



# EF Clif

EUROPEAN  
FOUNDATION  
FOR THE STUDY  
OF CHRONIC  
LIVER FAILURE

## SUMMARY OF ACTIVITIES

## 2018



**EF Clif**

EUROPEAN  
**FOUNDATION**  
FOR THE STUDY  
OF CHRONIC  
LIVER FAILURE



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LIVER FAILURE

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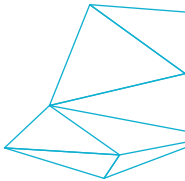
**SUMMARY  
OF  
ACTIVITIES**



**2018**

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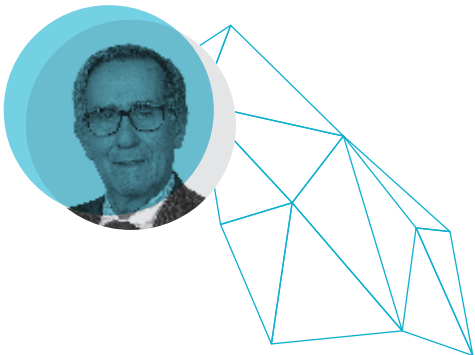
LETTER  
OF THE  
CHAIRMAN

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Vicente Arroyo

# 1. MISSION, VISION AND VALUES

The **EF Clif** is intended to support high quality research and education on **Acute on Chronic Liver Failure**, in order to improve the **quality of life** and to increase the survival of patients with **liver cirrhosis**.

Our aim is **helping investigators** to achieve their objectives and being a referent in **Acute on Chronic Liver Failure** research.

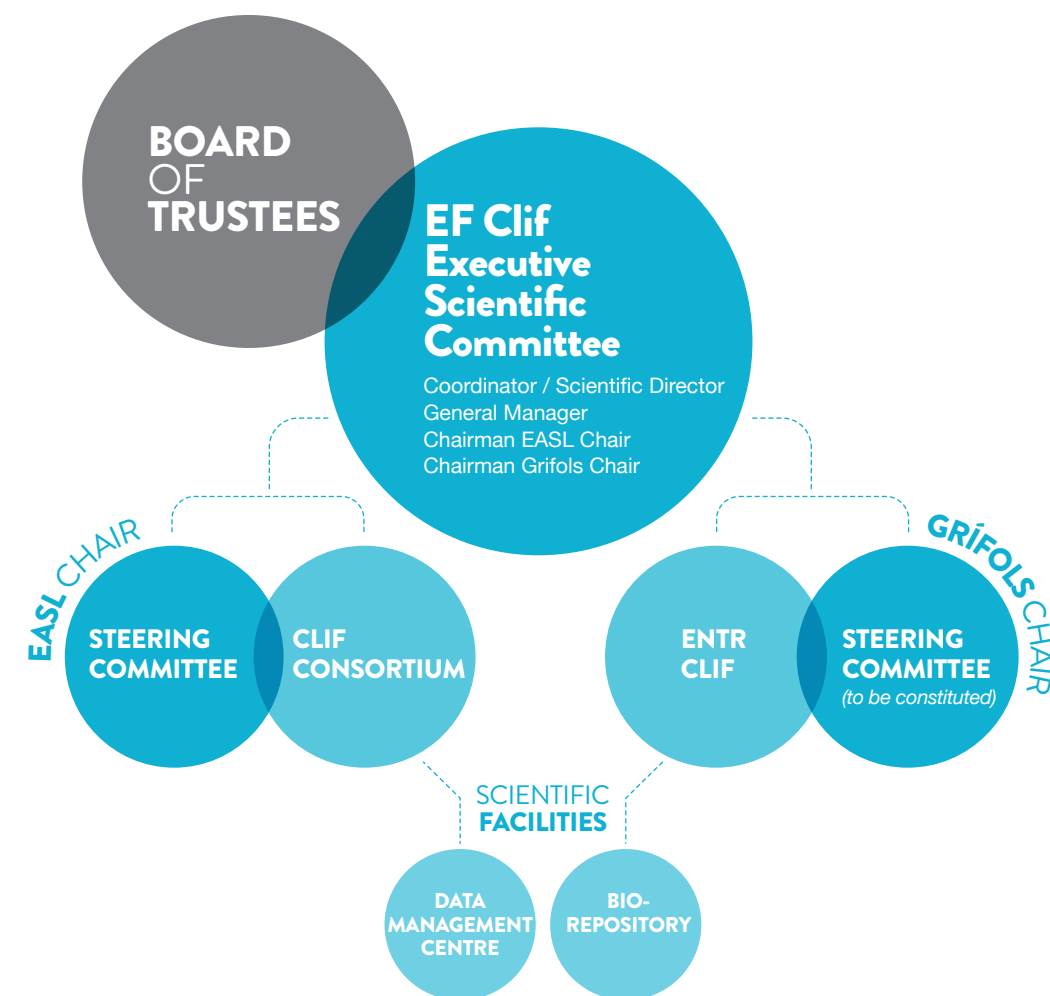


SERVICE  
INNOVATION  
HEALTH  
RESEARCH  
UNITY  
EDUCATION  
COMPROMISE

**QUALITY  
OF LIFE**

DEDICATION  
ACCURACY  
WELFARE  
DYNAMISM  
TRANSPARENCY  
COMMITMENT  
INDEPENDENCE

## 2. OUR ORGANISATION



## 3. BOARD OF TRUSTEES



**Vicente Arroyo**  
M.D.

Emeritus Professor of Medicine, University of Barcelona Medical School, Spain. Chairman of the EASL Clif Consortium. Recognition Award. European Association for the Study of the Liver.

**Main research interest**

Chronic Liver Failure, ascites, acute bacterial infection in cirrhosis and Acute-on-Chronic Liver Failure.



**Mauro Bernardi**  
M.D.

Professor of Internal Medicine at Bologna University, Italy. Director, Postgraduate School in Internal Medicine. Treasurer, European Association for the Study of the Liver. Vice-Chairman of the EASL Clif Consortium. Distinguished Service Award, Italian Association for the Study of the Liver.

**Main research fields**

Cirrhosis and related complications, hepatocellular carcinoma, chronic viral hepatitis, liver transplantation clinical aspects and treatment of alcoholism.



**Antoni Páez**  
M.D. B. Sc.

Director, Medical & Technical Department. Grifols Bioscience Industrial Group. Graduated in Medicine and Surgery from the Autonomous University of Barcelona. Graduated in Physical Science. Open University (United Kingdom).

**Main research fields**

New functions of plasma proteins.



**Ignacio Calero**  
Lawyer

Lawyer at Osborne Clarke. Graduated in Law from the Autonomous University of Madrid. Master's Degree in Corporate Legal Advice from the Instituto de Empresa Business School (Madrid, 2003).

**Main research fields**

Chronic Liver Failure, ascites, acute bacterial infection in cirrhosis and Acute-on-Chronic Liver Failure.

# 4. THE EASL CHAIR

## EASL CLIF CONSORTIUM STEERING COMMITTEE

The scientific activities of the network of hospitals organized in the setting of the **EASL Chair** are performed under the direction of a Chairman and a Vice-Chairman and of an **EASL- Clif Consortium Steering Committee** of 15 additional members.

