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Project full title: TRAINING IN TRANSLATIONAL PROTOCOLS FOR MINIMAL INVASIVE DIAGNOSIS AND THERAPY IN PANCREATICO-BILIARY CANCERS

D1.2 ACTION PLAN
FIRST UPDATE

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1. Excellence

Pancreatico-biliary cancers are a leading healthcare concern and their burden is increasing in many EU countries, but especially in Central and Eastern Europe. The International Agency for Research on Cancer (IARC) has published new data on the worldwide incidence of cancer in which they estimate 19.3 million new cancer cases diagnosed and almost 10 million cancer-related deaths worldwide in 2020. **Pancreatico-biliary cancers account for ~5% of the global cancer burden** and the incidence of these cancers has been constantly increasing in the past years. This is complicated by the fact that the real number of biliary tract cancers is difficult to assess, as intrahepatic biliary cancers are generally combined with hepatocellular carcinoma for reporting purposes. Despite extensive efforts to improve treatment, including the development of new drugs, the prognosis for advanced stages of hepato-pancreatico-biliary (HPB) cancers still remains very poor. Thus, the mortality rate of pancreatic cancer (PC) is almost equal to its incidence, making it one of the most fatal malignant tumors. Furthermore, **estimates show that PC is predicted to be the second leading cause of cancer death around 2030**. Moreover, Central and Eastern Europe is already ranked 1st or 2nd place in the E.U. in terms of age-standardised incidence and mortality for pancreas, gallbladder and liver (including intrahepatic bile ducts) cancers, respectively. Better diagnostic and treatment strategies are needed to improve the grim prognosis of these diseases. Multiple studies have confirmed the utility of minimally invasive techniques in dealing with patients with pancreatico-biliary cancer, whilst multidisciplinary approaches brought substantial benefits for patients, health systems, and society as a whole.

The most important challenges that face the use of precision medicine tools in pancreatico-biliary cancer patients are the lack of well-established training programs and the fact that most of the procedures are technically demanding. To address these issues, we propose the **TRIP** project where trainees from UMFCD will gain first-hand knowledge and experience in the field of early diagnosis and therapy of pancreatico-biliary cancers from leading institutions such as UCL, AMC and RHH. The trainees will initially practice procedures without involving patients, e.g. by using simulators, physical phantoms or live animals. This approach can lead to a faster and more complete achievement of procedural competence, as it allows the novice to train in a stress-free and low-risk environment, which in turn spares patients from undue complications. Furthermore, clinical or translational researchers from the involved Gastroenterology, Oncology or Surgical Departments will be embedded in PhD tracks, based on the infrastructure that promotes and supports both education, but also excellence in the doctorate level training of PhD candidates, as highly qualified future professionals in an international environment.

The overall aim of the project is to strengthen the strategic partnership of UMFCD (and its affiliated hospitals), located in Romania, one of the Widening countries, with two internationally-leading counterparts at the EU level (RHH in DENMARK, AMC in the Netherlands and UCL in the UNITED KINGDOM) in order to enhance scientific collaboration and networking activities among these institutions and to combine their skills and competences in the field of pancreatic cancer screening strategies, minimal invasive endoscopic / laparoscopic interventions used for early diagnosis / staging, but also for personalised therapy.

1.1 Objectives

The proposed consortium of this project will be coordinated by the **University of Medicine and Pharmacy "Carol Davila"** (with its affiliated hospitals: **Central Emergency Military Hospital Dr. Carol Davila**, **Elias Emergency University Hospital**, **Fundeni Clinical Institute - CEMT**), based in Bucharest, ROMANIA, one of the countries in the Widening region. The consortium will include two European leading research institutions: **RHH with Copenhagen University Hospitals Herlev (RHH)** – DENMARK, **University College London (UCL)** – UNITED KINGDOM and Amsterdam Medical Center (AMC) – NETHERLANDS.

The current proposal is the result of **previous long standing collaboration and joint multicentric research projects** developed and performed by the three partners of the consortium. Thus, in the past 20 years, there was a sustained **clinical research activity in the field of minimal invasive endoscopic and laparoscopic procedures, supported by various national and international grants of the key-persons involved in the TRIP proposal.** These lead to a constantly growing research track record, across the EU, in the field of image-guided minimally invasive procedures used for the diagnosis and treatment of pancreatico-biliary diseases. This joint effort has already resulted **in clinical practice guidelines, structured reviews, original peer-reviewed science publication, congress presentations and participation during endoscopy and surgery live-demos. The partnership is further detailed in section 3.2.**

Table 1.1 Short description of partners and their contribution to the TWINNING project TRIP

Participant	Role in the project	Contribution to twinning	Benefit for the partner
UMF Carol Davila, Bucharest (Central Military Emergency Hospital Dr. Carol Davila, Elias Emergency University Hospital, Fundeni Clinical Institute - CEMT), Bucharest, R**OMANIA**	Project coordinator	UMFCD will provide access to CEMT facilities and data regarding gastrointestinal disorders from the Eastern Europe region that is not sufficiently covered in most European studies.	UMFCD will be the coordinator and the main beneficiary of the project in terms of its impact (and budget). The project implementation will improve the research profile of UMFCD and its staff. Upgrading the current research management unit of UMFCD will be achieved by fully utilising the experience and best practices of the internationally leading partners.
RHH (Copenhagen University Hospitals Herlev), Copenhagen, **DENMARK**	Partner 1	RHH will bring multidisciplinary expertise covering advanced pancreatico-biliary endoscopic procedures and utilization of organoid cultures for pharmacotyping. RHH will provide access to CAMES (Copenhagen Academy for Medical Education and Simulation) for hands-on training activities.	RHH will use capacities of the UMFCD clinical affiliated hospitals to support new research activities with impact on pancreatico-biliary disorders in the region.
Academisch Medisch Centrum bij de Universiteit van Amsterdam, **NETHERLANDS**	Partner 2	AMC will bring multidisciplinary expertise in minimally invasive hepato-pancreatico-biliary (HPB) surgery and GI cancer screening strategies. AMC experts will contribute to the development of a pancreatic cancer screening program and a high-risk clinic at PAH.	AMC will benefit from the development of research activities with impact on HPB disorders at UMFCD by the widening of its current research to other parts of Europe - current HPB research include very few Eastern European cohorts.
University College London (UCL Hospital and Royal Free Hospital), London, **UNITED KINGDOM**	Associated Partner	UCL's previously established joint research initiatives overlapping developments related to endoscopic interventions will be key to identifying novel areas for multi-disciplinary clinical development and research innovations. UCL currently leads the pancreatic cancer screening initiatives, the expertise being instrumental for this proposal.	UCL will benefit from the instrumental capacities and expertise available at UMFCD clinical affiliated hospitals for hybrid endoscopic minimal invasive interventional procedures. The new partnerships and joint projects facilitated through the TRIP proposal will lead to new research and clinical opportunities in this key interface.

To reach the overall aim, the **specific objectives of the project** are:
O1. **To strengthen the research excellence of UMFCD in the field of precision medicine tools** used for the early diagnosis and minimal-invasive therapy of pancreatico-biliary cancers;
O2. **To enhance the scientific visibility of UMFCD and open new strategic networking opportunities** (joint project applications, secondments of young researchers and senior staff) with the internationally leading counterparts (RHH/UCL/AMC);
O3. **To increase the competitiveness of UMFCD in national, EU and international research grant competitions** (competitive individual grant applications, joint collaborative project applications);
O4. **To develop new (and ongoing) joint research projects in the field of endoscopic minimal invasive interventions of pancreatico-biliary cancers**, with emphasis also on translational components;
O5. **To develop a multicentre protocol for a research project on pancreatic organoid cultures** derived from EUS-FNB specimens in patients with pancreatic cancer;
O6. **To improve UMFCD researchers' and research support staff profiles with a special reference to early stage researchers (ESRs)** (PhDs / postdocs of the Widening country institution & mentors from the partner institutions) that will benefit from the increased inwards and outwards mobility;
O7. **To expand innovation and raise reputation at UMFCD (and its affiliated hospitals)** based on intensive training in clinical research through:
- O7.1 **Introduction of new innovative medical services performed for the patients, including a second opinion platform and a high-risk clinic**;
- O7.2 **Dissemination and outreach activities based on specific research results of the early-stage researchers** including common workshops, conference attendance, publication of articles and reviews;
- O7.3 **Development of a second opinion website** to be used for cases uploaded from all over the country, with tumor board functions used to determine the best possible cancer treatment and care plan for individual patients;
O8. **To strengthen the research management capacities and administrative skills of the staff working in institutions from the Widening country** (UMFCD and its affiliated clinical hospitals).

The objectives will be achieved through a carefully planned and coordinated set of activities, including visits and lectures of international experts participating in the twinning project, joint workshops, seminars and summer schools, research visits of junior scientists at the partner institutions, co-tutoring of Ph.D. students and post-doctoral fellows, participation in conferences, and trainings to enhance competencies of researchers and research support staff. The proposed activities will help to unlock and fully exploit the UMFCD (and its affiliated hospitals) research and innovation potential and allow it to become a sough- after partner in international research consortia.

1.2 Coordination and/or support measures and methodology

1.2.1 Coordination and/or support measures

The proposed project fully complies with the specific challenges and scope of the Twinning Coordination and Support Action as set out in the Widening Participation and Spreading Excellence Horizon Europe (HORIZON) Work Programme (**HORIZON-WIDERA-2021-ACCESS-03-01**). It responds to the need of strengthening research and innovation performance of low-performing Member States and Associated Countries through knowledge transfer, networking activities and exchange of best practice with internationally-leading research institutions.

Table 1.2. Individual challenges of the project and how these are being addressed

HORIZON-WIDERA-2021-ACCESS-03: Twinning	How TRIP addresses the Call	Covered by WP
"Twinning aims to enhance networking activities between the research institutions of the Widening countries and top-class leading counterparts at EU level by linking it with at least two research institutions from two different Member States or Associated Countries."	The key aim of the TRIP project is to broaden the existing expertise of UMFCD (and its affiliated hospitals) in the management of pancreatico-biliary cancers by building new expertise in the field of **pancreatic cancer screening strategies** and **minimal invasive hybrid endoscopic / laparoscopic procedures**. This will allow for closer collaboration of UMFCD with advanced partners on development of new approaches to study the opportunities of early diagnosis / staging, as well as personalised therapy for patients with pancreatico-biliary cancers. The project partners will transfer their expertise (RHH / AMC / UCL) to UMFCD, with emphasis on PhD students and ESRs, which will significantly enhance the UMFCD profile in the area of screening and early cancer detection, as well as minimal invasive therapies. **This knowledge**	WP 2-3-4

	transfer and capacity building will be achieved through: (i) joint research activities and academic collaboration, (ii) enhanced staff mobility, secondments and exchanges, (ii) education and training activities for academics and support staff, (iii) joint workshops, summer schools and dissemination events.	
"Twinning proposals should have to clearly outline the scientific strategy for stepping up and stimulating scientific excellence and innovation capacity in a defined area of research as well as the scientific quality of the partners involved in the twinning exercise. A research component not exceeding 30% of the total Horizon Europe grant may include an exploratory research project. This will open opportunities for integrating smaller research activities and by this strengthening the commitment and the engagement of the twinning partners."	The twinning project introduces a **strong translational research training programme** with emphasis on pancreatic cancer screening, hybrid endoscopic / laparoscopic surgical techniques and personalised therapy for pancreatico-biliary cancers. Apart from the increased research performance of UMFCD and contributing to building the critical mass of research expertise, the ambition of the project is to translate the research results into innovative services and a high-risk clinic at UMFCD for HBP patients. **Another aim of the TRIP project is to develop a multicentre research protocol on pancreatic organoid cultures derived from EUS-FNB specimens in patients with pancreatic cancer**, thus closing the still apparent research and innovation gap within Europe in this field.	WP 2-3; WP 7
"Proposals should also focus on strengthening the research management and administration skills of the coordinating institution from the Widening country. This should take the form of a dedicated work package or task, placing emphasis to specific activities, in view of helping the staff of the coordinating institution to improve their proposal preparation and project management/administration skills."	The Twinning project will introduce PhD students and ESRs from UMFCD to the advanced research culture established in the partner institutions (UCL/RHH/AMC). Such practices will also be adopted in UMFCD, including improvement of the human resources development policy, better career planning, regular staff evaluation, increased mobility, international evaluation of the institution, support for preparation of competitive grant applications. **Upgrading the current research management / administration unit of UMFCD** is certainly beneficial, being achieved by fully utilizing the experience and best practices of the internationally leading partners. **This is a concrete deliverable of the Twinning exercise.**	WP 1, 2-4
"Such a strategy should include a comprehensive set of activities to be supported. These should include at least a number of the following: short-term staff exchanges; expert visits and short term on-site or virtual training; workshops; conference attendance; organisation of joint summer school type activities; dissemination and outreach activities. As far as appropriate these activities should take into account the gender equality plans of the participants."	**ESRs at all three institutions, but particularly in UMFCD, will be key players in all project activities**, including the mobility actions (short-term staff exchanges, expert visits and short-term on-site or virtual training workshops), conference attendance, joint summer schools, internships and best practice sharing. A specific work package is dedicated to the enhancement of the research profile of ESRs, including PhD students. They will benefit not only from training activities, workshops and summer schools, but especially from exchanges and joint research activities, as well as co-tutoring of their research projects, papers and thesis coordinated jointly by senior staff from all project partners. Gender equality plans are clearly covered in the framework of the TRIP project.	WP 4
"The Twinning proposals should illustrate quantitatively and qualitatively the expected potential impact of the twinning exercise within the coordinating institution (and possibly at regional/national level)"	Indicators such as expected future publications in peer reviewed journals, collaboration agreements with businesses, intellectual property, new innovative products or services, number of international students, number of women scientists and their roles in the research institutions are clearly detailed in a dedicated WP concerning Dissemination and Communication.	WP 6

Early detection of HPB cancers allows definitive local treatment, resulting in excellent survival rates. Primary prevention and early detection have therefore become a major goal worldwide. **Pancreatic cancer screening programs** currently include high-risk patients, defined as patients with family history (including first-degree relatives of patients with pancreas cancer with at least 2 affected genetically related relatives), patients with genetic syndromes and no family history (ATM, CDKN2A/p16, STK11, PRSS1), as well as patients with genetic syndromes and pancreatic cancer family history (BRCA1, BRCA2, PALB2, MMR, Tp53) (Aslanian et al, 2020). Nevertheless, **there are no screening programs or high-risk clinics in Romania**, sustained training efforts in this field being highly beneficial for the research and healthcare system. Furthermore, new-onset diabetes can be considered an early manifestation of pancreatic cancer, leading to various predictive models aimed for risk assessment analysis (Gallo et al, ESMO Open 2021). Clear delineation of biomarkers (CA 19-9, circulating tumor DNA, micro-RNA alterations, etc.), as well as development of state-of-the-art imaging methods like artificial intelligence (AI) - assisted contrast enhanced ultrasound (CEUS) or computer tomography (CECT) might further improve early detection of pancreatic cancer (Pereira et al, Lancet Gastroenterol Hepatol 2020). More direct interventions among those at elevated risk of HPB malignancies are thus highly encouraged in an effort to improve their grim prognosis. RHH has long-standing experience for the early diagnosis and minimal invasive therapy of pancreatico-biliary cancers, whilst UCL and AMC are one of the leading institutions for the pancreatic cancer screening program. **Consequently, enhanced networking, translated expertise and educational support from these institutions are needed to develop screening and early detection strategies in Romania and neighbouring countries.**

Organoids are a promising new development for translational research and precision medicine in oncology. At RHH, pancreatic **organoid culture development** and **organoid response to a variety of chemotherapeutic agents** is currently tested and the methodology will be transferred to UMFCD. **A multicentre research protocol will be developed on pancreatic organoid cultures, genomic characterization and pharmacotyping for patients with pancreatic cancer**. Moreover, the diagnostic and therapeutic paradigm of HPB cancers is shifting from an open surgical approach to a minimally invasive endoscopic / laparoscopic alternative, especially for early diagnosis, but also for accurate staging and minimal invasive therapies like radio-frequency or microwave ablation (RFA / MWA) or irreversible electroporation (IRE). Drainage procedures are nowadays performed based on advanced endoscopic techniques like endoscopic ultrasound (EUS) and/or endoscopic retrograde cholangiopancreatography (ERCP). As imaging technologies expand to include image-guided anatomical navigation and endoscopic / laparoscopic techniques evolve to accommodate increasingly complex interventions with minimally invasive approaches, endoscopists and surgeons have developed a novel area of hospitals around the world known as the hybrid operating room.

As technology continues to accelerate, endoscopists, surgeons and oncologists rely on each other to bring these new advances to patient care, improving patient outcomes. Hybrid minimal-invasive interventions are a very effective treatment method especially for high-risk patients and for the treatment of complex pancreatico-biliary diseases. Leading hospitals RHH / UCL / AMC have developed hybrid operating rooms to diagnose and treat pancreatico-biliary malignancies and there is a need to exploit these techniques to Eastern EU countries such as Romania in order to improve overall EU citizen health. Translated expertise, in the form of training and educating early ESR, from RHH / UCL / AMC in the field of pancreatico-biliary diseases and minimal invasive endoscopic / laparoscopic interventions is needed to increase the number and quality of innovative services. Furthermore, development of the field of palliation and supportive care research is an essential component for the development of improved healthcare patient services, with minimization of further disparities in between EU centres.

1.2.2 Overall methodology

The translational / clinical training activities proposed in the TRIP project will be focused on the following focused research areas (**Figure 1.1**):

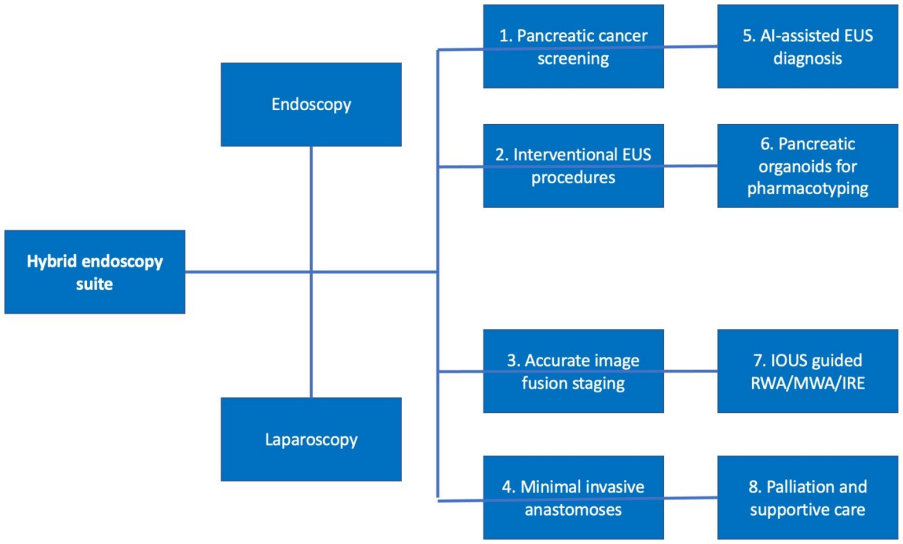


Figure 1.1 Areas of translational / clinical research training and mentoring proposed in the TRIP project.

1. Structuring of a high-risk clinic and training for pancreatic cancer screening program

A pancreatic cancer screening algorithm will be specifically developed for UMFCD (and its affiliated hospitals), using a multidisciplinary approach and taking into consideration circumstances particular to UMFCD, including the following: specific patient population, services, structure and clinical information. The screening algorithm will be developed in close collaboration with the partner institutions (UCL / RHH / AMC). This pilot screening program will provide guidelines and protocols for screening and early diagnosis of pancreatic cancer and will offer training for clinicians / researchers in cancer prevention and control. The ultimate goal is to create a **high risk clinic** (**Figure 1.2**) where patients with key risk factors for pancreatic cancer will be offered services such as risk assessment, screening investigations (AI-enhanced contrast-enhanced US & EUS, and/or MRI/MRCP), genetic counselling and ongoing surveillance (a personalized plan will be developed for regular monitoring).

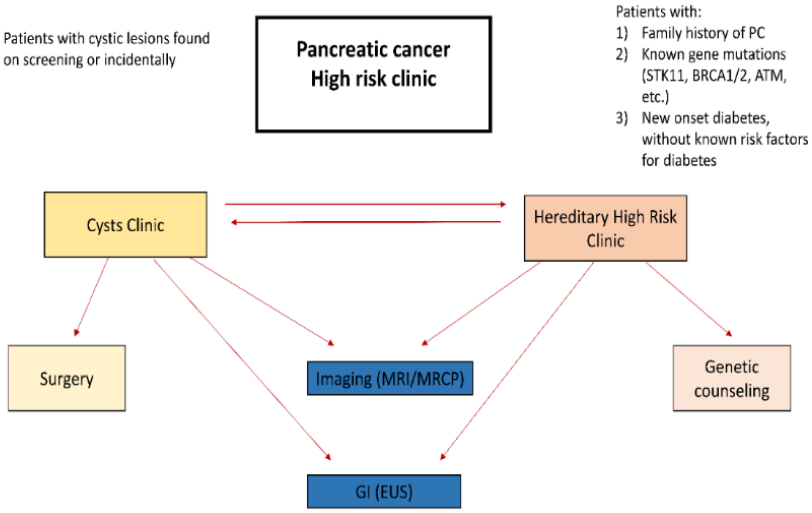


Figure 1.2 Development of a high-risk clinic at UMFCD.

Definition of high-risk patients will be based on published clinical practice guidelines (in accordance with the expertise of internationally leading institutions RHH / UCL / AMC), including patients with familial PC (first-degree relatives of patients with PC with at least 2 affected genetically related relatives), as well as patients with specific genetic syndromes (incl. Peutz-Jeghers, hereditary pancreatitis, Lynch, Li-Fraumeni, etc.) (Aslanian et al, 2020). One of the most important subgroups is represented by **patients with new-onset diabetes**, which have an 8-fold increased risk of PC in the first 36 months following diagnosis. As various predictive models are currently developed for risk analysis of these patients, **we envision a complex AI platform developed by the consortium members**. The model should include various biomarkers (CA 19-9, circulating tumor DNA, micro-RNA alterations, etc.), as well as state-of-the-art imaging methods like contrast-enhanced ultrasound (CEUS) or computer tomography (CECT) / magnetic resonance imaging (MRI/MRCP). Based

on the multidisciplinary expertise of project partners in the field of AI, PhD students and young clinicians will be actively involved in the **training and testing of an AI-assisted clinical practice screening algorithm** for these patients.

2. AI-assisted EUS imaging diagnosis

EUS is the method of choice for the examination of focal pancreatic masses, even for small masses with a negative contrast-enhanced CT (Dietrich et al, Gastrointest Endosc 2016). Various imaging techniques like elastography and contrast-enhanced EUS are currently employed for the differential diagnosis of pancreatic masses, yielding the concept of **multiparametric EUS examinations.** Furthermore, the team in UMFCD and RHH was leading the field of advanced imaging through the publication of several multicentre studies that highlighted the role of these techniques (Costache MI, Endosc Ultrasound 2020; Saftoiu A, Jinga M et al, Endosc Ultrasound 2019; Ignee A et al, Endoscopy 2018; Saftoiu A et al, Gastrointest Endosc 2015; Saftoiu A et al, Clin Gastroenterol Hepatol 2012; Saftoiu A et al, Gastrointest Endosc 2008;). Artificial intelligence has been recently employed to enhance the capabilities of multiparametric EUS differential diagnosis of focal pancreatic masses, with a deep learning model based on a hybrid convolutional and long short-term memory neural network recently proposed (Udristoiu AL et al, PLoS One 2021). One of the desired approaches is to further implement real-time AI techniques into the clinical practice, whilst the resulting software algorithms could be used for the clinical decision management in all the institutions of the TRIP consortium. Development of a future multicentre study will lead to future publications in peer reviewed journals and collaboration agreements with software businesses interested in the marketing of AI solutions for EUS.

The methodology for AI will integrate deep learning (DL) with EUS-FNB in order to improve the intra- and inter-observer analysis for fast and accurate pathology diagnosis of focal pancreatic masses. The machine learning algorithms related to image feature extraction and classification, convolutional neural networks (CNNs) have been widely proven to be superior to traditional algorithms. These networks provide the flexibility of extracting discriminative features from images preserving the spatial structure and could be developed for region recognition and classification of medical images. In our project, DL algorithms for localization and segmentation will be trained and optimized to: 1) find normal / tumor tissue regions of interest (ROIs) in WSI; 2) label ROIs (normal acini, pancreatic adenocarcinoma, neuroendocrine neoplasia, metastases, chronic pseudotumoral pancreatitis, etc.); 3) compute ROIs bounding box with the corresponding coordinates and 4) segment ROIs by producing a mask that gives pixel-wise segmentation of focal pancreatic mass.

3. **Advanced pancreatico-biliary procedures**

Several multicentric trials and multi-institution surveys have also been performed related to the accuracy of **EUS-guided fine needle aspiration (FNA) and fine needle biopsy (FNB)** (Vilmann P, Saftoiu A et al, Scand J Gastroenterol 2013; Guo, Saftoiu, Vilmann et al, Endosc Ultrasound 2020). Usage of **through-the-needle confocal laser endomicroscopy (nCLE) during EUS examinations** has also been established as a ground-breaking technique for the differential diagnosis of solid and cystic pancreatic masses. Several papers were published in collaboration with RHH concerning the usage of EUS-nCLE in solid pancreatic masses (Karstensen JG et al, Pancreas 2015; Karstensen JG et al, Endosc Int Open 2018). However, new avenues of research are still open for this fascinating technique, especially by using real-time image-analysis with conventional or targeted stains for the evaluation of patients with pancreatic diseases (Ungureanu BS et al, Diagnostics 2020). For cystic masses, **EUS-guided through-the-needle microbiopsy** has also found its utility, as shown in a recent systematic review of our group (Balaban VD et al, Endosc Ultrasound 2021). All these pathology techniques can also be assisted by various deep learning algorithms (Naito Y et al, Nature 2021) that could improve the accuracy of diagnosis, opening up potential research studies in the involved institutions and acting as a source for increased mobility (inwards and outwards) of qualified young researchers (including doctoral candidates).

4. Pancreas organoids and pharmacotyping

At RHH, protocols have been recently established on **utilization of pancreas organoid cultures derived from the aspirated EUS-FNB tumor cells and further used for pharmacotyping**. Training in organoid cultures includes purification and culturing of epithelial and stromal cells from EUS-FNB samples, pathological and mutational analysis (including NGS techniques) of the grown organoids as well as the baseline EUS-FNB sample for comparison. Furthermore, **organoid response to a variety of chemotherapeutic agents** is currently tested and the methodology will be transferred from the leading EU institutions to UMFCD. The trainees will have the chance to increase their knowledge of translational research & practice through short-visits at the partner institutions to obtain hands-on experience in ongoing projects under the mentorship of established investigators. Furthermore, various workshops and virtual presentations will be organized with focus on time management, scientific presentations, scientific writings, grant preparation and professional development skills.

5. Accurate image-fusion staging

Image fusion is an emerging concept that refers to the integration and merging of visual information from various imaging modalities, for e.g. EUS and (PET)-CT/MR. The major advantages of combining various imaging techniques include the ability to compare findings from one modality to another and the overall improved visualization of the target lesions for diagnosis and image-guided interventions. Therefore, image fusion seems to be promising for managing pancreatic-biliary cancer as it is expected to allow for a more precise lesion characterization with higher accuracy in tumor detection, staging, and therapy guidance. A specific software and hardware platform of **EUS image fusion based on electromagnetic navigation** has been developed through the IDEAR project (in collaboration with SINTEF and Trondheim Hospital, Norway), where a few of the project members were actively involved. Furthermore, a similar platform has been developed at UCL through a grant awarded by Cancer Research UK. Thus, clinical training of young clinical researchers will be performed using an advanced fusion imaging platform for diagnosis, staging, and follow-up of pancreatico-biliary cancer patients. The system will be initially tested on phantoms and animal models. Feasibility testing and training will also be performed with an assisting robotic system for navigating flexible instruments like biopsy needles, guidewires or catheters (including Spy-Glass cholangioscopes / pancreatoscopes) inside the pancreatico-biliary tract.

