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27th October 2010

Clinical Trials Unit
Medicines and Healthcare Products Regulatory Agency
Market Towers
1 Nine Elms Lane
London
SW8 5NQ

Dear MHRA

REC ref. 07/Q1605/40
MHRA reference 21439/0215/001-0002
Eudract No. 2005-002417-20
Full protocol title: A Phase II Trial of erlotinib as first line therapy in Non-Small Cell Lung Cancer over-expressing EGFR

Re: End of Trial
Please find enclosed End of Trial form for this study with premature closure undertaken due to final NICE guidance on the use of first line gefitinib for the treatment of mutation positive non-small-cell lung cancer.

Yours sincerely

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Enc.
- ☐ 1. End of Trial form dated: 27 October 2010

Cc
- ☐ Shahista Hussain, Research Governance Coordinator, R&D Dept., Oxford Radcliffe Hospitals NHS Trust;
- ☐ Chair, Early Phase Trial Steering Committee, Oxford Cancer Centre

Declaration of the End of Trial Form (cf. Section 4.2.1 of the *Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial*[1])

NOTIFICATION OF THE END OF A CLINICAL TRIAL OF A MEDICINE FOR HUMAN USE TO THE COMPETENT AUTHORITY AND THE ETHICS COMMITTEE

For official use

Date of receipt :	Competent authority registration number : Ethics committee registration number:

To be filled in by the applicant

A MEMBER STATE IN WHICH THE DECLARATION IS BEING MADE : United Kingdom

B TRIAL IDENTIFICATION

B.1 EudraCT number :	**2007-001264-72**
B.2 Sponsor's protocol code number:	**A Phase II Trial of Erlotinib as first line therapy in Non-Small Cell Lung Cancer over-expressing EGFR**
B.3 Full title of the trial : ORH/PID/5298. Version 4.1 Apr 2010	

C APPLICANT IDENTIFICATION (please tick the appropriate box)

C.1	**DECLARATION FOR THE COMPETENT AUTHORITY**	❑
C.1.1	Sponsor	❑
C.1.2	Legal representative of the sponsor	❑
C.1.3	Person or organisation authorised by the sponsor to make the application.	X
C.1.4	**Complete below:**	
C.1.4.1	Organisation : University of Oxford, Department of Medical Oncology	
C.1.4.2	Name of person to contact : Dr Denis Talbot, Consultant Medical Oncologist	
C.1.4.3	Address : Cancer and Haematology Centre, Churchill Hospital, Old Road, Headington, Oxford, OX3 7LJ	
C.1.4.4	Telephone number : 01865235312	
C.1.4.5	Fax number : 01865 235986	
C.1.4.6	E-mail denis.talbot@medonc.ox.ac.uk	

C.2	**DECLARATION FOR THE ETHICS COMMITTEE**	❑
C.2.1	Sponsor	❑
C.2.2	Legal representative of the sponsor	❑
C.2.3	Person or organisation authorised by the sponsor to make the application.	❑
C.2.4	Investigator in charge of the application if applicable[2]:	
•	Co-ordinating investigator (for multicentre trial):	❑
•	Principal investigator (for single centre trial):	X
C.2.5	**Complete below** :	
C.2.5.1	Organisation: University of Oxford, Department of Medical Oncology	
C.2.5.2	Name : Dr Denis Talbot, Consultant Medical Oncologist	
C.2.5.3	Address : Cancer and Haematology Centre, Churchill Hospital, Old Road, Headington, Oxford, OX3 7LJ	
C.2.5.4	Telephone number : 01865235312	
C.2.5.5	Fax number : 01865 235986	
C.2.5.6	E-mail : denis.talbot@medonc.ox.ac.uk	

D END OF TRIAL

D.1	**Date of the end of the complete trial in all countries concerned by the trial?**
D.1.1	(YYYY/MM/DD): 2010/10/13

D.2	**Is it an early termination?[3]**	yes X no ❑

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1 OJ, C82, 30.3.2010, p. 1; hereinafter referred to as 'detailed guidance CT-1'.

2 According to national legislation.

3 Cf. Section 4.2. of the detailed guidance CT-1.

D.2.1 If yes, give date (YYYY/MM/DD): 2010/10/13
D.2.2 Briefly describe in an annex (free text):
D.2.2.1 The justification for early termination of the trial;
D.2.2.2 Number of patients still receiving treatment at time of early termination in the MS concerned by the declaration and their proposed management;
D.2.2.3 The consequences of early termination for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product.

D.2.2.1
This study has closed prior to target recruitment due the recent evidence and NICE (National Institute for Health and Clinical Excellence) guidance on the first line treatment of patients with non-small cell lung cancer (NSCLC) with gefitinib. (Gefinitib is an alternative tyrosine kinase inhibitor to erlotinib, the agent being utilised in our phase II trial).

In July 2010, NICE released its final technology appraisal titled "Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer". This stated that gefinitib is a recommended option for the first-line treatment of people with locally advanced or metastatic NSCLC if they test positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation. This recommendation was based on data from the IPASS trial, a phase III randomised controlled trial which compared gefitinib to chemotherapy (carboplatin/paclitaxel) as first-line therapy in patients with advanced-stage adenocarcinoma[1]. The results demonstrated that the 12 month rate of progression free survival (PFS) was 24.9% with gefitinib and 6.7% with chemotherapy ($p<0.001$). Furthermore, the PFS was significantly longer among patients on gefitinib with an EGFR-TK mutation, while patients without a mutation had a longer PFS with chemotherapy. In terms of overall response rate, this was 43% among all patients, but among the subgroup of patients with an EGFR-TK mutation this improved to 71.2% ($p<0.001$). This data forms the basis of gefinitib being recommended first line therapy for those patients with an EGFR-TK mutation, and the three month period required in the NHS for the institution of NICE guidance has now passed.

The Phase II erlotinib is being closed based on the introduction of the NICE guidance and that the hypothesis of the study has been proven, i.e. that tyrosine kinase inhibitors are a valuable therapy in the first line treatment of NSCLC (erlotinib is an alternative tyrosine kinase inhibitor agent to gefinitib as stated). The phase II study was based on EGFR over-expression rather than mutational analysis and an increasing body of evidence supports mutational analysis as the current best biomarker of response to tyrosine kinase therapy.

Reference
Mok T. N Engl J Med. 2009; 361:10

D2.2.2
There are no patients currently receiving treatment in this trial.

D2.2.3
This study has been terminated early with 26 patients having completed treatment within the trial of a proposed initial target of 35 patients. This is likely to affect the statistical power of this study in terms of efficacy but useful data for secondary endpoints such as toxicity has been collected. We will compare the study results to other Phase II studies of erlotinib in this patient population and hope to contribute to the current body of evidence for its use in NSCLC.

E SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

E.1 I hereby confirm that/confirm on behalf of the sponsor that (delete which is not applicable):
- The above information given on this declaration is correct; and
- That the clinical trial summary report will be submitted within the applicable deadlines in accordance with the applicable guidance by the Commission.[4]

E.2 APPLICANT TO THE COMPETENT AUTHORITY (as stated in C.1) ☐

E.2.1 Date : October 27, 2010
E.2.2 Signature :
E.2.3 Print name: Dr Denis Talbot

E.3 APPLICANT TO THE ETHICS COMMITTEE (as stated in C.2) : ☐

[4] Section 4.3. of the detailed guidance CT-1.

E.3.1	Date : October 27, 2010
E.3.2	Signature :
E.3.3	Print name: Dr Denis Talbot