Health Research Authority

Dr James Larkin
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Sutton
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Email: hra.approval@nhs.net

03 November 2017

Dear Dr Larkin

Initial Assessment Letter

Study title:	**Renal Adjuvant MultiPle Arm Randomised Trial (RAMPART): An international investigator-led phase III multi-arm multi-stage randomised controlled platform trial of adjuvant therapy in patients with resected primary renal cell carcinoma (RCC) at high or intermediate risk of relapse**
IRAS project ID:	**219487**
EudraCT number:	**2017-002329-39**
Protocol number:	**RE06**
REC reference:	**17/LO/1875**
Sponsor	**University College London**

Thank you for your application for HRA Approval for the above referenced study. You will have already received notification that your application is valid for REC and proceeding to a REC meeting.

I have been assigned to this application and have undertaken my initial assessment, the findings of which are detailed in *Appendix B*. Please note that **this is not a letter of HRA Approval**, and the research should not begin at any participating NHS organisations in England before HRA Approval is issued.

Purpose

The purpose of this letter is to provide initial information from the HRA assessment to you, the sponsor and participating NHS organisations in England to enable the process of arranging capacity and capability to begin.

You should now provide a copy of this letter and the local document package to participating NHS organisations in England and work with them to coordinate local arrangements in preparation for HRA Approval on the basis described in this letter, even where certain arrangements detailed in *Appendix B* are still to be finalised.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Notification of Outcomes

I will continue to work with you to resolve any outstanding questions whilst local arrangements are finalised prior to HRA Approval. I may contact you by phone or email to seek clarification as I complete my assessment.

You will receive written notification of HRA Approval once the assessment has been completed and subsequent to any regulatory approvals required for your study (e.g. REC Favourable Opinion, MHRA Clinical Trial Authorisation, etc.). HRA Approval will not be issued until any specific conditions on these approvals have been met.

There is no need for you to send me the REC opinion or any other regulatory approvals, as I will receive these directly, although I may contact you to confirm that any applicable conditions have been met.

Appendices

This Initial Assessment Letter contains the following appendices:

- A – List of documents to be reviewed during HRA assessment
- B – Summary of initial HRA assessment

Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

HRA training

We are pleased to welcome researchers and research management staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

Your IRAS project ID is **219487.** Please quote this on all correspondence.

Yours sincerely

Joanna Ho

Assessor

Email: hra.approval@nhs.net

Copy to: *RAMPART Trial Management Team, Sponsor Representative, MRC Clinical Trials Unit at UCL*

Ms Jane Lawrence, The Royal Marsden NHS Trust

Appendix A - Documents received

The documents to be assessed as part of HRA Approval are as follows.

Document	*Version*	*Date*
Contract/Study Agreement template [mNCA and MTA]	1.0	25 September 2017
Contract/Study Agreement template [RAMPART Statement of Activities]	1.0	12 October 2017
Contract/Study Agreement template [RAMPART Schedule of Events]	1.0	12 October 2017
Covering letter on headed paper [Cover Letter]		12 October 2017
Details of any Data Monitoring Committee [IDMC Letter]		02 October 2017
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance]		24 July 2017
GP/consultant information sheets or letters [GP Letter]	1.0	03 October 2017
Investigator's brochure / IMP Dossier [Durvalumab IB]	11.0	28 April 2017
Investigator's brochure / IMP Dossier [Tremelimumab IB]	6.0	07 June 2016
IRAS Application Form [IRAS_Form_13102017]		13 October 2017
IRAS Application Form XML file [IRAS_Form_13102017]		13 October 2017
IRAS Checklist XML [Checklist_13102017]		13 October 2017
Letter from funder [AZ Confirmation of funding]		29 September 2016
Letter from sponsor [Confirmation of sponsorship]		02 October 2017
Letter from statistician [Letter from Statistician]		04 October 2017
Participant consent form [Participant Consent Form]	1.0	03 October 2017
Participant consent form [Partner Consent Form]	1.0	03 October 2017
Participant information sheet (PIS) [Participant Information Sheet]	1.0	03 October 2017
Referee's report or other scientific critique report [RAMPART Funding and Scientific peer-review]		08 May 2017
Research protocol or project proposal [RAMPART Protocol]	1.0	03 October 2017
Summary CV for Chief Investigator (CI) [CI CV]		03 October 2017
Summary, synopsis or diagram (flowchart) of protocol in non technical language [RAMPART Lay Summary]	1.0	03 October 2017
Validated questionnaire [EQ-5D]	1.0	12 October 2017
Validated questionnaire [QLQ-C30]	1.0	12 October 2017

Appendix B – Information for Sponsors and Participating NHS Organisations

The appendix below provides all parties with information that will be beneficial when discussing the arranging of capacity and capability with participating NHS organisations in England. The information in this appendix is intended to be an accurate reflection of the study at the time of issue of this letter. As part of the HRA Approval process, details may change prior to a Letter of HRA Approval being issued. NHS organisations should be assured that the HRA will continue to work with the sponsor on any HRA assessment criteria which are 'pending', and this should not impact on the arranging or capacity and capability.