6. Endoscopic / intraoperative ultrasound (EUS/IOUS) guided ablation procedures

Because of the aggressive behaviour and the poor outcome of PC after medical treatment, ablative therapies became an appealing option in local treatment for pancreatic tumors. RFA is currently the most frequent ablative technique used for pancreatic tumor ablation and can be performed with ultrasound guidance either percutaneously, intraoperatively or using EUS. Advantage of MWA over RFA ablation is mainly represented by the lower heat sink effect, shorter time of ablation, higher temperatures and a better predictability of the ablation area. In comparison with RFA ablation, studies using MWA are scarce. The challenge is whether to introduce this local therapy as a part of the multimodal treatment (chemo-radiotherapy) in patients with locally advanced, inoperable, non-metastatic PC in order to obtain a better local tumor control, an increase in overall survival and identifying predictive and prognostic factors induced by immunomodulation. To the best of our knowledge, these methods are not available currently in Romania. Hence, introduction of **IOUS- or EUS-guided RFA / MWA** would be very important for the clinical research environment, but also for the patients that might benefit from a newly introduced innovative procedure. Furthermore, based on the recent experience with irreversible electroporation (IRE) developed at RHH, this could be also introduced as a pilot study in a small number of patients.

7. Minimal-invasive EUS-guided anastomoses

Young doctors involved in clinical research protocols will be trained to perform different interventional **pancreatico-biliary procedures under EUS / ERCP guidance**. This includes various procedures like choledocoduodenostomy, hepaticogastrostomy and pancreaticogastrostomy. All techniques of **EUS-guided tissue access** (FNA / FNB), but also **various types of drainages** (including double flanged covered expandable metal stents) will be initially performed for structured training purposes on various experimental models (hands-on training in 3D printed synthetic models, *ex-vivo* animal models and small animal live models), followed by supervised hands-on training in the hybrid endoscopy rooms. A dedicated model of competence measures will be used, derived from the experience of tutors coming from the leading EU institutions (RHH / UCL / AMC). Theoretical experience will be derived from established professional societies guidelines (EFSUMB / ESGE), where members involved in the TRIP proposal hold key positions.

8. Palliation and supportive care research

Palliative EUS / ERCP procedures in complex pancreatico-biliary cancer patients have been described in various settings, including for e.g. EUS-guided celiac plexus radiofrequency ablation as a novel pain treatment option. Nevertheless, advanced cancer patients are inherently plagued by inequalities of patients' access to specialist palliative care (SPC), yielding to an increased symptom burden and low quality of life for these patients, especially in the setting of Eastern European healthcare systems. Most of the training activities for the medical / nursing procedures will be set-up on hands-on training in 3D printed synthetic models, ex-vivo animal models, small animal (pig) live models) or directly in the hybrid operating rooms (for selected patients with complicated drainage procedures in advanced pancreatico-biliary cancers) at the participating institutions (RHH / UCL / AMC). Selected movies will be uploaded in the specialized educational platform of the project (DIGITS). A program of training for **advanced palliative endoscopic techniques** would be also started based on the skills transfer from RHH/UCL/AMC, for the SPC of complex patients. This will lead in the future to an improved management of these complex patients, through the unfolding of a joint workshop involving SPC researchers, but also other caregivers and patient family representatives.

The following projects are ongoing and will certainly unfold during the following 3 to 6 years, especially based on the support from the funding provided in the TRIP proposal. These projects will **generate** sustainability and will lay the ground for future collaborative grants submitted by the TRIP consortium (**Table 1.4**).

Project	Short description	Key persons involved
PEACE protocol (not funded) **-** Perfusion Assessment With Contrast-Enhanced EUS in Locally Advanced and Metastatic Pancreatic Cancer – international study (National Institute of Health ClinicalTrials.gov Identifier: NCT03513198), including UMFCD in collaboration with other centers from EU, USA and Asia [2019-2023]	Patients with unresectable pancreatic cancer have a poor prognosis. The analysis of prognostic factors before treatment may be helpful in determining the best therapeutic strategies. The aim of the PEACE study is to assess the vascularity of pancreatic malignant tumors using contrast-enhanced harmonic EUS (CEH-EUS) and to clarify the prognostic value of tumor vascularity in patients with locally advanced and metastatic pancreatic cancer. Hereby, we present the protocol of a prospective, nonrandomized, single-arm, multicenter study aiming to assess changes in tumor vascularity using CEH-EUS before and after treatment initiation in patients with unresectable, locally advanced/metastatic pancreatic cancer and to examine the correlation between vascular changes and treatment response, progression-free survival and overall survival. **Output:** 1 protocol published in Endoscopic Ultrasound https://www.ncbi.nlm.nih.gov/pubmed/31249159	**Mariana Jinga Adrian Săftoiu Irina Cazacu Peter Vilmann Stephen Pereira**
PANC-ORG protocol - Prediction of chemotherapeutic response using pancreatic cancer organoids derived from diagnostic biopsies	In this study, we aim to establish advanced co-cultures consisting of patient derived organoids from pancreatic ductal adenocarcinoma (PDAC) and stromal cancer-associated fibroblasts. Tissue for culture establishment is acquired from the diagnostic sample using endoscopic ultrasound guided fine needle biopsies. We will perform drug screening tests on the co-cultures, with the intent to compare their response with the clinical outcome of patients receiving chemotherapy. In this way, we attempt to validate patient derived organoids and co-cultures as a predictive tool for patient chemotherapy response, paving the way for precision medicine in the treatment of PDAC.	**Peter Vilmann, Pia Klausen, Simon Ezban Gruetzmeier**
PancFusion project (not funded) - Pancreas Image Fusion Platform [2019-2023]	To summarize, the main objective of the proposal is to create an endoscopic / laparoscopic (robotic) ultrasound image integration platform with (PET)CT / MR imaging in order to: a. Improve accuracy of targeted biopsies leading to better diagnosis and less toxicity ; b. Allow for better placement of fiducial markers c. Identify areas where more radiation therapy could lead to ablation and increase survival and control; d. Allow for repeat biopsies after each treatment regimen (chemotherapy, surgery, and radiation) to gauge therapy success and drive future care in a personalized manner; e. Allow for focused delivery of alternative treatments such as ablation + brachytherapy or drug delivery; f. Improve assessment of tumor microenvironment including immune infiltrates before and after therapies; g. Improve the planning and guidance during laparoscopic surgery	**Adrian Săftoiu Stephen Pereira Irina Cazacu**

2. Impact

2.1 Project's pathways towards impact

TRIP project will have a significant impact on the research performance and excellence of the UMFCD in the field of minimal invasive interventions performed for pancreatico-biliary patients in the hybrid endoscopy room. Both qualitative and quantitative impact factors will be assessed during the project period based on the reinforcement of a sustainable framework for the scientific strategy of the UMFCD and its affiliated hospitals. This will certainly increase the visibility of researchers, as well as the competitiveness of clinical research teams in the field of minimal invasive procedures, thus enhancing the attractiveness and reputation of UMFCD both within Romania and the other EU/EAA countries. These effects will be evident on both short-term and long-term. In the short-term there will be an increase in the number of publications with high impact and visibility, as well as submission of common project proposals asking for funding; and, in the medium- and long-term there will be an active and sustainable participation in research and innovation networks developed during the project.

2.1.1. Improvement of the research excellence and innovation capacity of UMFCD

- **The upgraded research unit of UMFCD** (with integrated research management and technical support services) will support a critical mass of ESRs and senior doctors / professors, needed to boost the number and quality of national, EU and internationally competitive research funding applications, as well as the number of successfully implemented prospective collaborative multicentre projects.
    - This will be linked with **grant applications** for the European Regional Development Fund (ERDF), the European Social Fund (ESF) and the Cohesion Fund to set-up new infrastructures as needed to support new research themes and an increased number of PhD and ESRs.
- The **increased number of translational research trials and prospective multicentric protocols** generated by the TRIP proposal skills transfer will consequently induce an increased number of PhD students and early-stage researchers (ESRs) in all consortium institutions, including successful applications for national or international funding for such academic positions.
    - Two of the projects (**PEACE** and **PANC-ORG**) will certainly unfold during the project period, involving ESRs from all 4 institutions in a collaborative, multicentric work environment
    - Another project concerning fusion imaging in the hybrid endoscopy room will be based on the collaboration established between the EU partners and MD Anderson Cancer Center, Houston, Texas, USA. Thus, an image-guided (based on magnetic navigation) fusion platform will be used for training purposes in the OR, during combined endoscopic / laparoscopic procedures.
- Development of a new **high-risk clinic** at UMFCD (initially for patient with pancreatic diseases, especially pancreatic cysts) will be based by the skill transfer and increased mobility (inwards and outwards) from AMC and UCL, leading institutions for the PC screening program, as well as from RHH which had a long-standing implication in the colorectal cancer screening program. An increase in the quality of services is expected to be offered to pancreatico-biliary patients from Romania and neighbouring countries.
- Translated expertise from UCL / RHH / AMC in the field of hybrid endoscopy rooms and minimal invasive interventions will certainly increase the number and quality of **innovative services** introduced at UMFCD such as: minimal-invasive fusion imaging guided endoscopic procedures, minimal invasive EUS-guided anastomoses, EUS/IOUS-guided radiofrequency ablation (RFA) or microwave ablation (MWA), palliative procedures like EUS-guided radio-frequency ablation (RFA) of the celiac trunk etc.
- Quality in **human resources education and training** at UMFCD will be significantly enhanced by the transfer of structured competence measures for training developed at CAMES (based at RHH) or the systematic approach to clinical guidelines and technical reviews developed at UCL and AMC, thus enhancing the mutual long-term exchange of people in between the involved institutions.

2.1.2. Enhanced reputation and attractiveness of UMFCD based on improved networking channels

- Training activities set-up at UMFCD will be based on the long standing expertise of the leading EU institutions and will significantly increase the number and quality of jointly organized hands-on training workshops.
    - Three **postgraduate training courses** will be organized, with courses and hands-on training in 3D printed synthetic models, ex-vivo animal models, small animal live models and hybrid simulation.
    - Three **workshops with teamwork hands-on training and live-demo** will be organized during the project period, benefiting from the local presence of EU experts.
    - One **summer school** will be organized at UMFCD with participation of experts from all centres.

- **Common organization of webinars and live video courses** with transmission from partner centres with real-time but also store-and-forward of educational movies into a common repository created during the project period will certainly enhance the quality of educational and training programs for all institutions involved.
- Interlinked management of human resources encouraging international mobility of PhD students / ESRs and senior doctors based on the scientific networks developed during the project unfolding.
    - **Co-tutoring of the projects** between the involved institution will be successfully performed through involvement of ESRs and senior clinical researchers from leading institutions.
- Introduction of **new innovative medical services** performed for the patients, including a second opinion platform will increase the reputation of UMFCD as a tertiary hospital with integrated multidisciplinary services for high-risk oncology patients.
    - A continuous process of networking will ensure the **translation of information** from the flagship affiliated hospitals of UMFCD to other hospitals and clinics in Romania and neighbouring countries, through the workshops organized yearly and other dissemination channels (**website, webinars, social media**), as well as involvement of professional societies.

2.1.3. Improved capability to compete for national and international competitive research funding

- Capacity building for **successful funding of multicentric basic and clinical protocols, as well as translational grant applications** based on the **upgraded research unit management and administrative services**. These will include the enhancement of training capabilities of ESRs in the setting of pancreatico-biliary cancers, as a support framework for future research grant applications.
    - **Virtual and LiveDemo workshops** will be organised with focus on time management, scientific presentations, scientific writing, grant preparation and professional development skills, thus leading to an increased excellence and competitiveness of individual researchers of UMFCD.
- Development of **at least 5 individual and multicentre clinical protocols** together with all partners, with the active support of the administration of clinical affiliated hospitals.
    - Personalized approach for pancreatico-biliary cancer patients, including NGS and organoids.
    - Innovative minimal-invasive endoscopic procedures: EUS-guided fiducial placement, EUS-guided anastomoses, EUS / IOUS-guided RFA / MWA / IRE, etc.
    - Clinical applications of image-fusion (based on magnetic navigation).
    - Competence measures for the translational research procedures environment.
- Individual applications for **competitive funding for mobility and PhD / postdoctoral fellowship applications** (individual Romanian Executive Unit for Financing Higher Education, Research, Development and Innovation - UEFISCDI, Marie Sklodowska-Curie) will benefit of improved training of ESRs involved and co-tutored by EU leading scientists.
- Writing of **at least 2 major research grant applications**, based on the research excellence developed during the project and the continuous professional development of human resources supported by the project. These will be submitted as either competitive Research Intensive Actions of the newly launched Horizon Europe, or other EU or EEA structural funding programs (for e.g. Norway grants).
- **Increased patient flow towards the high-risk clinic** with inclusion of patients into innovative clinical trials, leading to a lower morbidity and mortality of these high-risk populations.
- A **second opinion website** will be built for cases uploaded from all over the country, with tumor board functions used to determine the best possible cancer treatment and care plan for individual patients.

2.1.4. Increased number and quality of scientific output

- Increased number of **original collaborative and multidisciplinary oral presentations and posters** presented at important gastroenterology, oncology and surgery congress (UEG, DDW, ASCO, ESGE Days, EUROSON, ECR, ESMO, EURO-EUS, EGEUS will be preferentially targeted) international meetings.
- Increased quantity and quality of publications with a **constant output of original articles and systematic reviews**, published in first quartile international journals (Q1) indexed in ISI Web of Science and/or Scopus, targeting mostly gastroenterology and surgery domains (Gastroenterology, Gut, Gastrointestinal Endoscopy, Endoscopy, Surgical Endoscopy, Endoscopic Ultrasound, European Journal of Ultrasound, Medical Ultrasonography). An OpenAccess policy will be sought whenever possible targeting also journals with a high impact factor. A total number of 15 articles will be published by the consortium partners during the unfolding of the TRIP project.

