



ORBIT STUDY – NEWSLETTER

Dear all

Welcome to the fourth edition of the ORBIT newsletter!
The purpose of the newsletter is to provide you with ORBIT updates and will be circulated on an ongoing basis.

Update on approval of sites.

The following sites are still awaiting local R&D approval:

Site	PI
Cardiff University School Of Medicine	Prof. Ernest Choy
Ipswich Hospital - Ipswich	Dr Richard Watts
Torbay Hospital – Torquay Devon	Dr Kirsten Mackay
Derriford Hospital – Derriford-Plymouth	Dr Mark Perry
West Suffolk Hospital	Dr David O’Reilly
University Hospitals Coventry	Dr Tanya Potter
Royal Devon And Exeter NHS Trust	Dr Richard Haigh
Betsi Cadwaladr University Health Board	Dr Yasmeen Ahmad
South London Healthcare NHS Trust	Dr Louise Dolan
Essex - Queens Hospital	Prof Kuntal Chakravarty
Royal Cornwall Hospitals NHS Trust	Prof Anthony Woolf
Basildon And Thurrock University Hospital	Dr Nagui Gendi
Essex – King George Hospital	Dr Thalia Roussou

For the new sites, we have global permission from CSP (CSP Study ID no. 12570) and the trial has been adopted on to the UKCRN portfolio. Some sites still need to complete a Site Specific Information (SSI) form to gain local NHS approval.

Please note: as this is a ‘Devolved Nations Study’ originating from Scotland; the SSI needs to be MANUALLY uploaded onto CSP and then validated, clock started and local checks completed as normal. Please see “CSP Procedures for studies requiring UK-wide permissions V2.1”; and the latest “CSP Operating Guidelines” for further guidance.

We are continuing to work very hard to assist you with this, and please don’t hesitate to get in contact if you are running into problems, or have a query. The sooner we can get sites approved, the sooner you can start recruiting!



Recruitment

Arthritis Research UK has set us the target of recruiting 14 patients per month between May and July 2011. If recruitment falls short, the funder may decide to discontinue funding for the trial. It is therefore a critical period for the success of the project! As a number of sites are still awaiting local R&D approval, the challenge of recruiting to target in this key period lies with the sites that have been given the Green For Go. Thank you for the hard work; however given this critical period can we re-double our efforts?

Remember - this study is one of the few investigator-initiated trials of biologic therapy ever performed, and only the second ever head-to-head biologic Randomised Controlled Trial. Well worth all our efforts! Please find below the present recruitment rate per site.

Site Number	Site	Randomised	Withdrawn
1	Gartnavel General Hospital, Glasgow	16	0
2	Glasgow Royal Infirmary, Glasgow	6	0
4	Stobhill General Hospital, Glasgow	2	0
5	Inverclyde Royal Hospital, Greenock	1	0
6	Western General Hospital, Edinburgh	2	0
6	Raigmore Hospital, Inverness	5	0
9	Wishaw General Hospital, Wishaw	7	2
10	Aberdeen Royal Infirmary, Aberdeen	4	0
11	Whyteman's Brae Hospital, Fife	2	0
15	Barts and the London NHS Trust, London	7	0
16	University of Birmingham	0	0
19	Borders General Hospital, Borders	0	0
20	Ninewells Hospital, Dundee	1	0
22	Royal Victoria Infirmary, Newcastle	0	0
23	James Cook University Hospital, Middlesbrough	0	0
Total		53	2

How well do you know the protocol?

