Health Research Authority
London - Riverside Research Ethics Committee
Level 3 Block B
Whitefriars
Lewins Mead
Bristol
BS1 2NT

18-Apr-2019

EudraCT number: 2004-000193-31
REC number: 17/LO/1875
Sponsor reference number: MRC RE06

Dear Colleague,

RE: Renal Adjuvant MultiPle Arm Randomised Trial (RAMPART): An international investigator-led phase III Multi-Arm, Multi-Stage (MAMS), multi-centre, randomised controlled platform trial of adjuvant therapy in patients with resected primary renal cell carcinoma (RCC) at high or intermediate risk of relapse

I am writing to notify the HRA and London Riverside REC of substantial amendments to the RAMPART Protocol (v1.0, November 2017). I have enclosed a copy of the Substantial Amendment Notification Form, along with tracked and clean versions of all amended documents. The relevant information has also been sent to the MHRA for approval.

The main reason for amending the Protocol and its supporting documents is to reflect new information provided in the most recent version of the Durvalumab Investigator Brochure (v14.0, February 2019). The updated Investigator Brochure identified several new Adverse Events of Special Interest (AESIs), which we have now incorporated into the Protocol. There were also changes to the Reference Safety Information (RSI) – both new expected side-effects and changes to the frequency of those previously listed – and we are keen to ensure patients are being adequately informed of these risks through an updated Participant Information Sheet.

We have taken the opportunity to make some additional small changes to the Protocol and its supporting documents, as noted below:

- Corrected an error in the Cockcroft Gault formula.
- Increased the window (from 3 to 5 days) for completing pre-infusion safety checks - this was proving to be a logistical issue for some of our sites and the Trial Management Group (TMG) were satisfied that this would not affect patient safety.
- Removed mandatory requirement for Hep A testing prior to randomisation – the TMG were in agreement that no Hep A result would present a safety issue for patients entering the study.
- An updated version of the Toxicity Management Guidelines was recently issued by AstraZeneca and the changes have been incorporated into the guidelines in the Protocol appendices.
- The Protocol and our patient documents (Information Sheets and Consent Forms) have been updated to reference and comply with the GDPR regulations. The language used in the patient documents has previously been approved by the HRA on 19-Mar-2019 for use in all MRC CTU at UCL trials after correspondence with Fleur Hudson, Head of Clinical Operations.
- Introduction of a new Patient Diary Card so that patients have a list of upcoming visits and emergency contact details to hand.

All the amendments, both substantial and non-substantial are listed in full in the supporting document Summary of Changes from RAMPART Protocol v1.0 to v2.0.

Please note that this amendment also comprises some changes to Principal Investigators and new sites since November 2017 (as documented in the Substantial Amendment Notification Form) that have previously been approved by the HRA, but are listed for the approval of the MHRA.

I would like to thank you for considering this submission. We welcome the opportunity to respond to any comments or questions you may have.

Kind regards,

Ben Smith

On behalf of the RAMPART Trial Development Group

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Enclosed documentation

Document	Version	Date
Cover letter	n/a	18-Apr-2019
Notification of Substantial Amendment Form	n/a	18-Apr-2019
Investigator Brochure (Durvalumab)	14.0	11-Feb-2019
Investigator Brochure (Tremelimumab)	9.0	27-Nov-2018
Protocol (clean)	2.0	18-Apr-2019
Protocol (tracked)	2.0	18-Apr-2019
Participant Information Sheet (clean)	2.0	18-Apr-2019
Participant Information Sheet (tracked)	2.0	18-Apr-2019
Pregnant Partner Information Sheet (clean)	2.0	18-Apr-2019
Pregnant Partner Information Sheet (tracked)	2.0	18-Apr-2019
Participant Consent Form (clean)	2.0	18-Apr-2019
Participant Consent Form (tracked)	2.0	18-Apr-2019
Pregnant Partner Consent Form (clean)	2.0	18-Apr-2019
Pregnant Partner Consent Form (tracked)	2.0	18-Apr-2019
Patient Diary Card (Arm A)	1.0	18-Apr-2019
Patient Diary Card (Arm B & C)	1.0	18-Apr-2019