- All publications (in the particular field of research) of the coordinator during the three years preceding the start date of the project, will be introduced in the first 3 months by the UMFCD team in the reporting tool on the Participant Portal, as requested by the Commission to evaluate the impact of activities in **Horizon Europe Key Performance Indicators (KPI)**. These will be followed longitudinally during the project (2022-2024) and 5 years after in order to look at the sustainability at the proposed measures.
- Both early stage and senior researchers will benefit from the **inclusion into clinical practice guidelines and technical reviews**, based on the expertise of several experts involved in the professional development of these documents by various societies: UEG, ESGE, EFSUMB, etc.

2.1.5. Increased number of innovative services introduced

- A **culture of clinical research and innovation** will be developed at UMFCD through close interactions and networking with leading EU institutions involved in the project (UCL, RHH, AMC). The collaboration will be expanded to the **Technology Transfer** offices of these entities, which can share their own experience in providing innovative services into clinical practice.
- Introduction of **innovative services for UMFCD** will certainly bring added value for patients, including:
    - introduction of several innovative minimal invasive procedures: EUS-guided fiducial placement, EUS-guided anastomoses and rendez-vous, EUS / IOUS-guided RFA / MWA
    - minimal-invasive endoscopic and/or laparoscopic procedures guided by fusion imaging based on the expertise of UCL / RHH / AMC;
    - development of a personalised treatment strategy for pancreatic cancer patients, based on pancreatic cancer organoids and pharmacotyping

2.1.6. Enhanced research and innovation capacity and more efficient networking of the whole consortium

- Increased connectivity and mobility (inwards and outwards) of ESRs and highly skilled scientists based on short-term visits and virtual meetings leading to a highly skilled networking environment:
    - Several **short-term exchange visits** are envisaged at the leading EU institutions (2 short-term exchange visits of 1-2 weeks duration for ESRs, each year)
    - **Virtual meetings** will be organized for the protocols developed, for co-tutoring of PhDs and ESRs, as well as for webinars organized and broadcasted periodically (twice yearly).
- Mutual benefits will be driven also to the internationally leading scientific institutions, **through increased networking capabilities** and the possibility of developing ongoing or generating new protocols, as well as developing cooperative EU or international grants.
- Organization of **joint activities such as hands-on and live demonstration workshops and summer schools** open to the international research community to bring in talented individuals and introduce the research potential of the UMFCD, as well as the available instrumental capacities and high-end expertise of project partners (UCL, RHH, AMC).

2.1.7. Benefits to the internationally leading partners and how the partnership will be maintained long-term

- The proposed TWINNING partnership will be beneficial to all partners of the TRIP proposal due to producing collaborative high-quality science / clinical publications, meeting presentations and other research outputs, including **technology transfer of relevant ideas / patents**.
- The internationally leading institutions will also benefit from the TRIP proposal, by having an **open access to the training facilities of the clinical affiliated hospitals of UMFCD**, thus providing excellent clinical research options in the field, with complementary expertise needed to achieve the critical mass needed to apply for larger international research projects.
- The E.U. leading institutions will also gain **access to the human resources** (including PhD and postdoc researchers), which may enhance the mutual exchange of ESRs between countries. Scientific mobility is an important aspect of the life of ESRs and senior researchers. The improved research excellence of TRIP will provide international partners with extended possibilities of collaboration in both research and education activities, with a systematic and **long-term exchange options for ESRs**. An increased number of PhD graduates will most probably apply for their **postdoctoral research mobility grants abroad**, choosing one of the leading institutions.

Barriers and obstacles in reaching the desired impact of the proposal are presented in the following **SWOT analysis**.

Strengths
> Appropiate infrastructure
> Multidisciplinary team
> Investment in equipment
> Personalized care
> Increased international mobility

Weaknesses
> Weak administrative units
> Slow
> Bureaucracy
> Low number of ESRs
> Continuous braindrain

Opportunities
> High quality education a
> Enhanced training programs
> Research opportunities
> International competitive funding
> Added innovative services

Threats
> Unrealistic expectations
> Low public awareness for R&D
> Low interes of researchers
> Low success rate for grants
> Increased pandemic barriers

Impact	Obstacle	Mitigation
Improvement of the research excellence and innovation capacity of UMFCD	Continuous brain drain of ESRs and postdocs towards other excellence centers	The international mobility for the ESRs could lead to an exodus to more attractive centers. If that were to happen, the outgoing PhD students and post-doctoral researchers would maintain the collaboration with the original institution and engage in joint research projects.
Enhanced reputation and attractiveness of UMFCD	The project would not gain the public awareness as expected	UMFCD is the biggest medical university in Romania, but it might experience difficulties disseminating the project outcomes in order to engage stakeholders and target groups.
Improved capability to compete successfully for national, EU and international competitive research funding. Increased number and quality of scientific output	Unrealistic expectations	The development of multicentric translational protocols will increase the success rate as the impact of the projects will lead to improved excellence. Moreover, close interactions and networking will attract more research partners and

		improve training, which will result in excellent research proposals.
Increased number of innovative services	Competition could develop sooner for new services in the area of interest	Competition could be used in the team's benefit as a boost for innovation and promote creativity and the development of new approaches. Moreover, the partnership offers a source for increased mobility of qualified researchers which would result in delivering high-quality strategies and services.

2.2 Measures to maximise impact - Dissemination, exploitation and communication

2.2.1 Dissemination and exploitation of results

Project dissemination is a very important part of the proposal, targeting various users and uses, including research, but also development and innovation (commercialization), social, policy-making, competency standards and skills, as well as education. Thus, the results of the TRIP project will be broadcasted to relevant stakeholders, policy makers, business partners, ESRs and postdoctoral researchers, healthcare professionals (doctors) and general public. **The Communication and Dissemination Plan**, including target groups and dissemination channels is proposed below.

Dissemination and exploitation activities are described in a dedicated work package (**WP6**). The leader for WP6 is the Dissemination Manager of the Project that will work closely with the Project Manager, with the aim of maximizing dissemination activities and broadcasting project results. The Dissemination Manager will continuously monitor project results and will propose the most efficient ways for dissemination. The Dissemination Manager will maintain the dissemination plan which will be discussed with partners, and in addition to that, the partners will be given prior notice before any dissemination activity (according to the EC guidelines). The support of the European Commission will be acknowledged in all project outcomes as requested by the EC guidelines and given rules. The dissemination plan will be prepared by the Dissemination Manager based on the already discussed activities proposed in the preparatory phase of the project and will be approved at the first meeting of the Steering Committee.

TRIP project will comply with the extended '**Pilot on Open Research Data in Horizon Europe**' ('open research data by default'), except if they indicate otherwise ('opt-out'.) Once the action has started, those beneficiaries which do not opt-out, will need to create a more detailed Data Management Plan (D6.4) for making their data findable, accessible, interoperable and reusable (**FAIR**). Dissemination activities will be discussed with project partners, especially in order to protect relevant **Intellectual Property Rights (IPR)** derived from the project activities. The project partners will always be asked to give their formal approval to dissemination activities containing or affecting their expertise (including background IPR). They will have the veto right-to-refuse any dissemination activity which could potentially harm their interests – including the publication of research results in scientific papers.

The **Open Access and Data Management** policies are not fully relevant for the TRIP Twinning project as it does not support the realization of research activities, being a Coordination and Support Action. On the other hand, and with respect to the expected impact of the project, which is to increase research results, publications and joint research projects, **Open Access and Data Management** policies will be discussed within **WP6** and the best practice in this area will be shared among the project partners. Project partners support an Open Access policy for publications (the so-called green model of Open Access being the preferred way for publication), with some of the publication costs supported by either the institutions itself (UCL / RHH / AMC / UMFCD), or through some of the project activities Other public repositories, for e.g. **ResearchGate**, will also be used to host the research papers obtained during the project. Sensitive data will be treated in compliance with the new EU GDPR regulations. The prospective studies (PEACE and PANC-ORG) proposed in this project **will be approved** by the local **Ethical Committee** of UMFCD. Thus, the statutory requirements, internal regulations and ethical requirements were all met, particularly focused on the privacy protection, protection of personality and human dignity of patients, their possibility of a free withdrawal from the study, as well as transparency of collection and storing of data and biological samples.

The IPR strategy of the TRIP project consortium will follow the rules adopted by the E.C. and best practice of IPR protection published by the EC and the internal rules of all partners involved. IPR protection rules will be codified in the Grant Agreement and Consortium Agreement in order to protect the IP generated before and within the project (background and foreground), minimize potential risks and eliminate possible conflicts raised. The key principles of the IPR strategy are as follows:

• Each partner is and remains the sole owner of its IPR over its background. The background needed for the project realization will be defined in the specific Annex of the Consortium Agreement. Every partner will be entitled to describe its own pre-existing background;

• Foreground will be owned by the project partner who will generate it. If it is not possible to determine the exact share of generated IPR (more partners participated on the foreground), the parties will have joint ownership of such

foreground according to the pro ratio effort invested by each partner. Every joint foreground consisting of a joint patent or patent application is subject to establishment of joint ownership agreement prior to any application;
• Each project partner will make available its foreground and background according to the previously mentioned Consortium Agreement to be signed before the project starts, on a royalty-free basis to all partners, to the extent necessary for the execution of the project and with respect to other obligations (non-disclosure agreements, etc.). Background and foreground should be made available for partners for exploitation purposes with fair conditions;
• If the possibility of exploitation of results arises (patenting, commercialization, industrial cooperation), all partners to whom the IPR belongs will be contacted to participate in the negotiations. The IPR strategy will follow the rules of EU and participating institutions. The dissemination activities and the publication of scientific papers may be delayed in order to protect commercial interest. Such a procedure will be detailed in the Consortium Agreement.

2.2.2 Communication activities

The communication activities of the TRIP project will be complementary to the communication strategy of the UMF Carol Davila. The strategy sets the overall concept and framework of how the hospital should communicate and engage with the relevant audiences. Based on the planned measurements and expected impact of the project, the communication plan of the project will be continually evaluated and adjusted. The underlying goal of the communication is to contribute to the outstanding reputation of UMF Carol Davila and increase awareness of the hospital with relevant target groups.

Communication plan, corresponding to the UMFCD communication strategy includes:

- **increasing awareness of the UMFCD**, partners (UCL / RHH / AMC) and the scientific area of the project;
- **drawing the attention of national governments, regional authorities** and other public and private funding sources to the need for and ultimate benefits of our research;
- **encouraging highly skilled scientists and students** to join partner institutes/hospitals;
- **enhancing the reputation and visibility of UMFCD** at local, national and international levels;
- **exploiting research results and outcomes**; and
- **generating market demand** for the innovative services developed and offered.

The basic role of communication and marketing is to help support the reputation of the UMFCD. The reputation is built on high-quality outputs and positioned and delivered with consistently high standards across the organization. Proper communication and marketing should tell the stories of UMFCD in the most compelling and attractive way, which will be appealing to relevant target groups (see below). The reputation and brand strength of UMFCD rely upon the actual and, thanks to the project, increased research performance of the hospital, and also upon the experience of students, early stage researchers and other important players with the hospital. Communication is included in the Action Plan of the project and is part of WP6. Its leader will be the Communication Manager of the project, who will collaborate with corresponding professionals of the project partners.

Target groups

The target groups of our communication strategy are relatively broad and diverse. To simplify the communication, targeting and development of communication channels, we grouped the target audiences and individuals we plan to reach into six main target groups:

- Internal staff – to create an internal culture of strong teamwork and inform staff about key activities and possible changes
- PhD students – to support a collaborative culture among early stage researchers and staff, to attract new PhD students and to retain the interest of alumni in UMFCD activities.
- Users, clients and industry – to increase the interest of users, clients and industry in research results, services and relevant activities of UMFCD.
- Policy-makers and stakeholders – to help the stakeholders adopt and use relevant research results in policy making and to ensure the financial sustainability of UMFCD.
- Media – to explain to the media the scientific problems and to position UMFCD as a contact point for relevant scientific and societal questions.
- General public – to explain to the general public the sense and importance of science and to increase awareness of UMFCD as a socially responsible institution.

