

**REQUEST FOR APPLICATION
HIGH IMPACT CLINICAL TRIALS IN
PANCREATIC &
BILIARY TRACT CANCER**

- Funding Guidelines -

PLEASE READ ALL INSTRUCTIONS CAREFULLY

For any questions, please call (+32 2 268 48 16) or e-mail us (apply@anticancerfund.org).

About the Anticancer Fund

The Anticancer Fund (ACF) is a Belgian non-profit organisation with an international scope, dedicated to expanding the range of treatment options for cancer patients. The fund depends on donations and private funding to finance its work. With no commercial shareholders or interference from special interest groups or the pharma industry, it focuses exclusively on the evidence-based potential of new cancer treatments to respond to unmet patients' needs.

The ACF's vision

The ACF is committed to expanding the range of treatment options available to cancer patients, regardless of their commercial value. Its ultimate goal is to extend lives, increase quality of life and provide cures for cancer patients.

The ACF's mission

The ACF believes no promising treatment options should be left untapped and therefore works on commercially neglected therapies. It aims to complement the commercial drivers of cancer care with exclusive patient-first thinking. Hence, the ACF puts the focus on evidence-based development of high impact therapies for the benefit of cancer patients.

The ACF's work has three main pillars:

Research & Clinical trials

It promotes research, finances and/or coordinates clinical trials, investigating scientifically promising treatments that have the potential for significant positive impacts on patients lives but lack a market push for more research. If the effectiveness of a treatment is scientifically proven, it will further its access to patients.

Information & knowledge-sharing

It offers personalized, non-judgmental and evidence-based information about cancer treatments to patients who want to make informed decisions.

Policy-making

The ACF engages with stakeholders on both national and European levels to influence decision makers and eliminate barriers to rapid, affordable access to more cancer treatments.

Further information can be found on our website - <https://www.anticancerfund.org>

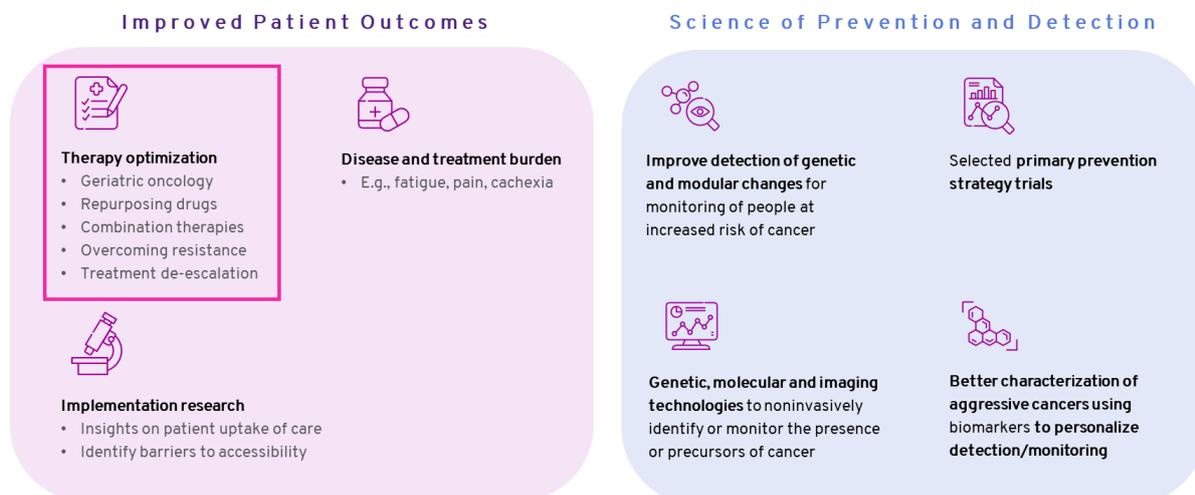
About the Rising Tide Foundation for Clinical Cancer Research

Rising Tide Foundation for Clinical Cancer Research (RTFCCR) is a charitable, non-profit organization established in 2010 and is located in Schaffhausen, Switzerland. Our mission is to promote freedom to improve quality of life everywhere. Using a patient-centred approach, we support research grants that enable patients to better understand their treatment options and to have a voice in trial design, thereby empowering them to be active agents in enhancing their quality of life.

RTFCCR's primary consideration in granting support is given to truly innovative, unique, patient-centered clinical research. The long-term ambition of the foundation is to **optimize partnerships** and attract the best in Phase I to Phase III clinical trials that aim to bring **maximum patient benefit** in the **shortest time possible**. With patients at the core of the mission, the foundation strives to support clinical trials resulting in the creation of less toxic therapeutic approaches, better disease burden management, earlier cancer detection, and innovative prevention strategies that will lead to increased quality of life and survival.

RTFCCR provides funding for research that directly benefits patients in the short term. We do not provide funding for basic research. We seek to provide support for clinical research topics that would not likely be funded by the pharma industry or other for-profit sources. Funding can be provided to any relevant institution in any country where meaningful grant oversight is possible.

RTFCCR Strategic Focus Areas



Further information can be found on our website - <https://www.risingtide-foundation.org/clinical-cancer-research>

Funding guidelines

INTRODUCTION

Rationale for pancreatic ductal adenocarcinoma and biliary tract cancer

Despite all the recent advances in cancer therapies, pancreatic cancer patients have very poor prognosis. In 2020, the incidence rates worldwide were 5.7 per 100,000 in men and 4.1 per 100,000 in women and accounted for 466,000 deaths¹. Incident rates are on the rise and pancreatic cancer has been reported to be the second largest cancer-related cause of the death^{2,3}.

Pancreatic cancer is regarded as a silent disease, with many patients remaining undiagnosed until an advanced stage, where the 5-year survival is 3%³. The most prevalent of which is pancreatic ductal adenocarcinoma (PDAC) accounting for 94% of pancreatic malignancies. At present, surgery, radiation, and chemotherapy are the main treatment options. However, less than 20% of patients are eligible for surgery, as many patients have unresectable, locally advanced, or metastatic disease at the time of diagnosis³. FOLFIRINOX is a regimen based on folinic acid, 5-FU, irinotecan and oxaliplatin, which has shown an increase in overall survival for patients with metastatic pancreatic cancer⁴. However, due to the toxicity, several side effects have also been reported that reduce patient's quality of life. More recently, immunotherapy has been explored as a treatment option. However, due to the complex tumour microenvironment, immunotherapy options have not yet demonstrated the same success as that observed for melanoma. It has been reported that combination therapies may provide a method for enhancing the immune responses to achieve a better therapeutic effect⁵.

Biliary tract cancer (BTC) includes cancer of the gallbladder (GBC), intrahepatic (ICC) and extrahepatic cholangiocarcinoma (ECC), and ampulla of Vater (AVC). BTC is a rare disease with poor prognosis⁶. In contrast to pancreatic cancer, the incidence rates are more difficult to compare, as in many cases, survival statistics are not provided for BTC. Nonetheless, statistics for intrahepatic bile duct cancer and extrahepatic bile duct cancer report 5-year survival rates of 10% for all stages combined⁷. Similar to pancreatic cancer, biliary tract cancers are usually diagnosed at a late stage and depending on the stage and the location, treatment options include surgery, chemotherapy, radiation, or combinations of chemotherapy and radiation after surgery to reduce reoccurrence.

With incidence rates on the increase and the 5-year survival rates of less than 10 % for both PDAC and BTC, there is a real need to provide better solutions for pancreatic and biliary cancer patients. To this end, this collaboration is seeking to support clinical trials testing novel and unique strategies in the treatment of patients diagnosed with pancreatic ductal adenocarcinomas and/or biliary tract cancer.

References

¹ International Agency for Research in Cancer- World Health Organization Pancreatic Cancer Fact Sheet 2020 Source: <https://gco.iarc.fr/today/data/factsheets/cancers/13-Pancreas-fact-sheet.pdf>

² Pancreatic cancer action network (PanCAN) Source: <https://www.pancan.org/press-releases/pancreatic-cancer-still-on-path-to-become-second-leading-cause-of-cancer-related-death-in-u-s-by-2020/>

³ American Cancer Society, Source: <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf>

⁴ Conroy T et al. Canadian Cancer Trials Group and the Unicancer-GI-PRODIGE Group. FOLFIRINOX or Gemcitabine as Adjuvant Therapy for Pancreatic Cancer. *N Engl J Med.* 2018 Dec 20;379(25):2395-2406. doi: 10.1056/NEJMoa1809775. PMID: 30575490.