The following person is the sponsor contact for the purpose of addressing participating organisation questions relating to the study:

Name: Ben Smith / Francesca Schiavone
Tel: 0207 670 4683/4743
Email: mrcctu.rampart@ucl.ac.uk

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
1.1	IRAS application completed correctly	Pending	IRAS A72 indicate 70 UK sites included into the study, however, IRAS Part C only cites 47 research host organisations. Sponsor to confirm additional site, if applicable. See also 5.3 below
2.1	Participant information/consent documents and consent process	Pending	Sponsor has been requested to amend the participant information and consent documents to align with HRA assessment criteria and standards. See also 5.1 and 5.3 below. Additional participant information sheets have also been requested for pregnant partner for which a consent form has been submitted and also sub-studies that are cited in the main informed consent form.
3.1	Protocol assessment	Pending	No comments
4.1	Allocation of responsibilities and rights are agreed and	Yes	A sponsor agreement will act as an

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
	documented		agreement of an NHS organisation to participate. The model agreement for non-commercial research in the NHS has been confirmed for use; this has not been modified from the standard template and includes a schedule for material transfer. No other agreement is expected. The Statement of Activities and Schedule of Events have been provided for information only.
4.2	Insurance/indemnity arrangements assessed	Yes	Sponsor indemnity arrangements are in place for the management and design of the study. NHS indemnity applies to the conduct of the study. Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the activities expected of them for this research study
4.3	Financial arrangements assessed	Yes	Funding has been secured from Kidney Cancer UK and AstraZeneca UK LTD for this study. Funding will be provided to participating NHS organisations as detailed in the Statement of Activities and will be arranged via the sponsor agreement.
5.1	Compliance with the Data Protection Act and data security issues assessed	Pending	The use of participant data has only been partially described in the current version of the participant information and consent forms. Personal data will be required for long-term follow-up and should be described clearly in the information sheet. Sponsor has been requested to include further details into the participant documents to comply to the Data Protection Act and to meet HRA assessment criteria and standards.

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Yes	No comments
5.3	Compliance with any applicable laws or regulations	Pending	IRAS indicates blood samples will be taken for the study. Sponsor to confirm and provide additional information for any other tissue samples to be provided for the study. The participant information sheet requires additional details on the use of participant tissue samples to comply with the Human Tissue Act and to meet HRA Assessment Criteria and Standards.
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Pending	REC meeting scheduled for 06 November 2017. A REC Favourable Opinion is required to be in place before HRA Approval can be issued.
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Pending	MHRA CTA has yet to be issued. Sponsor to provide MHRA Approval, when available. HRA Approval will not be issued until this is in place.
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.

This is a non-commercial multicentre study, where all participating NHS organisations will be undertaking all research activities as described in the IRAS application. There is therefore only one site-type in this study.

Sponsor to confirm additional participating sites, if applicable, that are not currently listed in IRAS Part C.

The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. For NIHR CRN Portfolio studies, the Local LCRN contact should also be copied into this correspondence. For further guidance on working with participating NHS organisations please see the HRA website.

If Chief Investigators, sponsors or Principal Investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the Chief Investigator, sponsor or Principal Investigator should notify the HRA immediately at hra.approval@nhs.net. The HRA will work with these organisations to achieve a consistent approach to information provision.

Confirmation of Capacity and Capability

This describes whether formal confirmation of capacity and capability is expected from participating NHS organisations in England.

Participating NHS organisations in England **will be expected to formally confirm their capacity and capability** to host this research.

- The sponsor should ensure that participating NHS organisations are provided with a copy of this letter and all relevant study documentation, and work jointly with NHS organisations to arrange capacity and capability whilst the HRA assessment is ongoing.
- Further detail on how capacity and capability will be confirmed by participating NHS organisations, following issue of the Letter of HRA Approval, is provided in the *Participating NHS Organisations* and *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections of this appendix.
- The Assessing, Arranging, and Confirming document on the HRA website provides further information for the sponsor and NHS organisations on assessing, arranging and confirming capacity and capability.

Principal Investigator Suitability

This confirms whether the sponsor's position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England, and the minimum expectations for education, training and experience that PIs should meet (where applicable).
A Principal Investigator should be in place at participating NHS organisations. Prior to site activation, sponsor will provide training to include an overview of eligibility, treatment, follow-up and safety reporting, CRF completion guidelines, drug supply management system and image repository systems. Training will also be provided by sponsor after any relevant updates on protocol changes. GCP training is not a generic training expectation, in line with the HRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken.
Local staff substantively employed by the participating NHS organisation will be undertaking research activities as described in the IRAS application. No HR access arrangements are therefore expected for this study. Where arrangements are not already in place, network staff employed by another Trust or University (or similar) undertaking any of the research activities listed in A18 or A19 of the IRAS form (except for administration of questionnaires or surveys), would be expected to obtain an honorary research contract from one NHS organisation (if university employed), followed by Letters of Access for subsequent organisations. This would be on the basis of a Research Passport (if university employed) or an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed). These should confirm enhanced DBS checks, including appropriate barred list checks, and occupational health clearance. For research team members only administering questionnaires or surveys, a Letter of Access based on standard DBS checks and occupational health clearance would be appropriate.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England in study set-up.
The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio.