

## CA18122 EURO-CHOLANGIO-NET

### Management Committee Virtual Meeting Minutes

Monday, October 5, 2020

Time: 15:00-17:00 CEST

15:00- Vincenzo Cardinale opened the meeting and summarized the previous grant period performance- approx. €80,000 spent, which reflected the impact of the COVID-19 pandemic. The planned training school in Glasgow in March could not be held, and only 1 STSM was able to be completed. CA18122 currently has 27 countries represented on the management committee (MC). The latest additions to the action are BE, CZ, IE, LT, and RO. The training schools, mentorship program, relevant publications, Action website, standard operating procedures for the collection and storage of CCA biological samples, and GEM/CIS patient information sheets were briefly introduced.

15:05- Nathalie Warengien made a presentation on virtual meetings and networking tools during COVID-19. Dissemination was discussed. Open access can be funded for articles published by at least 3 COST full-member countries or cooperating members. Info material, graphic design (up to €1000), the action website, multimedia content, conference books and roll-ups, marketing gifts (pens, USB sticks, notebooks, bags, umbrellas), proofreading, editing, and layout expenses can also be funded under dissemination. The COST association recommends virtual meetings for the immediate future. Individual country restrictions should be carefully checked before planning any future in-person meetings. If an in-person meeting is planned, travel insurance is recommended (and is an eligible expense) and force majeure will apply for any travel prohibitions issued within 48 hours of the meeting. License fees for virtual communication tools are eligible to be reimbursed (up to €500 for the entire grant period, VAT not eligible). Local organizing support for virtual meetings will cover technical set-up expenses, IT tests with technicians, registration, attendance management, configuration and setup, communication and monitoring attendees, customer support for live-stream technical support via email or chat, and post meeting management. As a temporary measure, local organizers should obtain cancellation insurance. Local organizing support remains at €10,000, regardless of whether the meeting is in-person, virtual, or hybrid.

15:30- Vincenzo Cardinale presented a proposed modified work and budget plan (WBP) due to the COVID-19 pandemic. The modified WBP would allow more money for dissemination, particularly open access publications (open-access publications shall be a direct result of work performed by Action Participants within the topic of the Action and shall be co-authored by Action Participants representing at least 3 different participating countries. Any journal that is situated in the first three quartiles Q1-Q3 is considered of sufficient impact. COST funding must be specifically acknowledged). Prior approval of open access funding is needed and the Action Chair should be informed prior to

publication. The modified WBP also includes 2 virtual training schools and a hybrid MC meeting in Madeira Island (PT).

MC Meeting: €45,000

Training schools (2)- €20,000

STSM- €4,500

ITC- €1000

Dissemination (website)- €3000

Dissemination (meeting). €1000

Publication fees (open access)- €20,000

OERSA (bank transfer fees incurred by grant holder)- €1000

FSAC- €14,325

Total= €109,825

**The modified WBP will be sent to the MC via email for their approval.**

Rui Castro spoke about the planned hybrid MC meeting in Madeira Island (PT) (proposed dates April 8/9-April 11/12, 2021, proposed budget €35,000 for attendees, €10,000 for local organizing support). Other COST events have been held on Madeira Island. At the moment, all travelers arriving in Madeira Island are tested via PCR test for COVID-19, with results available on the same day. The test is not necessary if travelers present negative test results from within 72 hours prior to arrival. At the moment, there are 67 active cases on the island (0 deaths, 1 ICU).

15:50- Chiara Braconi briefly discussed the virtual training school in novel experimental models: from ex vivo patient-derived organoids to in vivo animal models. Speakers and the agenda remain similar to those from the previously scheduled training school in March that was canceled due to COVID-19, pending speaker confirmation. Presentations will be 20 minutes followed by a 10-minute discussion.

If Zoom is used, participants could stay connected (with possibility of sharing desktop). The moderator will introduce the speakers and guide the discussion at the end. Questions for discussion will be presented live and via chat. Presentations can be recorded.

