



ATTRACT

Accelerate Together Rare Cancer Treatment

International call for research proposals on rare cancer drug development

Six European anti-cancer charities are joining forces to stimulate international research on rare cancer drug development. The focus of this joint international call, the ATTRACT-Call, is on late phase (2/3) clinical trials on rare cancer drugs. Improving treatment for rare cancers as well as bringing drug development to the next developmental stage are two of the current target goals.

MOTIVATION

Rare cancers account for as many as 20% of new cancer cases. Yet, for most rare cancers there are hardly any specific, targeted drugs available, leaving patients with limited or no treatment options. There is also limited knowledge and confidence in clinical decision-making for rare cancers, and often incorrect or late diagnosis due to their rarity and their complex pathological results and lack of recognition of rare cancers. Though better treatments have been proposed for rare cancers, death rates have not yet been reduced and the cost of management of rare cancers remains one of the healthcare financial burdens worldwide. We aim to tackle this unmet medical need and increase survival and quality of life of patients with rare cancer by facilitating the development of drugs for rare cancer treatment, including repurposing of existing drugs, with this call.

According to conventional methodologies for drug development, late phase clinical trials need to include large numbers of patients to collect robust clinical evidence for obtaining market authorisation or for expanding indications after registration. However, in rare cancers, including large numbers of patients in clinical trials is difficult. Thus, rare cancer trials face long recruitment timelines. In addition, validated surrogate endpoints may be lacking and ultimately, the small sample sizes may possibly not support traditional randomised designs. These factors impede fast assessment of clinical efficacy and may make it less optimal to use a traditional randomised clinical trial design. Therefore, gathering robust clinical evidence is more difficult for rare cancers than for more common cancers. Moreover, clinical scientific understanding of rare cancers is usually gained from case reports or anecdotal evidence, analogies with more common cancers, single-institution case series or small multicentre trial series. Yet, methodologies need to adhere to stringent regulatory requirements in order to obtain authorisation by agencies such as the European Medicines Agency, as well as to support reimbursement decisions. Moreover, international collaboration in late-phase clinical research plays a pivotal role in fostering standardisation, gaining acceptance among clinicians, and facilitating the realisation and the implementation of guidelines.

In addition, funding bodies rarely offer funding for collaborative multicentre trials that span across multiple countries. In general, rare cancers receive less scientific consideration and financial support

than more common cancer types. All these factors hamper innovation of treatment for rare cancers and affect the average outcome of patients diagnosed with a rare tumour.

SCOPE

One of the main goals is to make better treatment available for rare cancer patients and to accelerate development of drugs for rare cancers. Efforts to set up large, international, collaborative clinical trials deserve special attention in rare cancers, and need to be funded properly. Therefore, the focus of this call is on late phase, collaborative, international clinical trials that aim to develop better drug treatment for rare cancers. We encourage researchers and clinicians from different countries to join forces, share knowledge, and collaborate.

By defining the requirements and recommendations for research proposals below, this call aims to provide funding for current development gaps.

REQUIREMENTS

- Participating parties:
 - o Trials need to be multicentre, collaborative, and organised internationally.
 - o The Project Leader as well as research consortium partners (i.e. national coordinators) need to be located in the countries of the participating funding organisations (i.e. Belgium, France, the Netherlands or Spain), with a minimum participation of 3 countries. Participation of all 4 countries is highly encouraged. In order to support swift enrolment of study patients in clinical trials, it is allowed to include external inclusion centres outside of the funding countries.
 - o Funding recipients should fall within the following categories: Academic research groups (from universities or other higher education or research institutions); or Clinical/public health sector research groups (from hospitals/public health and/or other health care settings and health organisations).
 - o Young researchers are welcome to apply; taking into account that the right expertise and experience should be available within the consortium and that the project should be led by the most suitable candidate.
 - o Public/Private collaborations are accepted if needed for the execution of the project, and as long as co-funding as well as appropriate agreements on intellectual property and fair pricing are in place. Commercial partners cannot be the Project Leader and may only be involved if collaborating with Academic or Clinical/public health research groups. Commercial parties will not receive funding directly and are required to provide co-funding and/or in-kind contribution to the project.
 - o External inclusion centres are preferably located within geographical Europe, in order to encourage and enhance European collaboration. If the applicant wishes to include inclusion centres outside of Europe, it should be a limited number and a strong rationale and justification should be provided on the need, feasibility, and prior existence (if any) of the intercontinental collaboration. Funding for external inclusion centres will be dependent to the available funding resources.
 - o Sponsorship: the sponsor of the trial must be an academic or research party; industry sponsored trials are not accepted.
- Research type: multicentre, multinational, clinical trial
Research phase: phase 2 and/or 3 clinical trials (including single arm phase 2 trial).
Preference for confirmatory or pivotal trial.

- A strong scientific rationale that supports the hypothesis and objective of the trial is required.
- Trial designs and methodologies: Well-controlled prospective studies, using the best-fitting trial design. This may include but is not limited to randomised trials, innovative trial designs such as basket- and umbrella design, platform trial design, designs that use methodologies to enhance patient inclusion, designs that leverage existing patient registries, etc. Designs that make use of validated clinically relevant endpoints or validated surrogate endpoints both are allowed. Including real world data (for example as control arm) may be considered. Design should include the most suitable and representative study population, with respect to the studied disease.
- Cancer type: rare cancers, defined as those with an incidence of less than 6 per 100,000 persons per year (definition by RARECARE; for list of rare cancers, see www.rarecarenet.eu/rarecarenet/cancerlist). Rare cancer in both adult and paediatric populations are accepted.
- Product type: medicinal products (including but not limited to chemo-, hormone-, immune-, radionuclide-, and advanced cell- and gene therapy (ATMPs)). This includes repurposing/label extensions of existing drugs that are out of data protection and marketing protection, and development of drug/device combinations.
- Intervention type: medicinal products intended to be used for treatment (including but not limited to monotherapy, treatments in combination with standard treatment, (neo)adjuvant therapy, add-on therapy).
- Active involvement of patients is mandatory throughout the entire project lifecycle (project set-up and execution, communication of results etc).
- Under no circumstances can funding be requested for translational research activities.

RECOMMENDATIONS AND CONSIDERATIONS FOR APPLICANTS AND REVIEWERS

The organising funding organisations use a pre- and full-proposal process for this call to be able to steer by providing recommendations/encouragements to researchers or steer the scientific evaluations of the final proposals by means of criteria and/or guidance for the reviewing committee.

Those criteria for proposals or guidance for prioritisation are:

- Strong regulatory and go-to-patient/clinical implementation strategies, including regulatory support and/or regulatory oversight for international projects, are strongly encouraged (e.g. EMA and/or National Competent Authorities advice).
- Trials on new or repurposed drugs that are close-to-patient/registration/market are encouraged.
- Trials that target unmet medical need are encouraged (include description of unmet medical need in application, based on the target population, current standard of care and current life expectancy).
- Trials on agnostic treatments (treatments effective for multiple (rare) cancer types) are encouraged.
- Trials with a potential high impact on survival and/or quality of life are encouraged.
- The best-fitted trial design for the trial objective should be used. Use of novel trial designs is accepted, in order to overcome challenges specific for studies on rare cancers. For example, master protocols, use of Bayesian methods, decentralised trials, real world data control arms.
- Trial designs that use validated biomarkers (e.g. genetic mutations or molecular markers typical for rare cancers) to identify and/or stratify eligible patients or subgroups to one or multiple treatment arms, are allowed as long as the primary endpoint of the trial is clinically relevant (survival, QoL) and not biomarker validation. Please note that the aim of this call is to accelerate drug development towards clinical implementation and is therefore not meant for translational research.

- Projects are expected to contribute to reproducible science and have a plan to disseminate their data and results, in particular:
 - Sharing of results in public databases, particularly after initial publication;
 - Publication of data in addition to the results adhering to FAIR principles (<https://www.gofair.org/>);
 - Publication of results in open-access journals.
- Biobanking is only allowed if required to carry out the proposed project.

INDICATIVE BUDGET

The indicative total budget for the ATTRACT-call is up to 12.4 million euro, provided by the 6 collaborating funding organisations: Anticancer Fund, Fondation ARC, Kom Op Tegen Kanker, KWF Dutch Cancer Society, Rising Tide Foundation for Clinical Cancer Research and Scientific Foundation of the Spanish Association Against Cancer. Definitive budget allocations per funding organisation will be published on the call-website prior to opening of the call.

MORE INFORMATION

Specific guidelines on the process, characteristics and eligibility terms for the ATTRACT-Call will be based on the current funding bodies' Guidelines and are to be announced on the call-website prior to opening of the call. Guidelines will include specific information on application requirements, preferences and recommendations, review procedure and timelines, funding conditions, estimated total budget, estimated budget per trial, and estimated number of trials to be funded.

TIMELINES

The target date of opening the ATTRACT-Call is September 2024. Detailed and definitive timelines will be published on the call-website prior to opening of the call.