Communication channels

Channels are the different paths through which the stakeholders are reached with information or communicate with or within UMFCD. Channels can be oral or written, printed or digital. The communication strategy describes which channels should be prioritized. The channels of UMFCD communication are following:

- UMFCD website – the website contains relevant information about TRIP proposal, e-newsletter, links to partners, short movies, interviews and news; KPI: 30000 visits over project duration
- Intranet & other internal communication platforms– the intranet provides a tool for internal communication, provides the necessary information for the internal staff and students and access to all relevant documents;
- Professional websites - relevant information presented on professional websites and research related portals; KPI: a total of 20000 visits of all related portal and websites over project duration

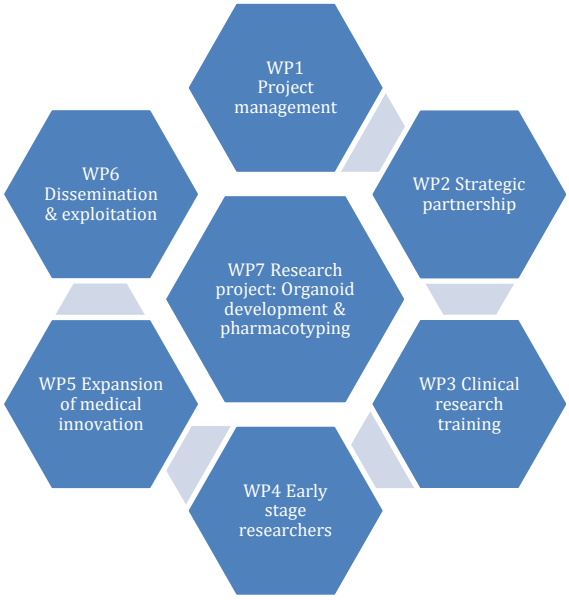
- Events for professional public and general public – e.g. workshops, seminars, congresses, trainings or summer schools, the European Researchers' Nights and Open Days which aim either at the general public or specifically at prospective early stage researchers (ESRs); KPI: at least 10 events attended over project duration
- Events for internal staff and ESRs – these events are one of the basic channels of the internal communication supporting the creation of common culture where all the staff and students are part of the team, take their role in delivering the results and contribute to the UMFCD goals; KPI: at least 10 events attended over project duration
- Presentations at conferences – talks, posters, session presentations at conferences such as ESGE Days, EUROSON congresses and schools, EAES congress, UEG Week, DDW; KPI: at least 20 conferences attended over project duration
- Print media – including leaflets and brochures – physical and pdf versions to be distributed at project events, conferences, summer schools, etc.; KPI: At least 2000 online views (digital versions) and distributed to at least 3000 people at events (physical version)
- Public media –local and national media will be used as a channel to the general public. The media used will be selected based on the target audience and message to be communicated; KPI: 4 press releases, 4 videos/interviews
- Social media – relevant social media used to publicize the project and UMFCD. The usage of LinkedIn, Facebook and Instagram is expected based on the nature of the message to be communicated; KPI: 200,000 combined views on social media

2.3 Summary

KEY ELEMENT OF THE IMPACT SECTION

Specific needs	**Expected results**	**D & E & C measures**
Project dissemination	The results of the TRIP project will be broadcasted to relevant stakeholders, policy makers, business partners, ESRs and postdoctoral researchers, healthcare professionals (doctors) and general public	Communication and dissemination plan; project website;
Open Access policy for publications	To increase research results, publications and joint research projects	Open Access and Data Management policies
Ethical approvals, transparency of collection and storing of data and biological samples	To meet all statutory requirements, internal regulations and ethical requirements, particularly focused on the privacy protection, protection of personality and human dignity of patients, their possibility of a free withdrawal from the study	Approval of prospective studies included in the TRIP proposal by the local Ethical Committee of UMFCD
Protection of relevant **Intellectual Property Rights (IPR)** derived from project activities	PR protection rules will be codified in the Grant Agreement and Consortium Agreement in order to protect the IP generated before and within the project (background and foreground), minimize potential risks and eliminate possible conflicts raised	IPR strategy plan
Communication activities	Increasing awareness of the UMFCD, partners (UCL / RHH / AMC) and the scientific area of the project; drawing the attention of national governments, regional authorities and other public and private funding sources to the need for and ultimate benefits of our research; encouraging highly skilled scientists and students to join UMFCD or partner institutes enhancing the reputation and visibility of UMFCD at local, national and international levels;	Communication and dissemination plan

Target groups	**Outcomes**	**Impacts**
Internal staff (doctors)	Events to inform staff about key activities and possible changes	to create an internal culture of strong teamwork
PhD students and ESRs	Events for ESRs, presentations, conferences, professional websites,	to support a collaborative culture among ESRs and staff, to attract new PhD students and to retain the interest of alumni in UMFCD activities;



Users, clients and industry	UMFCD website updated with relevant information about TRIP proposal	to increase the interest of users, clients and industry in research results, services and relevant activities of UMFCD.
Policy-makers and stakeholders	Events for SMEs -Publications, reports and recommendations, important tool for innovation management, increasing the awareness of the UMFCD, research topics and possibilities of collaboration with SMEs	to help the stakeholders adopt and use relevant research results in policy making and to ensure the financial sustainability of UMFCD.
Media	Print media, public media and social media event to publicize the project and UMFCD	to explain to the media the scientific problems and to position UMFCD as a contact point for relevant scientific and societal questions
General public	Events for professional public and general public	to explain to the general public the sense and importance of science and to increase awareness of UMFCD as a socially responsible institution

3. Quality and efficiency of the implementation

3.1 Work plan and resources

The project will be implemented in interconnected work packages (WPs), each dedicated to specific project objectives. Training objectives spawn across all WPs, which will unfold in a coordinated interlinked approach, as detailed in the following **PERT chart**:

3.2 Capacity of participants and consortium as a whole

3.2.1 A Consortium of Excellence and Complementarity

To accomplish the objectives of the widespread call, a consortium contains world leaders in all key scientific and management components has been build. The TRIP Consortium comprises 4 partners, the **Widening partner, UMFCD** and three **international-leading** counterpart European research institutions **(RHH, AMC and UCL)** in the field of diagnostic and therapeutic techniques in gastroenterology. The TRIP project has been developed by considering the internal and external limitation, to achieve scientific excellence by UMFCD.

UMFCD is one of the leading Romanian higher education institutions, with long academic tradition in education, clinical activities and excellent reputation on research. The University host to more than 8000 students, over 1607 academic staff, a doctoral school in medical sciences. Clinical practice teaching takes place in departments from over 20 clinical hospital or institutes (more than 18000 hospital beds). In addition, for preclinical teaching and research activities the university has an extended technical-material base for educational and research activities, 19 research centers. The university has achieved international recognition for the quality of both its teaching and research. In international university rankings, **Top Shanghai 500**, the latest positioning of UMF "Carol Davila" was 151-200 for "Medical Science" segment, and 101-150 for "Clinical Medicine". UMFCD is a leading partner in medical education, having built over the years a dedicated team of experts with focus on pancreatic pathology. Owing to a strong connection with its affiliated hospitals, along with partnerships from other universities and collaborations with world-renown pancreatologists, UMFCD has organized over the past decade an annual pancreatology event, **Bucharest Pancreatic Fest** (2012-2021), comprising a workshop with live demonstrations and postgraduate teaching course. The event, hosted by the **APPR, Association for Pancreatic Pathology Romania**, gathers over 200 participants yearly including gastroenterologists, radiologists, oncologists, surgeons, pathologists and other related medical specialties, and has promoted collaborations between faculty experts and attendees, evidence-based knowledge in pancreatic diseases and development of biliopancreatic centers in Romania. Research, development of new approaches, innovation comprise an important part of the University's mission. This aspect is also reflected in the establishment within the UMFCD of the Genomics Development Research Institute.

Central Military Emergency University Hospital Dr. Carol Davila (SUUMC) is a top academic hospital affiliated to UMFCD, ranked as level 1 in the national healthcare system. The Gastroenterology Department along with its Endoscopy unit is a referral center for pancreatic diseases, owing to its expertise in clinical pancreatology and bilio-pancreatic endoscopic procedures. In fact, SUUMC has been a pioneer of endosonography in Romania (first EUS-FNA done in 2002) and is currently a high-volume center for pancreatic EUS. Practical demonstrations and training for postgraduate courses are accommodated in the Endoscopy Unit, which is fully equipped for advanced bilio-pancreatic endoscopy and provides the opportunity for tissue sampling for the TRIP project. Expertise of the medical staff, along with the high number of pancreatic cancer patients managed by the pancreas-focused multidisciplinary team, contributes to good recruitment for the TRIP project.

Elias Emergency University Hospital (EEUH) is a multidisciplinary emergency hospital covering a broad spectrum of medical specialties. Dedicated Gastroenterology and General Surgery Departments are covering various diseases such as IBD, gastrointestinal and hepato-bilio-pancreatic cancers. Both departments have state-of the art endoscopic and ultrasound equipment, with laboratory facilities and a pathology department serving as routine units as well as research facility with ability to process samples for Genetics and Molecular Biology. Due to the high flow of patients and strong connections with the other hospitals, it would represent a perfect location for a high-risk clinic with second opinion abilities for patients coming from the rest of the country.

Fundeni Clinical Institute (FCI) - The Center of Excellence in Translational Medicine (CEMT). Affiliation of FCI to the TRIP project provides a great advantage for the enrolment of patients in the research project (WP7) due to the high number of patients with PDAC treated annually at FCI. CEMT has currently an infrastructure that includes sequencing technology using multiple platforms and technologies, NGS (Ion Torrent and NextSeq 500) that allows analysis of the whole genome, transcriptom, exom and target gene panels. More details of the equipment are mentioned on the ERRIS platform at: https://eeris.eu/ERIF-2000-000F-1826. **The role in the project**: ICF brings staff with extensive **experience in pancreatic cancer diagnostic through pancreatic EUS**, **EUS-FNA** and in **laboratory genomic and proteomic techniques** (quality analyses of DNA, RNA and protein fragments with the TapeStation 2200 system, microfluidic capillary electrophoresis with the Bioanalyzer 2100, pancreatic tumor cultures, molecular analysis of fine needle aspirations samples from pancreatic lesion, new compounds screening and morpho-functional studies, CRISPR-CAS, biobanking) validated in multiple international projects and proven by publications in international journals. FCI is well ranked in Romanian medical research, which hosted **EU research, research related educational projects, cancer screening projects**.

The Academic Medical Center is one of the largest and leading hospital in The Netherlands which houses the university hospital and the faculty of medicine of UvA as well as the Emma Children's Hospital, the Netherlands Institute for Neuroscience, the Spinoza Centre for Neuroimaging, the medical department of the Royal Tropical Institute and the Amsterdam Institute for Global Health and Development. A number of biotech companies are also located on the premises. This concentration of expertise makes the centre a breeding ground for fruitful scientific collaboration. The three core activities of the AMC are patient care, research, training and education. The aim of the AMC is to conduct these tasks on top referees and top clinical level.

Together with VUmc colleagues, the AMC collaborates in eight research institutes. 1500 members of staff are either fully or partially employed in medical research, which is regularly subjected to scrutiny by a panel of international scientists. Many of the departments and research groups at AMC work closely with leading foreign institutions, for example, Oxford and Harvard and the Karolinska University Hospital in Sweden. Medical and biomedical research at the Academic Medical Center enjoys international prestige. Their publications are among the

best in the world. In the past three years AMC acquired various prestigious personal research grants. Within AMC there is a fast track outpatient clinic for hepato-pancreatico-biliary (HPB) malignancies, **The Gastro-Intestinal Oncologic Centre Amsterdam (GIOCA)**, which strives to deliver the best possible and most innovative patient centred care within a short time span. The aim of the GIOCA is to be the best center for Gastro-Intestinal oncology in the Netherlands with the ambition to become an international key player.

The chiefs of the department of surgery and gastroenterology started created GIOCA in 2008. The main reason was the long waiting time for patients with gastrointestinal malignancy that was in part caused by the division structure of hospitals. Since the opening in 2009 all patients with a gastro-intestinal malignancy are diverted to the GIOCA. The care is centred round patients by allocating specific days to the different gastro-intestinal malignancies. Between 2009 and 2014 the number of new HPB-GIOCA patients had grown by 133% - in 2014 the total number of referrals of new patients was 1138, which 565 specifically to the HPB-GIOCA.

UCL is consistently ranked as one of the top performing organisations worldwide under the EU Framework Programmes for research. UCL was the best performing Higher Education Institution (HEI) under the first two years (2014–2016) of Horizon 2020, the EU's current, €80 billion research and innovation programme. It has consistently remained within the top three performing HEIs to date and UCL is also currently ranked as the top HEI in Europe for H2020 collaborative projects. In addition to that, UCL's well-recognized cutting-edge technology and resources place it in the top 4 universities in the world for anatomy and human physiological sciences. UCL has participated in more than 1,000 EU Framework Programme projects, of which more than 400 (equalling around €250 million) are funded through Horizon 2020. We have also hosted close to 200 prestigious European Research Council grants. **The role in the project:** RHH has long-standing experience for the early diagnosis and minimal invasive therapy of pancreatico-biliary cancers, whilst UCL is one of the leading institutions for the pancreatic cancer screening program. Consequently, enhanced networking, translated expertise and educational support from these institutions are needed to develop screening and early detection strategies in Romania and neighbouring countries. UCL is an associated partner in TRIP with a foreseen budget of € 114,310.78.

The Capital Region of Copenhagen (RHH) consists of major 5 hospitals all of which are regarded as one entity. Each of these hospitals are serving a population of around 500,000 inhabitants regarding general diseases, including general gastrointestinal diseases. For specialized GI diseases each of the 5 hospitals have their own profile. Herlev hospital has a gastrounit consisting of gastroenterology and surgical gastroenterology mainly focusing on colorectal cancer and IBD. For surgical treatment of pancreatic cancer and other upper GI cancer diseases the hospitals must transfer these patients to the main university hospital, Rigshospitalet whereas benign upper specialised GI diseases such as endoscopic or surgical treatment of obesity is handled at Hvidovre hospital. Oncological treatment of GI cancers is referred to Herlev hospital. This centralisation in the RHH has resulted in high volume centers with great expertise. The gastro unit at Herlev hospital has a world recognised endoscopic department with 8 high-end endoscopy rooms, performing around 14,000 endoscopies per year. The department has for many years been an official ESGE training centre, receiving young grantees for training from the ESGE but also other endoscopist who wants to learn endoscopic methods, and in particular EUS. Since the year 2000, more than 300 endoscopist have been visiting the department for training purposes. The endoscopic department at Herlev hospital is also one of a few Pentax Centers of Excellence testing new endoscopic equipment as well as participating in scientific studies regarding new endoscopic methods for GI diseases. The department has a recognised scientific profile lead by Professor Peter Vilmann and his scientific team. The main focus of studies are optimising diagnosis, treatment and care for patients with pancreatic cancer using EUS guided methods for either harvesting of cells from pancreatic lesions or internal drainage of obstructed bile ducts or EUS guided anastomoses for outlet obstructions from the guts.

All participants requesting funding in this project which are public bodies, research organisations or higher education institutions in a Member State or Associated Country have a gender equality plan in place.