The patients are being treated according to 'Treat-to-Target' principles – this means that the Research Nurse and the PI needs to keep a close eye on the patients' disease activity to decide every month if the treatment should be continued or not. Each edition of the newsletter will contain an MCQ that will test your knowledge of the protocol:

Mrs X comes for her 3 month assessment. She has been randomised to anti-TNF therapy, and is feeling a bit better. Her DAS28 scores are as follows:

Baseline	Month 1	Month 2	Month 3
5.6	4.8	4.3	4.2

- Q1 – Is the patient a:
- a) non-responder?
 - b) moderate responder?
 - c) good responder?
- Q2 – should you:
- a) continue anti-TNF therapy?
 - b) switch to rituximab?
- Q3 – at subsequent visits, how high should her DAS28 be for you to consider switching to rituximab?
- a) >3.2
 - b) >4.4
 - c) >5.1

The answers and explanation can be found at the end of the newsletter. If you got any wrong, then have another look at the protocol, and drop us a line if you need any clarification.

Serious Adverse Events.

We all know the benefits our patients can receive from Biologic therapy, but we are also conscious of the potential for serious drug-related toxicity. It is very encouraging, therefore, that only 5 Serious Adverse Events have occurred to date (One patient had 2 Serious Adverse Events). One of these was a Suspected Unexpected Serious Adverse Reaction – a patient developed a brisk transaminitis following a rituximab infusion; whilst there were other possible contributory factors (methotrexate therapy, alcohol) the time course suggested to the PI that rituximab may have been involved. The other SAEs reported have been 1) community acquired pneumonia (2 SAE forms); 2) probable rheumatoid vasculitis, and 3) New onset interstitial lung disease; all occurring in patients receiving anti-TNF therapy.

Serious Adverse Event Reporting.

All Serious Adverse Events (SAEs) in the study must be reported within 24 - 48 hour to the Sponsor Pharmacovigilance (PV) Office. These reports are processed by the PV office team -Fiona Selfridge- PV Administrator and Dr Eleanor Dinnett-PV Officer. Fiona and Eleanor are happy to answer any questions you may have and can be contacted by phone at 041 330 4744 or by email at: pharmacovig@glasgowctu.org

SAE reporting is carried out using the SAE form available at www.glasgowctu.org. The form is downloaded, printed off, completed and signed. The form is then faxed to 0141 357 5588. The PV Office will acknowledge receipt of the form and will contact you if there are any queries.

A verbal report can also be made by contacting the PV Office on 0141 330 4744. This must be followed up as soon as possible with a signed written report.

Cost questionnaire – patient diary.

At various times throughout the study the Cost questionnaires will be required to be forwarded to the statistical centre for analysis. Jurgen will be in touch with all the sites in due course to explain the procedure.

Blood sampling procedures - new contact.

Please note that the PEAC Biobank recently appointed a new member of staff join the team; Dr Vidalba Rocher Ros. Vidalba will now be responsible for dealing with the processing of samples and clinic supplies. Please add Vidalba's email address v.rocher@qmul.ac.uk to your records and direct all requests and notifications to her.

Please continue to CC Dr Becki Hands r.e.hands@qmul.ac.uk into all ORBIT emails so that Becki can still deal with any issues/requests if Vidalba is away.

With regards to the revised sample collection protocol for ORBIT. The sign off of necessary contracts is imminent. As from the moment this is in place then Jurgen will notify all sites; Vidalba will supply additional equipment to all sites in order to undertake the revised procedure.

QUERIES.



Should you have any queries then please contact:

- For SSI information please contact Ann on: Ann.Tierney@ggc.scot.nhs.uk
- For general information / queries please contact Jurgen on: Jurgen.van-melckebeke@ggc.scot.nhs.uk or Duncan on: Duncan.Porter@ggc.scot.nhs.uk

THANK YOU FOR YOUR SUPPORT IN THE STUDY!

Duncan & Jurgen.

A1 – b) moderate responder – her DAS28 has fallen by >1.2 (and she is therefore a responder), but is still above 3.2 (and so isn't a good responder)
A2 – a) continue anti-TNF therapy – only switch patients who are non-responders. You can change the patient's DMARDS, give IA/IM steroid
A3 – b) >4.4 – if the patient's DAS28 rises to within 1.2 of their baseline, then they have lost response and a switch to rituximab should be considered, assuming there is no reason to suspect that the DAS28 has been elevated falsely (e.g. by a UTI causing her ESR to be high).