GRF-CRIS Real-Life Trials in Oncology Programme.
Call for Applications 2024

Awards certificate

Members of the GRF-CRIS Real-Life Trials in Oncology Programme Evaluation Committee

Certifies

- On **25th October 2024** the RLTiO Evaluation Committee held the evaluation meeting of the **GRF-CRIS Real-Life Trials in Oncology Programme**, at virtual meeting.

  The **attendees** to the evaluation meetings were:
  Prof. Michel Ducreux – Gustave Roussy - FR
  Prof. Alexandra Leary – Gustave Roussy - FR
  Prof. Emiliano Calvo – HM CIOCC - SP
  Prof. Fernando Rico-Villademoros – COCIENTE S.L. - SP
  Mr. Antonio López – CNIO – SP – Secretariat Lead
  Dr. Jesús Sánchez – CRIS contra el cáncer
  Dr. Tamara Mondéjar – CRIS contra el cáncer

  Excused their absence to the meeting:
  Prof. Fabrice André – Gustave Roussy - FR
  Prof. Benjamin Besse – Gustave Roussy - FR
  Prof. Ignacio Durán - IDIVAL – SP

- After the evaluation meeting there was a post-meeting discussion, by email, participating the whole Evaluation Committee (attendees and non-attendees to the meeting)

- Considering the Evaluation Meeting and the Post-Meeting discussion, the Evaluation Committee decided to Award the Candidacy **RLTiO2024_01 (BRAVA)**:

Project: Two-arm, Phase II, Non-Randomized Study to Assess the Role of BRCAness Biomarkers in the Treatment of Patients with AdVanced Uterine LeiomyosarcomA with Niraparib and Temozolamide

Principal Investigators: **Patricia Pautier** (Institut Gustave-Roussy)
César Serrano García (VHIO Vall d'Hebron Instituto de Oncología)

Budget: **798.632,07€** (377.741,66€ at GRI / 420.890,41€ at VHIO)

What is signed by all Members of the Evaluation Committee.

DocuSigned by:
Fabrice André
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Dr. Fabrice Andre

DocuSigned by:
Fernando Rico-Villademoros
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Dr. Fernando Rico-Villademoros

DocuSigned by:
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Dr. Alexandra Leary

DocuSigned by:
Calvo
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Dr. Emiliano Calvo

DocuSigned by:
Michel Ducreux
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Dr. Michel Ducreux

Dr. Ignacio Durán

DocuSigned by:
Benjamin Besse
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Dr. Benjamin Besse

Real-Life Trials in Oncology Programme. Call for applications 2024

EVALUATION MEETING MINUTES

25th October 2024

Venue:
Virtual Meeting Zoom: https://us02web.zoom.us/j/82486166039

Participants:
Prof. Michel Ducreux – Gustave Roussy - FR
Prof. Alexandra Leary – Gustave Roussy - FR
Prof. Emiliano Calvo – HM CIOCC - SP
Prof. Fernando Rico-Villademoros – COCIENTE S.L. - SP
Mr. Antonio López – CNIO – SP – Secretariat Lead
Dr. Jesús Sánchez – CRIS contra el cáncer
Dr. Tamara Mondéjar – CRIS contra el cáncer

Excused their absence:
Prof. Fabrice André – Gustave Roussy - FR
Prof. Benjamin Besse – Gustave Roussy - FR
Prof. Ignacio Durán - IDIVAL – SP

17:00 - 17:10 Welcome and Introduction

Antonio López (ALo) welcomed and introduced all members of the GRF-CRIS Evaluation Committee, and Tamara and Jesús as CRIS cancer team. **ALo** excused the absence of Dr. André, Dr. Besse and Dr. Durán.

ALo reminded to the panel the Terms and Conditions of the Real-Life Trials in Oncology Programme and the criteria for evaluation, emphasizing the necessity of clarifying the "Real-Life Trial" definition.

Tamara Mondéjar (TM) asked to the evaluators if they would mind recording the

meeting to prepare the minutes. **ALo** explained that it will be only for preparing the minutes and after that, CRIS will delete this file. Evaluators agreed in recording the meeting.

Alexandra Leary (ALe) agreed about the trouble of defining what is considered a "Real-Life Trial", considered it necessary to remind people before they submit what we mean by a real-life pragmatic trial.

ALe explained that the tested strategy has to be simple, feasible across the world (meaning, various clinical settings, not only in tertiary expert centers), low-level infrastructure, key endpoint, simple inclusion/exclusion criteria, minimal data point, minimal extra trial related procedures, affordable... And, whether the result of the trial is positive or negative (actually, a negative trial could be informative), it should change, or inform, oncology practice, broadly.

ALe concluded that, basically, real-life trials are **simple** trials, and **affordable**, and it is necessary to communicate it better.

ALe also pointed that the requested amounts of funds for this call are probably the highest until date, so found the need to remind candidates that trials need to be affordable, and to provide more guidance.

ALo asked the rest of evaluators about their opinion.

Fernando Rico-Villademoros (FRV) agreed with most of the characteristics of a pragmatic trial, and he stated that it would be nice to add that the endpoints, at least the primary endpoints, should be a **patient relevant endpoint**. **ALe** agreed with the comment.

FRV suggested that instead of "simple inclusion criteria" he would say "**simple selection criteria**". Because most of the problems with the trials are the exclusión criteria. **ALe** agreed with "Simple selection criteria"

Emiliano Calvo (EC) agreed and considered the definition of pragmatic trials very well described by Alexandra. **EC** stated that, with pragmatic trials, you must really look for indications and specific needs or areas to be able **to change practice or to inform** in a relevant way the standard practice. **ALe** agreed to define it as "**change or inform oncology practice"**.

About the committee reviewing process during the final selection, **ALe** said that instead of describing every trial in detail it might be easier to review the proposals having a look at the comments with the strengths and weaknesses.

ALo asked if evaluators considered entering any point of scoring in the questionnaire to this specific issue of pragmatic or real-life trial. **ALe** explained that she evaluated the first section whether it was pragmatic, feasible, low-cost...

EC pointed out that there might be a specific question at the questionnaire asking for if the evaluator thinks this is a pragmatic study that can change or inform the practice. **ALe** stated that it was not a specific question as to whether it's pragmatic and suggested adding that question to future calls. **FRV** suggested to set up the type of studies that are wanted to see.

ALe mentioned that this season the budgets were too high. **FRV** suggested using "**tested strategy is affordable**" instead of "tested strategy is low-cost". **ALe** agreed.

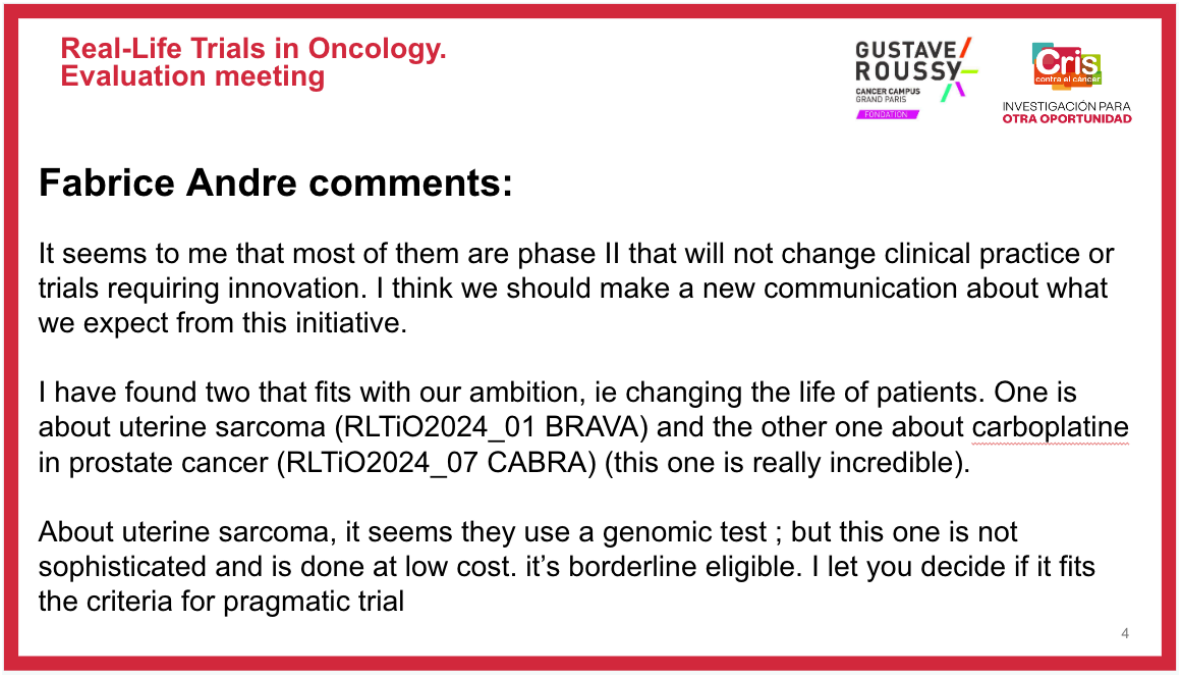
17:15 - 18:00 Discussion of proposals

CANDIDACY	PROJECT	FR_IP name	SP_IP name	FRANCE	SPAIN	TOTAL
RLTiO2024_01	BRAVA	Patricia Pautier	César Serrano García	377.741,66 €	420.890,41 €	**798.632,07 €**
RLTiO2024_02	Chemoimmunotherapy	PI: Claudia Pasqualini Co-PI: Pablo Berlanga	PI: María Adela Cañete Nieto Co-PI: Lucas Moreno Martín-Retortillo	449.900,00€	449.900,00€	**899.800,00 €**
RLTiO2024_05	MRDSarc	Benjamin Verret	César Serrano García	543.087,60 €	514.090,86 €	**1.057.178,46 €**
RLTiO2024_04	PREVEMM	Alina Danu	Joaquín Martínez López	612.683,50 €	612.683,50 €	**1.225.367,00 €**
RLTiO2024_08	AmeloBRAF	François-Régis Ferrand	Irene Braña Garcia	747.043,00€	752.276,82€	**1.499.319,82 €**
RLTiO2024_07	CABRA	Alice BERNARD-TESSIER	Elena Castro Marcos	507.375,00 €	251.551,30 €	**758.926,30 €**
RLTiO2024_03	ARTURO	Capucine Baldini	PI: Maria Vieito Co-PI: Joan Seoane Suarez	376.750,00 €	379.120,06 €	**755.870,06 €**
RLTiO2024_06	TRANSFORMER	Cristina Smolenschi	Jorge Barriuso Feijoo	441.848,00 €	441.848,00 €	**883.696,00 €**

ALo shared the slides with the information of each proposal and pointed out that some of them have some relevant differences in the evaluation between the two evaluators.

TM pointed out that the Spanish PI from BRAVA (number one; first scored) and MRDSarc (number five; third scored) proposals were the same. So, they both cannot be awarded.

ALo shared some comments from Fabrice, who considered that some of them are phase II trials so not really changing practice.



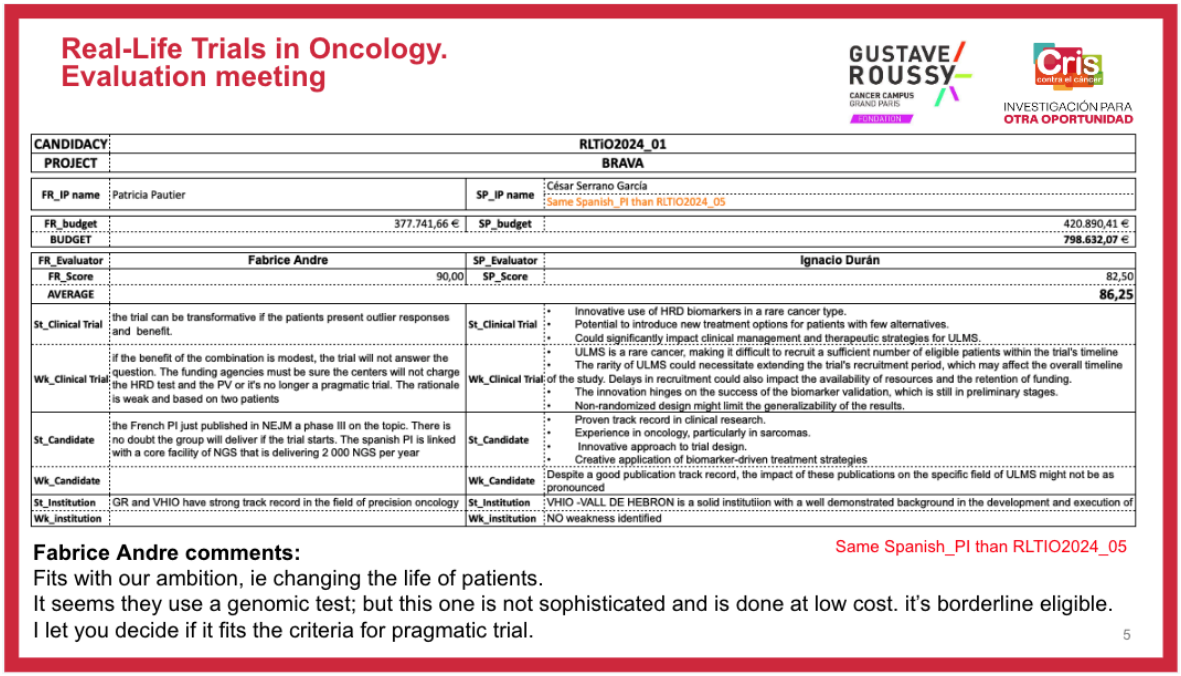
FRV noted that a phase II can change the clinical practice. **ALe** found single arm trials that were pragmatic trials. Phase II trials that could inform at least and possibly even change practice but pragmatic are not for testing new drugs.

FRV noted that a phase II trial could not be so pragmatic because of the endpoints used for demonstrating or supporting the proof of concept. But definitely phase II trials can change clinical practice.

ALo gave the CRIS Cancer point of view that phase II is not a bad proposal itself, in terms of practice changing, it depends on the proposal.

RLTiO2024_01 - BRAVA

ALo shared the first proposal's slide, titled "Two-arm, Phase II, Non-Randomized Study to Assess the Role of BRCAness Biomarkers in the Treatment of Patients with AdVanced Uterine LeiomyosarcomA with Niraparib and Temozolamide".



Real-Life Trials in Oncology. Evaluation meeting

CANDIDACY	RLTiO2024_01		
PROJECT	BRAVA		
FR_IP name	Patricia Pautier	SP_IP name	César Serrano García Same Spanish_PI than RLTIO2024_05
FR_budget	377.741,66 €	SP_budget	420.890,41 €
BUDGET			798.632,07 €
FR_Evaluator	Fabrice Andre	SP_Evaluator	Ignacio Durán
FR_Score	90,00	SP_Score	82,50
AVERAGE			86,25
St_Clinical Trial	the trial can be transformative if the patients present outlier responses and benefit.	St_Clinical Trial	• Innovative use of HRD biomarkers in a rare cancer type. • Potential to introduce new treatment options for patients with few alternatives. • Could significantly impact clinical management and therapeutic strategies for ULMS.
Wk_Clinical Trial	if the benefit of the combination is modest, the trial will not answer the question. The funding agencies must be sure the centers will not charge the HRD test and the PV or it's no longer a pragmatic trial. The rationale is weak and based on two patients	Wk_Clinical Trial	• ULMS is a rare cancer, making it difficult to recruit a sufficient number of eligible patients within the trial's timeline • The rarity of ULMS could necessitate extending the trial's recruitment period, which may affect the overall timeline of the study. Delays in recruitment could also impact the availability of resources and the retention of funding. • The innovation hinges on the success of the biomarker validation, which is still in preliminary stages. • Non-randomized design might limit the generalizability of the results.
St_Candidate	the French PI just published in NEJM a phase III on the topic. There is no doubt the group will deliver if the trial starts. The spanish PI is linked with a core facility of NGS that is delivering 2 000 NGS per year	St_Candidate	• Proven track record in clinical research. • Experience in oncology, particularly in sarcomas. • Innovative approach to trial design. • Creative application of biomarker-driven treatment strategies
Wk_Candidate		Wk_Candidate	Despite a good publication track record, the impact of these publications on the specific field of ULMS might not be as pronounced
St_Institution	GR and VHIO have strong track record in the field of precision oncology	St_Institution	VHIO -VALL DE HEBRON is a solid institution with a well demonstrated background in the development and execution of
Wk_institution		Wk_institution	NO weakness identified

Fabrice Andre comments:
Fits with our ambition, ie changing the life of patients.
It seems they use a genomic test; but this one is not sophisticated and is done at low cost. it's borderline eligible.
I let you decide if it fits the criteria for pragmatic trial.

Same Spanish_PI than RLTIO2024_05

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None of the evaluators of the BRAVA project were present at the meeting and read some of the comments from the evaluators (Fabrice and Ignacio):

- The trial can be transformative if the patients present outlier responses and benefits.
- Innovative use of HRD biomarkers in a rare cancer type.
- Potential to introduce new treatment options for patients with few alternatives.
- Could significantly impact clinical management and therapeutic strategies for ULMS.

ALo remarked the final comment from Fabrice that "this proposal fits with our mission of changing the lives of patients, that is not sophisticated, that is done at low-cost and that is a borderline eligible proposal" and shared the proposal document.

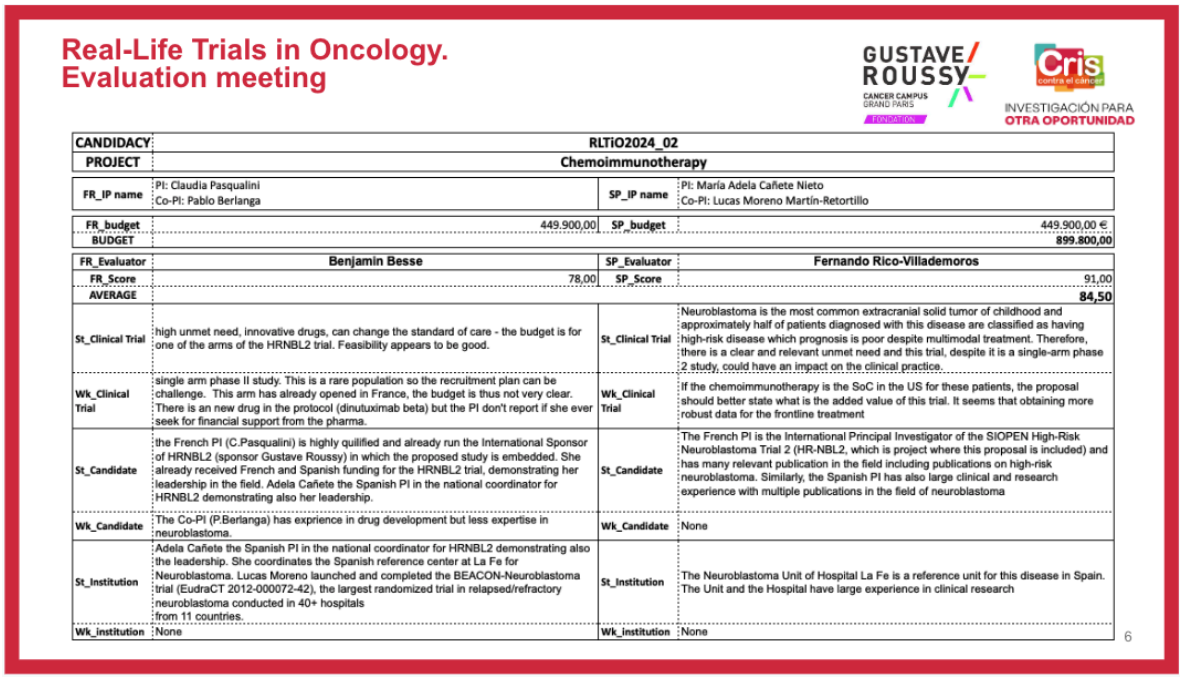
EC asked if there is money for one proposal. ALo confirmed that It is up to the total budget of the call, that is 1.5 million euros.

EC suggested to see the first three ones in the score, focusing more on having an agreement in which ones are fundable and, if there is any major objection in any of the evaluators, say about it.

TM remarked that the first one and the third one in the score were from the same Spanish PI. so, they cannot be both awarded and perhaps you prefer to check also the fourth one.

RLTiO2024_02 - Chemoimmunotherapy

ALo shared the second proposal`s information.



Real-Life Trials in Oncology. Evaluation meeting

CANDIDACY	**RLTiO2024_02**		
PROJECT	**Chemoimmunotherapy**		
FR_IP name	PI: Claudia Pasqualini Co-PI: Pablo Berlanga	**SP_IP name**	PI: María Adela Cañete Nieto Co-PI: Lucas Moreno Martín-Retortillo
FR_budget	449.900,00	**SP_budget**	449.900,00 €
BUDGET			899.800,00
FR_Evaluator	**Benjamin Besse**	**SP_Evaluator**	**Fernando Rico-Villademoros**
FR_Score	78,00	**SP_Score**	91,00
AVERAGE			**84,50**
St_Clinical Trial	high unmet need, innovative drugs, can change the standard of care - the budget is for one of the arms of the HRNBL2 trial. Feasibility appears to be good.	**St_Clinical Trial**	Neuroblastoma is the most common extracranial solid tumor of childhood and approximately half of patients diagnosed with this disease are classified as having high-risk disease which prognosis is poor despite multimodal treatment. Therefore, there is a clear and relevant unmet need and this trial, despite it is a single-arm phase 2 study, could have an impact on the clinical practice.
Wk_Clinical Trial	single arm phase II study. This is a rare population so the recruitment plan can be challenge. This arm has already opened in France, the budget is thus not very clear. There is an new drug in the protocol (dinutuximab beta) but the PI don't report if she ever seek for financial support from the pharma.	**Wk_Clinical Trial**	If the chemoimmunotherapy is the SoC in the US for these patients, the proposal should better state what is the added value of this trial. It seems that obtaining more robust data for the frontline treatment
St_Candidate	the French PI (C.Pasqualini) is highly quilified and already run the International Sponsor of HRNBL2 (sponsor Gustave Roussy) in which the proposed study is embedded. She already received French and Spanish funding for the HRNBL2 trial, demonstrating her leadership in the field. Adela Cañete the Spanish PI in the national coordinator for HRNBL2 demonstrating also her leadership.	**St_Candidate**	The French PI is the International Principal Investigator of the SIOPEN High-Risk Neuroblastoma Trial 2 (HR-NBL2, which is project where this proposal is included) and has many relevant publication in the field including publications on high-risk neuroblastoma. Similarly, the Spanish PI has also large clinical and research experience with multiple publications in the field of neuroblastoma
Wk_Candidate	The Co-PI (P.Berlanga) has exprience in drug development but less expertise in neuroblastoma.	**Wk_Candidate**	None
St_Institution	Adela Cañete the Spanish PI in the national coordinator for HRNBL2 demonstrating also the leadership. She coordinates the Spanish reference center at La Fe for Neuroblastoma. Lucas Moreno launched and completed the BEACON-Neuroblastoma trial (EudraCT 2012-000072-42), the largest randomized trial in relapsed/refractory neuroblastoma conducted in 40+ hospitals from 11 countries.	**St_Institution**	The Neuroblastoma Unit of Hospital La Fe is a reference unit for this disease in Spain. The Unit and the Hospital have large experience in clinical research
Wk_institution	None	**Wk_Institution**	None

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FRV explained that this proposal is a Phase II Study. **Michel Ducreux (MD)** fingered down about this proposal. But sometimes it may change clinical practice.

FRV considered both investigators well experienced in this area, especially the French PI, but also the Spanish one. He thought this proposal looked nice.

FRV does not understand why there is a certainly high lack of concordance, because the other collaborator scored trial us 78.

MD was concerned about the PTB teams, the budget is not very clear, the recruitment may be challenging and there is a new drug in the protocol (dinutuximab beta), but the PI doesn't report if she ever seeks financial support from the pharma. **MD** consider that are the major negative comments from Benjamin.

ALe noted that these two studies were testing a new drug. In Chemo-immunotherapy trial it is dinutuximab, and in BRAVA trial it is Niraparib, which is not approved in uterine leiomiosarcoma and has never been studied. So,

in terms of applicability, if these studies were positive, people will still not have access to these drugs. **FRV** considered it a good point. **ALe** noted that pragmatic trials were not meant to test new therapy. That's her only minor comment about these two studies.

MD said it's becoming more difficult because if you want to have trials that are changing the standard of care, that is not too big (because the finance that we can put it's not too bad, but it's not a large amount of money). So, if you cannot have a new drug in the project, at the end we are looking for something that is very, very difficult.

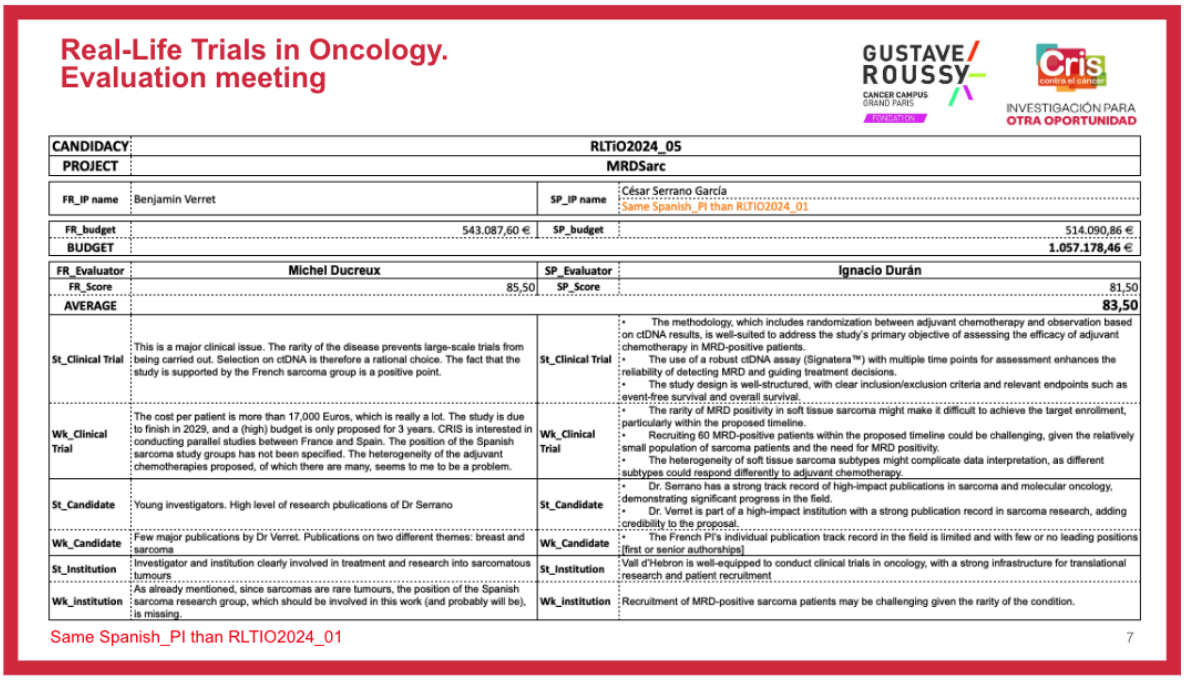
ALe responded that is what they are after: things that are de-escalating, sequencing, radiotherapy, surgery... For example, there's a study where she didn't get a good grade, testing carboplatinum BRCA mutated prostate cancer. That's a simple question, very pragmatic and it's cheap.

ALe conveyed the idea that maybe in two years they will realize that this practice idea of pragmatic trials doesn't make sense anymore but, at least for now, there's plenty of other ways to finance drug trials. She thinks that's not what they're supposed to be doing there.

MD said that BTS and we have not a lot of popular concerning equations about radiotherapy or even surgery, because this is very, very difficult to find financing or funding for this kind of studies, that had absolutely no question about new drug and support from industry or something like that. **MD** explained that he had not read all the proposals, but at least the two proposals that he had reviewed were absolutely not in the way.

ALe summarized that in the past calls they have had really nice projects on surgery or radiotherapy. They didn't make the cut that time but we should remind people none of them resubmitted it. And we should remind them because some of them are really good projects. We had trouble deciding, there were sometimes young investigators, the idea was good, and they corresponded to the philosophy of this call.

RLTiO2024_05 - MRDSarc



Real-Life Trials in Oncology. Evaluation meeting

CANDIDACY	RLTiO2024_05		
PROJECT	MRDSarc		
FR_IP name	Benjamin Verret	SP_IP name	César Serrano García Same Spanish_PI than RLTiO2024_01
FR_budget	543.087,60 €	SP_budget	514.090,86 €
BUDGET			1.057.178,46 €
FR_Evaluator	Michel Ducreux	SP_Evaluator	Ignacio Durán
FR_Score	85,50	SP_Score	81,50
AVERAGE			83,50
St_Clinical Trial	This is a major clinical issue. The rarity of the disease prevents large-scale trials from being carried out. Selection on ctDNA is therefore a rational choice. The fact that the study is supported by the French sarcoma group is a positive point.	St_Clinical Trial	• The methodology, which includes randomization between adjuvant chemotherapy and observation based on ctDNA results, is well-suited to address the study's primary objective of assessing the efficacy of adjuvant chemotherapy in MRD-positive patients. • The use of a robust ctDNA assay (Signatera™) with multiple time points for assessment enhances the reliability of detecting MRD and guiding treatment decisions. • The study design is well-structured, with clear inclusion/exclusion criteria and relevant endpoints such as event-free survival and overall survival.
Wk_Clinical Trial	The cost per patient is more than 17,000 Euros, which is really a lot. The study is due to finish in 2029, and a (high) budget is only proposed for 3 years. CRIS is interested in conducting parallel studies between France and Spain. The position of the Spanish sarcoma study groups has not been specified. The heterogeneity of the adjuvant chemotherapies proposed, of which there are many, seems to me to be a problem.	Wk_Clinical Trial	• The rarity of MRD positivity in soft tissue sarcoma might make it difficult to achieve the target enrollment, particularly within the proposed timeline. • Recruiting 60 MRD-positive patients within the proposed timeline could be challenging, given the relatively small population of sarcoma patients and the need for MRD positivity. • The heterogeneity of soft tissue sarcoma subtypes might complicate data interpretation, as different subtypes could respond differently to adjuvant chemotherapy.
St_Candidate	Young investigators. High level of research pbulications of Dr Serrano	St_Candidate	• Dr. Serrano has a strong track record of high-impact publications in sarcoma and molecular oncology, demonstrating significant progress in the field. • Dr. Verret is part of a high-impact institution with a strong publication record in sarcoma research, adding credibility to the proposal.
Wk_Candidate	Few major publications by Dr Verret. Publications on two different themes: breast and sarcoma	Wk_Candidate	• The French PI's individual publication track record in the field is limited and with few or no leading positions [first or senior authorships]
St_Institution	Investigator and institution clearly involved in treatment and research into sarcomatous tumours	St_Institution	Vall d'Hebron is well-equipped to conduct clinical trials in oncology, with a strong infrastructure for translational research and patient recruitment
Wk_institution	As already mentioned, since sarcomas are rare tumours, the position of the Spanish sarcoma research group, which should be involved in this work (and probably will be), is missing.	Wk_institution	Recruitment of MRD-positive sarcoma patients may be challenging given the rarity of the condition.

Same Spanish_PI than RLTIO2024_01 7

ALe explained that the project does not use a MRD test or a MRD biomarker, however it's basically a prognostic trial to figure out who needs adjuvant treatment versus doesn't need adjuvant treatment, and they use this to classify patients into levels of risk, to guide and personalize adjuvant treatment. She believes it is not an expensive technique. She believes that's why they said HRD because it sort of resembles genomic instability score.

MD explained that the idea of the project was to select patients for adjuvant chemotherapy in the soft tissue platform of sarcoma using circulating tumor DNA. In his opinion, the idea was not bad because there is no drug. It is not a very new concept but there is no demonstration of interest in the concept of ctDNA in ongoing trials, and especially not in soft tissues sarcoma. So, not too bad.

MD pointed out this is a rare disease, so it's a little bit more complicated to build a large file and, in terms of number of patients, there are not so many patients. So, he showed some doubt about the fact that, in the end, it could change a clinical practice because the clinical trial project is only done on 60 patients.

ALe gave the opinion that this proposal would inform practice and then justify the study, because **MD** had pointed out that the proposal was very good. She suggested to them to do something cheap that will change practice, and it should cost less than 300.000€.

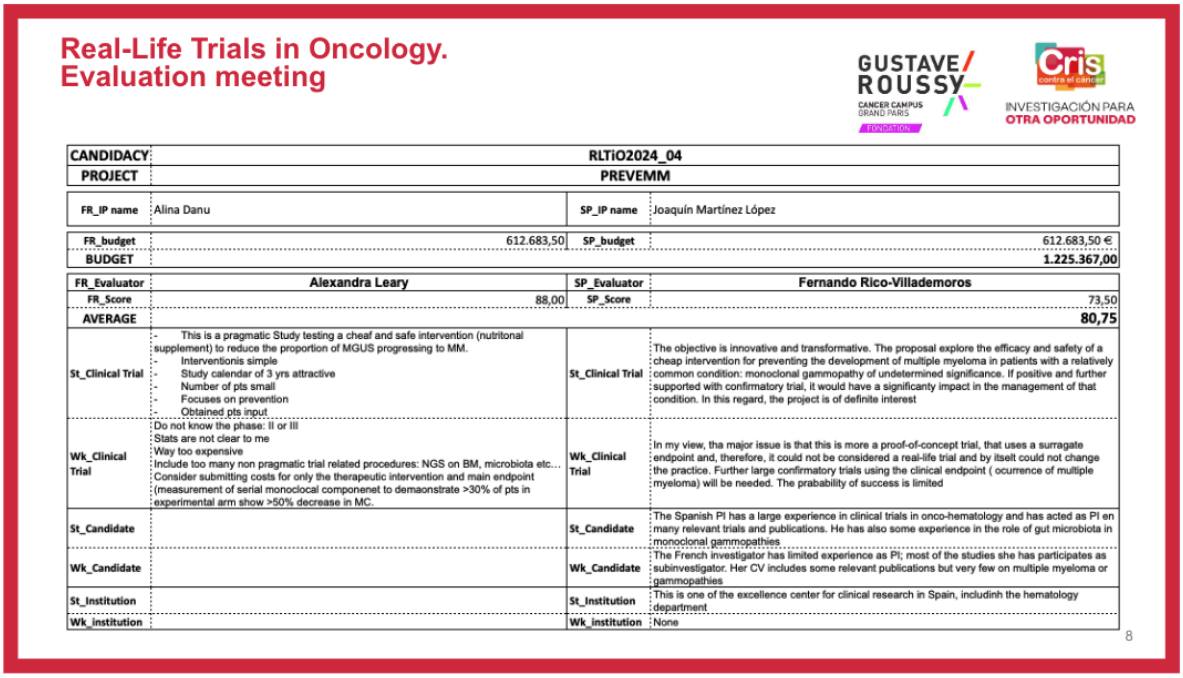
MD pointed out that comments were quite consistent between Ignacio Duran and himself.

ALo emphasized that the current budget was 1 million and indicated that the budget was quite well balanced.

ALe asked how they are funding Signatera™. Because, with Signatera™ you have to do NGS on a tumor, and it is actually the whole exome of the tumor on an FFPE sample, and then they do a personalized ctDNA.

MD answered that Signatera™ will be provided by Natera, and that they have included the extra cost in the budget, but that the test's cost is given. **ALe** liked the proposal.

RLTiO2024_04 - PREVEMM



Real-Life Trials in Oncology. Evaluation meeting

CANDIDACY	**RLTiO2024_04**		
PROJECT	**PREVEMM**		
FR_IP name	Alina Danu	**SP_IP name**	Joaquín Martínez López
FR_budget	612.683,50	**SP_budget**	612.683,50 €
BUDGET			**1.225.367,00**
FR_Evaluator	**Alexandra Leary**	**SP_Evaluator**	**Fernando Rico-Villademoros**
FR_Score	88,00	**SP_Score**	73,50
AVERAGE			**80,75**
St_Clinical Trial	- This is a pragmatic Study testing a cheaf and safe intervention (nutritonal supplement) to reduce the proportion of MGUS progressing to MM. - Interventionis simple - Study calendar of 3 yrs attractive - Number of pts small - Focuses on prevention - Obtained pts input	**St_Clinical Trial**	The objective is innovative and transformative. The proposal explore the efficacy and safety of a cheap intervention for preventing the development of multiple myeloma in patients with a relatively common condition: monoclonal gammopathy of undetermined significance. If positive and further supported with confirmatory trial, it would have a significanty impact in the management of that condition. In this regard, the project is of definite interest
Wk_Clinical Trial	Do not know the phase: II or III Stats are not clear to me Way too expensive Include too many non pragmatic trial related procedures: NGS on BM, microbiota etc… Consider submitting costs for only the therapeutic intervention and main endpoint (measurement of serial monoclocal componenet to demaonstrate >30% of pts in experimental arm show >50% decrease in MC.	**Wk_Clinical Trial**	In my view, tha major issue is that this is more a proof-of-concept trial, that uses a surragate endpoint and, therefore, it could not be considered a real-life trial and by itselt could not change the practice. Further large confirmatory trials using the clinical endpoint (ocurrence of multiple myeloma) will be needed. The prabability of success is limited
St_Candidate		**St_Candidate**	The Spanish PI has a large experience in clinical trials in onco-hematology and has acted as PI en many relevant trials and publications. He has also some experience in the role of gut microbiota in monoclonal gammopathies
Wk_Candidate		**Wk_Candidate**	The French investigator has limited experience as PI; most of the studies she has participates as subinvestigator. Her CV includes some relevant publications but very few on multiple myeloma or gammopathies
St_Institution		**St_Institution**	This is one of the excellence center for clinical research in Spain, includinh the hematology department
Wk_institution		**Wk_institution**	None

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ALe explained that it is a Phase II trial, interventional, that the intervention is just an oral tablet, which is like a bacterium that's supposed to just modulate the gut microbiota, and that the aim of the intervention is to try to diminish the risk of MGUS escalating, reduce the chance that MGUS progresses to Multiple Myeloma. The oral tablet is fairly a dietary supplement with basically bacteria in it, and the point is to change intestinal microbiota. The stats looked weird to her, but she pointed out that she is not a statistician. **ALe** added that the treatment intervention is cheap and safe, and that the aim is to intervene in a pre-invasive disease to prevent it from going to an incurable cancer.