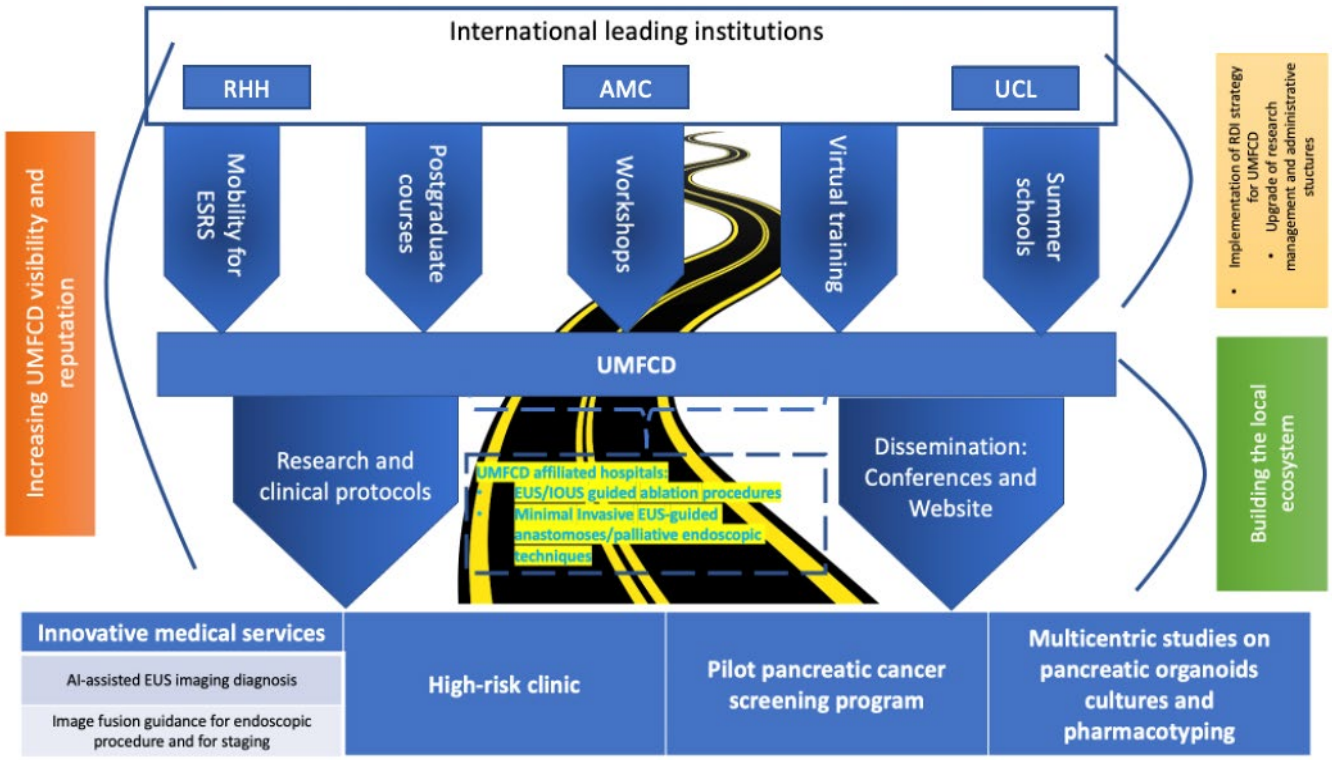
3.2.2 A Consortium with a proven track record of successful cooperation

TRIP project will work on the old synergies created between the TRIP consortium members. During the last 20 years a firm scientific collaboration has been established by professor Mariana Jinga, the coordinator PI, and Professor Adrian Săftoiu, team member of UMFCD partner, with high-level leading scientist, such as Professor Steven Pereira from UCL in UK and Professor Peter Vilmann, together with his scientific team from RHH in Denmark. These lead to a constantly growing research track record, across the EU, in the field of image-guided minimally invasive procedures used for the diagnosis and treatment of pancreatico-biliary diseases. This joint effort has already resulted **in clinical practice guidelines, structured reviews, original peer-reviewed publications, congress presentations and participation during endoscopy and surgery live-demos.** During the years a firm scientific collaboration has been established, thus resulting in several PhD studies.

Furthermore, the team in UMFCD and RHH / UCL was leading the field of advanced imaging through the publication of several multicentre studies that highlighted the role of these techniques (Costache MI, Endosc Ultrasound 2020, Saftoiu, Jinga et al, Endosc Ultrasound 2019; Ignee A et al, Endoscopy 2018; Saftoiu et al, Gastrointest Endosc 2015). The team has an extensive track record of collaboration on GI cancer field (**PANCNGS, THERRES, PREDYCT**) that will contribute to the successful outcome of the research project (WP7). In addition, Drs. Mariana Jinga, Adrian Săftoiu, Cristian Gheorghe, Simona Dima, Irina Cazacu and Vlad Croitoru provide complementary expertise covering particular areas under investigation in the research project.

The project will be **coordinated by UMFCD**, which has a **small R&D grants office** and appropriate dissemination and European communication facilities**, including ongoing H2020 projects**. **Work Package** leaders will report to the SC at regular intervals, updating them on work progress, any delays, changes to the Work Plan or arising potential obstacles which may affect the smooth running of the project implementation. The **Project Coordinator** will be assisted by a dedicated **Project Management Team** (detailed below). The principal decision-making and strategic body will be the **Steering Committee** (SC).

Figure 3.1 Project activities and outcomes



Tables for section 3.1

Table 3.1a: List of work packages

Work package No	Work Package Title	Lead Participant No	Lead Participant Short Name	Person-Months	Start Month	End month
1	**Project management and coordination activities**	1	UMFCD	17.13	1	36
2	**Strategic partnerships with leading EU institutions**	3	AMC	10.45	1	36
3	**Education and clinical / translational research training**	2	RHH	18.35	1	35
4	**Early stage researchers career development**	1	UMFCD	33.03	1	32
5	**Expansion of medical innovation, including second opinion and a high-risk clinic**	1	UMFCD	14	24	36
6	**Dissemination, exploitation of results**	1	UMFCD	11.35	1	36
7	**Research project: Organoid development & pharmacotyping**	2	RHH	22.35	6	36
				Total: 126.66		

Table 3.1b: Work package description

Work package number	1		**Lead beneficiary**			**UMFCD**	
Work package title	**Project management and coordination activities**						
Participant number	1	2	3	AP			
Short name of participant	UMFCD	RHH	AMC	UCL			
Person months per participant:	13.13	2.6	1.4	1.2			
Start month	1			**End month**	36		

Objectives

- Definition and implementation of the RDI strategy for UMFCD
- Upgrading of research management / administrative structures
- Overall management and decision making for the TRIP project
- Administrative and financial management, as well as monitoring progress
- Ethical issues, according to sub-chapter Ethics and Security

Description of work

Task 1.1 Definition and implementation of the RDI strategy for UMFCD (Leader UMFCD)

The lead partner of this WP is the coordinator of the project (UMFCD, Bucharest, ROMANIA), which will be assisted by the other partners in the definition and implementation of the RDI strategy of the university and clinical affiliated hospitals. The existing research unit will be upgraded in the university, whilst the abilities for the staff and early researchers will be coagulated together in order to improve the proposal preparation and project management skills needed to attract increased research funding in the following period (2022-2027) from both EU structural funds and/or Horizon Europe. The research unit will be strongly connected to the other administrative services of the University (human resources, etc.).

Task 1.2 Upgrading of research management / administrative structures (Leader UMFCD)

During the first 6 months of the project, a detailed roadmap for the research group will be developed, as a general strategic and operational plan for the most exciting research topics aligned with the engagement of early researchers involved in clinical research at UMF Carol Davila, but also with the health needs of the local population. This will be based on a transparent program of internal consultation with the researchers and clinicians from the involved institutions, but also industry and other local stakeholders (patient associations, etc.). The

roadmap will cover the period of Horizon Europe (2021-2027), extending well beyond the end of the TRIP project, thus achieving a synergy between the project objectives, with other national or international funding opportunities.

Task 1.3 Overall management and decision making for the TRIP project (Leader UMFCD)

The overall coordination and implementation of the project will be the responsibility of the **Project Coordinator** in compliance with the project strategy approved by the **Steering Committee** representing the principal decision-making body of the project. The Steering Committee will meet at least once a year physically and at 6 months electronically, and whenever necessary to discuss any issues related to the scientific direction of the project, project implementation and further matters as described in Section 3.2 (and detailed in the Consortium Agreement). The **Project Manager** will assist the Project Coordinator in day-to-day administrative and financial management of the project as well as risk management. The PM will support preparation and realization of project activities such as invited lectures, training events, and internships. The WP Leaders and Task Leaders will be responsible for day-to-day management and problem solving with respect to their assigned tasks.

All three beneficiaries (UMFCD, RHH and AMC) and the associated partner (UCL) will be involved in Task 1.3 (They are all part of the Steering Committee and will participate to all meetings). Along the scope of this action, AMC and UCL will have a support role to the Coordinator providing their expertise in management via consultations whenever necessary and discussions in project meetings.

Task 1.4 Administrative and financial management, as well as monitoring progress (Leader UMFCD)

To ensure proper and smooth implementation of project activities, an **Action Plan** will be prepared by the **Project Coordinator**, assisted by the **Project Manager**, and approved by the **Steering Committee**. Work progress will be monitored continuously by Task Leaders and WP Leaders. Any deviations will be reported immediately to the respective WP Leader or the Project Coordinator. Assessment of work progress, fulfilment of objectives, deliverables and milestones according to the Action Plan will be conducted quarterly by the PC who will further prepare a concise yearly report in collaboration with the PM. The Action Plan will be updated according to work progress, actual requests and needs and possible deviations and obstacles that may arise. The scientific and technical progress, including financial reporting, will be part of the periodic reports submitted regularly to the EC.

RHH / AMC / UCL will approve the Action Plan and will also dedicate time for preparing the reporting (technical and financial). Along the scope of this action, AMC and UCL will have a support role to the Coordinator providing their expertise in management via consultations whenever necessary and discussions in project meetings.

Task 1.5 Ethics (Leader UMFCD)

Ethical issues will be carefully considered and addressed. Clinical and translational studies and protocols developed during the project will be approved by the Ethical Committee of **UMFCD**.

Task 1.6 Gender balance (Leader UMFCD)

Relevant gender issues were considered in the TRIP project proposal – not only gender in the training and research content but also by promoting equal opportunities and a balanced participation of women and men at all levels in research. TRIP does not struggle with insufficient percentages of women in research, support, and management positions. About 50% of the UMFCD and clinical affiliated hospitals employees and ESRs are women, which is above average in the Romanian healthcare and research environments.

Deliverables

D1.1 Roadmap for the RDI strategy & procedures of UMFCD research unit **[M6]**
D1.2 Action Plan approved by the Steering Committee **[M6]**
D1.3. Progress report **[M17]**

Milestones

M1.1 Project kick-off meeting **[M1]**
M1.2 Action Plan completed and approved by SC **[M6]**

Work package number	2		**Lead beneficiary**		**UMFCD**	
Work package title	**Strategic partnerships with leading EU institutions**					
Participant number	1	2	3	AP		
Short name of participant	UMFCD	RHH	AMC	UCL		
Person months per participant:	9.25	0.8	0.4	1.2		
Start month	1		**End month**	36		

Objectives

- Strengthening the research excellence of UMFCD in the field of pancreatic cancer screening strategies and minimal invasive pancreatico-biliary interventions
- Enhancing the scientific visibility of UMFCD and open new networking opportunities (joint project applications, secondments of young researchers and senior staff);

- Increasing the competitiveness of UMFCD in national, EU and international research grant competitions (competitive individual grant applications, joint collaborative project applications);

Description of work

Task 2.1 Strengthening research excellence (Leader UMFCD)

The research excellence and scientific visibility of UMFCD will be certainly enhanced during the project based on the continuous training support received from all 3 partners from internationally-leading research institutions. The practical collaboration will enable us to share the knowledge in the field of minimal invasive endoscopic interventions and pancreatic cancer screening strategies. This will increase the reputation and attractiveness of UMFCD as an excellent partner for future collaborative grants or multicenter trials. The complementary expertise of all partners is the key element that sustains the collaborative efforts.

Task 2.2 Enhancing the scientific visibility and open new networking opportunities (Leader UMFCD)

All publications (in the particular field of research) of the coordinator during the three years preceding the start date of the project, will be introduced in the first 3 months by the UMFCD team in the reporting tool on the Participant Portal, as requested by the Commission to evaluate the impact of activities in Horizon 2020 Key Performance Indicators (KPI). Also, there will be a clear framework for the clinical research and training programs, including short-term staff exchanges, expert visits, short-term on-site and virtual training. RHH / AMC / UCL will all be involved in the development of the framework. The dissemination and outreach activities defined in WP will be also defined in terms of hospital policy: common workshops, conference attendance, publication of articles and reviews, patents and innovative medical services.

Task 2.3 Increasing the competitiveness in national and international grant competitions (Leader UCL)

Clear protocols for the implementation of the RDI research strategy will be also developed during the first 6 months, by the newly established research unit of the UMFCD, Bucharest, Romania. These will clearly define the joint research projects unfolding in the hospital in collaboration with other national and international partners. RHH / AMC / UCL will offer support in the development of protocols for the implementation of the RDI research strategy at UMFCD.

Deliverables

D2.1 Collaborative ongoing and new projects **[M36]**

Milestones

M2.1 Scientific work plan running as expected **[M36]**

Work package number	3		**Lead beneficiary**			**RHH**	
Work package title	**Education and clinical / translational research training**						
Participant number	1	3	4	AP			
Short name of participant	UMFCD	RHH	AMC	UCL			
Person months per participant:	10.25	4.4	3.7	1			
Start month	1			**End month**	35		

Objectives

- Sharing knowledge and building expertise in the field of minimal invasive pancreatico-biliary endoscopic procedures and pancreatic cancer screening strategies
- Enhancing professional competencies and acquiring knowledge for the staff and ESRs

Description of work

Task 3.1 Mobility for clinical early stage researchers (Leader UMFCD)

One of the aims of the TRIP proposals is to increase international mobility based on co-tutoring of the PhD students from UMFCD by the leading EU project partners (UCL / RHH/ AMC). This will result in better professional and transferable skills, with improvement of the competitiveness of the PhD program at both the national and international level. Mobility will include 3 short-term / exchange visits of ESRs from UMFCD to the other project partners (RHH / AMC / UCL). Joint research activities, postgraduate training courses and workshops, as well as virtual trainings, thus supporting ESRs to develop the scientific career and to build their own scientific network.

