and/or metastasised malignancy
o Severe deconditioning with a life expectancy of less than 6 months according to the treating physician
o Immunocompromised patients
- recipient of a solid organ transplant
- regular intake of anti-inflammatory therapy due to concomitant auto- immune diseases (e.g., biologics)
- primary immune deficiency
2. Evidence of other significant uncontrolled concomitant diseases or serious and/or uncontrolled diseases with a bad prognosis that are likely to interfere with the evaluation of the patient's safety and with the study outcome as judged by the treating physician
3. Women pregnant or breastfeeding
4. Males or females of reproductive potential not willing to use effective

contraception for the duration of the study period (defined as PEARL index <1 e.g., contraceptive pill, IUD or true sexual abstinence, bilateral tubal occlusion or male partner with vasectomy; also see chapter 19.2 for guidance)
5. Current participation in another interventional clinical trial with IMP or participation within the last 30 days

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:	Pending
Start date (anticipated):	01-07-2022
Enrollment:	100
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	FX06
Generic name:	FX06

Ethics review

Approved WMO

Date:	23-07-2022
Application type:	First submission

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-01-2023
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
Other	2021-005059-35
EudraCT	EUCTR2021-005059-35-NL
CCMO	NL80448.068.22