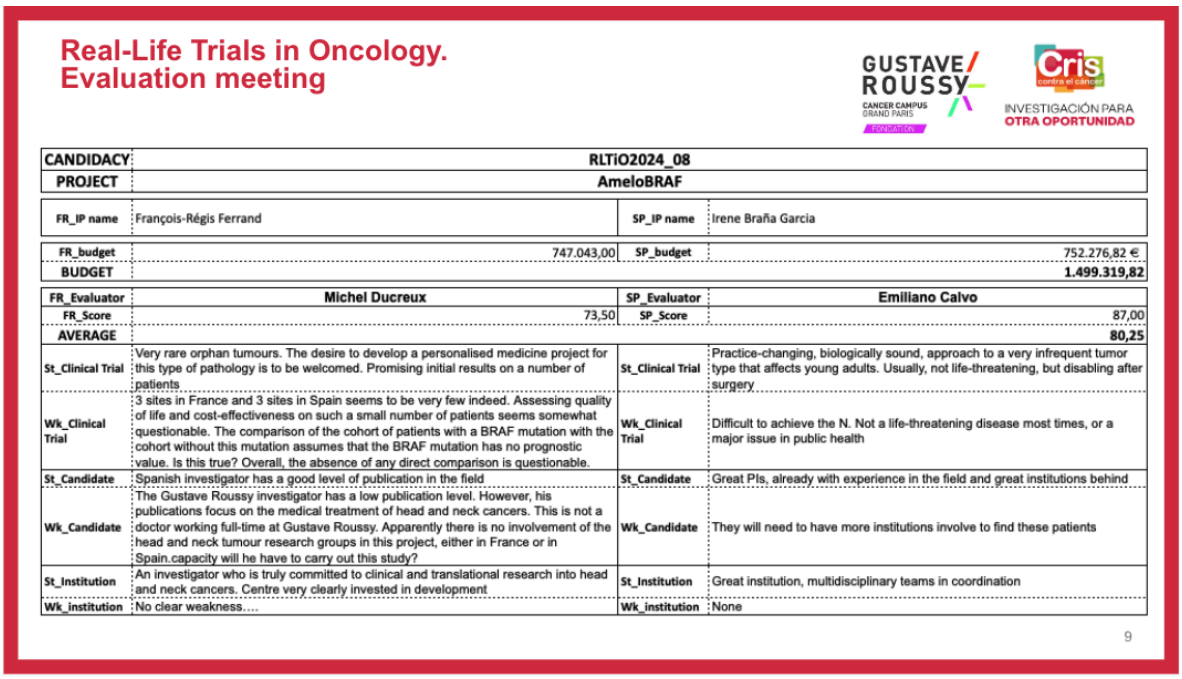
ALe summarized the positive points of the proposal. It is a pragmatic study testing a cheap and safe intervention, a nutritional supplement to reduce the proportion of MGUS progressing to Multiple Myeloma. The intervention is simple. The study calendar is attractive because it's three years, so you get results quite quickly. You do not have to wait 10 years. The number of patients is very small. Focuses on prevention. They obtain the patient's input.

Ale said she couldn't figure out if it was a Phase II or a Phase III trial. She couldn't

interpret the stats. They can't include NGS on bone marrow and microbiota. So, it just has to be the intervention and that way they'll bring their costs down.

FRV agreed with Alexandra's comment that, from that point of view, it is a pragmatic trial. But the issue for him are the clinical endpoints, the primary endpoint, because they try to make a proof-of-concept trial using a surrogated endpoint, instead of a clinical one. **ALe** agreed with FRV arguing that their primary endpoint is a 50% reduction of the monoclonal component of the MGUS. **FRV** wondered if, with a surrogate endpoint, investigators would be able to change or inform the practice, **FRV** found it quite difficult. **ALe** agreed and added that this was why she had said that the statistical plan was a weakness.

RLTiO2024_08 - AmeloBRAF



Real-Life Trials in Oncology.
Evaluation meeting

CANDIDACY	RLTiO2024_08		
PROJECT	AmeloBRAF		
FR_IP name	François-Régis Ferrand	SP_IP name	Irene Braña Garcia
FR_budget	747.043,00	SP_budget	752.276,82 €
BUDGET			1.499.319,82
FR_Evaluator	Michel Ducreux	SP_Evaluator	Emiliano Calvo
FR_Score	73,50	SP_Score	87,00
AVERAGE			80,25
St_Clinical Trial	Very rare orphan tumours. The desire to develop a personalised medicine project for this type of pathology is to be welcomed. Promising initial results on a number of patients	St_Clinical Trial	Practice-changing, biologically sound, approach to a very infrequent tumor type that affects young adults. Usually, not life-threatening, but disabling after surgery
Wk_Clinical Trial	3 sites in France and 3 sites in Spain seems to be very few indeed. Assessing quality of life and cost-effectiveness on such a small number of patients seems somewhat questionable. The comparison of the cohort of patients with a BRAF mutation with the cohort without this mutation assumes that the BRAF mutation has no prognostic value. Is this true? Overall, the absence of any direct comparison is questionable.	Wk_Clinical Trial	Difficult to achieve the N. Not a life-threatening disease most times, or a major issue in public health
St_Candidate	Spanish investigator has a good level of publication in the field	St_Candidate	Great PIs, already with experience in the field and great institutions behind
Wk_Candidate	The Gustave Roussy investigator has a low publication level. However, his publications focus on the medical treatment of head and neck cancers. This is not a doctor working full-time at Gustave Roussy. Apparently there is no involvement of the head and neck tumour research groups in this project, either in France or in Spain.capacity will he have to carry out this study?	Wk_Candidate	They will need to have more institutions involve to find these patients
St_Institution	An investigator who is truly committed to clinical and translational research into head and neck cancers. Centre very clearly invested in development	St_Institution	Great institution, multidisciplinary teams in coordination
Wk_institution	No clear weakness....	Wk_institution	None

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EC explained that this was a Phase II study in ameloblastoma, a very infrequent tumor type, an odontogenic tumor in the teeth that doesn't generate metastasis and doesn't kill the patient, but after the surgery, when it is locally advanced, there is some loss in quality of life and some physical distortion or disability. So, what is affecting those patients that have this type of tumor, infrequently (less than 1.1 million). This group alludes to the BRAF mutation that occurs in half, or even higher percentage of patients, so they would like to do a Phase II study with the combination of encorafenib and binimetinib like an adjuvant approach before surgery, and improve quality of life and the disability. **EC** thought that this might change the practice if it is positive because no studies will be done for this indication. However, the impact in oncology is really minor, because this is not a lethal tumor, and the frequency is very small.

EC added that the group seems to be well connected to get these patients, because that is the challenge also, to get the patients.

MD pointed out that they were speaking about three sites in France and three sites in Spain and added that in Gustave Roussy there is probably the largest

Department of Head and Neck Cancer. So probably in France GRI is where they see the highest number of patients. Although it's a lot of patients, the pure mathematician is that it is seen only in more than 50 percent of the patients, but it means that 50 to 70. He indicated that they don't know, and in the local series, it is put in the background that it is only 50 percent.

MD added that, in terms of feasibility, he accepted the proposal. He did not see if they will really show the change of surgery, because there is a comparison, but this is an indirect comparison, there's no clear randomizations. The comparison is done with observational data. In the end, **MD** showed not too rich a fan of this study.

EC understood MD's points and pointed that it is also true that there are no other studies in the world for this indication. So, even though it is very infrequent, if they are able to communicate the possibility of this study to these patients or wherever they are, they might follow the study from any other place, because it is like a clear orphan tumor. **EC** totally agreed that it was a challenge to get patients. **EC** summarized that, for him, the most important thing is that it is true that it might change practice, but the reality is that this has almost no impact in oncology, because he has never seen a case of this type of tumor and these tumors do not kill the patient. So, it was important for the patient because they will get some improvement in quality of life.

MD intervened, agreeing it was a rare disease, a mutation on the rare disease that was only 50% of the question and planning to get with the medical treatment up to 40% response rate. At the end, the proposal was taking 40 percent of 50 percent of patients with the rare disease. So, they were speaking about less than 20 percent of the patients with a rare disease. **MD** summarized that they were doing an evaluation of quality of life on a very, very small number of patients. **MD** added the point that it was not known if the natural story of patients without the BRAF mutation is exactly the same as patients with this kind of BRAF mutation.

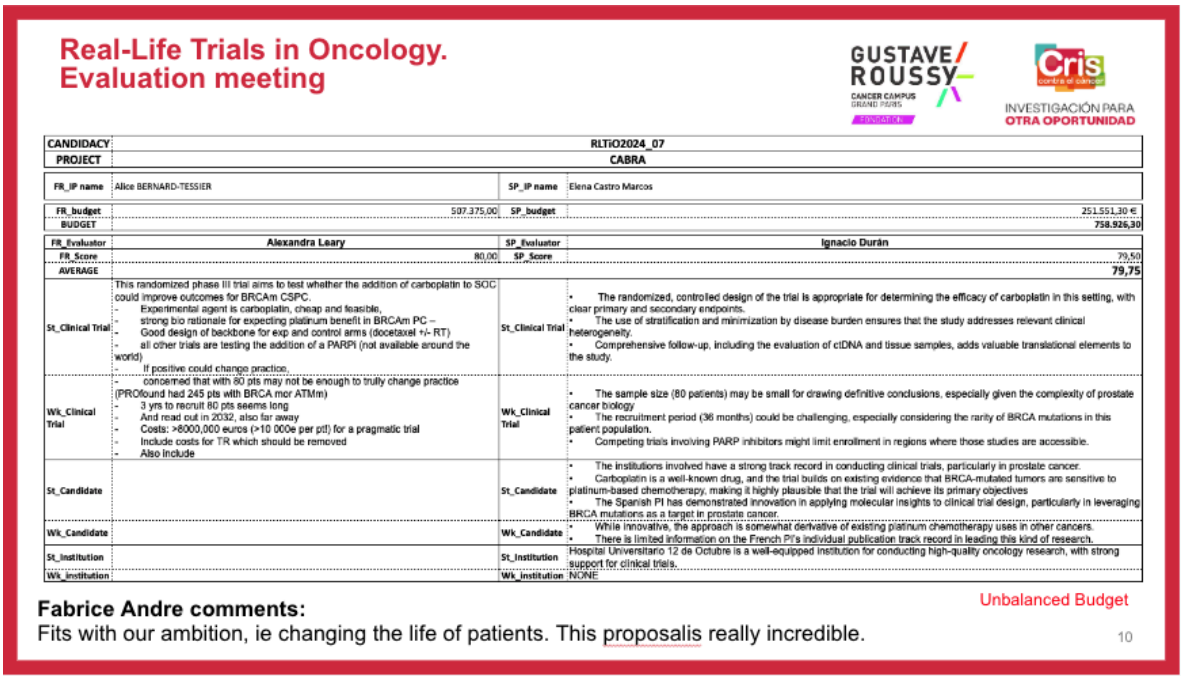
EC agreed with **MD** and added that was the reason for having different scores. **EC** pointed out that his impression is that, for this type of disease where there are no patients and it's not possible to do a formal comparison, and that actually there was not a real need. It is like trying to randomize if parachutes are saving lives, having no data of control arm, is a percentage of parachute saving life because

we already know the alternative. So here if a patient has a big tumor, that the only way to help him/her is to do a big surgery and because of the treatment, the surgery is not needed because there is a switch-case and the surgery could be more conservative and that happens to 40 percent of the patients, all of them with BRAF mutation... then, there is no need to compare because it will be something that we will only turn back. **EC** explained he understood MD's points, shared the challenges of this study and considered that having different scores is good and natural.

