Health Research Authority

London - South East Research Ethics Committee

Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

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

01 March 2018

Dr Graham Collins
Churchill Hospital
Old Road, Headington
Oxford
OX3 7LE

Dear Dr Collins,

Study title:	**A phase II study of nivolumab monotherapy in patients with relapsed/refractory Hodgkin lymphoma, fit for autologous stem cell transplant, who fail to reach complete metabolic remission after first or second line salvage therapy**
REC reference:	**18/LO/0204**
Protocol number:	**UCL/15/0515**
EudraCT number:	**2017-002544-32**
IRAS project ID:	**216147**

The Research Ethics Committee reviewed the above application at the meeting held on 14 February 2018. Thank you for attending to discuss the application, along with Dr Pip Patrick and Mr Oliver Schofield.

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 hra.studyregistration@nhs.net outlining the reasons for your request.
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.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below. .

Conditions of the favourable opinion

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

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

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk 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 management permissions 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 the HRA. 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 taking part in the study, 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(s) (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. I 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.

Summary of discussion at the meeting

Recruitment arrangements and access to health information, and fair participant selection

The Committee acknowledged that the recruitment to the study would happen before the Standard of Care PET/CT Scan, the results of which would confirm eligibility for the study.

You confirmed that all data and tissue collected up to that point would be kept and used within the terms of the participant's consent.

Dr Patrick confirmed that consent would be in place to store and use all data and tissue collected up to the point of withdrawal from the study.

The Committee noted that it was stated that approximately 120 patients would be recruited to the study to achieve the required sample size of 30 and asked for clarification which was the fixed number.

You confirmed that the fixed number of participants to go through to treatment was 30, as many patients as required would be recruited to achieve that number.

The Committee were satisfied with the responses given.

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

The Committee queried whether data obtained from participants that withdrew from the study would be included in the overall intention to treat study data. It was slightly unclear how long the duration period would be between the initial recruitment and the point at which participants would be confirmed into the study.

Dr Collins confirmed that if the PET/CT scan showed a positive result then participants would take part in the additional study screening tests to confirm eligibility into the trial and beginning treatment with the IMP. This would take approximately 1-2 weeks and everything would be done to minimise any waiting period.

The Committee was satisfied with the response.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering letter on headed paper [Cover Letter]	N/A	11 January 2018
Details of any Data Monitoring Committee [IDMC membership list]		15 December 2017

Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance letter from Sponsor and Policy document]		06 November 2017
GP/consultant information sheets or letters [GP Letter]	1.0	04 January 2018
Investigator's brochure / IMP Dossier [Nivolumab Investigator Brochure]	16	23 June 2017
IRAS Application Form [IRAS_Form_11012018]		11 January 2018
IRAS Checklist XML [Checklist_11012018]		11 January 2018
Letter from funder [Funding confirmation letter]		29 December 2016
Letter from sponsor [Confirmation of Sponsorship letter]		06 November 2017
Letter from statistician [Letter from statistician]		13 December 2017
Participant consent form [Consent Form (Main)]	1.0	04 January 2018
Participant consent form [Pregnancy Monitoring Consent Form (Partners)]	1.0	04 January 2018
Participant information sheet (PIS) [Patient Information Sheet (Main)]	1.0	04 January 2018
Participant information sheet (PIS) [Pregnancy Monitoring Information Sheet (Partners)]	1.0	04 January 2018
Referee's report or other scientific critique report [Peer reviews (independent, statistics and CSG)]		10 January 2018
Research protocol or project proposal [Protocol]	1.0	04 January 2018
Sample diary card/patient card [Patient Contact Card]	1.0	04 January 2018
Summary CV for Chief Investigator (CI) [Graham Collins CV]		08 January 2018

Membership of the Committee

The members of the Ethics 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.

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/

18/LO/0204	**Please quote this number on all correspondence**

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

Yours sincerely

pp
Ms Stephanie Cooper
Chair

E-mail: nrescommittee.london-southeast@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 Oliver Schofield* *Ms Heather House, University of Oxford*

London - South East Research Ethics Committee

Attendance at Committee meeting on 14 February 2018

Committee Members:

Name	*Profession*	*Present*	*Notes*
Ms Stephanie Cooper	Retired Solicitor	Yes	
Mr Ron Driver	Retired University Lecturer/Statistician	Yes	In the Chair
Professor John Eastwood	Consultant Renal Physician	Yes	
Professor Anthony Fox	Pharmaceutical Medicine	Yes	
Mr Guy Gardener	Retired Assistant Chief Constable	No	
Ms Janelle Hill	Former Banking Administrator	Yes	
Professor Atholl Johnston	Professor of Clinical Pharmacology	No	
Dr Morven Leese	Reader in Biostatistics	Yes	
Professor Eleni Palazidou	Consultant Psychiatrist	Yes	
Ms Lois Rogers	Journalist	No	
Mr Graham Smith	Business Consultant	Yes	
Ms Vanda Taylor	Senior Cancer Information Nurse	No	
Ms Brigid Tucker	Head of Policy & Communications, General Osteopathic Council	Yes	
Professor Zahur Zaman	Retired Clinical Pathologist	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Ms Julie Acourt	REC Assistant
Mrs Margaret Hutchinson	REC Manager