NHS
Health Research Authority

Dr James Larkin
Royal Marsden Hospital
Downs Road
Sutton
SM2 5PT

Email: hra.approval@nhs.net

08 January 2018

Dear Dr Larkin

Letter of HRA Approval

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**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

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 the HRA website.

Appendices

The HRA Approval letter contains the following appendices:

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

After HRA Approval

The document *"After Ethical Review – guidance for sponsors and investigators",* issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website.

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 through IRAS.

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

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website.

HRA Training

We are pleased to welcome researchers and research management staff at our training days – see details on the HRA website.

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, Lead NHS R&D Contact, The Royal Marsden NHS Trust

Appendix A - List of Documents

The final document set assessed and approved by HRA Approval is listed below.

Document	*Version*	*Date*
Confirmation of Clinical Trial Authorisation from MHRA and relevant correspondence [Clinical Trials Authorisation]	1.0	24 November 2017
Confirmation of Clinical Trial Authorisation from MHRA and relevant correspondence [Re-Submission Cover Letter]	1.0	22 November 2017
Confirmation of Clinical Trial Authorisation from MHRA and relevant correspondence [Grounds for Non-Acceptance Letter]	1.0	08 November 2017
Confirmation of Clinical Trial Authorisation from MHRA and relevant correspondence [Initial Submission Cover Letter]	1.0	13 October 2017
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
Covering letter on headed paper [HRA Response Cover Letter]	1.0	15 December 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_15122017]		15 December 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
Other [RAMPART_Cover_Letter_MHRA_GNA_Response_2017-11-22]		22 November 2017
Other [CTA_2017-11-24]		24 November 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 (clean)]	1.0	15 December 2017
Participant information sheet (PIS) [Pregnant Partner Information Sheet]	1.0	15 December 2017
Referee's report or other scientific critique report [RAMPART Funding and Scientific peer-review]		08 May 2017
Research protocol or project proposal [Protocol]	1.0	22 November 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 - Summary of HRA Assessment

This appendix provides assurance to you, the sponsor and the NHS in England that the study, as reviewed for HRA Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England to assist in assessing and arranging capacity and capability.

For information on how the sponsor should be working with participating NHS organisations in England, please refer to the, *participating NHS organisations*, *capacity and capability* and *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections in this appendix.

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	Yes	IRAS Part C: Sponsor has confirmed that only sites who have confirmed their interest in the study through an Expression of Interest have been included in Part C. Any additional sites will need to be added via a substantial amendment. IRAS Part B Section 5 – use of newly obtained human tissue should also include urine. This will be used for pregnancy testing only and the sample will not be stored. Safety bloods have also been omitted from this section. Sponsor has confirmed that these will be collected and analysed locally at sites; they will not be stored and should be disposed of as per standard practice.
of			
2.1	Participant information/consent documents and consent	Yes	Sponsor was requested to include the IRAS ID to participant information and

Section	HRA Assessment Criteria	Compliant with Standards	Comments
	process		consent documents. This has been updated into the participant information sheets; however, sponsor has stated that they did not feel it necessary to include this into the informed consent forms.
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	A sponsor agreement will act as an 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.

Section	HRA Assessment Criteria	Compliant with Standards	Comments
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No 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	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	REC Provisional Opinion issued 16 November 2017; REC Favourable Opinion issued 097 January 2018
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Yes	MHRA grounds for non-acceptance issued 08 November 2017; MHRA CTA notice of acceptance of amended request issued 24 November 2017
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. 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**.

- Following issue of this letter, participating NHS organisations in England may now confirm to the sponsor their capacity and capability to host this research, when ready to do so. How capacity and capacity will be confirmed is detailed in the *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* section 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 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 each participating NHS organisation.

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/MHRA 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 to aid study set-up.

The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio.