ATTRACT

Accelerate Together Rare Cancer Treatment

Joint International Call

for research proposals on

Rare Cancer Drug Development

Guidelines for Applicants

Final
Version 3, 5 April 2023

Background

Five European anti-cancer funds 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.

Why rare cancer drug development

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 authorization 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 possible not support traditional randomized designs. These factors impede fast assessment of clinical efficacy and may make it less optimal to use a traditional randomized 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 multicenter trial series. Yet, methodologies need to adhere to stringent regulatory requirements in order to obtain authorization by agencies such as the European Medicines Agency, as well as to support reimbursement decisions. In addition, funding bodies rarely offer funding for collaborative multicenter 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 tumor.

Scope

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.

Requirements

Application Requirements		**Guidance**
Main applicant	Hospital or institute based in one of the funding-countries (i.e. Belgium, France, the Netherlands, or Spain)	- Main applicants as well as research consortium partners (i.e. participating parties/work package leaders) (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 organizations). - Inclusion centers and other participating parties in other countries than the funding countries are allowed (*see other participating parties*). - 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 best suitable candidate.
Research consortium partners	Multicenter, collaborative, internationally organized (> 2 participating countries)	- The main applicant as well as research consortium partners (i.e. work package leaders) need to be located in the countries of the participating funding organizations (i.e. Belgium, France, the Netherlands or Spain), with a minimum participation of 2 countries. - In order to support swift enrolment of study patients in clinical trials, it is allowed to include external inclusion centers outside of the funding countries (i.e. outside of Belgium, France, the Netherlands, Spain) (*see other participating parties*).
Other participating parties	External inclusion centers	- **External inclusion centers** outside of the funding countries (i.e. outside of Belgium, France, the Netherlands, Spain) are allowed, in order to support swift enrolment of study patients in clinical trials. Preferably, the external inclusion centers are located within Europe, in order to encourage and enhance European collaboration. If the applicant wishes to include inclusion centers outside of Europe, it should be limited in number and a strong rationale and justification should be provided on the need, feasibility and prior existence (if any) of the intercontinental collaboration.
	Industrial partners	- **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 a main applicant 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. This contribution should be of an extent appropriate for the type and size of the project. In case of financial contribution, a justification is required explaining the nature of the contribution, and why the remaining budget cannot be foreseen by the commercial party and why non-profit funding would be needed to execute the project. • Intellectual Property (IP): the background owned by any applicant will remain the sole property of the applicant (or his/her affiliated research structure (i.e. institutes, research centers and investigators). In addition, all data and results that are generated during the project remain the property of the applicants or his/her affiliated research structure (i.e. institutes, research centers and investigators)) for the duration of the project. • Commercial parties are requested to express their commitment and guarantee their maximal and reasonable efforts to

		accommodate further development, implementation and access for patients after the end of the project. Clear agreements between industry partners and researchers should be in place prior to the trial, assuring independent research and publishing. • Agreements between applicants and commercial parties as well as letters of intent should be provided for review as part of the full proposal application process.
Study Sponsor	The sponsor of the trial must be an academic or research party.	- Industry sponsored trials are not accepted.
Research type	Multinational multicenter clinical trial	
Research phase	Phase 2 or phase 3 clinical trial, or comparable (including single arm phase 2 trial)	- Preference for confirmatory or pivotal.
Scientific Rationale	A strong scientific rationale that supports the hypothesis and objective of the trial is required.	
Trial design	Prospective, well-controlled studies, using the best-fitting trial design	- Including but not limited to randomized 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 are both allowed. Including real world data (for example as control arm) may be considered. Design should include the best suitable and most representative study population, with respect to the studied disease.
Cancer type	Rare cancer	- Incidence of less than 6 per 100,000 persons per year. - As defined by RARECARE; see RARECARE for list of rare cancers (https://www.rarecarenet.eu/rarecarenet/cancerlist). - Rare cancer in both adult and paediatric populations are accepted.
Product type	Medicinal product	- Medicinal products, including but not limited to chemo-, hormone-, immune-therapy, and advanced cell- and gene therapy (i.e. ATMPs). This includes repurposing/label extensions of existing drugs and development of drug/device combinations. Drugs that are still under data-or marketing protection are allowed under certain conditions; see 'Public/Private collaborations' above.
Intervention type	Medicinal products intended to be used for treatment	- 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).
Project Manager	A Project manager must be allocated to the project.	- A Project manager is obligated to be allocated to the project, in order to perform the international clinical trial management. The allocated Project manager preferably has strong international clinical trial management and regulatory (EC/CA) experience.
Patient Involvement	It is required to actively involve patients in the set up and execution of the trial.	- Involvement of patients in the set up and execution of the trial is required. This may include, but not limited to, one or more of the following: letter of support from a patient organization, patient review of the Informed Consent Form, patient input on the protocol, dissemination of results to patients (including study participants), patient participation in steering committee.

Preferences and recommendations

This call will be a two-step process with a pre- and full proposal stage. The following criteria (see table) are provided as preferences and recommendations, which will steer the scientific evaluations of the final proposals.

Application Recommendations	
	Strongly recommended
Regulatory Strategy	It is strongly encouraged to have a shown strong regulatory strategy (i.e. EMA advice), including regulatory support and/or regulatory oversight for international projects.
Regulatory Lead	It is strongly suggested to allocate a Regulatory lead to the project, i.e. a person with regulatory expertise, in order to advise, oversee and perform international regulatory affairs. The regulatory lead can be a person from the main applicant or research consortium partners, as well as from an external consultancy agency.
EMA/NCA advice	It is strongly encouraged to have obtained scientific advice at the EMA (i.e. protocol assistance with the SAWP (Scientific Advice Working Party) and COMP (Committee for Orphan Medicinal Products) or NCAs (National Competent Authorities). *(This may be integrated in the full proposal review process in collaboration with EMA/NCAs)*
Orphan designation	It is a plus if orphan drug designation at the EMA-COMP has been obtained.
Implementation Strategy	It is strongly encouraged to have a shown go-to-market/clinical implementation strategy (including market registration, ensured accessibility for patients, scale-up possibilities, possible industry cooperation, reimbursement strategy with insurance companies).
Early HTA	It is a plus to have an early HTA (Health Technology Assessment) analysis of the compound.

Note: It is not obliged to have those criteria completed at time of the application; applicants may describe the current status and future plans on these topics. However, the better elaborated and the further in progress, the higher the developmental potential.

	Preferred/a plus
Close-to-patient	It is encouraged to submit trials on new or repurposed drugs that are Close-to-patient/registration/market.
Unmet medical need	It is encouraged to submit trials that target unmet medical need (include description of unmet medical need in application, based on the target population, current standard of care and current life expectancy).
Agnostic treatments	It is encouraged to submit trials on agnostic treatments (treatments effective for multiple (rare) cancer types).
Impact	It is encouraged to submit trials with a potential high impact on survival and/or quality of life.

	Other guidance
Novel trial designs	The best-fitted 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, decentralized trials, real world data control arms.
Biomarker validation	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. The aim of this call is to accelerate drug development towards clinical implementation and is therefore not meant for translational research.
Dissemination plan	A plan to disseminate project data and results is expected. 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	Biobanking is only allowed if required to carry out the proposed project.

Submission

This call is a two-stage submission procedure, i.e. a pre- and full proposals stage. Both pre- and full proposals must be written in English and submitted exclusively by the main applicant through the electronic submission system (Grant Management System, hosted by KWF). Please note that registration in the system is required prior to submitting your application. It is recommended to register as soon as possible. If you are new in the system, your registration must be approved by KWF. Please check at least six weeks before the call deadline if your registration is approved. Instructions how to register are provided in the Instructions for GMS for Applicants (available on the ATTRACT-website).

Applicants should use the application forms available from the electronic submission system, the Grant Management System GMS (GMS, see https://gms.kwf.nl/). Applicants should also take note of individual national rules/funding conditions (ATTRACT website, https://www.kwf.nl/en/attract), and contact their national contact persons for specific questions. In addition, applicants should agree that all information and documents that will be submitted in either the pre- or full proposal stage and as part of monitoring, are to be shared between all funding organisations in the context of the eligibility check, the project evaluation and monitoring. Selected applications might be shared with regulatory authorities during the review process or successful applicants may receive the recommendation to seek pre-grant scientific advice and share their application with regulatory authorities.

The pre- and full proposals must be submitted to the electronic submission system no later than the exact Application Deadline of **31 January 2023** for the pre-proposal and **27 June 2023** for the full application. Please note that full proposals are only accepted from applicants who are explicitly invited. Moreover, the information provided in the pre-proposal application is binding for the entire application process. Any substantial changes between the pre-proposal and the full proposal (e.g. composition of the consortia, objectives of the project, etc.) must be communicated in advance and will only be accepted under exceptional circumstances.

Eligibility check

All pre-proposals and full proposals will be checked in terms of eligibility.

All pre-proposals are examined to ensure that they meet all criteria specified in the Call Application Requirements and Recommendations (see above), date of submission, number of participating countries/regions and groups, inclusion of all necessary information in English, adherence to the application forms, document length). The relevant national funding organisations also perform a formal check of compliance with their respective regulations/funding conditions. Pre-proposals not considered eligible are rejected without further review. The coordinating applicants of the non-eligible pre-proposals are informed accordingly and there will be no possibility to object to this decision.

An eligibility check of the full proposals is performed to ensure that they meet the formal criteria of the call and have not changed substantially from the respective pre-proposals. A full proposal may be excluded from further review, if criteria are not met or if the proposal objectives or the composition of the consortium deviate substantially from the previously submitted pre-proposal. In any case, major changes must be communicated in advance.

Evaluation Process

Because of the two-stage application procedure, there will be a two-stage evaluation procedure, based on the evaluation criteria indicated in the following section.

Evaluation criteria

Pre- and full proposals are assessed according to the criteria specified in the Call Application Requirements and Recommendations (see tables above) and in general, the Scientific Evaluation Committee (SEC) review will focus on the following criteria:

1. Excellence

a. Relevance in relation to the topic of this call (fit-to-call): primary endpoint aiming for improvement of treatment of rare cancer, limited commercial interest/need for international funding, international collaboration.
b. Scientific quality: including sound trial design (i.e. statistics, methodology) and scientific background, previous research and evidence supporting the objective of the trial (i.e. state of the art).
c. Feasibility: including feasible workplan and recruitment plan, good quality consortium, project management
d. Proven anti-tumour effect, or a strong rational in favour of an anti-tumour effect (available data showing efficacy for the call of molecule/treatment in the given cancer site)

2. Developmental potential

Depending on the presence (if any)* and quality of:

a. Regulatory and Go-to-Market/Registration/Implementation Strategy (either academic or commercial)
b. EMA advice
c. Orphan designation
d. Early HTA

**It is not obliged to have those criteria completed at time of the application; applicants may describe the current status and future plans on these topics. However, the better elaborated and the further in progress, the higher the developmental potential.*

3. Patient Impact potential

Which may be impacted by:

a. Close-to-patient/clinical implementation innovations
b. Targeting an unmet medical need
c. Agnostic treatment potential
d. Potential impact on survival and/or quality of life of patients with rare cancer

Evaluation of the pre-proposals

Pre-proposals passing the formal eligibility checks are reviewed

- by the Scientific Evaluation Committee (SEC). Each pre-proposal is allocated to members of the SEC, who will review the proposal in accordance with the criteria described above.
- by the Patient Advocacy Committee (PAC). Selected pre-proposals will be evaluated by the PAC. For this purpose, a specific patient-friendly application section should be completed by the applicants as part of pre-proposal form of the initial application (see Guidelines regarding Patient Centricity & Patient Involvement below). Each selected pre-proposal will be provided to members of the PAC for review, resulting in a PAC Advise report. The pre-proposals will be evaluated by the PAC for patient-centricity of the research, taking into account the following criteria:

- Patient relevance, taking into account:
  - The patients' needs
  - The proposed solution
  - The patient-friendliness of the solution
  - The impact of the solution on the life expectancy and quality of life
- Patient participation, taking into account:
  - Effective involvement of patients in the design and preparation of the trial
  - Involvement of patients (study participants and non-participants) during the execution of the trial
- Patient burden, taking into account:
  - (un)acceptability of burden for participants in the clinical trial
  - appropriate burden/benefit assessment

Decision of the pre-proposal

The decision on the results of the pre-proposals and feedback will be communicated to all the applicants (successful and unsuccessful) by **end March 2023**. Successful applicants will be invited to submit a full proposal. The invitation will include a summary of the evaluation and possible recommendations on the project from the SEC as well as the PAC for implementation in the full proposal.

Evaluation of the full proposals

Each full proposal is reviewed:

- by members of the SEC, possibly those who had reviewed the corresponding pre-proposal, and an additional methodology review by a SEC methodologist member.
- by external reviewers.
- by the PAC. For this purpose, the applicant must submit a specific patient-friendly application form as part of the full proposal application. In this form, the goal and the patient-centricity of the project is described in layperson's terms, as well as if the prior comments listed in the PAC Advise report of the PAC have been implemented. In addition, the applicant is requested to provide a short video where the project is explained to the patient (in English). Review will result in a PAC Evaluation Report, including a PAC score. The PAC will score all full proposals according to the following criteria relevant to patient-centricity:
  - Concrete need: does the project address a concrete need among patients?
  - Added value: the added value of the research for the patient in terms of life expectancy and/or quality of life
  - Patient burden: the burden for the patients participating in the clinical trial is kept to a minimum
  - Patient participation: the patients are actively involved in the research

As part of the review process of the full proposals, the SEC members and external reviewers will independently assess the full proposals according to the evaluation criteria mentioned above.
The total score of the SEC and external reviewers will count for 70% of the total score for the project. The scores of the PAC account for 30% of the total score of each project proposal.

Rebuttal stage

Once the evaluation by the SEC members, the PAC and the external reviewers is completed, each applicant will have access, through the electronic submission system, to the anonymous evaluation reports (not to the assigned scores) by the SEC members, PAC and the external reviewers. Coordinators are allowed to reply to reviewers' questions and to comment on factual errors or misunderstandings on the evaluations. However, issues which are not related with reviewers' comments or questions cannot be addressed and the work plan cannot be modified. The resubmission

of the full proposal is not permitted in any case. This response to reviewers' comments is optional (but encouraged) and must be submitted exclusively by the coordinating applicant of the proposal through the electronic submission system, which only will be available during the Rebuttal Comment Window (7-10 days), as specified in the Timelines (see below). An interview for an oral explanation by the applicant on the proposal might be requested.

Decision of the Full proposal

Based on the total project scores and the optional responses in the rebuttal stage, a ranking list is established and discussed during the evaluation meeting with all members of the SEC, the PAC chair and delegate, and the Call Steering Committee (CSC) to reach a consensus on the proposal to be funded. The decision on the results of the full proposals evaluation meeting will be communicated to all the coordinating applicants (successful and unsuccessful) by the end November 2023, as specified in the Timelines (see below). The coordinating applicants of the full proposals will receive a conclusion of the evaluation.

Timelines

ATTRACT-Call Milestone	Timeline
Application Open Pre-proposal	22 Nov 22
Application Deadline Pre-proposal	31 Jan 23 12:00
Review process Pre-Proposal	Feb-Mar 23
Invitations Full Proposal	End Mar 23
Application Open Full proposal	End Mar 23
Application Deadline Full proposal	27 Jun 23 12:00
Review Process Full proposal	Jul-Aug 23
Rebuttal week	Second half of Sep 23
Finalize funding decisions and letters	Oct-Nov 23
Funding Letters	End Nov 23

Funding conditions

Applicants should take note of individual national rules/funding conditions (ATTRACT website, https://www.kwf.nl/en/attract) and contact their national contact persons for specific questions.

