Health Research Authority
London - Riverside Research Ethics Committee
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03-Dec-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 REC of substantial amendments to the RAMPART Protocol (v2.0, April 2019). 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 is to reflect changes to the Tremelimumab vials that will be used within the RAMPART study. AstraZeneca currently supplies 400mg vials of Tremelimumab, however this will change to 25mg vials as of February 2020. Aside from the change in volume, there will be no change to the contents of the Tremelimumab vials. As a result of the changes to the Tremelimumab vials, it was necessary for us to update our Protocol guidance on the preparation and administration of our IMP.

We have also taken the opportunity to make some additional small changes to the Protocol, as noted below:

- Inclusion/exclusion criteria updated to allow microscopically positive margins after radical nephrectomy, but not after partial nephrectomy.
- HIV testing added to the screening procedures table. The exclusion criteria have always ruled out HIV positive patients, however the requirement for the test was implied rather than explicitly stated.
- Additional section providing more detailed guidance for the follow-up of patients after disease progression.
- Additional guidance about the reporting of lab-based adverse events.
- 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.

All the amendments, both substantial and non-substantial are listed in full in the supporting document Summary of Changes from RAMPART Protocol v2.0 to v3.0.

In addition to the amended Protocol, we are also submitting some updated supporting documents, as noted below:

- *Durvalumab Investigator Brochure (v15.0)* – AstraZeneca have released this updated version and it is our intention to use the relevant tables (34 & 35) within the document as our reference safety information (RSI) once approval for this amendment has been received.
- *Participant Information Sheet (v3.0)* – We have revised our PIS in response to the new Durvalumab IB to ensure our patients are adequately informed of the potential side-effects associated with Durvalumab monotherapy and in combination with Tremelimumab. An additional summary document is included with this submission to highlight our changes and their justifications.

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	03-Dec-2019
Notification of Substantial Amendment Form	n/a	28-Nov-2019
Protocol (clean)	3.0	28-Nov-2019
Protocol (tracked)	3.0	28-Nov-2019
Summary of Changes from RAMPART Protocol v2.0 to v3.0	n/a	28-Nov-2019
RAMPART Participant Information Sheet (clean)	3.0	03-Dec-2019
RAMPART Participant Information Sheet (tracked)	3.0	03-Dec-2019
Summary of Changes from RAMPART Participant Information Sheet v2.0 to v3.0	n/a	03-Dec-2019
Durvalumab Investigator Brochure (clean)	15.0	08-Oct-2019
Durvalumab Investigator Brochure (tracked)	15.0	08-Oct-2019