FRV pointed that for a rare disease, or orphan disease, he thought it is not strictly necessary to make a randomized trial, adding that they use historical controls and it's affected by regulatory authorities. Related to Emiliano's comment, **FRV** stated that it is really difficult to find support for this type of indication, for doing this research. So, at least in his opinion, he thought it's a nice opportunity for organizations such as CRIS to support something that has clinical interests, because these patients exist, and they could offer a support to a trial, providing the trial is feasible, providing the trial is able to achieve the goal of changing the practice.

MD added another constant that, without being specialist in Gastrointestinal or Head and Neck Cancer, he didn't see any reference to the GETTHI, which is a very important Head and Neck Network in science. He was surprised that it is a rare disease and there is no mention of this network, at least he didn't find that in the application form. There is no mention about the network that could be involved in, finding these patients and taking this patient from small centers to put them, to send them to share to specialized centers that could include them into the trial. **MD** insisted that in six centers (3 in France and 3 in Spain) would be able to find 40 patients, if it is really a rare disease, he pointed that he did not believe that.

RLTiO2024_07 - CABRA



Real-Life Trials in Oncology. Evaluation meeting

CANDIDACY	RLTiO2024_07		
PROJECT	CABRA		
FR_IP name	Alice BERNARD-TESSIER	SP_IP name	Elena Castro Marcos
FR_budget	507.375,00	SP_budget	251.551,30 €
BUDGET			758.926,30
FR_Evaluator	Alexandra Leary	SP_Evaluator	Ignacio Durán
FR_Score	80,00	SP_Score	79,50
AVERAGE			79,75
St_Clinical Trial	This randomized phase III trial aims to test whether the addition of carboplatin to SOC could improve outcomes for BRCAm CSPC. - Experimental agent is carboplatin, cheap and feasible, - strong bio rationale for expecting platinum benefit in BRCAm PC – - Good design of backbone for exp and control arms (docetaxel +/- RT) - all other trials are testing the addition of a PARPi (not available around the world) - If positive could change practice.	St_Clinical Trial	• The randomized, controlled design of the trial is appropriate for determining the efficacy of carboplatin in this setting, with clear primary and secondary endpoints. • The use of stratification and minimization by disease burden ensures that the study addresses relevant clinical heterogeneity. • Comprehensive follow-up, including the evaluation of ctDNA and tissue samples, adds valuable translational elements to the study.
Wk_Clinical Trial	- concerned that with 80 pts may not be enough to trully change practice (PROfound had 245 pts with BRCA mor ATMm) - 3 yrs to recruit 80 pts seems long - And read out in 2032, also far away - Costs: >8000,000 euros (>10 000e per pt) for a pragmatic trial - Include costs for TR which should be removed - Also include	Wk_Clinical Trial	• The sample size (80 patients) may be small for drawing definitive conclusions, especially given the complexity of prostate cancer biology • The recruitment period (36 months) could be challenging, especially considering the rarity of BRCA mutations in this patient population. • Competing trials involving PARP inhibitors might limit enrollment in regions where those studies are accessible.
St_Candidate		St_Candidate	• The institutions involved have a strong track record in conducting clinical trials, particularly in prostate cancer. • Carboplatin is a well-known drug, and the trial builds on existing evidence that BRCA-mutated tumors are sensitive to platinum-based chemotherapy, making it highly plausible that the trial will achieve its primary objectives • The Spanish PI has demonstrated innovation in applying molecular insights to clinical trial design, particularly in leveraging BRCA mutations as a target in prostate cancer.
Wk_Candidate		Wk_Candidate	• While innovative, the approach is somewhat derivative of existing platinum chemotherapy uses in other cancers. • There is limited information on the French PI's individual publication track record in leading this kind of research.
St_Institution		St_Institution	Hospital Universitario 12 de Octubre is a well-equipped institution for conducting high-quality oncology research, with strong support for clinical trials.
Wk_Institution		Wk_Institution	NONE

Unbalanced Budget

Fabrice Andre comments:
Fits with our ambition, ie changing the life of patients. This proposalis really incredible.

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ALe explained that this is a randomized Phase III trial of Carboplatin in combination with standard of care in men with de novo metastatic castration-sensitive Prostate Cancer that have a BRCA mutation.

ALe thought this proposal gave a pretty good evaluation, so her comments were mainly that this is a randomized Phase III trial that aims to test whether the addition of a very cheap, affordable and safe intervention, which is carboplatin, a standard of care, can improve outcomes for metastatic patients BRCA mutated in prostate cancer. The strengths were that the experimental agent is carboplatin, cheap, feasible, and it makes biological sense because it is known in breast cancer

and in ovarian cancer that Platinum works better in BRCA mutated tumors. So, there's a strong biological rationale. She thought that the design was good because the experimental and control arms use the same backbone and it's those drugs plus or minus radiotherapy and hormonal therapy. Whereas all other trials that are testing this approach are going for PARP inhibitors, which might not be available around the world, this could change practice around the world. **ALe** summarized that this could inform the practice. She was suddenly concerned because she thought the numbers were a little bit small, but considered it has already been talked about, and that, if it could at least inform practice, it would be good. **ALe** pointed out that recruitment time was a little bit long, so they'd have to reduce their cost. They're asking for 10.000€ per patient and a pragmatic trial can't have that. Part of the reason is that they included translational research into their costs so, if they remove that, then they would bring their costs down. And it is mentioned in our call that we don't fund translational research. **ALe** added that the institutions and the candidates are good. The French candidate is young, but very dynamic in prostate cancer, and that there's a good network for recruiting in prostate cancer in France.

Ignacio Durán was the other evaluator, shared the slide and read some comments from Ignacio: “randomized, controlled design of the trial is appropriate for determining the efficacy of carboplatin in this setting”, “The use of stratification and minimization by disease burden ensures that the study addresses relevant clinical heterogeneity”, “Comprehensive follow-up, including the evaluation of ctDNA and tissue samples, adds valuable translational elements to the study", "The sample size may be small for drawing definitive conclusions”, “Recruitment period of 36 months, could be challenging”, “Competing trials involving PARP inhibitors might limit enrollment", “Institutions are strong”, “Carboplatin is a well-known drug”, “The PI has demonstrated innovation in applying molecular insights to clinical trial design", “While innovative, the approach is somewhat derivative of existing platinum chemotherapy uses in other cancers”, “There is limited information on the French PI’s individual publication track ".

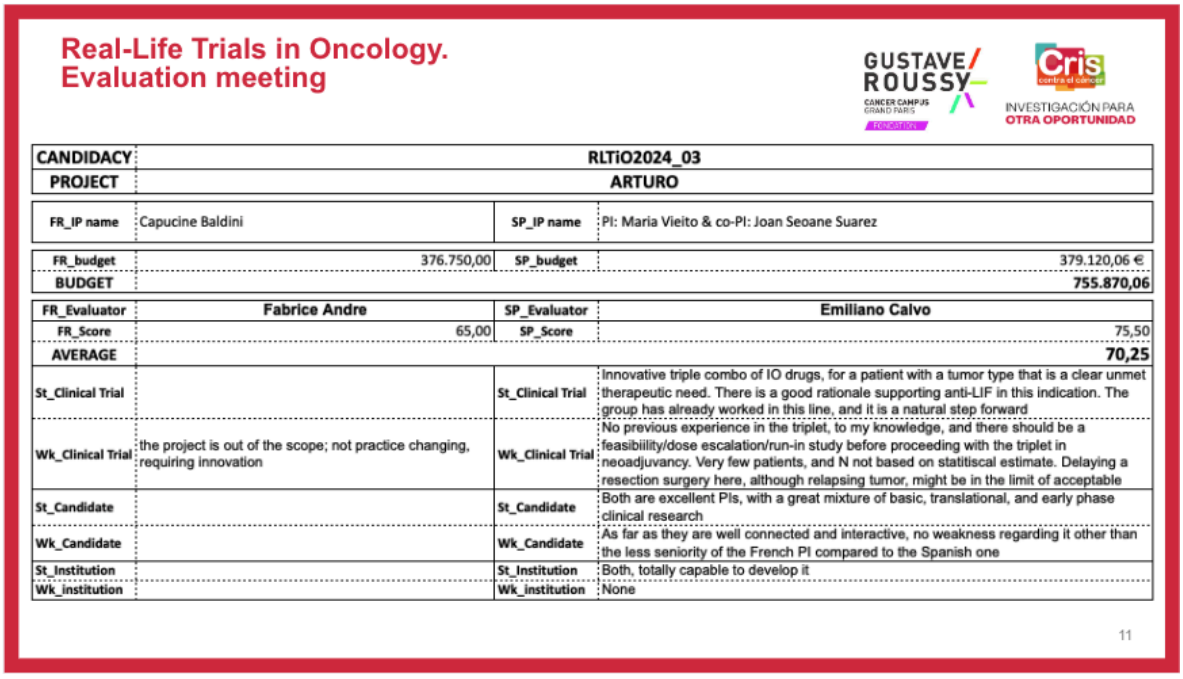
ALe pointed out that the French PI is young, that she is at the beginning of her career but she's backed by one of the biggest guys in prostate cancer, Karim Fizazi. ALe thought it's good that Karim is putting a young investigator on this

study and ALe is sure that the PI will benefit from his support and definite experience in prostate cancer.

ALo pointed out that Ignacio Durán is also working in this field and probably knows both investigators.

ALe emphasized that they have to bring down the budget and balance it, and that they can't put translational research in their budget. **ALo** pointed out the comment from Fabrice: “Fits with our ambition”.

RLTiO2024_03 - ARTURO



Real-Life Trials in Oncology. Evaluation meeting

CANDIDACY	**RLTiO2024_03**		
PROJECT	**ARTURO**		
FR_IP name	Capucine Baldini	**SP_IP name**	PI: Maria Vieito & co-PI: Joan Seoane Suarez
FR_budget	376.750,00	**SP_budget**	379.120,06 €
BUDGET			**755.870,06**
FR_Evaluator	**Fabrice Andre**	**SP_Evaluator**	**Emiliano Calvo**
FR_Score	65,00	**SP_Score**	75,50
AVERAGE			**70,25**
St_Clinical Trial		**St_Clinical Trial**	Innovative triple combo of IO drugs, for a patient with a tumor type that is a clear unmet therapeutic need. There is a good rationale supporting anti-LIF in this indication. The group has already worked in this line, and it is a natural step forward
Wk_Clinical Trial	the project is out of the scope; not practice changing, requiring innovation	**Wk_Clinical Trial**	No previous experience in the triplet, to my knowledge, and there should be a feasibility/dose escalation/run-in study before proceeding with the triplet in neoadjuvancy. Very few patients, and N not based on statitiscal estimate. Delaying a resection surgery here, although relapsing tumor, might be in the limit of acceptable
St_Candidate		**St_Candidate**	Both are excellent PIs, with a great mixture of basic, translational, and early phase clinical research
Wk_Candidate		**Wk_Candidate**	As far as they are well connected and interactive, no weakness regarding it other than the less seniority of the French PI compared to the Spanish one
St_Institution		**St_Institution**	Both, totally capable to develop it
Wk_institution		**Wk_institution**	None

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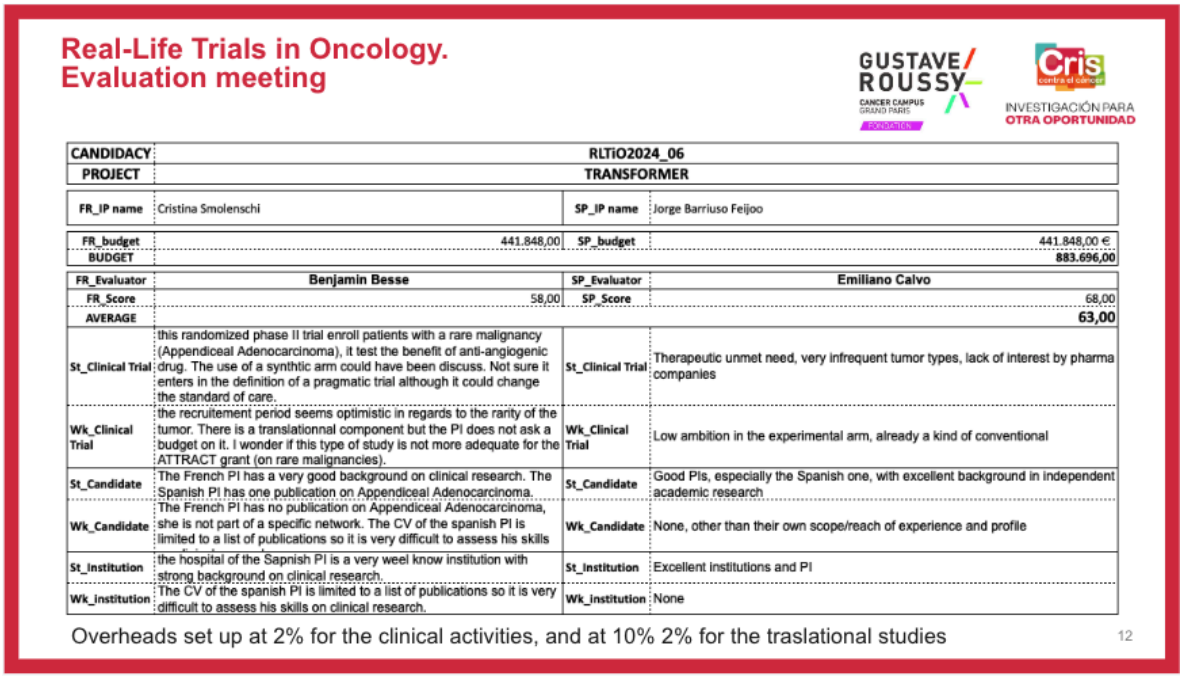
EC explained that the proposal is a “Window of Opportunity” study, of 12 patients with glioblastoma that need surgery. During the window before surgery, they give to the patients two cycles of triple immunotherapy: Anti PDL1 (Durvalumab), Anti CTLA-4 (Tremelimumab) and Anti MSC-1 (AZD0171). **EC** pointed out that the group has some experience in this setting.

ALe pointed out that a “window of opportunity” study doesn’t fit into a pragmatic call. The comment from Fabrice: “the project is out of the scope; not practice

changing, requiring innovation”

ALe summarized that it's a great study, but it's just not a pragmatic trial.

RLTiO2024_06 - TRANSFORMER



Real-Life Trials in Oncology.
Evaluation meeting

CANDIDACY	RLTiO2024_06		
PROJECT	TRANSFORMER		
FR_IP name	Cristina Smolenschi	SP_IP name	Jorge Barriuso Feijoo
FR_budget	441.848,00	SP_budget	441.848,00 €
BUDGET			883.696,00
FR_Evaluator	Benjamin Besse	SP_Evaluator	Emiliano Calvo
FR_Score	58,00	SP_Score	68,00
AVERAGE			63,00
St_Clinical Trial	this randomized phase II trial enroll patients with a rare malignancy (Appendiceal Adenocarcinoma), it test the benefit of anti-angiogenic drug. The use of a synthtic arm could have been discuss. Not sure it enters in the definition of a pragmatic trial although it could change the standard of care.	St_Clinical Trial	Therapeutic unmet need, very infrequent tumor types, lack of interest by pharma companies
Wk_Clinical Trial	the recruitement period seems optimistic in regards to the rarity of the tumor. There is a translationnal component but the PI does not ask a budget on it. I wonder if this type of study is not more adequate for the ATTRACT grant (on rare malignancies).	Wk_Clinical Trial	Low ambition in the experimental arm, already a kind of conventional
St_Candidate	The French PI has a very good background on clinical research. The Spanish PI has one publication on Appendiceal Adenocarcinoma.	St_Candidate	Good PIs, especially the Spanish one, with excellent background in independent academic research
Wk_Candidate	The French PI has no publication on Appendiceal Adenocarcinoma, she is not part of a specific network. The CV of the spanish PI is limited to a list of publications so it is very difficult to assess his skills	Wk_Candidate	None, other than their own scope/reach of experience and profile
St_Institution	the hospital of the Sapnish PI is a very weel know institution with strong background on clinical research.	St_Institution	Excellent institutions and PI
Wk_Institution	The CV of the spanish PI is limited to a list of publications so it is very difficult to assess his skills on clinical research.	Wk_Institution	None

Overheads set up at 2% for the clinical activities, and at 10% 2% for the traslational studies

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EC explained that the proposal refers to a platform study in a very rare tumor, appendiceal tumors, a first line therapy. It is a kind of study collecting data in the use of anti-VEGF and, in order to deliver better the other agents, which is a kind of first line therapy with different standards of care and to try to get some information from there.

EC pointed out that this proposal was a lower score by him, and **ALe** added that

Benjamin didn't give it a good score either.

18:00 – 18:05 Selection of Awardees

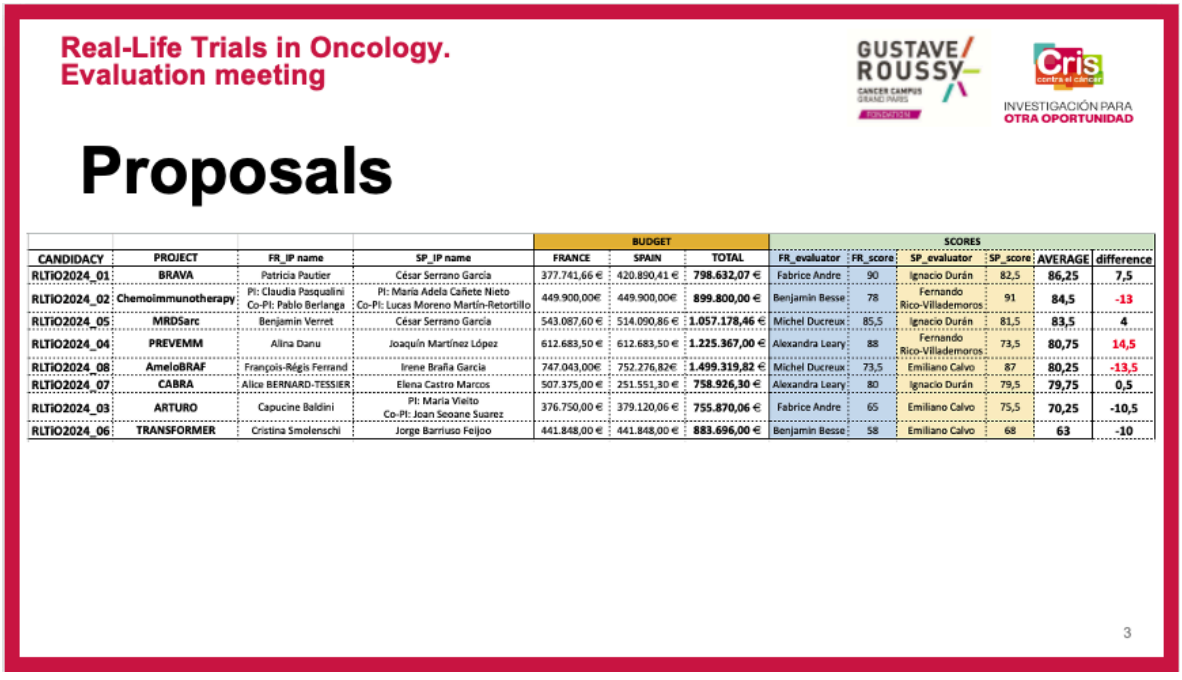
EC asked which proposals are the top ones and how many they can be funded. **EC** pointed out that what he would do, if there is no major objection by anybody, is to respect the order. EC referred to that there is the issue of the two studies with the same PI.

