

### 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

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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 <sup>st</sup> December 2000
Sponsor:	The University of Manchester

#### 3. Commencement and termination dates

Has the study started?	<b>Yes</b> / No
If yes, what was the actual start date?	1 <sup>st</sup> October 2001
If no, what are the reasons for the study not commencing?  What is the expected start date?	N/A
Has the study finished?	<b>Yes</b> / <b>No</b> If yes, complete and submit "Declaration of end of study" form, available at <a href="http://www.nres.npsa.nhs.uk">www.nres.npsa.nhs.uk</a>

<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>We started recruiting to a rituximab cohort in May 2008. To date we have recruited 953 patients receiving rituximab and our target is 1100 – recruitment to this cohort continues and all patients will be followed up for at least 5 years.</p> <p>Further to this, we have recently had ethical approval to begin the recruiting a cohort of patients starting certolizumab (Cimzia) along with a new cohort of anti-TNF patients (copy of ethical approval letter attached). We hope to recruit 2000 patients to the certolizumab cohort, and a further 2000 patients to the new anti-TNF cohort; follow up of these patients will be for at least five years.</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 local REC 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><b>Yes / <u>No</u></b></p> <p><i>Proposed in original application: Actual number recruited to date:</i></p> <p><b>Yes / No / <u>Not applicable</u></b></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><b><u>Yes</u> / No</b></p> <p>This is a national study; all rheumatology departments prescribing biologic therapy in the UK are participating. Local investigators are only required to inform LREC/R&amp;D of study participation (n= 645 rheumatologists at n=285 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><b><u>Yes</u> / No</b></p> <p>Only if new rheumatologists treat patients with anti-TNF therapy</p>

#### 5. Recruitment of participants

*Number of participants recruited:	<i>Proposed in original application: 16,000 biologic patients (plus 1,100 rituximab patients, 2,000 certolizumab patients and a further 2,000 patients to the new anti-TNF cohort). In addition to this, there was a recruitment target of 4,000 comparison patients. Actual number recruited to date: 15,014 biologic patients (plus 953 Rituximab patients) and 3,775 comparison patients. Recruitment to the certolizumab and the new anti-TNF cohorts has yet to commence.</i>
*Number of participants completing trial:	<i>Proposed in original application: 16,000 biologic patients (plus 1,100 rituximab patients, 2,000 certolizumab patients and a further 2,000 patients to the new anti-TNF cohort), and 4,000 comparison patients. Following a substantial amendment MREC approval (06/05/2008) we are now following all patients in the study until at least 2013.</i>
*Number of withdrawals due to:	
(a) lack of efficacy	0 (n/a)
(b) adverse events	0 (n/a)
(c) self-withdrawal	342
(d) non-compliance	0 (n/a)
Total number of withdrawals:	342
Have there been any serious difficulties in recruiting participants?	Yes / <b>No</b>
If Yes, give details:	N/A
Do you plan to increase the planned recruitment of participants into the study?  <i>Any increase in planned recruitment should be notified to the main REC as a substantial amendment for ethical review.</i>	Yes / <b>No</b>

\* 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 – <b><u>Not Applicable</u></b> This is an observational register to monitor long term safety on SAEs. It is therefore the responsibility of consultant/nurse 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 / <b><u>Not applicable</u></b>
Have any concerns arisen about the safety of participants in this study?	Yes / <b>No</b>

If yes, give details and say how the concerns have been addressed.	
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## 7. Amendments

Have any substantial amendments been made to the trial during the year?	<b><u>Yes</u> / No</b>
If yes, please give the date and amendment number for each substantial amendment made.	<p><b><u>Date approved:</u></b>                      <b><u>Reason:</u></b>  20/12/2010 - Addition of a certolizumab to the register and the introduction of a new anti-TNF cohort</p> <p>10/09/2010 - Future introduction of electronic data collection</p> <p>04/08/2010 - Addition of a tocilizumab to the register (please note that this has not yet commenced as the funding is not yet in place)</p>

## 8. Other issues

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

## 9. Declaration

Signature of Chief Investigator:	
<b>Print name:</b>	<b>Professor Deborah Symmons</b>
<b>Date:</b>	<b>10/01/2011</b>