Task 3.2 Postgraduate training courses (Leader UMFCD)

Postgraduate courses are a strong asset of UMFCD (and its affiliated hospitals), with a large number of short courses / workshops with hands-on trainings organized in the past 5 years. Based on the contribution from the other TRIP project partners, 3 postgraduate courses will be organized, with both theoretical courses and hands-on training in 3D printed synthetic models, ex-vivo animal models, small animal (pig) live models and hybrid

simulation. All three beneficiaries (UMFCD, RHH, AMC) and the associated partner (UCL) will contribute with speakers for the postgraduate courses.

Task 3.3 Workshops (livedemo + hands-on) at UMFCD (Leader UMFCD)

Three international workshops will also be organized in the framework of TRIP project. Based on the participation of invited experts from all 4 institutions (UMFCD/RHH/AMC/UCL), the workshops will include livedemos (recorded also from the website of the project for later broadcasting). Thus, the research potential of UMFCD will be introduced to national and international partners, showing the instrumental capacities and high-end expertise available for minimal invasive endoscopic pancreatico-biliary procedures.

Task 3.4 Virtual training (including webinars) (Leader AMC)

These will include virtual meetings organized for the protocols developed, for co-tutoring of PhDs and ESRs, as well as for webinars organized and broadcasted periodically (twice yearly). All three beneficiaries (UMFCD / RHH / AMC) and the associated partner (UCL) will be involved in the organization of the webinars. Several lectures will be transmitted over Zoom / GoToWebinar, including:

- Peter Vilmann (RHH): Interventional procedures based on EUS assistance / guidance
- Simon Ezban Gruetzmeier (RHH): EUS-guided FNA/FNB as a bridge towards translational research
- Pia Klausen (RHH): Organoid development for EUS-FNB material
- Stephen Pereira (UCL): Fusion imaging in advanced pancreatico-biliary procedures
- AMC: Screening strategies for pancreatic cancer screening

Task 3.5 Summer school (Leader UMFCD)

One **summer school** will be organized at UMFCD with participation of experts from all centers (UCL / RHH/AMC) for a total duration of 5 days, including courses and practical classes, with hands-on activities.

Task 3.6 Project management training meetings (Leader AMC)

These are budgeted separately for each partner, with a total of 6 meetings being established for the project (2 each year, one physical meeting and one virtual meeting). During each project meeting, there will be a dedicated session on project management training and AMC will be responsible for organizing these sessions.

Deliverables

D3.1 Reports on educational and training activities **[M35]**

D3.2 Report on the organization of summer school **[M12]**

Milestones

M3.1 Educational and training activities running as expected **[M35]**

M3.2 Summer school organization **[M12]**

Work package number	4		**Lead beneficiary**		**UMFCD**		
Work package title	**Early stage researchers career development**						
Participant number	1	2	3	AP			
Short name of participant	UMFCD	RHH	AMC	UCL			
Person months per participant:	22.13	1.3	9.6	0.4			
Start month	1			**End month**	32		

Objectives

- Acquiring knowledge and building expertise in the field of minimally invasive endoscopic techniques and cancer screening strategies
- Developing scientific and professional skills for clinical and translational ESRs
- Promoting international experience through short-term visits / exchanges, mentoring and co-tutoring
- Participation at postgraduate training courses, hands-on and livedemo workshops, virtual trainings (webinars and on-line educational repository) and summer school organized at UMFCD

Description of work

Task 4.1 Short-term exchange visits for clinical early stage researchers (Leader AMC)

As detailed in task 3.1, TRIP project will cover a total of 6 short / exchange visits for ESRs. 3 exchange visits will be organized as part of this task, with focus on postdoc researchers. This will enhance the exchange of research staff and increase the visibility and attractiveness of UMFCD. Despite the brain-drain that will occur because some of the PhD students will apply for postdoc positions at the leading EU institutions, the outgoing researchers will maintain their contacts and collaboration with the original institution and will support further collaboration via joint research projects. RHH / AMC/ UCL will each receive an ESR from UMFCD.

Task 4.2 Co-tutoring by project partners (Leader RHH)

Co-tutoring by experts from the advanced partners institutions (RHH / AMC / UCL) will be a key task of the TRIP project, as training activities will be certainly enhanced by the involvement of experts from leading EU institutions.

Co-tutoring ESRs by the international experts from each of the partner institutions will bring the students another experience connected with different research culture, providing innovative approaches and fresh insights.
Task 4.3 Training courses and workshops (Leader UMFCD)
These were all detailed in the previous WP. Besides professional development, the training activities will also support enhancing the transferrable skills (e.g. academic writing, IPR, project management, dissemination).

Deliverables
D4.1 Reports on early stage researchers career development **[M32]**
Milestones
M4.1 Early stage researchers career development activities running as expected **[M32]**

Work package number	5		**Lead beneficiary**			**AMC**	
Work package title	**Expansion of medical innovation**						
Participant number	1	2	3	AP			
Short name of participant	UMFCD	RHH	AMC	UCL			
Person months per participant:	8.25	2.5	3.25	1.9			
Start month	24			**End month**	36		

Objectives
- Enhancement of medical innovation at UMFCD with development of personalized therapy
- Pilot screening program (pancreatic cancer) and structuring of a high-risk clinic
- Second opinion website

Description of work
Task 5.1 Development of innovative medical services (Leader UMFCD)
Several innovative medical services will be introduced based on TRIP project activities, in accordance with the training activities that will support the young doctors to learn these procedures, including:
- fusion imaging guidance of endoscopic procedures
- personalized cancer therapy based on organoid culturing from EUS-guided fine needle biopsy samples

Task 5.2 Pilot screening program (pancreatic cancer) (Leader AMC)
Based on the training and support offered by AMC and UCL, a practical pancreatic cancer screening algorithm will be specifically developed for UMFCD, using a multidisciplinary approach and taking into consideration circumstances particular to UMFCD.
Task 5.3 High-risk clinic (Leader UMFCD)
This task aims to create a high risk clinic at UMFCD where patients with key risk factors for pancreatic cancer will be offered services such as risk assessment, screening investigations (EUS or MRI/MRCP), genetic counseling and ongoing surveillance (a personalized plan will be developed for regular monitoring). The high risk clinic will be developed with the support of experts from AMC / UCL / RHH.
Task 5.4 Development of a **second opinion website** (Leader UMFCD)
This will be created as an interface for other doctors to upload difficult cases from all over the country, with tumor board functions used to determine a personalised cancer treatment and care plan for individual patients. The second opinion website will be created by UMFCD with support of experts from AMC / UCL / RHH.

Deliverables
D5.1 Report on expansion of medical innovation **[M36]**
D5.2 Report on the organization of pancreatic cancer screening database **[M24]**
D5.3 Report on the organization of high-risk clinic **[M36]**
D5.4 Report on the organization of second opinion website **[M36]**
Milestones
M5.1 Pilot pancreatic cancer screening database **[M36]**
M5.2 High-risk clinic **[M36]**
M5.3 Second opinion website **[M36]**

Work package number	6		**Lead beneficiary**			**UMFCD**	
Work package title	**Dissemination, exploitation of results and communication activities**						
Participant number	1	2	3	AP			
Short name of participant	UMFCD	RHH	AMC	UCL			

Person months per participant:	9.25	1.6	0.5	1.1			
Start month	1			**End month**	36		

Objectives

- Dissemination, exploitation of results and communication activities

Description of work

Task 6.1 Communication and dissemination plan (Leader UMFCD)

A communication and dissemination plan will be prepared by the Dissemination Manager (WP6 Leader) in collaboration with the Project Manager and will be updated continuously. The Dissemination Manager and the Project Manager will be responsible for the communication and dissemination activities and will closely collaborate with the Innovation Manager. The management of data will be also ensured during the project according to the FAIR principles as described in section 2.2.1

Task 6.2 Project website (Leader UMFCD)

A dedicated website will be created to provide information about the TRIP project objectives and activities, research on the minimal invasive endoscopic therapies, work progress and project news. Additionally, basic information will be available publicly on the official UMFCD website (https://umfcd.ro/en/). Furthermore, detailed information and instructions related to project activities (e.g. realization of internships and mobilities) will be accessible internally for the UMFCD staff in the Intranet system.

Task 6.3 Dissemination activities (Leader RHH)

Project findings and outcomes will be disseminated within the **scientific community at** national and international conferences / congresses, local workshops and postgraduate training courses via the channels described in section 2.2.1. Early stage researchers from UMFCD will participate at these conferences (at least 2 per year), networking with experts from leading EU institutions. Most important conferences / congresses will be:

International

- ESGE Days (European Society of Gastrointestinal Endoscopy) / EURO-EUS (Endoscopic Ultrasound)
- EUROSON (European Federation Societies of Ultrasound in Medicine and Biology)
- EAES (European Association of Endoscopic Surgery)
- UEG Week (United European Gastroenterology Week)

National:

- Romanian National Conference of Gastroenterology, Hepatology and Digestive Endoscopy
- RAES (Romanian Association of Endoscopic Surgery)
- RSCP (Romanian Society of Coloproctology)

Furthermore, at least 9 joint publications will be prepared in collaboration with the international leading project partners and published in openly accessible high-impact journals. These include:

- PLoS One
- Endoscopy
- Gastrointestinal Endoscopy
- Gut
- Endoscopic Ultrasound
- Gastroenterology
- Journal of Gastrointestinal and Liver Diseases
- Surgical Endoscopy

All three beneficiaries (UMFCD/RHH/AMC) and the associated partner (UCL) will participate to conferences and will contribute to joint publications.

Task 6.4 Communication activities (Leader UMFCD)

Considering the relevance of this project to the whole healthcare and educational system, as well as the connection of the research topic to societal challenges identified by the European Union, we expect extensive public outreach through multiple communication strategies.

Popularization articles in newspapers, relevant magazines, web pages, etc. will be published to communicate the project, training and research focus of TRIP, project activities and science per se.

The potential of social networks such as Facebook (general public) and Instagram (students, youth), as well as specific professional networks like LinkedIn (professional healthcare / education) will be explored. We do not expect to create a new FB / Instagram page but to use already existing FB / Instagram channels to communicate the project and related activities with specific hashtag. UMFCD organizes already open public lectures on various topics, thus bringing science closer to the general public.

All three beneficiaries (UMFCD / RHH / AMC) and the associated partner (UCL) will actively participate to communication activities.

Deliverables
D6.1 Dissemination, communication and exploitation plan **[M6]**
D6.2 Updated dissemination, communication and exploitation plan **[M36]**
D6.3. Data management plan **[M6] – will be updated mid-term** [M17] and at the end of the project [M36]
Milestones
M6.1 Project website functional **[M3]**

Work package number	7		**Lead beneficiary**			**RHH**	
Work package title	**Research project: Organoid development & pharmacotyping**						
Participant number	1	2	3	AP			
Short name of participant	UMFCD	RHH	AMC	UCL			
Person months per participant:	10.75	9.6	2	0.6			
Start month	6			**End month**	36		

Objectives
- Development of pancreatic organoid cultures derived from EUS-FNB specimens from PDAC patients
- Mutational analysis of FNB samples, cfDNA and organoids using NGS
- Utilization of organoid cultures for pharmacotyping
- Stimulating scientific excellence and innovation capacity at UMFCD by transferring the methodology of organoid cultures from the leading EU institutions to UMFCD.

Description of work
Task 7.1 Development of pancreatic organoid cultures derived from EUS-FNB specimens from pancreatic adenocarcinoma patients (Leader RHH)
Organoids are a promising new development for translational research and precision medicine in pancreatic cancer. Through this task we aim to implement at UMFCD the methodology of organoid cultures from EUS-FNB samples in patients with PDAC. This research project will be a prospective trial including patients referred for the evaluation of a pancreatic mass by EUS at the partner hospitals in Romania (Elias University Emergency Hospital, Fundeni Clinical Institute, Central Military Hospital). EUS-FNB will be performed for initial diagnosis. Two additional needle passes will be performed with a 22-gauge FNB needle for organoid creation. The FNB specimens will be placed into basal organoid media and delivered immediately to CEMT for further processing and organoid generation. At RHH, protocols have been already established on **utilization of pancreas organoid cultures derived from EUS-FNB tumor cells and the methodology will thus be transferred at UMFCD.**
Task 7.2 Mutational analysis of FNB samples, cfDNA and organoids using NGS (Leader AMC)
Secondly, we aim to perform a thorough genomic characterization of organoid cultures by deep sequencing to determine whether the models represent the genomic constitution of the primary tumor, and if they retain their genetic characteristics over time. DNA will be extracted from the primary tumor, plasma, organoids and will be sequenced using the Illumina NextSeq500 platform and a custom targeted NGS panel. The main aim is to assess if there is genetic concordance between PDAC organoids and the primary tumor. Moreover, we plan to investigate the heterogeneity of the organoid population and the stability of genetic characteristics over time. Thus, single organoid DNA sequencing will be performed over time using multiple passages from the same patient. The molecular analysis will be carried out at UMFCD with support from AMC / RHH / UCL.
Task 7.3 Utilization of organoid cultures for pharmacotyping (Leader RHH)
Through this task, we aim to assess the feasibility of PDAC organoids for personalized drug screening. After genetic characterization, the established organoids will be exposed to a range of therapeutic agents to identify therapies that effectively kill the pancreatic tumor cells. The pharmacotyping will be carried out at UMFCD with support from AMC / RHH / UCL.
Task 7.4 Stimulating scientific excellence and innovation capacity at UMFCD by transferring the methodology of organoid cultures from the leading EU institutions to UMFCD (Leader UMFCD)
This tasks includes activities describing how the knowledge in Task 7.1-7.3 will be transferred. Training in organoid cultures includes purification and culturing of epithelial and stromal cells from EUS-FNB samples, pathological and mutational analysis (including NGS techniques) of the grown organoids as well as the baseline EUS-FNB sample for comparison. Furthermore, **organoid response to a variety of chemotherapeutic agents** is currently tested and the methodology will be transferred from the leading EU institutions to UMFCD. Regarding a deeper mutational analysis of FNA / FNB samples, training for whole exome sequencing of a pancreatic cancer relevant gene panel will be pursued by the ESRs involved in the translational research protocols, in close collaboration with the Pathology / Molecular Departments. The trainees will have the chance to increase their

knowledge of translational research & practice through short-visits at the partner institutions to obtain hands-on experience in ongoing projects under the mentorship of established investigators. Furthermore, various workshops and virtual presentations will be organized with focus on time management, scientific presentations, scientific writings, grant preparation and professional development skills.

