

European Cholangiocarcinoma Network (EURO-CHOLANGIO-NET)

www.cost.eu/actions/CA18122

Vincenzo Cardinale, Gastroenterology Unit, Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Rome, Italy

Jesus M. Banales, Head, Liver Diseases Group, Biodonostia Research Institute-Donostia University Hospital, San Sebastián, Spain

Miguel Servet, Ikerbasque, CIBERehd, Assistant Professor of Medicine/Sciences, Mayo Clinic (USA), University Navara, Spain and University Area Andina Colombia

Q. What is a COST Action and why apply for one?

COST Actions are European Horizon 2020 competitive programs aimed to create European science and technology networks. It is a unique opportunity to promote and boost pan-European and cross-sectional collaborations working on a common central topic. COST provides networking opportunities, such as internal meetings, working group meetings, workshops and conferences, short-term scientific missions, training schools, and even dissemination meetings, for researchers in order to strengthen their capacity to address scientific, technological and societal challenges. In a nutshell, if you have an important challenge and if you have colleagues/friends prepared to take part in the effort to tackle this challenge, all you need is COST (www.cost.eu)!

Q. What is the challenge this particular action is tackling and why is it relevant?

The COST Action EURO-CHOLANGIO-NET is focused on the multidisciplinary and interconnected study of CCA Cholangiocarcinoma (CCA). CCA includes a heterogeneous group of cancers affecting the biliary tree, whose etiopathogenesis remains largely unknown.^{1,2} CCA is considered one of the deadliest cancers¹⁻⁶ and its incidence is increasing constantly and dramatically in Europe.¹⁻⁷ Accordingly, the mortality from CCA has been increasing worldwide in recent decades.³⁻⁶ On the contrary, the mortality rate of the majority of cancers decreased in the same period.⁵ Notably, CCA is the most frequent cause of cancer metastases of unknown origin,⁸ suggesting underestimation of incidence and mortality rates for CCA. Although CCA subtypes share common features, there are important inter- and intra-tumor variability affecting both pathogenesis and outcome.¹ CCA heterogeneity has limited the discovery of biomarkers and novel therapeutic options, hampering the development of tools for early diagnosis and effective treatment. CCA is commonly asymptomatic in the early stages, often being diagnosed in advanced stages, when the disease has been disseminated.^{1,2} This limits the effectiveness of the current therapeutic strategies, which are preferably based on surgical resection, owing to high CCA chemoresistance limiting clinical efficacy of anti-tumor drugs.^{1,2} As a result, CCA prognosis is dismal, with a 5-year survival rate of <20%.¹⁻² Differences in survival exist among European countries. In general, relative survival is lower in Eastern Europe than in Central and Southern Europe.⁶

In summary, CCA is a rising clinical and social problem in Europe, constituting a major challenge for researchers, clinicians, national health systems and society. Yet, coordinated multidisciplinary pan-European studies are lacking.

Q. How was the network created and how is it composed?

The application was promoted and carried out by the European Network for the Study of Cholangiocarcinoma (ENS-CCA: www.enscca.org / www.cholangiocarcinoma.eu), an open, international and multidisciplinary network of scientists created in 2015 dedicated to the study of CCA. The network sustaining this Action is composed of 27 COST member countries with a pan-European distribution, and by an international partner country, the US. The network received the endorsement of the EASL International Liver Foundation, the CCA-UK charity AMMF, and the US Cholangiocarcinoma Foundation. EURO-CHOLANGIO-NET is a coordinated open pan-European network that could be viewed as the home of European CCA research, which will virtually employ all the European research groups in different specific fields of research/interest.

Q. What are the aims of this COST Action?

EURO-CHOLANGIO-NET aims to create a cooperative, interdisciplinary European network that gathers together basic scientists, clinical investigators, charities, and SMEs in order to:

1. Close the current gaps in CCA knowledge and applications by overcoming the limitation of small sample size studies and by developing and implementing a pan-European multidisciplinary collaboration, which is necessary to dissect the multilevel heterogeneity of CCA.
2. Improve translation by generating consensus on appropriate experimental models of CCA, including systematically revising the histomorphology, pathological background, and cells of origin of the distinct models of CCA with respect to human subtype counterparts.
3. Dissect inter and intratumor heterogeneity in order to define specific features for early diagnostic purposes and set up interconnected digitalized European registries for correlation studies on: i) epidemiology, risk factors, and clinical presentation, ii) histomorphology, and iii) radiologic imaging of tumor and preneoplastic tissue.
4. To gain insights into the determination of new sensitive and specific non-invasive biomarkers for the early diagnosis of each CCA subtypes.
5. Rationalize cost-efficient target therapy for CCA by defining the driver mutations, epigenetic alterations, and transcriptome of each CCA histomorphological subtype.
6. Develop or define novel drugs and strategies.
7. Contribute to the development of the mission, vision and aspirations for a global alliance against CCA.

Q. When did this Action start operating and how long will it continue its activities?

The kick-off meeting of this Action took place in Brussels on 18th March 2019, marking the beginning of the activity which will last for four years.

Q. How can one join the Action?

European countries (both EU and non-EU countries), EU candidates and potential candidates, which comprise less research-intensive countries referred as Inclusiveness Target Countries (ITC), are COST Member Countries. When a period of 12 months has elapsed from the date of the approval of the Action, November 13th 2018 in our case, the participation of additional COST Members becomes subject to formal approval by the Action Management Committee (MC). Individuals affiliated to universities, research centres, companies or other relevant legal entities NOT located in COST Member Countries can participate to the action according to the rules of the COST association (<https://www.cost.eu/wp-content/uploads/2018/10/20180501-Vademecum2.pdf>).

Q. How will the EURO-CHOLANGIO-NET be implemented?

EURO-CHOLANGIO-NET is a coordinated Action employing European research groups in different specific fields of research/interest interconnected through Working Groups by an iterative process involving people, data registries, information and bio-banking. This Action will be organized in 7 Working Groups (WGs) dealing with interrelated aspects of CCA: Preclinical, In-Depth Histomorphological Phenotyping, Molecular Profiling, Epidemiology, Clinical Characterization and Trials, Early Diagnostic Biomarkers, Development of Novel Therapeutic Targets and Tools, Legislation and Ethics. These WGs will work to construct efficient connections, exchanges and promote capacity-building objectives (i.e. data registries, young researchers' mobility, meetings, seminars, consensus guidelines and more).

Q. What are the expected key scientific outcomes?

1. Consensus articles establishing criteria for identifying the correct preclinical models of each subtype of CCA.
2. Scientific publications on the definition of histomorphological features and criteria for the diagnosis and classification of CCA subtypes.
3. Scientific publications on liquid biopsy and molecular profiling (single-nucleotide variants, FGFR2 fusions, copy number alterations, DNA methylation profiling) of different clinical, etiological, and histomorphological CCA subtypes.

Q. Where can information be found about this Action?

An Action website will go live soon. In the meantime, please visit the official link www.cost.eu/actions/CA18122, or send an email to vincenzo.cardinale@uniroma1.it, or to jesus.banales@biodonostia.org

References

1. Banales JM, et al. Nat Rev Gastroenterol Hepatol. 2016; 13:261-80.
2. Khan SA, et al. Gut. 2012; 61:1657-69.
3. Bertuccio P, et al. Ann Oncol. 2013; 24:1667-74.
4. Smittenaar CR, et al. Br J Cancer. 2016; 115:1147-1155.
5. Llovet JM, et al. Nat Rev Clin Oncol. 2015; 12:408-24.
6. Lepage C, et al.; EURO CARE-5 Working Group. Eur J Cancer. 2015; 51:2169-2178.
7. A Report from Public Health England, National Cancer Registration and Analysis Service.
http://www.ncin.org.uk/publications/rare_and_less_common_cancers
8. Varadhachary GR, Raber MN. N Engl J Med. 2014;21; 371:757-65.