Applicants with external inclusions centers outside Belgium, France, Spain or the Netherlands should also consult the funding terms for external inclusion centers (see Annex 1)

Budget

The estimated total budget for the ATTRACT-call is up to 11.5 million euro, provided by the 5 collaborating funding organisations: Spanish Association against Cancer Scientific Foundation, Anticancer Fund, Fondation ARC, Kom Op Tegen Kanker, KWF Dutch Cancer Society.

No estimated budget per trial is foreseen at the moment as the amount depends on the scientific and medical needs and should be justified in the requested budget. Therefore, no estimation on the number of trials to be funded can be made. However, it is highly recommended to respect the available budget mentioned in the individual national rules/funding conditions (ATTRACT website, https://www.kwf.nl/en/attract).

Guidelines on Patient Centricity & Patient Involvement

These guidelines form the instructions on how to write a project proposal for the patient advocacy committee (PAC). The guidelines are focused on patient centricity and patient involvement. Patient centricity signifies the focus of the project being on the need and wishes of patients, whereas patient involvement indicates the active involvement of patients and/or patient organizations in the study design, the conduction of the research, and the communication of the results to the patient community. Where the preproposal phase might be too early to follow all of these instructions, it is expected that during the full-proposal phase attention is paid to all of them.

Application Form

- Be objective and honest in your application. Ensure that your application for the PAC is in accordance with your application for the scientific expert committee (SEC).
- Be aware that your application for the PAC must be in layman's language and make sure that used jargon is explained.
- Use clear argumentation with a logical structure.
- Make use of clear figures and diagrams to support your text.
- Your applications for the PAC will be read and judged by patients, therefore we advise you to involve one or more patients/patient organisations in proofreading your application before applying. Actively ask them for suggestions regarding content and language.

Patient Centricity

- Pay sufficient attention to explaining the need of your research and the added value for patients. Address the question 'Did the demand for this research come directly from the patients of the target group?'. If so, explain the conversation you had with these patients.
- If the application is a follow-up of the results from (a) previous study/studies, please elaborate on the status and the results of this previous study. Explain in which way the previously gathered results will add value to the current proposal.
- Explain the choice for the used inclusion criteria for study participants
- Elaborate on the expected process after the project. Think about questions like: Will there be a need for a follow-up study? Will the treatment be practically feasible? Will the treatment be available for a wide spectrum of patients? Is contact already made with other centres? Etcetera.
- Explain the possible burden and benefits that patients can experience by participating in the study. Keep in mind that effects in quality of life are equally as important as effects in life expectancy. Pay attention to the follow-up of both physical and mental side-effects during the study.
- Explain the cost-benefit ratio for participants. Do the expected results outweigh the burden and risks? Did you consult patients in the evaluation of the cost-benefit ratio?
- Clearly explain the interventions and steps that participants will undergo in the process and make sure the burden for participants is minimized as much as possible.
- Explain the communication and dissemination plan of the results among the patients.

Patient Involvement

- Actively involve patients in your research by contacting a patient association from the start of developing the research. Actively involve them during the whole study process (the preparation of the project, the conduction of the research, and the dissemination of the results). Where passive involvement includes informing patients, active involvement indicates a form of co-creating and forming a substantial contribution to the research.
- Does your research concern a small group of patients of which there is no patient association? You can still actively involve patients by approaching patients (that are not part of a patient

organization) and ask them to collaborate and give feedback on your research. You can also involve ex-patients or loved ones.
- Pay attention to informing participants about (interim) results.
- Pay attention to the wide-spread dissemination of the study results. Point out which steps you are going to take to reach as many patients as possible and which media you are going to use for this.
- Make sure you explain your patient involvement in a concrete way: elaborate on your already made steps and the steps you are still planning to take. Think about: In which way did/will you collaborate with patients? Who are these patients? In which phases of your research will you involve patients? Which questions will be/where asked to these patients? How will be/was this feedback implemented? How are you planning to disseminate your results to participating patients and patients of your target group?

ANNEX 1. Conditions of external inclusion centers

Funding for external inclusion centers located in countries other than the funding parties of this call (i.e. centers located outside Belgium, France, Spain and the Netherlands), will be provided by Anticancer Fund (ACF) or the Dutch Cancer Society (KWF). ACF and KWF will provide this budget to the Main Applicant, and the Main Applicant is responsible for distribution of the budget among the external inclusion centers.	
External Inclusion Center is an organisation outside the funding consortium countries (i.e. outside Belgium, France, Spain or the Netherlands)	- The center only includes patients for a clinical study and has no active research role in the project. - The center is preferably located within Europe. If the applicant wishes to include inclusion centers outside of Europe, it should be limited and a strong rationale and justification should be provided on the need, feasibility, and prior existence (if any) of the intercontinental collaboration. - This center has no right to the overall project results and analyses. An exception to this may be that an external inclusion center retains the right on its own generated data, information, samples, knowledge and inventions. These agreements are specified in the project specific clinical trial agreement.
Budget	- The budget should be listed as 'External service provider' or equivalent. - The budget should be based on a per-patient-fee and estimated enrolment numbers. - The structure/build-up of the per-patient-fee should be specified and substantiated with a cost-specification of services that are included in the per-patient-fee. - The requested budget should be listed as amount per inclusion center, based on the per-patient-fee and site-specific enrolment target (i.e. estimated enrolment number per site, as specified in the Clinical Trial Agreement). - For each site, the requested budget should be substantiated with a quotation (including taxes, if applicable), or appendix of the Clinical Trial Agreement describing financial agreements. - The requested site-budget may include a start-up and close-out fee for support in the approval and reporting process of the Ethics Committee, or other applicable authorities; this fee should be substantiated by a specification of these costs.
Accountability	- Financial accountability will be the responsibility of the Main Applicant. - Actual realized expenditures on the inclusion centers should be reported in the financial end report of the project by the Main Applicant and be accounted for by substantiated invoices of each center. The financial end report will be shared with the applicable funding organisation (ACF or KWF) - In case major discrepancies between the estimated budget and actual expenditures arise, or other issues with the financial accountability of the external inclusion center-costs occur, the Main Applicant and/or the Main Applicant's funding organisation immediately will inform the applicable funding organisation (ACF or KWF), as well as the JCS, so appropriate corrective actions can be taken. - Expenses and quality will be further monitored by the Main Applicant's funding organisation, in accordance with the Main Applicant's funding organisation conditions.
Coordination	- Funding provided by ACF or KWF for external inclusion centers will be documented in a letter of grant, provided by ACF or KWF, as applicable, to the Main Applicant. - The letter of grant will specify at least the following information for each supported project: Project title, amount of provided budget; specified per inclusion center and per-patient-fee; estimated project start- and end-date. - Funding provided by ACF or KWF for external inclusion centers will be provided to the Main Applicant, by means of milestone-based payments. Milestones will be identified per project and documented in the letter of grant, prior to the start of the project.

	- At the end of the supported project, ACF or KWF, as applicable, will receive a report or justification on the realized costs for the external inclusion centers from the Main Applicant's funding organisation or from the Main Applicant directly. This may include a (copy of the) financial end report including quotes, expenditures, and corresponding invoices. In case any budget meant for external inclusion centers remains at the end of the project, this will be returned to the applicable funding organisation (ACF or KWF).
Further Guidance	Please contact one of the contact persons listed below if you have questions regarding the above.
Contact person	**Anticancer Fund (ACF)** Rica Capistrano Rica.capistrano@anticancerfund.org +32 2 268 48 16 **Dutch Cancer Society (KWF)** Tessa Nauta tnauta@kwf.nl +31205700437