Health Research Authority

**London - Riverside Research Ethics Committee**
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Whitefriars
Lewins Mead
Bristol
BS1 2NT

Telephone: 02071048044

**Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval**

16 November 2017

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

Dear Dr Larkin

| | |
|---|---|
| **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** |
| **REC reference:** | **17/LO/1875** |
| **Protocol number:** | **RE06** |
| **EudraCT number:** | **2017-002329-39** |
| **IRAS project ID:** | **219487** |

The Research Ethics Committee reviewed the above application at the meeting held on 06 November 2017. Professor Tom Powles, Trial Development Group Vice Chair, Dr Angela Meade, Project Leader and Professor Rick Kaplan, sponsor representative attended on your behalf to discuss the application.

**Provisional opinion**

The Committee would be content to give a favourable ethical opinion of the research, subject to receiving a complete response to the request for further information set out below.

Authority to consider your response and to confirm the Committee's final opinion has been delegated to the Chair.

**Further information or clarification required**

**1) Changes to the Participant Information Sheet (PIS)**

a) Please state clearly how many study visits there will be, and what each of the visits will involve for each of the study groups. The PIS should also state clearly how many additional clinical interventions will be involved in this study that are not part of the participant's routine care. The table titled Visit Plan (page 10 of the PIS) should be re-formatted accordingly to reflect clearly what the clinical interventions are for each study arm (including how many of which are additional to routine care) and how many study visits are required.

b) The PIS should state clearly that the participant's study data will be exported outside the EEA and that it will be anonymised to protect the participant's identity.

c) In Table 2 – Side Effects, section 11 of the PIS (page 11) please revise the table to state clearly the severity of the side effects. The Committee stated that some of the side effects may require hospitalisation and that this needs to be stated clearly in the PIS.

d) Please state clearly that the participant will be asked to complete a number of questionnaires as part of the study protocol. The PIS should state what these questionnaires will be and how long they will take to complete.

**2) Written assurance**

a) The Committee requested written assurance that the participant's personal study data will be anonymised and that their study data will be anonymised prior to exporting outside of the EEA.

**3) Written clarification**

a) It was noted in the PIS, under the heading Why am I being invited to take part? (page 2 of the PIS) that 'the doctor treating you believe that there is a risk that the cancer may return'. The Committee queried whether the doctor's treating the patient will inform them of this fact.

**If you would find it helpful to discuss any of the matters raised above or seek further clarification from a member of the Committee, you are welcome to contact the REC Manager, Tina Cavaliere.**

When submitting a response to the Committee, the requested information should be electronically submitted from IRAS. Please contact your REC Manager if you require guidance on how to submit your response to the REC provisional opinion.

Please submit revised documentation where appropriate underlining or otherwise highlighting the changes which have been made and giving revised version numbers and dates. You do not have to make any changes to the REC application form unless you have been specifically requested to do so by the REC.

The Committee will confirm the final ethical opinion within a maximum of 60 days from the date of initial receipt of the application, excluding the time taken by you to respond fully to the above points. A response should be submitted by no later than 16 December 2017.

**Summary of the discussion at the meeting**

The Committee welcomed Professor Tom Powles, Trial Development Group Vice Chair, Dr Angela Meade, Project Leader and Professor Rick Kaplan, sponsor representative to the meeting.

**Social or scientific value; scientific design and conduct of the study**

This is a large clinical trial to determine whether durvalumab alone or a combination of durvalumab and tremelimumab can delay the cancer from returning and increase life expectancy compared with the standard care of active monitoring patients. The study involves two drug arms; Arm A (durvalumab) and Arm B durvalumab and tremelimumab. A third arm is active monitoring of the participants for one year.

It was noted that participants will be randomised to one of the study arms.

The Committee commended the applicants on providing a clear lay summary for question A6-1 of the IRAS REC application form.

The applicants were commended by the Committee for involving patients, service users and the public in the design of the study protocol and PIS. The Health Research Authority advocate the involvement of patients, service users and the public in the design, management and conduct of the study as this will benefit both the participant and the research team to ensure the information provided in the study documentation is clear and easy to understand.

*Dr Meade replied to say that she was pleased to receive this recognition as the study protocol and documentation were developed with the specific patient population.*

**Care and protection of research participants; respect for potential and enrolled participants' welfare and dignity**

The participants will not receive a reimbursement for travel costs, however this was considered acceptable as there is only a small number of extra visits required for the study. It was noted that the applicants have been clear and upfront about this and the study is receiving a modest amount of funding.

The Committee noted that the participant's personal data will be exported outside the EEA (European Economic Community). The applicants were advised that the Committee would require written confirmation that the participant's personal data will be anonymised prior to exportation.

*The applicants agreed to provide assurance in a letter to the Committee that the participant's personal data will be anonymised prior to exportation.*

It was noted in the PIS, under the heading Why am I being invited to take part? (page 2 of the PIS) that 'the doctor treating you believe that there is a risk that the cancer may return.' The Committee queried whether the doctor's treating the patient will inform them of this fact.

*The applicants agreed to provide clarification in a letter.*

**Informed consent process and the adequacy and completeness of participant information**

The PIS is very well laid out and easy to read, however it is not clear in the PIS what each study visit will involve and how many study visits there will be. It appears that the Control group arm will be attending some of the study visits.

The study side effects are presented well in Table 2, section 11 (page 11 of the PIS), however the information provided is based on incidences and not on the severity of the side effects. The Committee added that some of the side effects could result in hospitalisation and that this needs to be stated clearly in the PIS.

*The applicants agreed to amend the PIS accordingly.*

The protocol states that this there will be a pharmacokinetics (PK) and antibody study planned later in the study duration, however there is no information on the PIS or an additional consent form to support this.

*Dr Meade replied to say that there will be samples taken for PK and antibody testing at a later date and that this will be submitted to the REC as separate application using a small sub-set of participants.*

The Committee accepted this response.

The PIS does not state that the participant will be asked to complete a number of questionnaires as part of the study non-clinical interventions.

The Committee summarised to the applicants that there were some minor amendments required to the Participant Information Sheet (PIS) to clarify the number of study visits required which would be outlined in the ethical opinion letter.

*The applicants agreed to amend the PIS accordingly.*

The Committee asked the applicants if they had any questions for the Committee to which they replied that they did not. The applicants were advised that the Committee would issue the

ethical opinion letter within 10 working days of the REC meeting. The applicants were thanked for attending the meeting and they left the room.

**Other ethical issues were raised and resolved in preliminary discussion before your attendance at the meeting.**

Please contact the REC Manager if you feel that the above summary is not an accurate reflection of the discussion at the meeting.

**Documents reviewed**

The documents reviewed at the meeting were:

| *Document* | *Version* | *Date* |
|---|---|---|
| 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 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 |

**Membership of the Committee**

The members of the Committee who were present at the meeting are listed on the attached sheet

**Statement of compliance**

This Committee is recognised by the United Kingdom Ethics Committee Authority under the

Medicines for Human Use (Clinical Trials) Regulations 2004, and is authorised to carry out the ethical review of clinical trials of investigational medicinal products.

The Committee is fully compliant with the Regulations as they relate to ethics committees and the conditions and principles of good clinical practice.

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

| **17/LO/1875** | **Please quote this number on all correspondence** |
|---|---|

Yours sincerely

**Pp**
**Tina Cavaliere, REC Manager**

**Dr Margaret Jones**
**Chair**

Email: nrescommittee.london-riverside@nhs.net

*Enclosures:* *List of names and professions of members who were present at the meeting and those who submitted written comments.*

*Copy to:* *RAMPART Trial Management Team*
*Ms Jane Lawrence, The Royal Marsden NHS Trust*

**London - Riverside Research Ethics Committee**

**Attendance at Committee meeting on 06 November 2017**

## Committee Members:

| *Name* | *Profession* | *Present* | *Notes* |
|---|---|---|---|
| Dr Marina Cecelja | Centre Career Establishment Fellow | Yes | |
| Dr Irina Chis Ster | Senior Lecturer In Biostatistics | Yes | |
| Ms Stephanie Ellis BEM | Former Civil Servant | Yes | |
| Dr Nuria Gonzalez-Cinca | Clinical Study Manager | No | |
| Ms Alison Higgs | Lecturer in Social Work | No | |
| Dr Matthew Hyde | Research Scientist | Yes | |
| Dr Margaret Jones | Retired General Practitioner | Yes | Chair of meeting |
| Ms Fanny Mitchell | Retired NHS Manager | Yes | |
| Dr Lorraine Murphy | Pharmaceutical Consultant | Yes | |
| Mr Kamen Shoylev | Lawyer | No | |
| Mrs Dinah Smith | Retired Head Teacher | Yes | |
| Ms Julia Williams | Senior Producer | Yes | |

## Also in attendance:

| *Name* | *Position (or reason for attending)* |
|---|---|
| Miss Tina Cavaliere | REC Manager |