Supplementary Material 12

Ethics/Research Ethics Committee Approval

Health Research Authority
NRES Committee East Midlands - Derby
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Telephone: 0115 883 9525

06 January 2015

Dr Gideon Hirschfield
University of Birmingham
Institute of Biomedical Research
Birmingham
B15 2TT

Dear Dr Hirschfield

Study title:	**A single arm, two-stage, multi-centre, phase II clinical trial investigating the safety and activity of the use of BTT1023, a human monoclonal antibody targeting vascular adhesion protein (VAP-1), in the treatment of patients with primary sclerosing cholangitis (PSC)**
REC reference:	**14/EM/1272**
Protocol number:	**RG_13-027**
EudraCT number:	**2014-002393-37**
IRAS project ID:	**146127**

Thank you for your letter of 19 December 2014, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-Chair and two other members of the Committee.

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, Tracy Leavesley, NRESCommittee.EastMidlands-Derby@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.

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*
Investigator's brochure / IMP Dossier [BTT1023 Investigator Brochure]	4	26 September 2014
IRAS Checklist XML [Checklist_19122014]		19 December 2014
Other [BUTEO PIS]	2.0	19 December 2014
Other [BUTEO PIS]	2.0	19 December 2014
Other [BUTEO GP LETTER]	2.0	19 December 2014
Other [BUTEO GP LETTER TRACKED CHANGES]	2.0	19 December 2014
Other [BUTEO IBD DIARY]	2.0	19 December 2014
Other [BUTEO IBD DIARY TRACKED CHANGES]	2.0	19 December 2014
Other [BUTEO Ethics re-submission letter 19-Dec-2014]		19 December 2014
Other [Buteo Indemnity Certificate]		11 December 2014
Participant consent form [BUTEO ICF]	1.0	23 October 2014
REC Application Form [REC_Form_14112014]		14 November 2014
REC Application Form [REC_Form_14112014]		14 November 2014
REC Application Form [REC_Form_19122014]		19 December 2014
Research protocol or project proposal [Buteo Protocol]	1.0	31 October 2014
Summary CV for Chief Investigator (CI) [CI CV]	1.0	

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/

14/EM/1272	**Please quote this number on all correspondence**

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

project. Yours sincerely

Mr Peter Korczak (Chair)

Email:NRESCommittee.EastMidlands-Derby@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Dr Sean Jennings*

Dr Chris Counsell, University Hospitals Birmingham NHS Foundation Trust