

Central Office for Research Ethics Committees (COREC)

ANNUAL PROGRESS REPORT TO MAIN RESEARCH ETHICS COMMITTEE (For all studies except clinical trials of investigational medicinal products)

To be completed in typescript and submitted to the main REC by the Chief Investigator. For questions with Yes/No options please indicate answer in bold type.

1. Details of Chief Investigator

Name:	Professor Alan Silman (substantial amendment submitted to change Chief Investigator to Professor Deborah Symmons and add Dr Kimme Hyrich as a Principle Investigator – 17/04/2007)
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2. Details of study

Full title of study:	Prospective Observational Study of the long term hazards of anti-TNF therapy in rheumatoid arthritis
Name of main REC:	North West MREC
REC reference number:	MREC 00/8/53
Date of favourable ethical opinion:	1 st December 2000
Sponsor:	British Society for Rheumatology

3. Commencement and termination dates

Has the study started?	Yes / No
If yes, what was the actual start date?	1 st October 2001
If no, what are the reasons for the study not commencing?	n/a
What is the expected start date?	
Has the study finished?	Yes / No <i>If yes, complete and submit "Declaration of end of study" form, available at www.corec.org.uk</i>

<p>If no, what is the expected completion date?</p> <p><i>If you expect the study to overrun the planned completion date this should be notified to the main REC for information.</i></p>	<p>Recruitment expected to be completed by June 2008 (all patients followed for 5 years so potential completion date is 2013: see previous progress report attached).</p>
<p>If you do not expect the study to be completed, give reason(s)</p>	<p>n/a</p>

4. Site information

<p>Is this a study requiring site-specific assessment (SSA) and ethical approval of each site and local Principal Investigator?</p> <p>If yes, how many UK research sites have been recruited</p> <p>Has the Site Specific Information Form (SSIF)* been submitted to the LREC for each local Principal Investigator?</p> <p><i>*or Part C or Annex D of the former MREC application form if submitted prior to 1 March 2004</i></p>	<p>Yes / No</p> <p><i>Proposed in original application: Actual number recruited to date:</i></p> <p>Yes / No / <u>Not applicable</u></p>
<p>Is this study "SSA-exempt"? *</p> <p>If yes, how many UK sites are currently involved in facilitating this research?</p> <p><i>* or was previously designated as a "no local investigator" or "no local researcher" study</i></p>	<p>Yes / No</p> <p>This is a national study so all rheumatology departments prescribing anti-TNF therapy in the UK are participating. Local investigators are only required to inform LREC/R&D of study participation (n=766 rheumatologists at n=271 centres).</p>
<p>Do you plan to increase the total number of UK sites proposed for the study?</p> <p>If yes, how many sites do you plan to recruit?</p> <p><i>In the case of studies requiring SSA, all sites must be approved by the main REC as part of the favourable opinion.</i></p>	<p>Yes / No</p> <p>Only if new rheumatologists treat patients with anti-TNF therapy.</p>

5. Recruitment of participants

<p>*Number of participants recruited:</p>	<p><i>Proposed in original application: 16000 biologic patients, 4000 comparison patients. Actual number recruited to date: 13855 biologic patients, 3109 comparison patients.</i></p>
<p>*Number of participants completing trial:</p>	<p><i>Proposed in original application: 16,000 biologic patients, 4000 comparison patients. Actual number completed to date: 275 biologic patients, 0 comparison patients.</i></p>
<p>*Number of withdrawals due to:</p>	

(a) lack of efficacy	0
(b) adverse events	0
(c) self-withdrawal	181
(d) non-compliance	0
Total number of withdrawals:	181
Have there been any serious difficulties in recruiting participants?	Yes / <u>No</u>
If Yes, give details:	
Do you plan to increase the planned recruitment of participants into the study?	Yes / <u>No</u>
<i>Any increase in planned recruitment should be notified to the main REC as a substantial amendment for ethical review.</i>	

* In the case of international trials, please provide separate figures for UK and non-UK participants.

6. Safety of participants

Have there been any <i>related</i> and <i>unexpected</i> Serious Adverse Events (SAEs) in this study?	Yes / No / <u>Not applicable</u> This is an observational register to monitor long-term safety on SAEs. It is therefore the consultant/nurse responsibility to assess causality and report to the regulatory authorities as necessary.
Have these SAEs been notified to the Committee? <i>If no, please submit details with this report and give reasons for late notification.</i>	Yes / No / <u>Not applicable</u>
Have any concerns arisen about the safety of participants in this study? <i>If yes, give details and say how the concerns have been addressed.</i>	Yes / <u>No</u>

7. Amendments

Have any substantial amendments been made to the trial during the year?	<u>Yes</u> / No								
If yes, please give the date and amendment number for each substantial amendment made.	<table border="1"> <thead> <tr> <th><u>Date</u></th> <th><u>Reason</u></th> </tr> </thead> <tbody> <tr> <td>14/12/2006</td> <td>Rituximab added</td> </tr> <tr> <td>05/03/2007</td> <td>Drug adherence data</td> </tr> <tr> <td>April 2007</td> <td>Change of Chief Investigator</td> </tr> </tbody> </table> <p><i>NB: Amendment numbers not stated on letters.</i></p>	<u>Date</u>	<u>Reason</u>	14/12/2006	Rituximab added	05/03/2007	Drug adherence data	April 2007	Change of Chief Investigator
<u>Date</u>	<u>Reason</u>								
14/12/2006	Rituximab added								
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8. Other issues

Are there any other developments in the study that you	Yes / <u>No</u>
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wish to report to the Committee?	
Are there any ethical issues on which further advice is required?	<p style="text-align: center;">Yes / <u>No</u></p> <p><i>If yes to either, please attach separate statement with details.</i></p>

9. Declaration

Signature of Chief Investigator:	
Print name:	
Date:	