Health Research Authority

Annual Progress Report to Research Ethics Committee

For all studies except clinical trials of investigational medicinal products

To be completed and submitted by the Chief Investigator or sponsor. Please email this report to the REC. For questions with Yes/No options please indicate answer in bold type.

1. Details of the Chief Investigator

Name:	Professor Kimme Hyrich
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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

IRAS ID:	64202
Name of REC:	NRES Committee Northwest - Haydock
REC reference number:	MREC 00/8/053
Date of favourable ethical opinion:	1st December 2000
Sponsor:	The University of Manchester

3. Commencement and termination dates

Has the study started?	***Yes*** / No
If yes, what was the actual start date?	1st October 2001
If no, what are the reasons for the study not commencing? What is the expected start date? Please note, if the study will not start within 24 months of the REC Favourable Opinion date the REC may review its' opinion.	***N/A***
Has the study finished? If yes, complete and submit "Declaration of end of study" form, available on the HRA website	*Yes* / ***No***
If no, what is the expected completion date? If you expect the study to overrun the planned completion date, what are the reasons for this?	Five cohorts are currently open to recruitment: i) IL-6 inhibitor cohort ii) Certolizumab cohort iii) Anti-TNF comparison cohort iv) Participants starting a biosimilar v) New targeted therapies (including JAK inhibitors) cohort All participants are being followed-up until at least 2028 (the current study end date is 30/09/2028) with an expectation that this may be further extended.
If you do not expect the study to be completed, give reason(s)	***N/A***

4. Registration

Is the study a 'clinical trial'? (Defined as the first 4 categories on the IRAS filter page) (For CTIMPs, please use CTIMP progress reporting template)	*Yes / **No***
Is the study registered on a publicly accessible database? (Registration of clinical trials is a condition of approval for studies approved after 30 September 2013)	Yes / No ***N/A***
If yes, please provide the name of the publicly accessible database and the registration number	Registration number: ***N/A***
If no:	a) What is the reason for non-registration? ***N/A*** b) What are your intentions for registration? ***N/A***

5. Recruitment of participants

In this section, "participants" includes those who will not be approached but whose samples/data will be studied.

Number of participants recruited:	*Proposed*: Original Anti-TNF cohort: 16,000 Non-biologic DMARD comparison cohort: 4,000 Mabthera cohort: 1,100 IL-6 inhibitor cohort: 4,000 Cimzia cohort: 2,000 Anti-TNF comparison cohort: 4,000 Biosimilar cohort: 6,000 Other advanced targeted therapies (including JAK inhibitors) cohort: 2000 per drug

	Actual number recruited to date: Original Anti-TNF cohort: 13254 (recruitment now closed) Non-biologic DMARD comparison cohort: 3685 (recruitment now closed) Mabthera cohort: 1603 (recruitment now closed) IL6 Inhibitor cohort: 1719 Cimzia cohort: 1519 Anti-TNF comparison cohort: 2198 Biosimilar cohort: 4708 Other advanced targeted therapies (including JAK inhibitors) cohort: 1018
Number of participants completing the study:	Actual number completed to date: All participants are being followed-up until at least 2028 (the current study end date is 30/09/2028).
Number of withdrawals from study to date due to: a) withdrawal of consent: 359 b) loss to follow-up: 1596 c) death (where not the primary outcome) 6206 Total study withdrawals:	8161
*Number of treatment failures to date (prior to reaching primary outcome) due to: Total treatment failures: **(N/A – not a trial)** *Applies to studies involving clinical treatment only a) adverse events **(N/A – not a trial)** b) lack of efficacy **(N/A – not a trial)**	
Have there been any serious difficulties in recruiting participants?	Yes / ***No***
If Yes, give details:	
Do you plan to increase the planned recruitment of participants into the study? Please note, any increase in planned recruitment or changes to the recruitment methodology should be notified to the REC as	Yes / ***No*** (unless new targeted therapies for RA are licensed in the UK in the future)

a substantial amendment for ethical review.	

6. Safety of participants

Have there been any related and unexpected serious adverse events (SAEs) in this study?	*Yes / No* ***Not Applicable***
Have these SAEs been notified to the Committee? If no, please submit details with this report and give reasons for late notification.	*Yes / No /****Not applicable***
Have any concerns arisen about the safety of participants in this study? If yes, give details and say how the concerns have been addressed. This information may be considered by the Committee when reviewing the report.	*Yes /* ***No***

7. Amendments

Have any substantial amendments been made to the study during the year?	***Yes*** / No
If yes, please give the date and amendment number for each substantial amendment made.	Substantial Amendment 28: REC approved 29/04/2021 HRA approved 19/05/2021

8. Serious Breaches of the Protocol

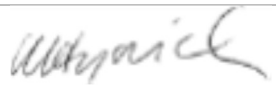
Have any serious breaches of the protocol occurred during the year? If Yes, please enclose a report of any serious breaches not already notified to the REC.	*Yes /* ***No*** *Yes / No* ***N/A***

9. Other issues

Annual progress report (non-CTIMP), version 4.6, dated January 2021

Are there any other developments in the study that you wish to report to the Committee?	***Yes*** / No Recruitment to the study has been impacted by the launch of the BSRBR-RA online database quickly followed by the COVID-19 pandemic, however remote consent procedures (for which the study already has ethical approval) have allowed the study to continue the recruitment of participants.

10. Declaration

*Signature/Electronic Signature of Chief Investigator or Sponsor representative: *Please print name below and insert electronic signature, if possible	
Print name:	Prof. Kimme Hyrich
Date of submission:	06/09/2022