Deliverables
D7.1 Multicentric protocol for organoid cultures development, pharmacotyping and molecular analysis [M36]
Milestones
M7.1 Ethical approval from local committee [M6]
M7.2 Implementation of research protocols [M24]

Table 3.1c: List of Deliverables

Deliverable (number)	Deliverable name	Work package number	Short name of lead participant	Type	Dissemination level	Delivery date (in months)
D1.1	Roadmap for the RDI strategy & procedures of UMFCD research unit	WP1	UMFCD	R	SEN	6
D1.2	Action Plan approved by the Steering Committee	WP1	UMFCD	R	PU	6
D1.3	Progress report	WP1	UMFCD	R	SEN	17
D2.1	Collaborative ongoing and new projects	WP2	UMFCD	R	PU	36
D3.1	Reports on educational and training activities	WP3	AMC	R	PU	35
D3.2	Report on the organization of summer school	WP3	UMFCD	R	PU	12
D4.1	Reports on early stage researchers career development	WP4	RHH	R	PU	32
D5.1	Reports on expansion of medical innovation	WP5	UMFCD	R	PU	36
D5.2	Report on the organization of pancreatic cancer screening database	WP5	AMC	R	SEN	24
D5.3	Report on the organization of high-risk clinic	WP5	UMFCD	R	SEN	36
D5.4	Report on the organization of second opinion website	WP5	UMFCD	R	PU	36
D6.1	Dissemination, communication and exploitation plan	WP6	UMFCD	R	PU	6
D6.2	Updated dissemination, communication and exploitation plan	WP6	UMFCD	R	PU	36
D6.3	Data management plan - will be updated mid-term [M17] and the end of the project [M36]	WP6	UMFCD	R	PU	6
D7.1	Multicentric protocol for utilization of organoid cultures for pharmacotyping	WP7	RHH	R	SEN	36

Table 3.1d: List of milestones

Milestone number	Milestone name	Related WPs	Due date (in month)	Means of verification
M1.1	Project kick-off meeting	WP1	1	Meeting minutes
M1.2	Action Plan completed and approved by SC	WP1	6	Submitting D1.2
M2.1	Scientific work plan running as expected	WP2	36	Submitting D2.1 and also submitting a list of jointly submitted/accepted/published in a special section in the portal

M3.1	Educational and training activities running as expected	WP3	35	Submitting D3.1
M3.2	Summer school organization	WP3	12	Submitting D3.2
M4.1	ESRs career development activities running as expected	WP4	32	Submitting D4.1
M5.1	Pilot pancreatic cancer screening database	WP5	36	Submitting D5.1 and D5.2
M5.2	High-risk clinic	WP5	36	Submitting D5.3
M5.3	Second opinion website	WP5	36	Submitting D5.4
M6.1	Project website functional	WP6	3	Trial of website available online
M7.1	Ethical approval from local committee	WP7	6	Certificate of approval from local committee obtained and checked by the Steering Committee
M7.2	Implementation of research protocols	WP7	24	Research protocols approved by Steering Committee

Table 3.1e: Critical risks for implementation

Description of risk (indicate level of (i) likelihood, and (ii) severity: Low/Medium/High)	WPs) involved	Proposed risk-mitigation measures
Low engagement of the partners with significant impact on the project delivery (Low/Medium)	All	Regular meetings will be set-up during the proposal to keep partners engaged and aligned. Workshops, trainings and visits exchanges will also be ensured as per work plan to keep partners engaged. A governance structure and its operation procedures will be outlined in the CA (as per Task 1.3 and 1.4), to monitor and ensure engagement of partners
Significantly delays and poor management of the project (Low/Medium)	1	Action plans and internal reports for monitoring project progress will be ensured by the Coordinator and Beneficiaries tasks and WP leaders. A governance structure will be set-up in the CA to monitor progress, identify delays early on and propose actions (as per Task 1.3 and 1.4).
Lack of communication - internal and between partners (Low)	1,6	Regular (online) meetings will be ensured during the project. These will be complemented by f2f meetings whenever possible and email communication. The governance bodies will have regular meetings. A meeting plan will be outlined at the kick-off meeting.
Risk to delay the International mobility An epidemic, such as COVID-19, lockdowns and border closures brings specific challenges, such as restrictions on the movement of people for webinars, demo workshops. (Low/Medium)	1,3,4,6,7	In case of a pandemic, meeting and exchanges will be held online regularly, and new formats will be discussed as to ensure objectives and outcomes of webinars and demo workshops are reached
Cost implications Health and safety protocols for a worker infected with the virus could lead to workplace closures and enhanced cleaning measures, both resulting in cost implications for an organization. (Low/Medium)	1,2,3,4,5,7	In case on an infection that leads to temporary workplace closure and enhanced cleaning measures we will i) in first instance evaluate its impact on the work and assess how this can be transferred to another facility ii) set-up the Steering Committee to agree on a plan to cover resulting costs

4. Ethics self-assessment

4.1 Ethical dimension of the objectives, methodology and likely impact

Human beings

All laparoscopic, endoscopic, and imaging methods mentioned in the TRIP project are current standard procedures, include informed consents, and are used routinely at each participating institution in the clinical care of patients with GI cancers. Oral and written information will be given to each patient, detailing the purpose for which the procedure is performed. If the patient agrees to participate, he/she will have to confirm this by signing the consent form. All patients will need to be able to read and understand both a "patient information sheet" and "consent form". To the greatest extent possible, the patient information sheet and consent form will be written in non-technical, non-scientific, simple language. No children or individuals not able to freely consent will be included. There will not be any positive discrimination for either gender in the selection of the patients.

Human tissues for research project (pancreatic organoids)

At RHH, protocols have been already established on the utilization of organoid cultures for pharmacotyping. The

protocol, written consent form, patient recruitment material have already received approval from the Ethics Committee of the Capital Region of Denmark and the Data Protection Agency. The same protocol will be sent for approval to the local ethical committee of the partners. The human tissues will be obtained from pancreatic cancer patients undergoing EUS-FNA biopsies for diagnosis. The samples will be anonymized prior to experiments and only the standard parameters like age and sex, the disease grade, and stage will be considered. All information will be kept under strict regulation of data protection. No biopsies samples will be taken specifically for this project.

Personal Data management and privacy

For training purposes, selected movies consisting of advanced endoscopic and surgical techniques will be uploaded to a specialized educational platform of the project. For data management, the national and (EU) 2016/679 - General Data Protection Regulation (GDPR) on the protection of individuals with regard to the processing of personal data and the free movement of such data will be applied. We will assure that the privacy of the subjects, including their personal identity and all other personal medical information, will be maintained at all times. For all documents or image material, subjects will not be identified by their names, but by an identification code. Electronic data (including movies and scans which are anonymized) will be stored in password-protected network storage which is regularly backed up to ensure the risk of data loss is minimized.

Animals

The live animal models play an important role in teaching and practicing new, minimally invasive techniques. Because of anatomic considerations, large animals provide the best approximation to humans and they are most commonly used for endoscopic training. The porcine live animals model will be used for training purposes in the TRIP proposal. EU Directive 2010/63/EU on the protection of animals used for scientific purposes (OJ L 276, 20.10.2010, p. 33) will be applied for each hands-on training activity on live animal models. All protocols must be approved by the Institutional Animal Care and Use Committee at each institution. All the 3R steps have been taken to comply with the principles of reduction, refinement, and replacement. In the TRIP proposal, the use of live animals will be limited to experienced trainees after practicing the endoscopic and surgical techniques in computer simulators or ex vivo models. Moreover, the use of these models will be reserved for advanced procedures that are not simulated realistically on ex vivo models. We will make sure that the minimum number of animals is selected. In vitro methods and ex vivo, animal models will be used to reduce the number of animals used wherever possible. All the animals will be treated with kindness and adequate living conditions will be provided. Trainees must be qualified for conducting animal research work. All the procedures will be performed with adequate sedation, analgesia, or anesthesia. and postoperative care of the experimental animals. Animals that cannot be relieved at the end of the procedure should be euthanized under anesthesia.

4.2 Compliance with ethical principles and relevant legislations

All the activities developed during the TRIP project will be carried out in strict accordance with ethical principles, as well as relevant national, EU, and international legislation, including the Charter of Fundamental Rights of the EU and the European Convention on Human Rights and its Supplementary Protocols, European Code of Conduct for Research Integrity

Additionally, the following ethical directives of the European Parliament and of the Council (with subsequent amendments) should be followed:

- Directive 2001/20/EC on the approximation of the laws, regulations, and administrative provisions of the MS relating to the implementation of Good Clinical Practice (GCP) in the conduct of clinical trials on medicinal products for human use.
- EU Regulation No 536/2014 on clinical trials on medicinal products for human use, repealing Directive 2001/20/EC (OJ L 158, 27.5.2014).
- Regulation (EU) 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (OJ L 119, 4.5.2016, p. 1)

World Medical Association Declaration of Helsinki (1964) where it is stated that “the well-being of the human subject should take precedence over the interests of science and society”, Oviedo Bioethics Convention on Human Rights and Biomedicine) for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: (Oviedo,4 April 1997)

5. Timeline of activities

WP 1 - Project management and coordination activities		
Deliverables WP 1	**Due date**	**Approved by the SC**
D1.1 Roadmap for the RDI strategy & procedures of UMFCD research unit	M6 (02.2023)	
D1.2 Action Plan approved by the Steering Committee	M6 (02.2023)	
D1.3. Progress report	M17 (01.2024)	
Milestones WP 1		
M1.1 Project kick-off meeting	M1 (09.2022)	
M1.2 Action Plan completed and approved by SC	M6 (03.2023)	

WP 2- Strategic partnerships with leading EU institutions		
Deliverables WP 2	**Due date**	**Approved by the SC**
D2.1 Collaborative ongoing and new projects	M36 (09.2025)	
Milestones WP 2		
M2.1 Scientific work plan running as expected	M36 (09.2025)	

WP 3 - Education and clinical / translational research training		
Deliverables WP 3	**Due date**	**Approved by the SC**
D3.1 Reports on educational and training activities	M35 (08.2025)	
D3.2 Report on the organization of summer school	M12 (09.2023)	
Milestones WP 1		
M3.1 Summer school organization	M12 (09.2023)	
M3.2 Educational and training activities running as expected	M35 (08.2025)	
TASKS		
Task 3.1 Mobility for clinical early stage researchers	3 exchange visits (09.2022-09.2024)	
Task 3.2 Postgraduate training courses	3 courses (09.2022-09.2024)	
Task 3.3 Workshops (livedemo + hands-on) at UMFCD	2 workshops (09.2022-09.2024)	
Task 3.4 Virtual training (including webinars)	6 virtual trainings (11.2022, 06.2023, 11.2023, 06.2024,	

	11.2024, 03.2025)	
Task 3.5 Summer school	1 - summer 2023	
Task 3.6 Project management training meetings	6 PM meetings (01.2023, 07.2023, 01.2024, 07.2024, 01.2025, 07.2025)	

1. Exchange visits (WP3/4) – period/persons involved

I Cazacu AMC
V Croitoru AMC
V Balaban AMC
C Tieranu AMC
D Tabacelia UCL
V Iovanescu UCL
M Fogarasi RHH
S Bunduc RHH
M Balaban RHH
EC Gheorghe AMC

2. Postgraduate training courses
Proposal: November 2023 (organized by UMFCD/CEMT); March 2024; August 2024

3. Workshops (live demo + hands-on) at UMFCD
Proposal: September 2023 (PancreaticFest)

4. Virtual training (including webinars)
November 2022 - done
Proposal: May 2023 (organized by UMFCD/Elias); December 2023 (organized by UMFCD/Fundeni)

5. Summer school
Proposal: 28.08-1.09/10-14.07 2023/21-25.08.2023

6. Project management meetings
01.2023 –done
Next: 07.2023

WP 4 - Early stage researchers career development		
Deliverables WP 4	**Due date**	**Approved by the SC**
D4.1 Reports on early stage researchers career development	M32 (05.2025)	
Milestones WP 4		
M4.1 Early stage researchers career development activities running as expected	M32 (05.2025)	

WP 5 - Expansion of medical innovation		
Deliverables WP 5	**Due date**	**Approved by the SC**
D5.1 Report on expansion of medical innovation	M36 (09.2025)	
D5.2 Report on the organization of pancreatic cancer screening database	M24 (09.2024)	
D5.3 Report on the organization of high-risk clinic	M36 (09.2025)	
D5.4 Report on the organization of second opinion website	M36 (09.2025)	

Milestones WP 4		
M5.1 Pilot pancreatic cancer screening database	M24 (09.2024)	
M5.2 High-risk clinic	M36 (09.2025)	
M5.3 Second opinion website	M36 (09.2025)	

WP 6 - Expansion of medical innovation		
Deliverables WP 6	**Due date**	**Approved by the SC**
D6.1 Dissemination,communication and exploitation plan	M6 (02.2023)	
D6.2 Updated dissemination,communication and exploitation plan	M36 (09.2025)	
D6.3. Data management plan	M6 (02.2023)	
Milestones WP 6		
M6.1 Project website functional	M3 (12.2022)	

WP 7 - Research project: Organoid development & pharmacotyping		
Deliverables WP 7	**Due date**	**Approved by the SC**
D7.1 Multicentric protocol for organoid cultures development, pharmacotyping and molecular analysis	M36 (09.2025)	
Milestones WP 7		
M7.1 Ethical approval	M6 (03.2023)	
M7.2 Implementation of research protocols	M24 (09.2024)	