⁵ Sarantis P et al. Pancreatic ductal adenocarcinoma: Treatment hurdles, tumor microenvironment and immunotherapy. *World J Gastrointest Oncol.* 2020;12(2):173-181. doi:10.4251/wjgo.v12.i2.173

⁶ Van Dyke AL et al. Biliary tract cancer incidence and trends in the United States by demographic group, 1999-2013. *Cancer.* 2019;125(9):1489-1498. doi:10.1002/cncr.31942

⁷ American Cancer Society Source: <https://www.cancer.org/cancer/bile-duct-cancer/detection-diagnosis-staging/survival-by-stage.html>

SCOPE

We are seeking to support clinical trials testing novel and unique strategies in the treatment of patients diagnosed with **pancreatic ductal adenocarcinomas (PDAC)** and/or **biliary tract cancer (BTC)***. The proposal needs to have the potential to have a **high impact** (e.g. improve cure rate or survival) on the treatment of these cancers.

We are looking for **innovative approaches** extrapolated from laboratory work in relevant cancer models or extrapolated from other cancer types but deemed applicable in PDAC and/or BTC. Both early phase trials as later phase trials with an **out-of-the-box concept** are permitted. In principal, generating proof-of concept data or exploring novel promising interventions not investigated yet or building on preliminary pilot data are welcomed. Proposals might not be deemed innovative if the intervention is being or has been investigated by other groups or if there is only a small incremental gain in knowledge and/or outcome.

We acknowledge that innovation might have inherent risks, the proposal must be realistic and deemed feasible to execute. We welcome applications from all research groups with a track record in PDAC and/or BTC.

As ACF and RTFCCR seek proposals in line with their vision and mission, the proposed intervention must be commercially neglected (as defined in detail in the eligibility criteria). We encourage applicants to contact apply@anticancerfund.org for any questions related to the RFA and to check eligibility of their proposal in case of doubt.

**Biliary tract cancers (BTCs) constitute epithelial malignancies of the biliary tree and include the following: gallbladder cancer, ampulla of Vater cancer, cancer of the extra-hepatic and intra-hepatic bile ducts.*

ELIGIBILITY CRITERIA

Clinical trials are eligible if they meet **all** of the following criteria.

1. Clinical trials in patients with pancreatic ductal adenocarcinoma, gallbladder cancer, ampulla of Vater cancer, cancer of the extra-hepatic and/or intra-hepatic bile ducts.
2. Clinical trials need to be an interventional trial with commercially neglected interventions, such as drug repurposing, surgery, radiotherapy.
3. Open to innovative clinical trials with “out of the box” thinking such as new design, innovative technology, and must have a high impact for patients.
4. Open for early to late-stage clinical trials (e.g., pilot study, Phase I, Phase II or Phase III).
5. The ultimate goal is to improve cure rate or survival with the intervention. Clinical trials should serve patients interests with primary endpoints that seek to provide clinical benefit. Trials should not have biological or translational primary endpoints, but applicants may include secondary non-clinical endpoints.
6. Trials should be patient centric. Applicants must include a patient engagement plan from research question through to dissemination.

7. All interventions are allowed, **except:**
 - a. Compounds (chemical/biological) that are still in drug development.
 - b. Drug products without marketing authorisation or approval from competent authorities (i.e., FDA, EMA, national) for any indication (cancer or not cancer related indication).
 - c. Cell-based therapy.
8. For on-patent drugs or non-drug products (e.g., machines, devices...) with commercial owner: a written statement should be provided that the commercial owner is not willing to give funding for the conduction of the trial. On-patent drugs or non-drug products (e.g., machines, devices...) intervention should be provided for the trial by the commercial owner (a written statement should be provided).
9. The leading clinical trial team has a track record of high-quality trials – preferentially investigator-driven trials – in the field of PDAC and/or BTC. Applicants without expertise in this field should seek collaboration with investigators who have demonstrated expertise in PDAC and/or BTC. A formal proof (letter) of collaboration should be provided.

We encourage applicants to contact apply@anticancerfund.org for any questions related to the RFA and to check eligibility of their proposal in case of doubt.

PATIENT ENGAGEMENT IN RESEARCH

We define Patient Engagement as meaningful engagement of patients in the development of therapeutic, detection or prevention approaches. It encompasses the active, meaningful, and collaborative interaction between patients and researchers across all stages of the research process, where research decision making is guided by patients' contributions as partners, recognizing their specific experiences, values, and expertise.

In this request for application we are adopting (Patient-Centered Outcomes Research Institute) PCORI's definition of Patient Partners: it includes patients (those with lived experience), family members, caregivers, and the organizations that are representative of the population of interest in a particular study.

It is important that Patient Partners are not confused with trial participants; Patient Partners are members of the research team and involved in the planning, conducting and dissemination of the research, whereas trial participants are those individuals actually enrolled into the study.

The strategy, modalities, and budgets for Patient Engagement, related deliverables, and expected outcomes must be clearly described in the application.

Guidance for planning your Patient Engagement in Research

Early involvement of Patient Partners, based on co-design principles allows a better formulation of relevant research questions, more credibility of the knowledge produced, identifying, and solving potential challenges faced during the trial, and better application of outcomes to specific contexts. Here is a checklist to help you plan Patient Engagement and complete our Patient Engagement Plan table required to be submitted as part of the Letter Of Intent. It encompasses points that should be considered before the trial starts, during the trial and beyond the trial.

Before the trial starts

- Patient Engagement is planned across the entire project lifecycle.
- The most appropriate Patient Engagement model is selected.
- The appropriate Patient Partners are involved early in formulating the concept, hypothesis.
- Appropriate budget for patient engagement activities and compensation of Patient Partners is reflected in the Patient Engagement Plan and the overall grant budget request.

During the trial

- Assessment of needs of trial participants by Patient Partners is included.
- Adaptation of trial and procedures where necessary to meet trial participants’ needs.
- Assessment of the impact of patient engagement in your trial at mid-term and at the end of the trial is considered.

Beyond the trial

- Communication and dissemination of study outcomes with patient / public partners is planned after trial end.
- Collaboration with patient community on trial outcomes is planned.

For more information, please refer to: <http://synapse.pfmd.org/resources/considerations-guide-to-implementing-patient-centric-initiatives-in-health-care-product-development/download>

Choice of model of Patient Engagement in research projects

Research teams should think carefully about the activities across the whole project lifecycle that the Patient Partners could undertake. Short term activities are easy to define upfront, but it is more challenging to think about sustained involvement across the entire project.

Therefore, depending on the research project, it is important to think about the most applicable role of a Patient Partner for contributing in a clinical trial:

Patient role	Examples	Engagement level
Consultant role	<ul style="list-style-type: none"> • Patients provide a priori and continuous consultation on outcomes of importance, study design, etc. • Patients are paid investigators or consultants • Patients have a governance role – “a seat at the table” 	High
Advisor role	<ul style="list-style-type: none"> • Patients serve as advisory committee members or provide a priori consultation on outcomes of importance and study design, but have no leadership role or governance authority 	Moderate
Reactor role	<ul style="list-style-type: none"> • Patient input is collected distally through surveys, focus groups or interviews, but patients are not consulted directly or a priori on such things as study design and outcomes of importance • Patients are asked to react to what has been put before them rather than being the origin of the concepts of interest 	Low

Patient Engagement Plan

We require you to submit a "Patient Engagement Plan" as part of your LOI and Full Application. The plan should describe Patient Engagement processes during the generation of the trial application as well as during the trial. It describes engagement e.g., how you engaged with the patient community when your research question was defined, while the proposal is written, when it is being submitted and resubmitted, and which patient engagement model you chose for the implementation of your project.

When developing your project budget, please make sure that adequate and realistic resources for Patient Engagement are reflected in the Patient Engagement Plan and the overall grant budget request. This could include e.g. appropriate budget for work time (staff or contractors in patient organizations) as well as project-related pass-through costs (e.g., travel expenses and meeting venue costs).