**Paolo Angeli**  
University of Padova  
(2018-2022 Chairman of the EASL Clif Consortium)

**Vicente Arroyo**  
EF Clif, Barcelona

**Mauro Bernardi**  
Policlinico S Orsola-Malpighi, University of Bologna

**Alexander Gerbes**  
Munich University Hospital

**Pere Ginès**  
Hospital Clínic, Barcelona

**Thierry Gustot**  
Erasme University Hospital, Bruxelles

**Rajiv Jalan**  
Royal Free Hospital, London

**Richard Moreau**  
Hôpital Beaujon, Clichy

**Frederik Nevens**  
Gasthuisberg University Hospital, Leuven

**Marco Pavesi**  
EF Clif, Barcelona

**Thomas Reiberger**  
Medical University of Vienna

**Francesco Salerno**  
Policlinico San Donato, University of Milan

**Faouzi Saliba**  
Hôpital Paul Brousse, Villejuif

**Fin Stolze Larsen**  
Rigshospitalet, University of Copenhagen

**Jonel Trebicka**  
Bonn University Hospital

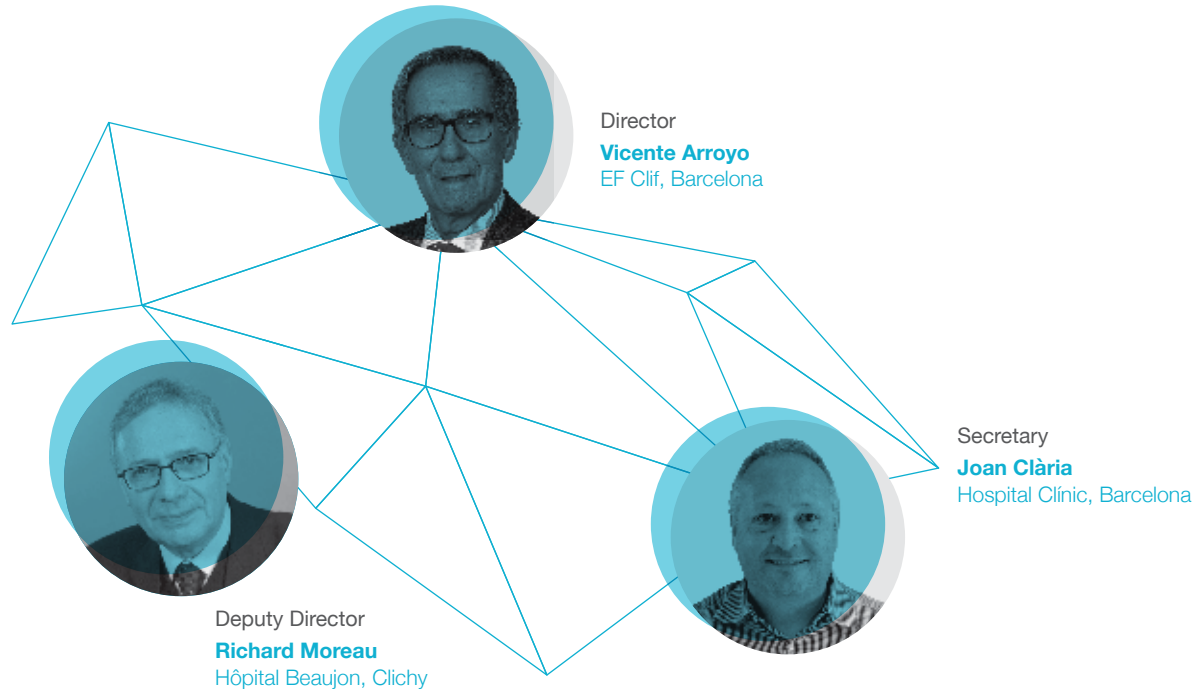
**Julia Wendon**  
King's College Hospital, London

**Reiner Wiest**  
University Clinic of Visceral Surgery and Medicine-Inselspital, Berne

# 5. THE GRIFOLS CHAIR

## EUROPEAN CLIF NETWORK OF TRANSLATIONAL RESEARCH (CLIF- ENTR). GOVERNING BOARD

The scientific activities of the **European Clif Network of Translational Research** centres, organized in the setting of the **Grifols Chair** are performed under the direction of a Director, a Deputy Director and a Secretary.



# 6. OUR STAFF

## MANAGEMENT

Managing Director

**Anna Bosch**  
**Josep M<sup>a</sup> Torner**

Administrative Assistant

**Montserrat Carreras**  
**Cecilia Ducco**

Scientific Assistant

**Yolanda Godoy**

## DATA MANAGEMENT CENTRE

Head

**Marco Pavesi**

Data Manager

**Anna Curto**  
**Carme Deulofeu**  
**Cristina Sánchez**

Statisticians

**Ferran Aguilar**  
**Àlex Amorós**  
**Anna Curto**  
**Elisabet García**  
**Carla Pitarch**

## RESEARCH ASSOCIATES

PI Predict Study

**Jonel Trebicka**

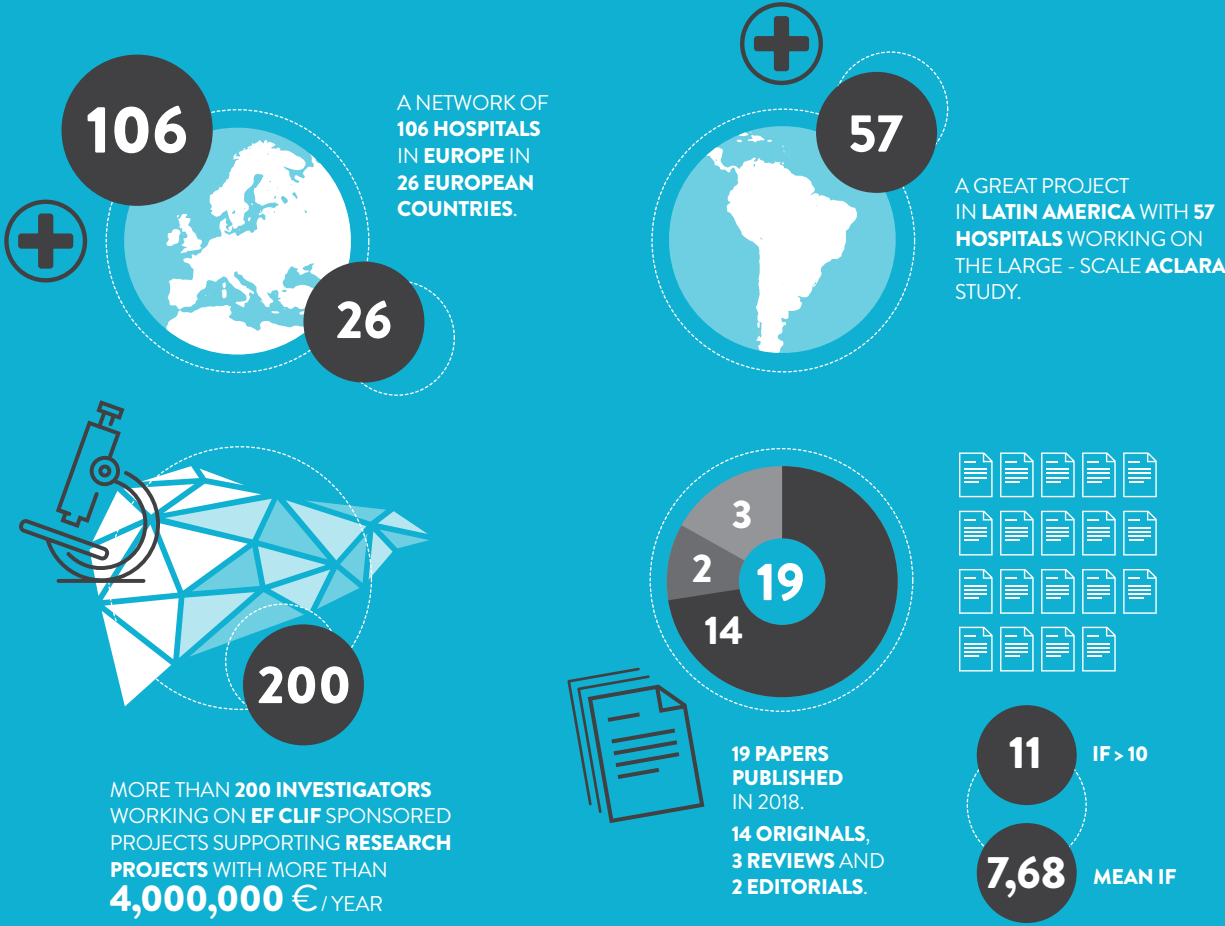
PI Apache and Preciosa Study

**Javier Fernández**

Grifols Chair Coordinator

**Joan Clària**

# 7. FACTS AND FIGURES





# 8. NEWS AND ACTIVITIES

February 07th 2018

## WELCOME TO PAOLO ANGELI AS THE NEW CHAIRMAN OF THE EASL-CLIF CONSORTIUM.

The EF Clif organized an international meeting at the Foundation headquarters, to welcome Paolo Angeli as the new Chairman of the EASL-Clif Consortium.

Among the participants, there were most of the Steering Committee Members of the EASL-CLIF Consortium, a selected group of investigators from the PREDICT Study, the Principal Investigators of the 2018 research program of the EF Clif, members of the Grifols Chair, Dr Tom Henning Karlsen, EASL General Secretary, Professors Roger Williams and Flair Carrilho.

The meeting included two sessions: In the first one, Pl's from the EASL-CLIF Consortium and the Latin-American CLIF Consortium presented the final ongoing investigations

from the CANONIC Study, the current state of the PREDICT Study and the launch of the ACLARA Study, an observational investigation starting in May 2018 assessing ACLF in 58 university hospitals from Argentina, Brazil, Chile, Colombia, Mexico, Panama, Paraguay, Peru and Mexico; and the OBSERVAH Study, a global (Europe, America and Asia) observational investigation of patients with Acute Alcoholic Hepatitis, which is planned to start in September 2018.

The second session covered the translational projects from the Grifols Chair, aimed at assessing the mechanism of systemic inflammation in acute decompensation and ACLF in cirrhosis, the immune modulatory effect of albumin, and the importance of integrated cohorts and big data in modern clinical and translational research.

After the end of the workshop, all the participants and the members of the EF Clif Staff enjoyed a dinner served by the Restaurant Gaig.



April 16th 2018

## THE EASL CLIF CONSORTIUM GENERAL ASSEMBLY AND STEERING COMMITTEE WERE HELD DURING THE EASL INTERNATIONAL LIVER CONGRESS 2018 AT PARIS.

More than 80 investigators of the EASL Clif Consortium took part in the Assembly, where the speakers gave a comprehensive overview of the latest researches in the setting of EF Clif and had the opportunity to exchange experiences.

In turn, the Steering Committee meeting broadly agreed with the inclusion of 9 new research unit in the Consortium, bringing to a total of 106 the number of centres in the EASL Clif Consortium.

May 01th 2018

## NEW VISITING RESEARCHER AT THE EF CLIF.

Dr Wenji Gu, medical investigator working on the group of Dr Hai Li in Shanghai, spent three months at the EF Clif central headquarters in Barcelona.

Dr Wenji Gu is a medical investigator, finishing her Master at the Department of Gastroenterology in Ren Ji Hospital, School of Medicine, and at Key Laboratory of Gastroenterology & Hepatology in Shanghai Jiao Tong University.

Her research is mainly focused on three related topics:

1. Describe the epidemiology of ACLF in China.
2. Establish diagnostic criteria for Chinese ACLF patients with HBV to determine whether there are universally accepted diagnostic criteria for both Eastern and Western types of the disease.
3. Explore the clinical course of ACLF patients, quantify the severity of the disease and establish a prognosis model for

both ACLF patients and AD patients. She spent 3 months working at our headquarters in Barcelona to extend her expertise on the ACLF, under the direction of Prof Vicente Arroyo, who helped her to finish some of her investigations initiated at the Shanghai Jiao Tong University.

These studies aim at improving early recognition of ACLF patients characterized by high short-term mortality, and eventually halting such epidemic.

Dr Gu stage pretends to be the first of many and falls within the initiatives of the EF Clif to pivot the role of the Foundation in the advancement of research in decompensated cirrhosis by strengthening ties between the international community and to enhances the collaboration between different study groups.



October 04th 2018

### THE PRINCIPAL INVESTIGATORS OF THE ACLARA STUDY MET DURING THE ANNUAL ALEH CONGRESS.

23 PIS participated in the work session on 21st September in Punta Cana, where they shared their views and prospects on the current state of the Project.

The discussion was focused on coordinating the efforts into reaching common act policies. Headed by the PIS of the Study, Dr Flair Carrilho, Dr Vicente Arroyo and Dr Richard Moreau and with the assistance of Dr Alberto Q Farias' Study coordinator, the meeting was also instrumental to work further on different technical aspects and establish further guidelines of the ACLARA STUDY.



October 12th 2018

### FIRST TRAINING WORKSHOP FOR THE PARTICIPANTS IN THE ACLARA STUDY.

The workshop was held on 1st and 2nd October 2018 at the Faculty of Medicine of the USP in Sao Paulo, with the participation of specialists from Argentina, Brazil and Chile.

The first session served as an introduction to the management of the samples, followed by a second one focused on the protocol guidelines and the use of the Clif-Consortium scores. During the second session, which lasted the whole day of October 2nd, the two working groups learnt about sample management and data introduction in the eCRF for the ACLARA Study through case studies.



November 7th 2018

### THE 2ND ACLARA WORKSHOP TOOK PLACE IN THE AUDITORIUM OF THE CLÍNICA MÉDICA SUR MEXICO CITY.

The workshop, which was a great success was celebrated under the patronage of Dr Misael Uribe on 30th and 31st of October 2018.

24 professionals from Brazil, Colombia, Panama, Mexico and Peru were trained in a two-days workshops, similar to the previous one held in Sao Paulo.

November 26th 2018

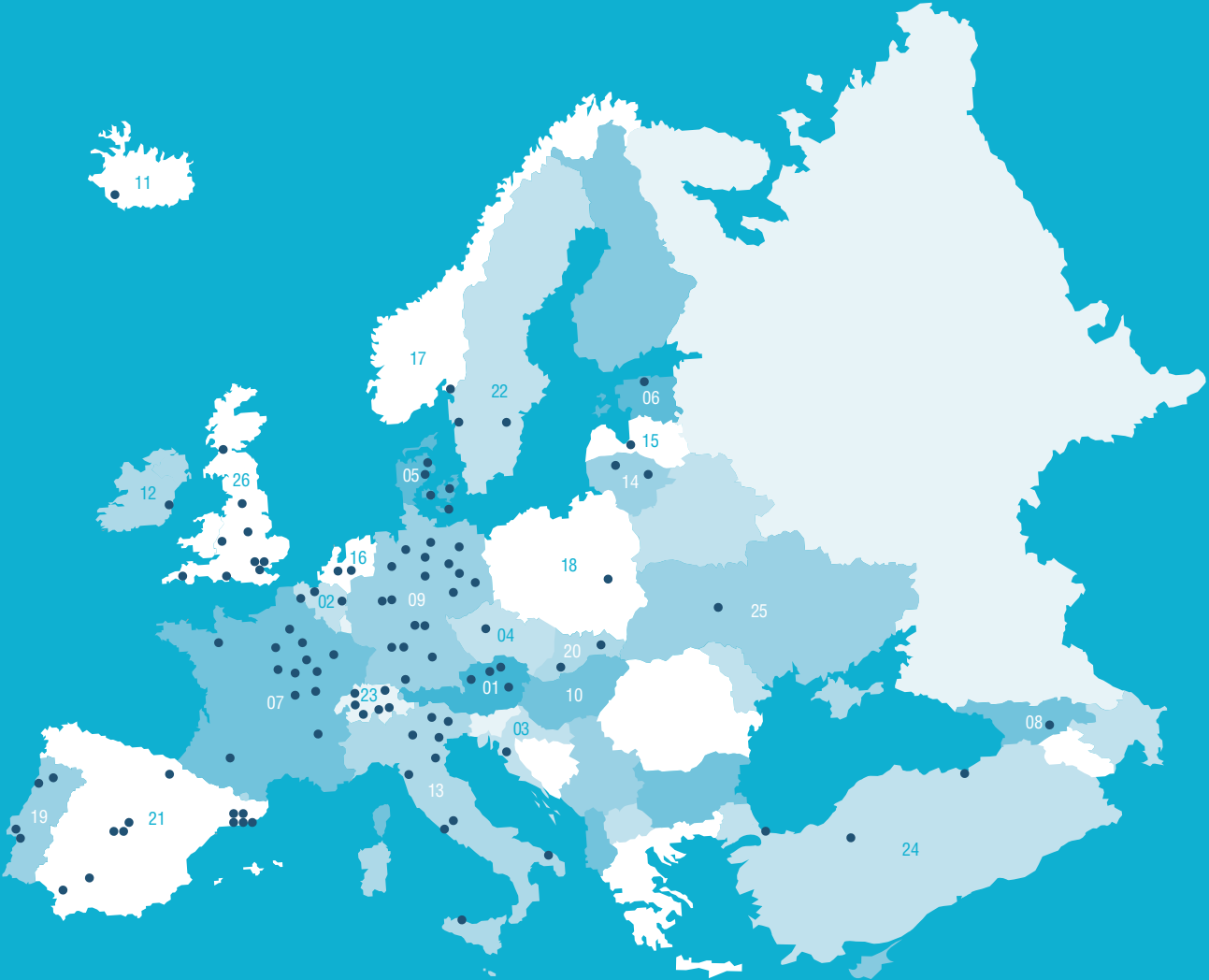
### THE ACLARA STUDY LAUNCHED.

First inclusions in the Aclara Study.

The first inclusion week of the Aclara study finished with two patients recruited in Hospital das Clinicas of Sao Paulo University.

At the end of November, there were 17 centres ready to start inclusion. The inclusion rate has grown apace, reaching 63 patients by the end of 2018.

# 9. THE CLIF CONSORTIUM HOSPITAL NETWORK & ASSOCIATED INVESTIGATORS



<b>AUSTRIA</b>  01	<b>MEDICAL UNIVERSITY OF GRAZ</b> <b>Rudolf Stauber</b> Karl Oettl Walter Spindelboeck <b>MEDICAL UNIVERSITY OF INSBROCK</b> <b>Wolfgang Vogel</b> <b>Heinz Zoller</b> Livia Dorn Ivo Graziadei <b>KLAGENFURT AM WÖRTHESSEE HOSPITAL</b> <b>Markus Peck Radosavljevic</b> <b>MEDICAL UNIVERSITY OF VIENNA</b> <b>Thomas Reiberger</b>	<b>CZECH REPUBLIC</b>  04	<b>INSTITUTE FOR CLINICAL AND EXPERIMENTAL MEDICINE</b> <b>Jan Sperl</b>
<b>BELGIUM</b>  02	<b>ERASME HOSPITAL. UNIVERSITÉ LIBRE DE BRUXELLES</b> <b>Thierry Gustot</b> <b>Christophe Moreno</b> Massimo Bocci Antonella Putignano <b>UNIVERSITY HOSPITAL ANTWERP</b> <b>GHENT UNIVERSITY HOSPITAL</b> <b>Sven Francque</b> <b>Hans Van Vlierberghe</b> Isabelle Colle Anja Geerts Xavier Verhelst <b>UZ GASTHUISBERG LEUVEN</b> <b>Frederik Nevens</b> Wim Laleman Jelle Matthijssens Len Verbeke Alexander Willmer	<b>DENMARK</b>  05	<b>AARHUS UNIVERSITY HOSPITAL</b> Henning Groenbaek Hendrik Vilstrup Niels Kristian Aagaard Stine Karlsen Moestrup oren Kragh Sidsel Rødgaard-Hansen <b>RIGSHOSPITALET</b> <b>Fin Stolze Larsen</b> Christian Mortensen <b>HVIDOVRE UNIVERSITY HOSPITAL</b> <b>Flemming Bendtsen</b> <b>NYKOEING FALSTER HOSPITAL</b> <b>Lars Martinsen</b> Stig Bondesen <b>ODENSE UNIVERSITY HOSPITAL</b> <b>Aleksander Krag</b>
<b>CROATIA</b>  03	<b>ZAGREB UNIVERSITY HOSPITAL</b> <b>Irena Hrstic</b>	<b>ESTONIA</b>  06	<b>WEST TALLIN CENTRAL HOSPITAL</b> <b>Vadim Brjalin</b> <b>Külliki Suurmaa</b>
		<b>FRANCE</b>  07	<b>CHU AMIENS – PICARDIE</b> <b>Nguyen-Khac</b> <b>CHU ANGERS</b> <b>Frédéric Oberti</b> <b>HÔPITAL MINJOZ</b> <b>Thierry Thevenot</b> <b>HÔPITAL AVICENNE BOBIGNY</b> <b>Dominique Roulot</b> <b>HÔPITAL JEAN VERDIER</b> <b>Roland Amathieu</b> <b>HÔPITAL BEAUJON</b> <b>Claire Francoz</b> François Durand Richard Moreau Pierre-Emmanuel Rautou Dominique Valla Catherine Paugam-Burtz

(\*) New centres

HÔPITAL HENRI MONDOR

**Christophe Duvoux**

HÔPITAL CLAUDE HURIEZ

**Philippe Mathurin**

HÔPITAL TENON- PARIS

**Jean Didier Grange**

HÔPITAL PITIÉ SALPÊTRIÈRE - PARIS

**Dominique Thabut**

RENNES UNIVERSITY HOSPITAL

**Pierre Brissot**

CHU TOULOUSE

**Christophe Bureau**

Jean-Marie Peron

HÔPITAL PAUL BROUSSE

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Eric Levesque

Didier Samuel

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Gocha Barbakadze

AACHEN UNIVERSITY HOSPITAL

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Pavel Strnad

UNIVERSITY OF BONN

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Frank Usner

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Tania Welzel

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HALLE-WITTENBERG

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**Valentin Fuhrmann**

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**Thomas von Hahn**

**Michael Manns**

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UNIVERSITÀ DI BOLOGNA

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**Filipe Nery**

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**José A Presa Ramos**

CURRY CABRAL HOSPITAL

**Filipe S. Cardoso**



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REPUBLIC

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UNIVERSITY IN KOSICE

**Peter Jarcuska**  
Martin Janicko

ROOSEVELT UNIVERSITY HOSPITAL  
BANSKA BYSTRICA

**Lubomir Skladany**

SPAIN

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HOSPITAL CLINIC BARCELONA

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Xavier Ariza  
Rogelio Barreto  
Joan Clària  
Javier Fernández  
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Elsa Solà  
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HOSPITAL DE LA SANTA CREU  
I SANT PAU

**Germán Soriano**

Concepción M<sup>a</sup> del Mar  
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Joan Genescà  
Macarena Simon-Talero

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Patricia Aguilar Melero  
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Francisco Mesonero

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Nigel Beaton  
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Rohit Sawhney

UNIVERSITY HOSPITALS NOTTINGHAM

**Stephen Ryder**

PLYMOUTH HOSPITAL TRUST

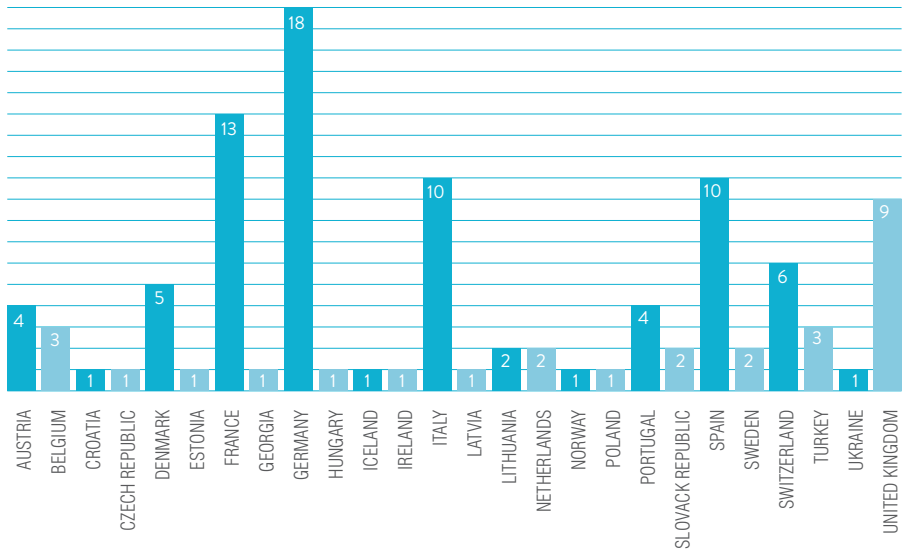
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**Matthew Cramp**

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PORTSMOUTH

**Richard Aspinall**

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**Luis Colombato**  
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**Shilpa Chokshi**  
*Foundation for Liver Research (London, UK)*

**Milagros Dávalos Moscol**  
*Hospital Edgardo Rebagliati (Lima, Peru)*

**Giovanni Faria Silva**  
*Faculty of Medicine of Botucatu, UNESP (Brazil)*

**Fernanda Fernandes Souza**  
*Hospital das Clínicas. Ribeirão Preto Medical School (Brazil)*

**Daniel Ferraz de Campos Mazo**  
*University of Campinas School of Medical Sciences (Brazil)*

**Adrián Gadano**  
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**David Gómez-Cabrero**  
*University of Navarra (Pamplona, Spain)*

**María Sarai González Huevo**  
*ISSEMyM Medical Center (Toluca, Mexico)*

**Cristophe Junot**  
*CEA (Gif-sur-Yvette, France)*

**Paulo Lisboa Bittencourt**  
*Hospital Português in Salvador (Brazil)*

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**Rita Martins Alves da Silva**  
*Regional Medical School Foundation of São José do Rio Preto (Brazil)*

**Manuel Mendizábal**  
*Hospital Austral (Buenos Aires, Argentina)*

**Gabriel Mezzano Puentes**  
*University Hospital of the Andes (Santiago, Chile)*

**Leila Maria Moreira Beltrão Pereira**  
*Institute of Liver and Transplantation of Pernambuco (Recife, Brazil)*

**Pedro Montes Teves**  
*Hospital Daniel A. Carrión (Lima, Perú)*

**Rafael Oliveira Ximenes**  
*Hospital das Clínicas. Federal University of Goiás (Brazil)*

**Martín Padilla Machaca**  
*Hospital Guillermo Almenara (Lima, Peru)*

**Alberto Queiroz Farias**  
*Hospital das Clínicas. University of São Paulo (Brazil)*

**Pierre Emmanuel Rautou**  
*Inserm (Paris, France)*

**Mario Reis Alvares da Silva**  
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**Juan Pablo Roblero**  
*Clinical Hospital San Borja Arriarán (Santiago, Chile)*

**Liliana Sampaio Costa Mendes**  
*Base Hospital of the Federal District (Brasília, Brazil)*

**Tarsicio dos Santos da Rocha**  
*University Hospital Walter Cantídio (Fortaleza, Brazil)*

**Gustavo Santos Pereira**  
*Federal Hospital of Bonsucesso (Rio de Janeiro, Brazil)*

**Carlos Terra**  
*University Hospital Pedro Ernesto (Rio de Janeiro, Brazil)*

**Claudio Toledo**  
*Austral University of Chile. Valdivia Hospital (Santiago, Chile)*

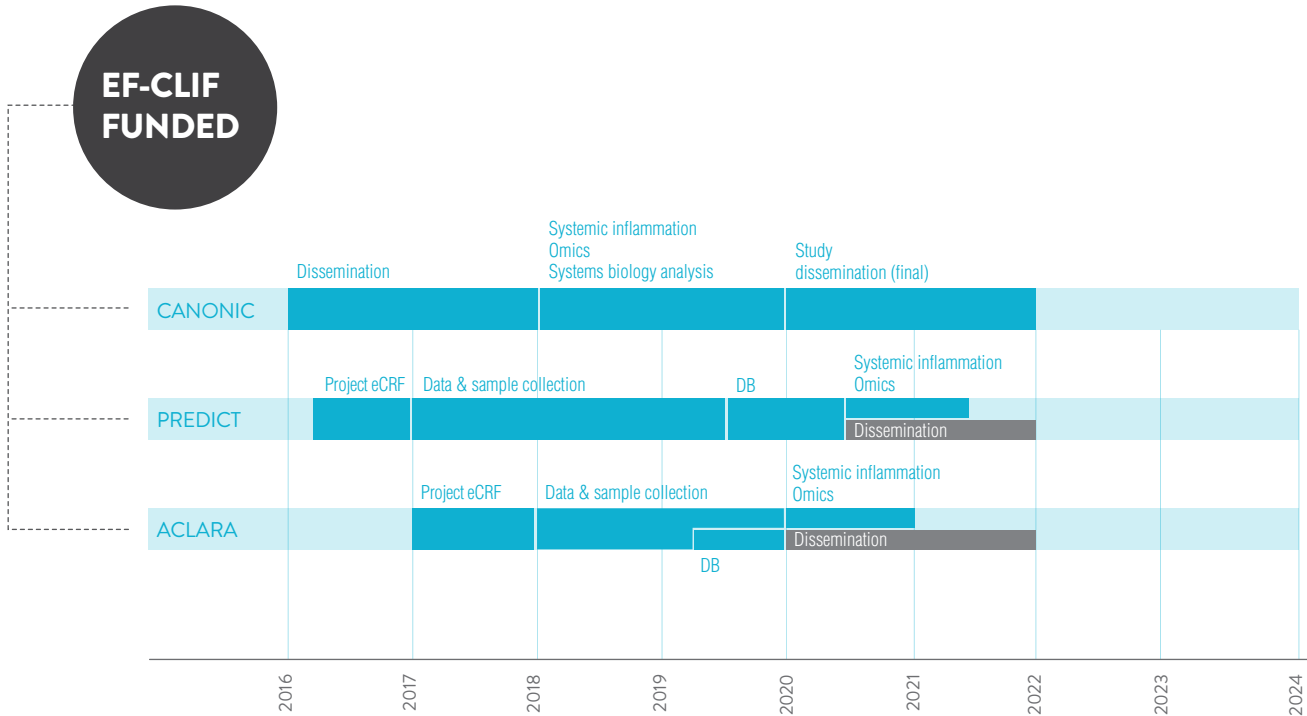
**Aldo Torre**  
*National Institute of Medical Sciences and Nutrition Salvador Zubirán (Mexico City, Mexico)*

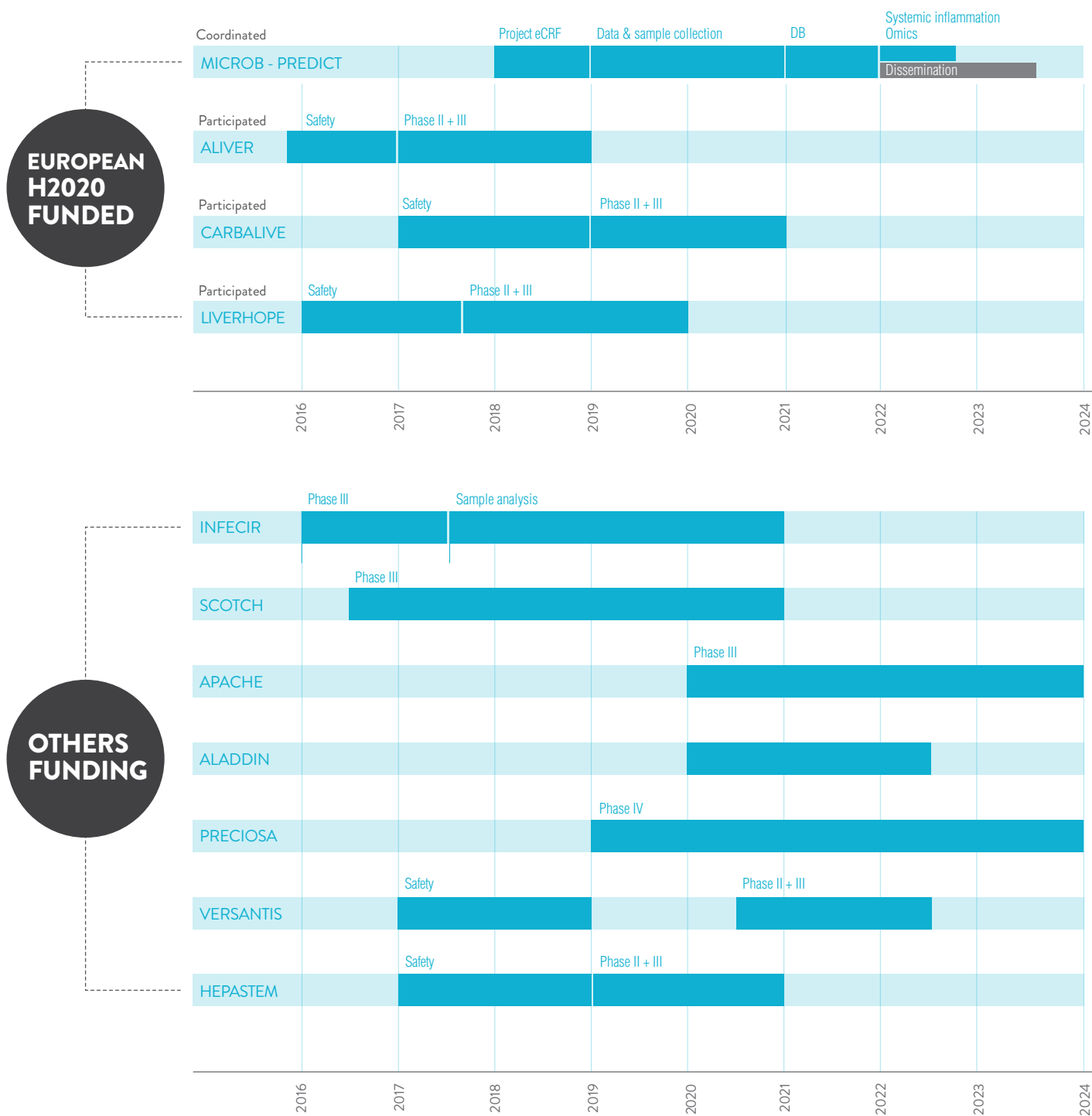
**Misael Uribe**  
*Clinica Foundation Médica Sur (Mexico City, Mexico)*

**Ângelo Zambam de Mattos**  
*Santa Casa de Misericórdia Hospital (Porto Alegre, Brazil)*

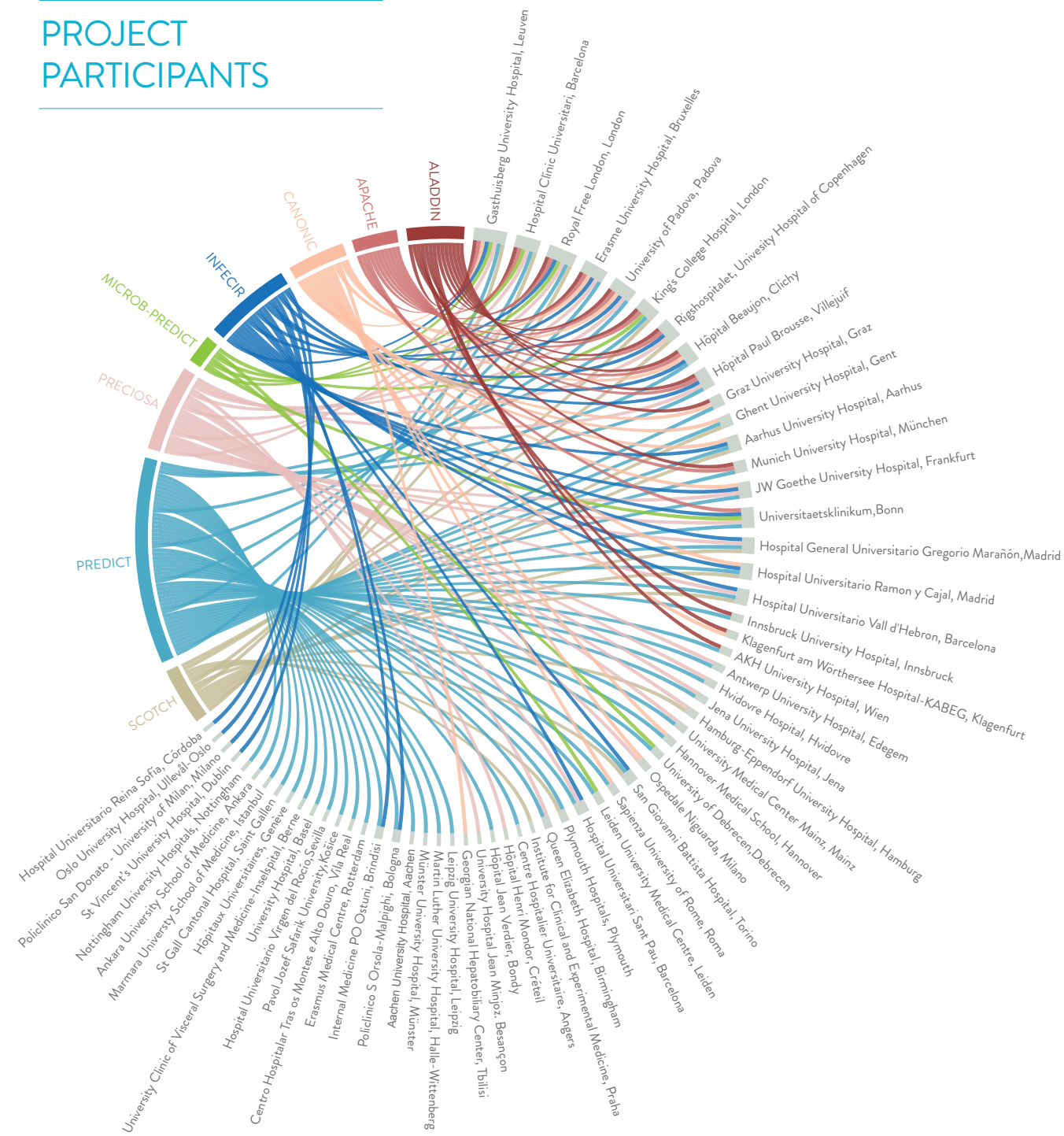
# 10. EASL-CLIF CONSORTIUM PROJECTS

## EASL CHAIR STUDIES CALENDAR



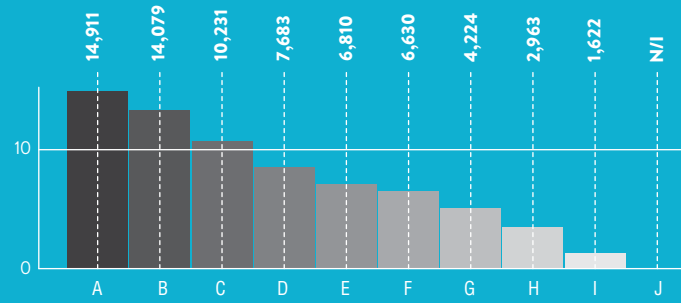


## PROJECT PARTICIPANTS



# 11. IMPACT FACTOR

## IMPACT FACTOR

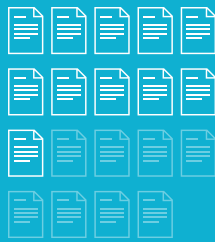


## SCIENTIFIC MAGAZINES

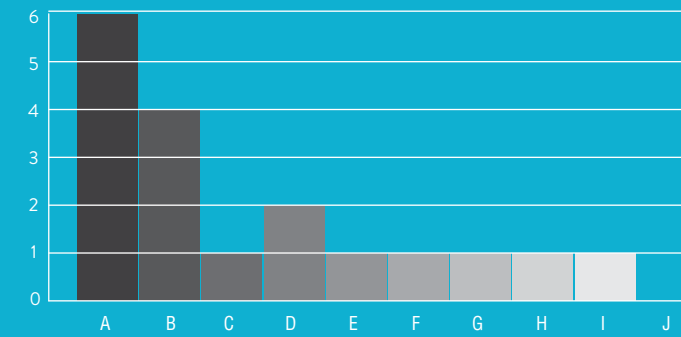
- A. Journal of hepatology
- B. Hepatology
- C. The american journal of gastroenterology
- D. Clinical gastroenterology and hepatology
- E. British journal of pharmacology
- F. Critical care medicine
- G. Journal of leukocyte biology
- H. Expert review of gastroenterology and hepatology
- I. Canadian journal of gastroenterology and hepatology
- J. Visceral medicine

## IF > 10

## TOTAL MEAN



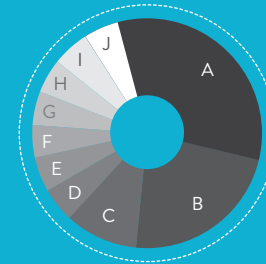
## PAPERS



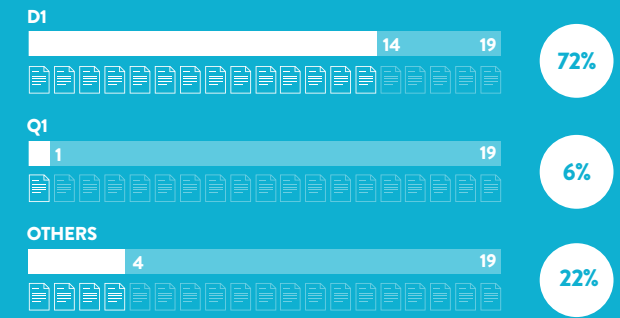
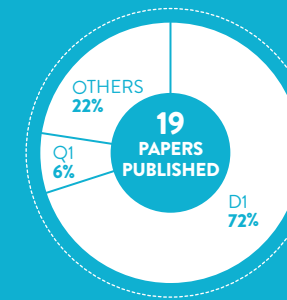
## SCIENTIFIC MAGAZINES

- A. Journal of hepatology
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- F. Critical care medicine
- G. Journal of leukocyte biology
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## CLASSIFICATION



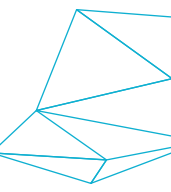
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- C. Q1 / 1D
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- E. Q1 / 1D
- F. Q1 / 1Q
- G. Q2 / 2D
- H. Q3 / 3Q
- I. Q4 / 4Q
- J. N/A







# 12. PROGRESS REPORT



# 13. SCIENTIFIC PUBLICATIONS

The scientific outcome in **2018** has consisted of **19 published articles**:

14

ORIGINALS

3

REVIEWS

2

EDITORIALS

**1. OXIDIZED ALBUMIN TRIGGERS A CYTOKINE STORM IN LEUKOCYTES THROUGH P38 MITOGEN-ACTIVATED PROTEIN KINASE: ROLE IN SYSTEMIC INFLAMMATION IN DECOMPENSATED.** Alcaraz-Quiles J, Casulleras M, Oettl K, Titos E, Flores-Costa R, Hepatology. 2018 Nov; 68:1937-1952. doi: 10.1002/hep.30135. OR

**2. MULTIDRUG-RESISTANT BACTERIAL INFECTIONS IN PATIENTS WITH DECOMPENSATED CIRRHOSIS AND WITH ACLF ACROSS EUROPE.** Fernandez J, Prado V, Trebicka J, Amoros A, Gustot T, J Hepatol. 2018 Nov 2. pii: S0168-8278(18)32511-X. doi: 10.1016/j.jhep.2018.10.027. OR

**3. LIVER TRANSPLANTATION IN PATIENTS WITH ACLF AND MULTIPLE ORGAN FAILURE: TIME FOR PRIORITY AFTER INITIAL STABILIZATION.** Fernández J, Saliba F, J Hepatol. 2018 Sep 18. pii: S0168-8278(18)32372-9. doi: 10.1016/j.jhep.2018.09.002. ED

**4. ACUTE-ON-CHRONIC LIVER FAILURE VS. TRADITIONAL ACUTE DECOMPENSATION OF CIRRHOSIS.** Gustot T, Moreau R, J Hepatol. 2018 Sep 6. pii: S0168-8278(18)32370-5. doi: 10.1016/j.jhep.2018.08.024. REV

**5. MIDODRINE&ALBUMIN FOR PREVENTING COMPLICATIONS INPATIENTS WITH CIRRHOSIS AWAITING LIVER TRANSPLANTATION.** Solà E, Solé C, Simón-Talero M, Martín-Llahí M, Castellote J, J Hepatol. 2018 Dec; 69:1250-1259. doi: 10.1016/j.jhep.2018.08.006. OR

**6. THE PROGNOSTIC VALUE OF ACUTE-ON-CHRONIC LIVER FAILURE DURING THE COURSE OF SEVERE ALCOHOLIC HEPATITIS.** Sersté T, Cornillie A, Njimi H, Pavesi M, Arroyo V, J Hepatol. 2018 Aug; 69:318-324. doi: 10.1016/j.jhep.2018.02.022. Epub 2018 Mar 8. OR

**7. DYNAMIC PROGNOSTICATION IN CRITICALLY ILL CIRRHOTIC PATIENTS WITH MULTIORGAN FAILURE IN ICUS IN EUROPE AND NORTH AMERICA: A MULTICENTER ANALYSIS.** Karvellas CJ, Garcia-Lopez E, Fernandez, Saliba F, Sy E, Crit Care Med. 2018 Aug 13. doi: 10.1097/CCM.0000000000003369. OR

**8. SYSTEMIC INFLAMMATION AND ACUTE-ON-CHRONIC LIVER FAILURE: TOO MUCH, NOT ENOUGH.** Laleman W, Claria J, Van der Merwe S, Moreau R, Trebicka J, Can J Gastroenterol Hepatol. 2018 Aug 1; 2018:1027152. doi: 10.1155/2018/1027152. eCollection 2018. REV

**9. ADVERSE EVENTS AND ACUTE CHRONIC LIVER FAILURE IN PATIENTS WITH CIRRHOSI UNDERGOING ENDOSCOPIC RETROGRADE CHOLANGIO-PANCREATOGRAPHY: A MULTICENTER MAT.** Leal C, Prado V, Colan J, Chavez-Rivera K, Sendino O, Am J Gastroenterol. 2019 Jan; 114:89-97. doi: 10.1038/s41395-018-0218. OR

**10. GUT-LIVER AXIS LINKS PORTAL HYPERTENSION TO ACUTE-ON-CHRONIC LIVER FAILURE.** Trebicka J, Reiberger T, Laleman W., Visc Med, Aug;34:270-275. doi: 10.1159/000490262. REV

**11. THE USE OF HUMAN ALBUMIN IN PATIENTS WITH CIRRHOSIS: A EUROPEAN SURVEY.** Caraceni P, Pavesi M, Baldassarre M, Bernardi M, Arroyo V, Expert Rev Gastroenterol Hepatol. 2018 Jun; 12:625-632. doi: 10.1080/17474124.2018.1460203. Epub 2018 Apr 4. OR

**12. COAGULATION FAILURE IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE (ACLF) AND DECOMPENSATED CIRRHOSIS: BEYOND INR.** Blasi A, Calvo A, Prado V, Reverter E, Carlos Reverter J, Hepatology. 2018 May 23. doi: 10.1002/hep.30103. OR

**13. ACUTE-ON-CHRONIC LIVER FAILURE, HUMAN SERUM ALBUMIN, AND IMMUNE MODULATION: THE BEGINNING OF AN EXCITING ADVENTURE.** Arroyo V, Clària J, Clin Gastroenterol Hepatol. 2018 May; 16:633-636. doi: 10.1016/j.cgh.2017.12.008. Epub 2017 Dec 12. ED

**14. ACUTE-ON-CHRONIC LIVER FAILURE: GETTING READY FOR PRIME TIME?** Bajaj JS, Moreau R, Kamath PS, Vargas HE, Arroyo V, Hepatology. 2018 Apr 24. doi: 10.1002/hep.30056. OR

**15. THE SOLUBLE GUANYLATE CYCLASE STIMULATOR IW-1973 PREVENTS INFLAMMATION AND FIBROSIS IN EXPERIMENTAL NON-ALCOHOLIC STEATOHEPATITIS.** Flores-Costa R, Alcaraz-Quiles J, Titos E, López-Vicario C, Casulleras M, Br J Pharmacol. 2018 Mar; 175:953-967. doi: 10.1111/bph.14137. OR

**16. CELL DEATH MARKERS IN PATIENTS WITH CIRRHOSIS AND ACUTE DECOMPENSATION.** Macdonald S, Andreola F, Bachtiger P, Amoros A, Pavesi M, Hepatology. 2018 Mar; 67:989-1002. doi: 10.1002/hep.29581. Epub 2018 Jan 24. OR

**17. FRONTLINE SCIENCE: SPECIALIZED PRORESOLVING LIPID MEDIATORS INHIBIT THE PRIMING AND ACTIVATION OF THE MACROPHAGE NLRP3 INFLAMMASOME.** Lopategi A, Flores-Costa R, Rius B, López-Vicario C, Alcaraz-Quiles J, J Leukoc Biol. 2018 Mar 30. doi: 10.1002/JLB.3HI0517-206RR. OR

**18. ASSOCIATION BETWEEN GRADE OF ACUTE ON CHRONIC LIVER FAILURE AND RESPONSE TO TERLIPRESSIN AND ALBUMIN IN PATIENTS WITH HEPATORENAL SYNDROME.** Piano S, Schmidt HH, Ariza X, Amoros A, Romano A, Clin Gastroenterol Hepatol. 2018 Jan 31. pii: S1542-3565(18)30105-8. doi: 10.1016/j.cgh.2018.01.035. OR

**19. PREVALENCE AND SHORT-TERM MORTALITY OF ACUTE-ON-CHRONIC LIVER FAILURE: A NATIONAL COHORT STUDY FROM THE USA.** Hernaez R, Kramer J, Liu Y, Tansel A, Natarajan Y, Hussain K, Gines P, Sola E, Moreau R, Gerbes A, Kanwal F, El-Serag H, J Hepatol. 2018 Dec 25. pii: S0168-8278(18)32637-0. doi:10.1016/j.jhep.2018.12.018. [Epub ahead of print]. OR

# 14. RELEVANCE SCIENTIFIC PUBLICATIONS

**A. Blasi, A. Calvo, V. Prado, E. Reverter, JC. Reverter, M. Hernández-Tejero, F. Aziz, A. Amorós, Cárdenas, J. Fernández.**

**Coagulation failure in patients with acute -on-chronic liver failure and decompensated cirrhosis: beyond the international normalized ratio.**

*Hepatology* 2018; 68: 2325-2337

The aim of the study was to characterize the coagulation profile in 24 patients patients with acute decompensation (AD) and 36 patients with acute-on-chronic liver failure (ACLF) and its relationship with systemic inflammation, transfusion requirements, bleeding events and short-term survival. Blood samples for thromboelastometry were obtained at admission and 72 hours thereafter. Patients with ACLF showed more hypocoagulable characteristics than patients with AD (prolonged time to initial fibrin formation and clot formation and decreased maximum clot firmness and  $\alpha$ -angle values) and higher prevalence of hypocoagulable profile (61% versus 16%). Hypocoagulativity was associated with systemic inflammation and higher short term mortality rate (45% vs 16%) but not with bleeding or transfusion requirements.

