COVend

A new therapy for the clinical management of Acute Respiratory Distress Syndrome (ARDS)

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THE COVend PROJECT

DURATION
01.08.2021 – 31.07.2025

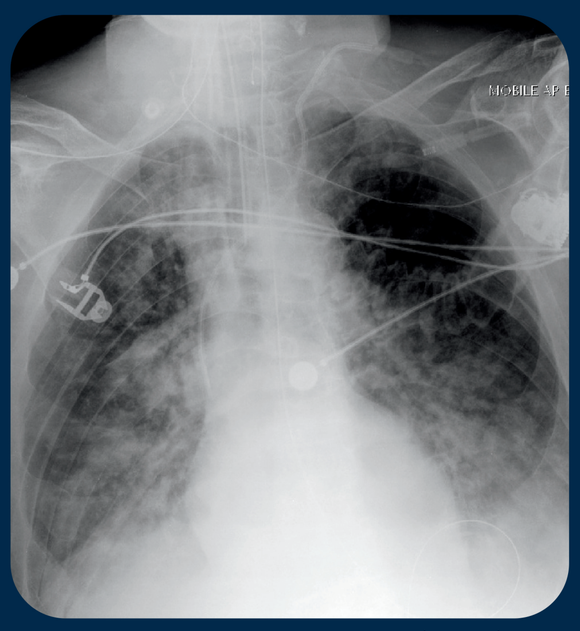
CALL TOPIC
HORIZON-HLTH-2021-CORONA

COORDINATOR
Goethe University Frankfurt, Germany

BUDGET
9.9 million euro

Advancing ARDS Treatment with FX06

The COVend project aims to clinically test a novel therapy for Acute Respiratory Distress Syndrome (ARDS) endothelial damage. ARDS is a life-threatening pulmonary dysfunction seen in intensive care patients, triggered by viral/bacterial infections, trauma, surgery, or blood transfusions. Currently, no effective pharmaceutical therapy for ARDS exist, and the COVend Trial seeks to close this gap.

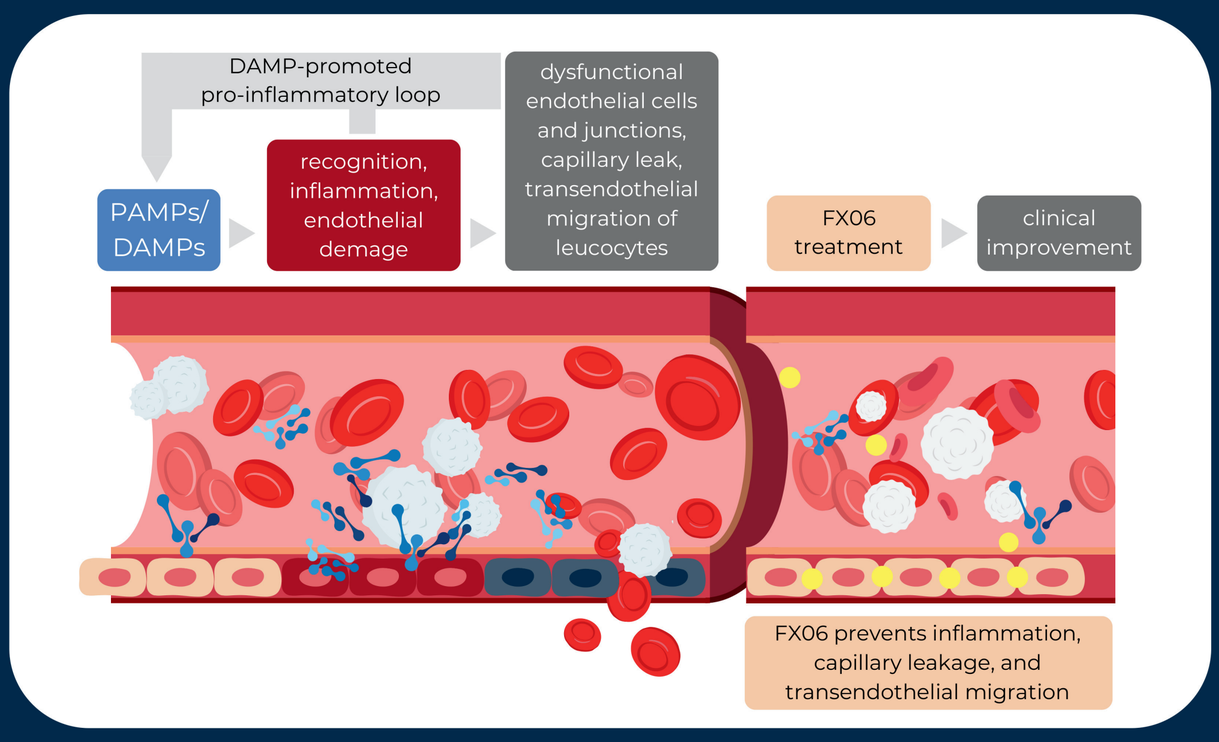


Source: radiopaedia.org/articles/858

FX06 - an innovative endothelium stabiliser

FX06 reduces endothelial leakage by competing with fibrin

FX06 binds to vascular endothelial (VE) cadherin and inhibits leukocyte transmigration. Animal models suggest therapeutic potential in conditions of increased vascular permeability (Gröger et al., 2009; Bergt et al., 2016). Human studies show that FX06 can reduce the size of the myocardial infarct zone during reperfusion (Hallén et al., 2010).



Quantitative biomarker analysis

Omics-based precision therapy profiling

OLINK ™ technology
Affinity-based, PCR-coupled, multiplexed high-throughout proteomics.

Selective and sensitive LC-MS/MS
Lipid mediators in blood plasma.

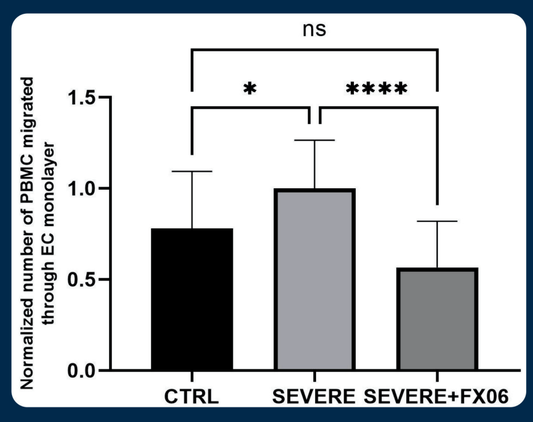
MxP® Quant 500 Assay, FIA-MS/MS, and LC-MS/MS
Small molecules, lipids, hexases to investigate metabolic pathways.

Multi-omics analysis has revealed molecular signatures of COVID-19 and the immune response with prognostic and drug targeting implications (Li et al., 2021; Su et al., 2021). Expanding on these findings, the COVend study will use proteomics, lipidomics and metabolomics of patient blood samples to elucidate the interaction between ARDS-associated systemic endothelial inflammation and the effects of FX06. In vitro studies will investigate effector molecules and the data will be used to train AI models for clinical applications.

FX06 alleviates hyperinflammation and capillary leak

COVID-19-triggered transendothelial migration of immune cells from the blood is suppressed by FX06 *in vitro*

Results from the University College Dublin (UCD) demonstrated successful mimicry of capillary shear stress conditions using computer-controlled laminar flow. After 24 hours of incubation with COVID-19-induced cytokines (SEVERE), transmission electron microscopy (TEM) of isolated peripheral blood mononuclear cells (PBMCs) through a monolayer of human pulmonary microvascular endothelial cells (HULEC-5a) is enhanced (*p = 0.0197).



Pre-incubation of endothelial cells (ECs) with FX06 for 2 hours (SEVERE+FX06) restores the non-inflammatory state (CTRL) and significantly reduces TEM (****p < 0.0001).

COVend's Plan of Action

Research

- IXION 2.0 phase II trial.
- Immuno-biomarker profiling.
- Endothelial cells assessment.

Development

- Drug production.
- AI decision support models.
- Personalised medication.

Outreach

- FX06 therapy.
- AI-based tools for healthcare workers.
- Clinical guidelines.

"Having cured a patient with Ebola, it was clear to me that FX06 could also be beneficial against COVID-19."

Professor Kai Zacharowski
MD PhD ML FRCA, FESAIC
Ambassador & Immediate President of the European Society of Anaesthesiology & Intensive Care (ESAIC)
COVend Project Coordinator

Funded by the European Union

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Potential of FX06 to improve disease severity in Acute Respiratory Distress Syndrome patients

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IXION 2.0 CLINICAL TRIAL

The IXION 2.0 study is an **exploratory, randomised, placebo-controlled, double-blind, parallel Phase II clinical trial** and is the centrepiece of COVend's work to make FX06 a viable therapy for ARDS.

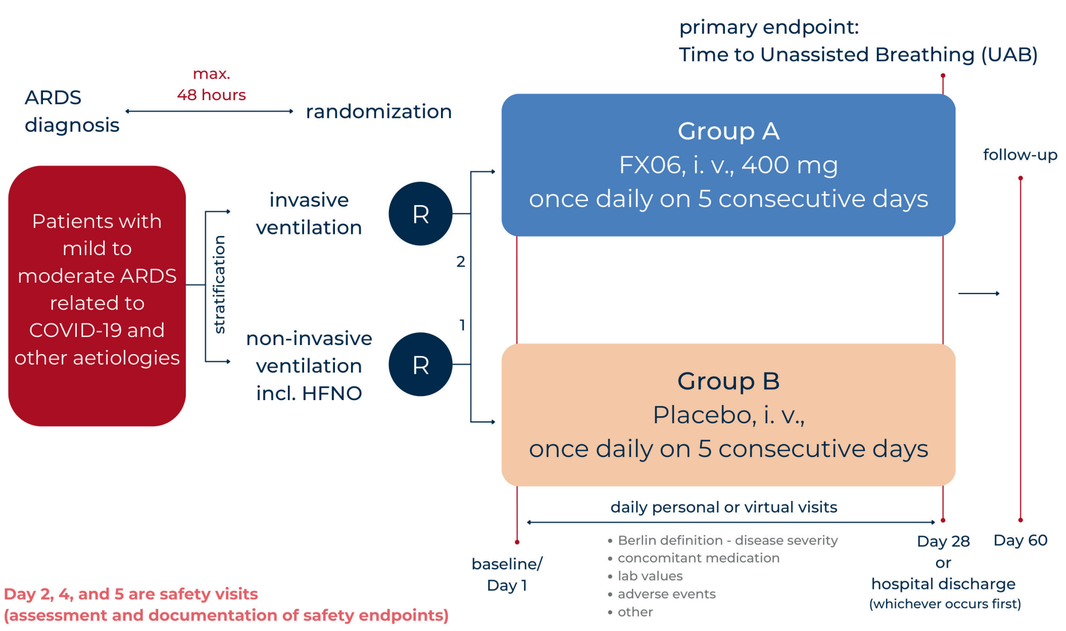
The burden of ARDS

ARDS develops as a result of an unbalanced immune response caused by viral or bacterial infections, severe trauma, major surgery or blood transfusion, and is a critical medical condition with no effective pharmaceutical treatment options. Patients with ARDS have impaired gas exchange due to dysfunctional capillaries, damaged alveoli and fluid accumulation in the lungs. ARDS it quite common, with certain studies reporting 7-23 cases of ARDS per 100,000 population per year in Europe. ARDS accounts for about 10% of all ICU admissions and about 20% of mechanically ventilated patients, with in-hospital mortality rates of up to 45%. Despite decades of research, an effective pharmacological treatment has not been developed thus highlighting the urgent need for innovative therapeutic approaches.

A new effective therapy for ARDS

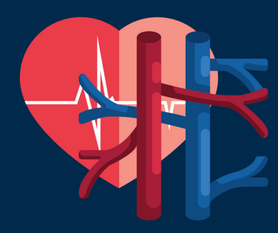
Clinical trials for ARDS are notorious for their lack of success. The results of the IXION 2.0 study aims to breakthrough this barrier via innovative patient-specific exploratory molecular analysis of proteins, lipids and metabolites in the blood of study participants (known as 'multi-omic analysis') to identify subtle pathophysiological differences between patient groups. AI tools complement the data, enabling personalised clinical practice to select patients who will benefit from the therapy and monitor its efficacy based on unique biomarkers. Advanced cell biology methods using endothelial cell lines will uncover the molecular mechanism of FX06, contributing to knowledge-based trust and transparency in medicine and potentially paving the way for further life-saving applications. Thus the IXION trial will lead the way in the ARDS research.

IXION 2.0 Clinical Trial



THE IXION STUDY IS REGISTERED UNDER EUDRACT NUMBER:
2021-005059-35

Innovative Medication Targeting Endothelial Dysfunction



Objectives

The overall goal of the COVend Research and Innovation Action is to provide a new effective therapy for the clinical management of ARDS in mild and moderate stages, including the prevention of progression to severe disease. We aim to achieve this by testing a promising medication, the peptide FX06, in a placebo-controlled, multinational Phase II study in mild and moderate ARDS cases related to SARS-COV-2 or other aetiologies.

FX06 or a placebo will be given over a course of 5 days and the patient will then be followed up for an additional 23 days. On day 60 a follow up phone call will also take place.

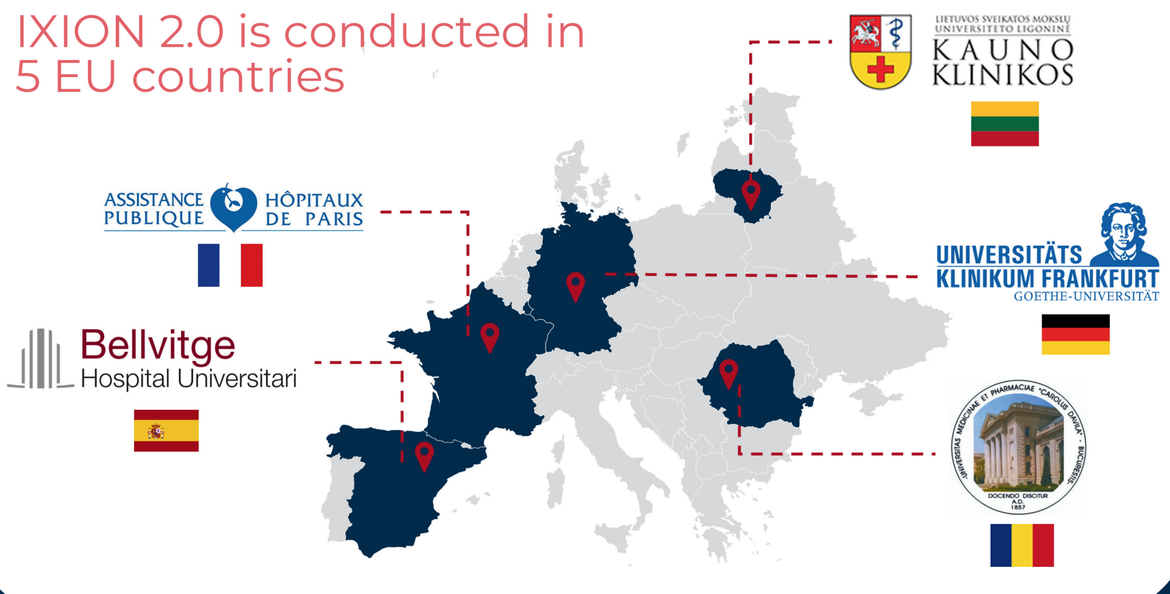
The study duration for individual patients will be maximally 28 days (plus up to 2 days of Screening period) for the main study period plus a follow up telephone call on day 60.

263 hospitalised patients with mild to moderate ARDS will be recruited for this study. Patients will be included according to inclusion and exclusion criteria.

INCLUSION CRITERIA

- Hospitalised patients with mild to moderate ARDS (Pa02/Fi02 Ratio >100 - <300 mmHg) according to the Berlin Definition of ARDS or patients with assisted breathing and high oxygen demand who fulfil the other criteria of the Berlin Definition of ARDS (modified Berlin criteria)
- Patients ≥ 18 years
- Randomization within 48h of ARDS diagnosis
- Written informed consent obtained prior to the initiation of any protocol-required procedures by the patient or his/her legal representative
- Patients or their legal representatives able to understand the requirements of the study and give written informed consent

IXION 2.0 is conducted in 5 EU countries



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