DECISION

DEcompensated CIrrhoSIs: identification of new cOmbiNatorial therapies based on systems approaches

WHY IT MATTERS

The fact that some patients suffering from decompensated cirrhosis recover, while many others die so fast, is both tragic and baffling because numerous treatments targeting specific aspects of the disease are already available, such as absorbable intravenous and oral antibiotics, oral non-absorbable antibiotics, antiviral agents, albumin, laxatives, diuretics, non-selective beta-blockers, vasoconstrictors, statins, anticoagulants, steroids, and proton-pump inhibitors. The fatal difference in the patients' response to treatment is likely explained by the large inter-individual variability of precipitating events and clinical presentations, but also by the fact that important factors involved in the pathophysiology of decompensation of cirrhosis have likely been overlooked so far. This clinical heterogeneity calls for novel and personalised combinatorial therapies according to underlying mechanisms based on each patient's genetics, gender, disease history, and physiology.

This is where DECISION comes in: The research consortium will perform multi-omic profiling of already existing large and clinically well-characterized patient cohorts, including 2200 patients with readily available standardised biobank samples. The gained knowledge will enable the development of a prognostic and a response test, and allow for novel combinatorial therapies tailored to mechanism-based groups of patients with acute decompensation of cirrhosis. The ultimate goal is, of course, to reduce the risk of short-term death following acute decompensation of cirrhosis as much as possible.

Under the aegis of EFCLIF, **DECISION** gathers the expertise from 21 different European partners to accomplish the following key aims and specific objectives:

KEY AIMS AND IMPACT

AIM 1
Understanding at systems level

- New pathophysiological concepts
- Integrative view of the pathophysiology
- Gender difference
- Relative contribution of each process
- New therapeutic targets

AIM 2
New combinatorial therapy

- Proof of concept of feasibility of systems approaches based therapy

- Mortality decline
- Limit side effects
- Reduction of economic burden
- Intellectual property
- Market opportunity
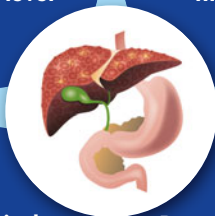
AIM 3
Preclinical models

- New models reflecting human disease
- Detailed characterization of existing models
- Parallel characterization of patients and rat features
- Ethical advances

AIM 4
Prognostic and response tests

- Identification of patients at risk
- Identification of patients that can be discharged

DECISION strives to better understand the pathophysiology of decompensated cirrhosis leading to acute-on-chronic liver failure (ACLF) at the systems level by taking advantage of already existing large and clinically well-characterized patient cohorts. The ultimate goal is to significantly reduce mortality through combinatorial therapies that are tailored to the specific needs of individual patients. Part of this endeavour is to develop a reliable prognostic test to identify patients that are at risk for a poor outcome following standard therapy but who may benefit from a novel and personalised combinatorial therapy, and a robust response test to predict the success of a novel combinatorial therapy as opposed to more aggressive solutions like a liver transplant.

Currently, amongst those patients that present with acute decompensation of cirrhosis in the clinic, 5% still die within the first month, 14% within three months, despite extensive efforts of standard medical treatment to preserve their live. We envision a future with much higher survival rates where a mechanism-based prognostic test robustly predicts which patients may have a poor outcome following standard treatment and would instead either benefit from a novel combinatorial therapy that is tailored to their specific needs or from a more aggressive strategy like a liver transplant.

OUR VISION

PARTICIPANTS

DECISION is an international research project that brings together 21 institutions from 10 European countries.

YouHealth AB (YouHealth)
Stockholm, Sweden

Nordic BioScience A/S (NordicBio)
Herlev, Dennark

Erasmus Universitair Medisch Centrum Rotterdam (EMC)
Rotterdam, Netherlands

European Liver Patients Assoicition (ELPA)
Brussels, Belgium

University College London (UCL)
London, United Kingdom

Universitätsklinikum Aachen (UKA) Aachen, Germany

Johann Wolfgang Goethe Universität Frankfurt am Main (GUF)
Frankfurt, Germany

Assistance Publique – Hopitaux de Paris (APHP)
Paris, France

concentris research management gmbh (concentris)
Fürstenfeldbruck, Germany

Commissariat à L'Énergie Atomique et aux Énergies Alternatives (CEA)
Paris, France

European Association for the Study of the Liver (EASL)
Geneva, Switzerland

Institut National de la Santé et de la Recherche Médicale (INSERM)
Paris, France

Università Degli Studi di Padova (UNIPD)
Padova, Italy

Alma mater studiorum – Università di Bologna (UNIBO)
Bologna, Italy

Fundación Pública Miguel Servet (NBM-FMS)
Pamplona, Spain

Università degli studi di Torino (UNITO)
Torino, Italy

Servicio Madrileño de Salud (SERMAS)
Madrid, Spain

European Foundation for the Study of Chronic Liver Failure (EFCLIF)
Barcelona, Spain

Fundació Clínic per a la Recerca Biomèdica (FCRB)
Barcelona, Spain

Institut Català de la Salut (ICS-HUVH)
Barcelona, Spain

Universitat de Barcelona (UB)
Barcelona, Spain

DECISION IN A NUTSHELL

FULL PROJECT TITLE
Decompensated cirrhosis: identification of new combinatorial therapies based on systems approaches

START DATE
01 April 2020

EC FUNDING
6 million €

DURATION
66 months (5.5 years)

PARTICIPANTS
21 institutions from
10 European countries

PROJECT WEBSITE
decision-for-liver.eu

DECISION ON TWITTER:
twitter.com/Decision4Liver

DECISION ON LINKEDIN:
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