**T. Sersté, A. Cornillie, H. Njimi, M. Pavesi, V. Arroyo, A. Putignano, L. Weichselbaim, P. Deltenre, D. Degré, E. Trépo, C. Moreno, T. Gustot.**

**The prognostic value of acute-on-chronic liver failure during the course of severe alcoholic hepatitis.**

*J Hepatol* 2018; 69: 318-324.

The study analyzed the impact of acute-on-chronic liver failure (ACLF) on outcomes in alcoholic hepatitis and the role of infections on the onset of ACLF and death. The study was performed in 165 patients hospitalized at the CUB Hôpital Erasme(Bruxelles) with biopsy proved severe

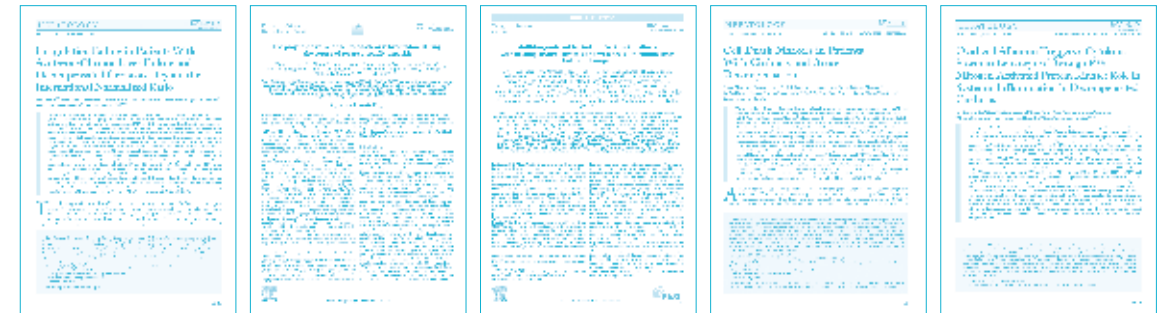
alcoholic hepatitis (investigation cohort) and in 97 patients with alcoholic hepatitis included in the Canonic study (validation cohort).The prevalence of ACLF at hospitalization in the investigation cohort was 47.9%; 17.5% additional patients developed ACLF during hospitalization. The 28-day mortality rate in the two groups were 31% and 42%, respectively. The prevalence, incidence and impact of prognosis was confirmed in the validation cohort. In the subgroup of patients developing ACLF during hospitalization, a previous infection was the only independent risk factor of ACLF. ACLF is extremely frequent in patients with alcoholic hepatitis, is associated with high short-term mortality rate, and is frequently preceded by material infections.

**J. Fernandez, Verónica Prado, Jonel Trebicka, Alex Amoros, Thierry Gustot, Reiner Wiest, Carme Deulofeu, Elisabet Garcia, Juan Acevedo, Valentin Fuhrmann, François Durand, Cristina Sánchez, Maria Papp, Paolo Caraceni, Victor Vargas, Rafael Bañares, Salvatore Piano, Martin Janicko, Agustin Albillos, Carlo Alessandria, German Soriano, Tania M. Welzel, Wim Laleman, Alexander Gerbes, Andrea De Gottardi, Manuela Merli, Minneke Coenraad, Faouzi Saliba, Marco Pavesi, Rajiv Jalan, Pere Ginès, Paolo Angeli, Vicente Arroyo, The European Foundation for the Study of Chronic Liver Failure.**

**Multidrug-resistant bacterial infections in patients with decompensated cirrhosis and with acute-on-chronic liver failure in Europe.**

*J Hepatol* 2018; doi: 10.1016/j.jhep.2018.10.027.

The aim of the study was to analyze epidemiological changes in patients with decompensated cirrhosis in 2 series of patients hospitalized with decompensated cirrhosis, the Canonic series including 1146 patients from Northern,



Southern and Western Europe investigated in 2011 and a second series of 883 patients from Eastern, Southern and Western Europe investigated between 2017-2018. A total of 455 patients developed 520 infections (39.7%) in the first series.

Nearly half of the infections were culture positive, of which 29.2% were caused by multiresistant bacteria. The prevalence of infections caused by multiresistant bacteria (38% of the culture positive infections) was higher in the second series of patients. In conclusion infections caused by multiresistant bacteria in cirrhosis is an increasing problem in Europe and extends throughout all European regions.

**S. Macdonald, Andreola F., Bachtiger P., Amoros A., Pavesi M., Mookerjee R., Zheng Y., Gronbaek H., Gerbes A., Sola E., Caraceni P., Moreau R., Gines P., Arroyo V., Jalan R.**

**Cell death markers in patients with cirrhosis and acute decompensation.**

*Hepatology* 2018; 67: 989-1002

The study was performed in 337 patients included in the Canonic study with acute decompensation (258) and ACLF (79) and additional cohorts of patients with stable cirrhosis and of healthy subjects. Caspase-cleaved keratin 18 (cK18) and keratin 18, which reflect apoptotic and total cell death, respectively, were measured in plasma. The concentration of both biomarkers increased with increasing severity of AD and ACLF. Close correlation existed between cell death markers and makers of systemic inflammation. The data suggest that cell death is an important feature of AD and ACLF and its magnitude correlates with clinical severity.

**J Alcaraz-Quiles, Alcaraz-Quiles J, Casulleras M, Oettl K, Titos E, Flores-Costa R, Duran-Güell M, López-Vicario C, Pavesi M, Stauber R, Arroyo V, Clària J.**

**Oxidized albumin triggers a cytokine storm in leukocytes through P38 mitogen-activated protein kinase: Role in systemic inflammation in decompensated cirrhosis.**

*Hepatology* 2018; 68: 1937-1953

The plasma levels of oxidized albumin forms (HNA and HNA2) were significantly increased in patients with decompensated cirrhosis (n= 256) included in the Canonic study with respect to healthy subjects (n= 48) and both forms increased gradually in the former group of patients in parallel with systemic inflammation (as estimated by the plasma levels of IL-6, IL-1 $\beta$ , TNF- $\alpha$  and ILK-8) and disease severity (from patients with compensated cirrhosis to patients with decompensated cirrhosis and with acute-on-chronic liver failure). To explore the ability of oxidized albumin to induce systemic inflammation by triggering the activation of circulating leukocytes, we prepared these oxidized albumin forms ex vivo and their posttranslational modifications monitored by liquid chromatography-quadrupole time-of-flight/mass spectrometry. HNA1 but not HNA2 increase IL-1 $\beta$ , IL-6 and TNF- $\alpha$  mRNA and protein expression in leukocytes from both healthy subjects and patients with cirrhosis. Moreover, HNA1 upregulated the expression of eicosanoid-generating enzymes and the production of inflammatory eicosanoids (PGE2, PGF2 $\alpha$ , Thromboxane B2 and leukotriene B4). Kynome analysis of peripheral revealed that HNA1 induced the phosphorylation of p38 mitogen-activated protein kinase. In conclusion, HNA1 triggers and inflammatory response in peripheral blood mononuclear cells providing a rationale for its removal and replacement by reduced albumin in the prevention of systemic inflammation in patients with advanced cirrhosis.



# 15. FINANCIAL REPORT

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**FOUNDATION**  
FOR THE STUDY  
OF CHRONIC  
LIVER FAILURE

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