Revised 11 June 2015

Health Research Authority

NRES Committee London - City & East
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23 February 2015

Professor Kwee Yong
UCL Cancer Institute
72 Huntley Street
London WC1E 4DD

Dear Professor Yong

Study title:	**Carfilzomib/Cyclophosphamide/Dexamethasone with maintenance carfilzomib in untreated transplant-eligible patients with symptomatic MM to evaluate the benefit of upfront ASCT**
REC reference:	**15/LO/0023**
Protocol number:	**UCL/12/0500**
EudraCT number:	**2014-000506-35**
IRAS project ID:	**148600**

Thank you for your letter of 16 Feb 2015, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered in correspondence by a Sub-Committee of the REC. A list of the Sub-Committee members is attached.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager, Mr Rajat Khullar, nrescommittee.london-cityandeast@nhs.net. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from NRES. Guidance on where to register is provided on the HRA website.

Clinical trial authorisation must be obtained from the Medicines and Healthcare products Regulatory Agency (MHRA).

The sponsor is asked to provide the Committee with a copy of the notice from the MHRA, either confirming clinical trial authorisation or giving grounds for non-acceptance, as soon as this is available.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites listed in the application, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

The Committee has not yet completed any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance Confirmation Letter]		20 May 2014
GP/consultant information sheets or letters [GP letter]	1.0	01 December 2014
Investigator's brochure / IMP Dossier [Carfilzomib Investigator Brochure]	v14	28 August 2014
IRAS Checklist XML [Checklist_03122014]		03 December 2014
IRAS Checklist XML [Checklist_16022015]		16 February 2015
Letter from sponsor [Final sponsor letter]		20 April 2014
Letter from statistician [Letter from statistician]		03 December 2014
Other [Dexamethasone SPC]		30 May 2014
Other [Carfilzomib prescribing information (US SPC equivalent)]		
Other [CTAAC endorsement]		06 June 2014
Other [REC response - reference Jakubowiak 2012]		
Other [REC response - reference Bringhen 2014]		
Other [REC response - reference Harvey 2014]		
Other [REC response - reference Sonneveld 2015]		
Other [Response to provisional opinion letter]		16 February 2015
Participant consent form [Cardamon Consent Form]	2.0	28 January 2015
Participant consent form [Pregnancy monitoring consent form (patient)]	2.0	28 January 2015
Participant consent form [Pregnancy monitoring consent form (partner)]	2.0	28 January 2015

Participant consent form [Lactational exposure consent form]	2.0	28 January 2015
Participant information sheet (PIS) [Patient information sheet]	2.0	28 January 2015
Participant information sheet (PIS) [Patient information sheet (tracked)]	2.0	28 January 2015
Participant information sheet (PIS) [Pregnancy monitoring information sheet (patient)]	2.0	28 January 2015
Participant information sheet (PIS) [Pregnancy monitoring information sheet (partner)]	2.0	28 January 2015
Participant information sheet (PIS) [Lactational exposure information sheet]	2.0	28 January 2015
REC Application Form [REC_Form_16022015]		16 February 2015
Research protocol or project proposal [Cardmon trial protocol]	1.0	01 December 2014
Sample diary card/patient card [Patient diary - consolidation]	1.0	01 December 2014
Sample diary card/patient card [Patient diary - induction]	1.0	01 December 2014
Summary CV for Chief Investigator (CI) [Kwee Yong CV]		
Summary of product characteristics (SmPC) [Cyclophosphamide SPC]		09 January 2013

Statement of compliance

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.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

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

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:

http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

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

15/LO/0023	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

pp Dr John Keen
Chair

Email:nrescommittee.london-cityandeast@nhs.net

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*
"After ethical review – guidance for researchers"

Copy to: *Mr Thomas Roberts*
Mr Philip Diamond, University College London Hospitals NHS Foundation Trust

NRES Committee London - City & East

Attendance at Sub-Committee of the REC meeting in correspondence

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr John Keen	GP (REC Chairman)	Yes	
Mr Roy Sinclair	Pharmacist	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mr Rajat Khullar	REC Manager