London - Fulham Research Ethics Committee

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05 September 2017

Amy Douglas
Trial Coordinator – Haematology Trials Group
Cancer Research UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London
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Dear Ms Douglas

Study title:	**UKALL14 - A randomized trial for adults with newly diagnosed acute lymphoblastic leukemia**
REC reference:	**09/H0711/90**
Protocol number:	**UCL/08/0167**
EudraCT number:	**2009-012717-22**
Amendment number:	**45**
Amendment date:	**10 August 2017**
IRAS project ID:	**23389**

- Changes to the PIS to reflect new safety information received regarding nelarabine.
- Also noted that patients had not been made aware in previous versions of the PIS that pegylated asparaginase may also cause somnolence and therefore are advised not to drive or use machines if they experience somnolence whilst receiving pegylated asparaginase treatment, therefore this has also been added.
- In addition to this update to the study PIS, will also reconsent all patients who have already consented to the study and are receiving/due to receive nelarabine or pegylated asparaginase during the trial in light of this new information. An additional Patient Information Sheet has been prepared for this purpose and is enclosed.

The above amendment was reviewed at the meeting of the Sub-Committee held on 23 August 2017.

Ethical opinion

The Sub-Committee reviewed the amendment and requested the following clarifications:

1. How would participants be re-consented E.g. letter, next visit, extra visit?
2. What happens to participants who don't sign the additional consent? This should be made clear in the additional patient information sheet.
3. Professional duty of candour: it appears that the warning regarding pegylated asparaginase was previously missed out of the participant information sheet in error. The wording in the current additional participant information sheet could make it seem that this is new information.
4. The wording in the additional participant information sheet should reflect that the warning was previously not included in error if this was the case e.g. - We have also found that the previous patient information sheet you were given missed out the advice that

pegylated asparaginase can cause drowsiness too. Baxalta, the manufacturer of pegylated asparaginase, advise that you do not drive or operate machinery if you experience drowsiness whilst receiving pegylated asparaginase.
5. Please put updated dates and version numbers on documents where applicable.

Trial Co-ordinator Pip Patrick responded to the above with the following clarification:

1. Patients would be re-consented face to face at their next visit. We would provide each of our sites with a list of their patients due to receive nelarabine and/or pegylated asparaginase in future and who therefore require re-consenting. Patients who are not due to receive either of the drugs (e.g. Philadelphia positive B cell patients or patients who have completed all treatment cycles containing the drugs) would not need to be re-consented, as the new information pertains to an immediate risk, rather than a late effect.
2. Patients would be withdrawn from trial treatment and receive treatment at their treating clinician's discretion. This has now been added to the patient information sheet.
3. The information sheet has been amended to make this clearer.
4. The suggested wording has been added to make this clearer.
5. These have been added.

The Sub-Committee reviewed the clarification and amended documents and were satisfied with the clarifications and amendments. The Sub-Committee had no further issues.

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering letter on headed paper [Covering Letter]		10 August 2017
Notice of Substantial Amendment (CTIMP) [Amendment Form]	45	10 August 2017
Participant information sheet (PIS) [UKALL14 - Patient Information Sheet - Clean]	8	09 August 2017
Participant information sheet (PIS) [UKALL14 - Patient Information Sheet - Tracked Changes]	8	09 August 2017
Participant information sheet (PIS) [UKALL14 Additional PIS Driving and Machines - Clean]	1.1	31 August 2017
Participant information sheet (PIS) [UKALL14 Additional PIS Driving and Machines - Tracked]	1.1	31 August 2017

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

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.

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

09/H0711/90:	**Please quote this number on all correspondence**

Yours sincerely

Dr Shaun Griffin
Chair

E-mail: nrescommittee.london-fulham@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Anna Jones, Royal Free London NHS Foundation Trust*
Adele Fielding, Royal Free Hospital

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Attendance at Sub-Committee of the REC meeting on 23 August 2017

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Shaun Griffin	Communications Manager	Yes	
Mrs Elizabeth Reeves	Clinical Trials Training Executive	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mr Ewan Waters	REC Assistant