15:55 Ana Lleo briefly discussed the planned virtual training school “Multidisciplinary management of cholangiocarcinoma clinical training school”. Main focus of the school is the multidisciplinary management of cholangiocarcinoma. The composite agenda includes all clinical specialties involved in clinical management, a clinical case presentation, and “Live Demo”. Learning objectives include the identification of challenges in the multidisciplinary management of CCA and interaction with different clinical specialties; learning about the suitability of novel CCA treatments, main

indications, and possible complications; a critical review of current clinical guidelines; identification of key open issues for cholangiocarcinoma clinical research; and learning how to advance the understanding of cholangiocarcinoma to translate basic research and preclinical findings into clinical practice.

It was stated that the training schools may receive EASL sponsorship (still waiting on confirmation of this).

16:00- Laura Fouassier presented the progress report for WG1 (preclinical) and briefly discussed the consensus published and the special issue of *Liver international* coordinated by Diego Calvisi. For the next six months, two reviews and the virtual training school on experimental models are planned, as well as the inclusion of Luke Boulter as another co-chair.

16:05- Guido Carpino presented the progress report for WG2 (in-depth histomorphological phenotyping) and briefly discussed the creation of the online ENSCCA registry (100 patients, 12 stains/patient (IHC and routine), 2 ongoing collaborative studies) and the published review and consensus. In the next six months, the ENSCCA registry will be improved through the inclusion of patients from other centers, knowledge will be developed by CCA histology and clinical pathology through the correlation of histologic data with clinical data from the ENSCCA clinical registry and with features from MRI (radiological registry) and through the application of an AI tool on specimens included in the histological registry, and a consensus on criteria for classification of CCA will be initiated by granting digital slides to 2-3 pathologists within the WG.

16:10- Trine Folseraas presented the progress report for WG3 (molecular profiling) and briefly discussed 6 recent publications from this WG. For the next six months, in order to define molecular profiling of each CCA subtype, Oslo University Hospital has agreed to fund 15-20 cases (funding application sent to AMMF but rejected for funding). To perform a genome wide association study, the WG has joined the CCA/GBC GWAS project coordinated by Prof. Lewis Roberts (Mayo Clinic, USA) and funded by the Cholangiocarcinoma Foundation.

16:15- In the absence of the chair and vice-chair of WG4 (epidemiology, clinical characterization, and trials), Jesus Banales presented the progress report. Three recent publications were briefly discussed. For the next 6 months, three tasks include the presentation, management, and outcome of patients with CCA in European countries, evaluation of the role of locoregional therapies in CCA, and validation of prognostic algorithms for CCA surgical resection, all through the use of the European CCA (E-CCA) registry.

16:20- Rocio Macias presented the progress report for WG5 (early diagnostic biomarkers). She briefly discussed five published collaborations on early tumor

biomarkers, a published consensus statement, the mentorship program (8 mentors + 8 mentees). For the next 6 months, planned projects include the international validation of a panel of protein biomarkers present in serum extracellular vesicles for the diagnosis and follow-up of PSC, CCA, and HCC, metabolomic-based prediction of prognosis in patients with PSC and early diagnosis of CCA, international validation of a panel of selected prognostic biomarkers (mRNA), validation of a panel of fibrosis- and cancer-associated biomarkers as a risk stratification tool for patients with PSC, metabolomics and miRNAs for the early and differential diagnosis of dCCA and PDAC. Two reviews are planned- 1 with WG1 and 1 with WG2.

16:25- Chiara Braconi presented the progress report for WG6 (development of novel therapeutic targets and tools). A systematic review and technical publications on the validation of tools for individualized prediction of the lack of response of cholangiocarcinoma patients to specific chemotherapy were published, with the active participation of junior members of the WG. The ACADEMIA-PHARMA meeting on drug development in CCA is planned as an in-person meeting of clinicians/researchers and representatives of the pharmaceutical industry and health authorities (European location/Q3-Q4 2021). Two original articles describing the molecular bases of mechanisms of chemoresistance to available drugs for the treatment of cholangiocarcinoma were published. Projects for the next six months include identification of targetable FGFR2 somatic mutations in iCCA patients, the use of preclinical models (organoids) as a flexible platform to investigate the effect of gene modulations in drug response in vivo, a vaccination program in cholangiocarcinoma, modulating necroptosis as therapeutic opportunities in CCA to entail both the inhibition of necroptosis to halt early liver cancer development and lineage commitment as well as the activation of necroptosis to overcome chemoresistance in liver cancer therapy, drug screening (established, repurposing, novel) on a platform of several preclinical CCA models, generation of a drug library including compounds developed by WG6 members that can be tested on a pool of preclinical models to identify leading compounds for first-in-human studies leading to clinical investigations.

16:30- Cecilia Rodrigues presented the progress report for WG7 (legislation and ethics). Ongoing work includes the organization and coordination of MTAs and the transfer of samples among countries, the supervision of data storage and data sharing, and the administration of the registry database. In the next 6 months, a virtual meeting with COST Action participants, the industry advisory committee (SME representatives), patient association, scientific society, and foundation advisory committee is planned in order to brainstorm around ethics and legal issues on academia-industry collaborations towards a “code of conduct”.

16:35- Helen Morement introduced AMMF: The Cholangiocarcinoma Charity. She briefly recapped some statistics, including that diagnosis is often late and few survive

beyond 1 year of diagnosis. This may be exacerbated by lack of awareness among medics, late diagnosis, lack of awareness regarding treatment and clinical trials, and the unavailability of molecular profiling. This situation can be improved with improved data recording (AMMF/Public Health England CCA data project) and recoding at an international level. ICD-11 has recoded CCA. This situation can also be improved by increased national and international awareness (ENSCCA, Global CCA alliance), supporting collaborative research, and the development of new improved therapies (new insights into early and correct diagnosis, molecular profiling, target therapies).

16:40- Stacie Lindsey introduced the Cholangiocarcinoma Foundation (CCF). Strategic plan involves supporting and educating patients, investing in and growing the CCA research field, and getting basic research resources into public space. Regarding patient services, CCF has maintained a discussion board since 2006 (16,000+ topics, 83,000+ posts) more than 360 videos on YouTube with almost 100,000 views, almost 14,000 Facebook followers, and monthly support groups through Zoom. Industry presence includes the industry council, patient advisory boards/surveys, investigator advisory boards/surveys, and collaborative projects (FDA, nutrition, newly diagnosed). Professional presence includes the scientific/medical advisory board, nursing advisory board, international cholangiocarcinoma research network and monthly webinars, and research fellowships/grants. A key resource is the patient-derived models repository (PDMR) which also includes the thai cell line project. Another resource is cBioPortal, which takes hard-to-interpret genomic and clinical data and provides a suite of user-friendly, easy-to-read visualization and analysis options. The CCF conference was held virtually in July and attended by 1650 registrants from 44 countries. The next conference is scheduled for March 31- April 2, 2021.

16:45- Rui Castro gave an update on the EURO-CHOLANGIO-NET website ([eurocholangionet.eu](http://eurocholangionet.eu)) and highlighted the ongoing updates, especially to the news section that is updated every 2 months. He recapped the call for a social media manager and introduced the two new social media managers, Francisco Romero and Diletta Overi, who are both early career investigators.

16:50- Chiara Gabbi gave an update on the mentorship program. Program consists of a 6-month distant mentoring activity in which contacts between Mentee and Mentor occur every 30-45 days via phone/teleconference and the opportunity to visit the Mentor's institution by applying for a COST short-term scientific mission. Mentees should be PhD students, medical residents, or postdoc students at an EU institution and have at least 1 paper or abstract published on CCA. Ten mentors from 6 countries and 9 mentees from 6 countries applied, and 8 were selected. Next steps include mentor/mentee surveys, STSMs for mentor/mentees, and the launch of the call for the next program (summer 2021).



17:00- Meeting was adjourned and participants were thanked for their attendance and contribution.