EC asked how CRIS and GRF would like to fund, how much money, how to proceed. **ALo** explained that the call is funding up to 1.5 million. So, if the first score does not enter in the budget for the call, the investigators may review the budget to be adjusted and try to manage to get them into the maximum of the 1.5 million.

ALo indicated that the top scoring studies are BRAVA (budget of around 800.000€) and Chemoimmunotherapy (budget of around 900.000€) so, if decided to fund the first two scores, it would be slightly over 1.5 million.

ALe suggested asking them to reduce the budget a little bit, as we have done every year. We've asked them to decrease it by far more than the previous call.

EC asked to see the final scores, the averages of the scores.



				BUDGET			SCORES					
CANDIDACY	PROJECT	FR_IP name	SP_IP name	FRANCE	SPAIN	TOTAL	FR_evaluator	FR_score	SP_evaluator	SP_score	AVERAGE	difference
RLTiO2024_01	BRAVA	Patricia Pautier	César Serrano García	377.741,66 €	420.890,41 €	798.632,07 €	Fabrice Andre	90	Ignacio Durán	82,5	86,25	7,5
RLTiO2024_02	Chemoimmunotherapy	PI: Claudia Pasqualini Co-PI: Pablo Berlanga	PI: María Adela Cañete Nieto Co-PI: Lucas Moreno Martín-Retortillo	449.900,00€	449.900,00€	899.800,00 €	Benjamin Besse	78	Fernando Rico-Villademoros	91	84,5	-13
RLTiO2024_05	MRDSarc	Benjamin Verret	César Serrano García	543.087,60 €	514.090,86 €	1.057.178,46 €	Michel Ducreux	85,5	Ignacio Durán	81,5	83,5	4
RLTiO2024_04	PREVEMM	Alina Danu	Joaquín Martínez López	612.683,50 €	612.683,50 €	1.225.367,00 €	Alexandra Leary	88	Fernando Rico-Villademoros	73,5	80,75	14,5
RLTiO2024_08	AmeloBRAF	François-Régis Ferrand	Irene Braña García	747.043,00€	752.276,82€	1.499.319,82 €	Michel Ducreux	73,5	Emiliano Calvo	87	80,25	-13,5
RLTiO2024_07	CABRA	Alice BERNARD-TESSIER	Elena Castro Marcos	507.375,00 €	251.551,30 €	758.926,30 €	Alexandra Leary	80	Ignacio Durán	79,5	79,75	0,5
RLTiO2024_03	ARTURO	Capucine Baldini	PI: María Vieito Co-PI: Joan Seoane Suarez	376.750,00 €	379.120,06 €	755.870,06 €	Fabrice Andre	65	Emiliano Calvo	75,5	70,25	-10,5
RLTiO2024_06	TRANSFORMER	Cristina Smolenschi	Jorge Barriuso Feijoo	441.848,00 €	441.848,00 €	883.696,00 €	Benjamin Besse	58	Emiliano Calvo	68	63	-10

EC pointed that the first and the third proposals (BRAVA and MRDSarc) had the same Spanish PI. EC considered that there's a discrimination of the first two ones, and then the next ones were like a different level in terms of scoring (79 points ...).

ALe summarized that they would select both, the top two, and asked for looking at the budgets to guide them on the costs that were probably not adapted to a pragmatic study and help them bring the budgets down.

Jesús Sánchez (JS) pointed out that, for CRIS Cancer, it makes a lot of sense because it's difficult for us to find good clinical trials in Pediatric Cancer and also because it would be the first pediatric Cancer in this call.

ALo thanked to all the attendees and explained that we were preparing the minutes from the meeting to share with everyone including Benjamin, Fabrice and Ignacio. And then inform the awardees and ask them to adjust the budget.

ALe added that it would be helpful if we can give the awardees the details to decrease the budgets, which sometimes is quite easy to see. For example, they put ctDNA in here, so they just have to take those out, and that helps them to reduce the budget.

ALo pointed out that in previous seasons what was done was to fund the first-scored proposal and ask the second proposal to adjust the budget. **ALe** agreed in just asking the second one.

Post-meeting discussion.

Fabrice Andre (FA): from our perspective, the chemoimmuno trial does not meet the criteria for « pragmatic trial » since this is a phase II trial that will not change the practice, and it requires the use of a new drug.

I would prefer we fund only one rather than funding trials that are not in the scope of our call. The trial on childhood cancer should be funded by the usual path of trial funding. If we fund this one, we will have 100 investigators coming next time with complex trials that do not change practice, and we will not be able to explain why we reject them

ALo: I see your point but, before taking any decision, I wanted to share with you the discussion we had during the meeting about the definition of RLT.

"Referring to the question that Phase II clinical trials could not change the clinical practice... specifically in the oncology area, a Phase II clinical trial may change the clinical practice. The endpoints, at least the primary endpoint, characteristically should be a patient relevant endpoint.

Some Phase II trials could not be so pragmatic because of the endpoints used for demonstrating or supporting the proof of concept but definitely, they can change the clinical practice.

Therefore, Phase II proposals are not “bad Proposals” themselves in terms of practice changing. It depends on the proposal.

It is very difficult to find pragmatic trials that are able, with one only pragmatic trial, to change practice.

In pragmatic trials you have to really look for indications and specific needs, areas or so to be able to change practice or to inform in a relevant way the standard practice."

In that sense, the panel evaluated and decided about the RLTiO2024_02 Chemoimmunotherapy project that it could be considered a practice-changing trial.

Please, you ALL feel free to comment or support this argument as you are all posted here. I would like to open the discussion in order to close the selection

process this week. This is an important issue, and we need to set the arguments up for the future calls in order to avoid non-RLTiO, as Fabrice mention, and we need a clear position on that.

If you prefer to have a short meeting, we may organize it.

ALe: The issue is not so much phase II vs III. During the discussion I raised exactly the same point as Fabrice regarding the pediatric trial, that trials testing novel therapies are not pragmatic, the aim should be to test affordable strategies that can be implemented across settings.

ALo asked to all the panelists if they you agreed with this definition s and that you consider that the RLTiO2024-02 Chemoimmunotherapy should not be funded. He asked to a telematic vote with YES / NOT FUNDABLE.

ALo will include at the minutes of the meeting as a Note after Meeting with the final decision.

CRIS Cancer will agree with the final resolution about this issue.

Ignacio Durán (ID): My opinion is that we should stick to what it was decided in the meeting the other day.

So it should be funded as that was the decision of the people who were in the meeting according to the evaluation obtained by the reviewers.

EC: Actually, I see that in Criterion #1 of the evaluation sheet ("Clinical Trial Proposal"), it has already collected the question we are now discussing through 2 criteria counting for 60% of the total 60 points for the assessment of this criterion ("is it an innovative and transformative project? It is a proposal of a practice-changing or practice-informing trial?" and "is the expected impact on the target population a significant gain on the clinical management of these patients?"), being the maximum total score of 100 points.

So, if the two reviewers that had the time to read in detail the proposal and

evaluated it, including this specific questions, gave such a high score as to deserve the funding, on one hand, and, on the other, in the final meeting it was considered a proper application for the characteristics of the grant by CRIS, then, I would abide by it and would not re-evaluate it: in the end, the rest of us did not go deep into details of this proposal, at least to the point of the two reviewers, and I think we could keep the study funded consequently.

Benjamin Besse (BB): NOT FUNDABLE

MD: I would say NOT FUNDABLE, I was not a great fan of this project

FA: I think the issue with this trial was not only the quality of evidence it would have generated but also the fact that it requires innovation, and this is not compatible with a low-cost trial. Also, while I fully agree that the single arm phase II trial is good for registration, I don't think the trial was designed to change practice.

ALo: I´ve got all the votes from everyone about the second project and the resolution is:

4 votes "Not Fundable"

3 Votes "Fundable"

We will revise the concept of Real-Life Trials at the Terms and Conditions of the call.

Awardee RLTiO 2024

The 2024 call for applications of the "Real-Life Trials in Oncology Programme" will fund the proposal **RLTiO2024_01 BRAVA**

Title: "Two-arm, Phase II, Non-Randomized Study to Assess the Role of BRCAness Biomarkers in the Treatment of Patients with AdVanced Uterine LeiomyosarcomA with Niraparib and Temozolamide"

French PI and Institution: Patricia Pautier. Institut Gustave-Roussy

Spanish PI and Institution: César Serrano García. Vall d'Hebron Instituto de Oncología.

Budget: 798.632,07 € (377.741,66€ France + 420.890,41€ Spain)

What is signed by all Members of the Evaluation Committee.

DocuSigned by:
78AA751DDBE8429...
Dr. Fabrice Andre

DocuSigned by:
B3300842C9F043A...
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