Different phases of research will need different activities to ensure patient engagement is implemented in the way defined in this document, *for example Phase I first in human studies may require a different approach than a survivorship study.*

We accept different formats of patient engagement plan, as long as:

- Activities proposed are listed and properly described;
- Activities proposed are designed for patients and with patients;
- The results of these activities are implementable in the clinical trial design or execution to ensure patient needs are met.

Be very clear at the outset about what you expect to achieve and what metrics – both quantitative and qualitative – you will use to measure progress against and achievement of both overall research goals and specific patient-centricity goals.

BUDGET

- The budget must be realistic and limited to the core activity of conducting the clinical trial.
- We foresee a total budget of **\$3M (\$1.5M ACF and \$1.5M RTFCCR)** and we anticipate supporting up to **1-3** trials with this budget.
- Investigator fees and institutional overhead costs will not be funded.
- Co-funding is welcome. All applicants must disclose the funding already secured and all past and ongoing funding applications.

SUBMISSION AND SELECTION PROCESS

This is a 2-step RFA

- **Step 1:** applicants are requested to submit a Letter of Intent (LOI).
- **Step 2:** after a pre-feasibility call with ACF and RTFCCR, successful applicants are requested to submit a full application, i.e., a trial protocol (ready or almost ready to be submitted to authorities and IRB/ethics committee), a detailed budget, a rebuttal letter on feedback about the LOI and a detailed patient engagement plan.

Step 1: Letter of Intent (LOI)

We ask all applicants to complete the LOI form which includes 2 main sections.

1. The **eligibility** section where applicants demonstrate that their proposal meets all the above-mentioned criteria as well as demonstrating Patient Engagement in the trial design from research question through to dissemination.
2. The **trial information** section where applicants provide details on their proposal.

----- **Deadline for submission of the LOI is Wednesday 30 June 2021, 23:59 CET** -----

The LOI template can be downloaded from <https://www.anticancerfund.org/request-application>.

Evaluation of the LOIs will be done by ACF and RTFCCR review team and will include:

- Checking the eligibility criteria;
- Evaluating the scientific rationale and the possible existence of counterevidence;
- Performing horizon scanning to assess competition;
- Reviewing alignment with mission, focus areas and core belief of RTFCCR and ACF;
- Assessing patient engagement in the trial design from research question through to dissemination.

From all applications, we expect to select 5-10 applications to go forward to step 2. Applicants will be notified whether their LOI has been selected by **16 August 2021**.

Applications will be automatically rejected if:

1. Other trial(s) of the same intervention in the same cancer and setting are ongoing (or registered) elsewhere and/or;
2. The applicant omitted to disclose secured funding or ongoing funding applications for the same trial.

Step 2: Full Application

Step 2 starts with a teleconference between the ACF and RTFCCR review team, and the applicant. The goal of this teleconference is to explain the process, perform a preliminary evaluation of the feasibility for running the trial, and assess whether any circumstances have changed since receipt of the LOI.

After the teleconference, the applicants will be asked to submit a full application containing:

- **Protocol:** we ask the applicants to submit a protocol ready (or almost ready) to be submitted to the competent authorities and to the IRB/EC.
- **Budget:** we ask the applicants to provide detailed breakdown of the budget.
- **Rebuttal:** we might ask further elaboration on specific questions and/or concerns that arose during the evaluation of the LOI.
- **Patient engagement plan:** we ask the applicants to further describe the strategy, modalities, and budgets for patient engagement based on the plan submitted during the LOI.

----- **Deadline for full application is Sunday 17 October 2021, 23:59 CET** -----

The evaluation of the full applications will be done by a grant review committee (GRC), consisting of patient expert, biostatistician, and subject matter experts, in addition to ACF and RTFCCR review team and RTFCCR scientific advisory board members. The GRC members will select the best applications for submission to the ACF and RTFCCR Board for approval.

The final selection is expected to be communicated on **20 December 2021**. Selected applications will receive a conditional go and will be contacted by both organisations individually regarding the next steps.

KEY DATES

