



## ORBIT STUDY – NEWSLETTER

Dear all

Welcome to the fifth 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.

Local R&D approval for the remaining sites is now imminent:

| Sites awaiting approval                 | PI                  |
|---|---------------------|
| Cardiff University School Of Medicine   | Prof. Ernest Choy   |
| Oxford University                       | Prof Peter Taylor   |
| West Suffolk Hospital                   | Dr David O'Reilly   |
| University Hospitals Coventry           | Dr Tanya Potter     |
| Betsi Cadwaladr University Health Board | Dr Yasmeen Ahmad    |
| Essex - Queens Hospital                 | Prof K. Chakravarty |
| Essex – King George Hospital            | Dr Thalia Roussou   |



Thanks to Dr Nixon (Countess of Chester NHS Foundation Trust); Prof Young (West Herts Hospital NHS Trust); Dr Smith (Salisbury NHS Foundation Trust); Dr Barkham (The Royal Wolverhampton Hospitals NHS Trust) and Dr Kinder (Leicester Royal Infirmary) for their kind offer to participate in the study. Work is underway to get the sites up and running as soon as possible.

### Recruitment

Arthritis Research UK continue to be very supportive of the study, but are anxious that we get results as soon as possible. Recruitment is the key to that, but unfortunately remains slower than we would like. Can you all re-double your efforts to find suitable patients? If you haven't yet got off the mark, then keep trying – the first patient is always the hardest! **THANKS!**

Congratulations to:

- Dr Fouz and team in Poole Hospital for their excellent recruitment rate since start up!
- the team at Gartnavel General Hospital for being the best overall recruiter!
- Dr Munro and his team in Wishaw for reaching double figures!

We are trying to assess why recruitment has been slower than expected. To that end, Arthritis Research UK have asked us to audit your screening logs. Could you make a special effort to fill these in for the next month? Jurgen will be in touch to get copies.

| Site                                   | Green For Go | Randomised |
|--|--------------|------------|
| Gartnavel General Hospital, Glasgow    | 02/04/2010   | 20         |
| Wishaw General Hospital, Wishaw        | 07/09/2010   | 10         |
| Glasgow Royal Infirmary, Glasgow       | 09/06/2010   | 9          |
| Raigmore Hospital, Inverness           | 16/08/2010   | 8          |
| Barts and the London NHS Trust; London | 04/11/2010   | 8          |
| Poole Hospital NHS Trust               | 15/06/2011   | 6          |
| Aberdeen Royal Infirmary, Aberdeen     | 23/09/2010   | 5          |
| Western General Hospital, Edinburgh    | 07/07/2010   | 4          |

|  |            |           |
|--|------------|-----------|
| Whytemans Brae Hospital, Fife                  | 08/11/2010 | 4         |
| Haywood Hospital, Stoke On Trent               | 23/02/2011 | 4         |
| Stobhill General Hospital, Glasgow             | 10/06/2010 | 3         |
| Inverclyde Royal Hospital , Greenock           | 05/08/2010 | 3         |
| James Cook University Hospital; Middlesborough | 13/05/2011 | 3         |
| Borders General Hospital, Borders              | 08/10/2011 | 2         |
| Ninewells Hospital, Dundee                     | 04/06/2010 | 2         |
| Royal Victoria Infirmary, Newcastle            | 11/03/2010 | 2         |
| University of Birmingham; Birmingham           | 01/02/2011 | 1         |
| Torbay Hospital                                | 01/08/2011 | 1         |
| <b>TOTAL</b>                                   |            | <b>95</b> |

### Changes to study documentation / processes.

Over the last 2 months there has been a flurry of paperwork. Important updates to the Protocol, Patient Information Sheet and Cost Questionnaires had to be made. Unfortunately this generated a lot of bureaucracy for everyone. Sorry! A summary of the changes is shown below

#### Substantial Amendments.

##### 1. Update to Protocol (version 2.2, 25/4/2011)

This clarified the 'window' during which study visits need to be made, the process whereby patients can receive IM steroid after screening but before baseline, the importance of the pre-medication for patients receiving rituximab, and an update on the procedures for safety reporting.

##### 2. Update to Patient Information Sheet (version 4, 22/06/2011)

Following case reports of fatal infusion reactions with rituximab, a sentence was added to the PIS stating:

"As with all therapies for arthritis, very serious side effects can occur rarely with either anti-TNF or rituximab. For instance, some patients treated with rituximab have developed allergic reactions, which rarely have proved fatal. Similarly, some patients treated with anti-TNF therapy have developed severe infections that rarely have proved fatal."

#### Blood sampling – revised blood sampling procedures for academic sites.

Under a revised sample collection we hope to improve the quality of the samples we collect for the Biobank. Thank you for the sites who can undertake the revised sampling procedure. Please see email dated 05/10/2011 detailing changes and actions required to implement locally.

#### Patient Diaries – Cost questionnaires.

One of the important outcomes of the study will be to assess the relative cost effectiveness of TNFi and rituximab therapy. For this analysis, the patient diary (also referred to as cost questionnaire) is vital. Can you all remember to forward this every month to Emma Miller (Project Assistant). Emma will remind you if you forget!

#### How well do you know the protocol? ORBIT quiz.

Mrs Y has been randomized to rituximab therapy. Her DAS28 score are as follows:

| Baseline | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 |
|----------|---------|---------|---------|---------|---------|---------|
| 5.8      | 4.8     | 4.1     | 3.0     | 2.8     | 2.9     | 3.1     |

Q1: At 6 months; is the patient a:

- Non-responder?
- Moderate responder?
- Good responder?

Q2: Should you:

- a) Prescribe a further course of rituximab?
- b) Switch to anti-TNF therapy?
- c) No change – just review in 1 month

Q3: At subsequent visits, how high should her DAS28 be for you to arrange another course of rituximab?

- a) >3.2
- b) >4.6
- 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.

#### **Safety update.**

Thankfully, we are not finding drug related toxicity to be a major problem. So far, only 14 serious events have been reported, and of these only 6 were thought to be possibly related to a study drug (3 adalimumab, 2 rituximab, 1 etanercept). There have been no further SUSARs.

#### **Blood sampling procedures – Contacts at day of shipping the samples.**

It is extremely important to notify PEAC Biobank staff by email **on the day of shipping the samples**. Failure to do so may result in unnecessary delays which can compromise the quality of the samples. Please read instructions as detailed on the sampling manuals

Staff to be contacted are:

- Dr Becky Hands: [r.e.hands@qmul.ac.uk](mailto:r.e.hands@qmul.ac.uk)
- Ms Rita Jones: [m.r.jones@qmul.ac.uk](mailto:m.r.jones@qmul.ac.uk)
- Dr Vidalba Rocher: [v.rocher@qmul.ac.uk](mailto:v.rocher@qmul.ac.uk)

#### **QUERIES.**

Should you have any queries then please contact:

- For SSI information: please contact Ann on: [Ann.Tierney@ggc.scot.nhs.uk](mailto:Ann.Tierney@ggc.scot.nhs.uk)
- cost questionnaires, please contact Emma on [Emma.Miller@ggc.scot.nhs.uk](mailto:Emma.Miller@ggc.scot.nhs.uk)
- For general information / queries please contact Jurgen on: [Jurgen.van-melckebeke@ggc.scot.nhs.uk](mailto:Jurgen.van-melckebeke@ggc.scot.nhs.uk) or Duncan on: [Duncan.Porter@ggc.scot.nhs.uk](mailto:Duncan.Porter@ggc.scot.nhs.uk)

**THANK YOU FOR YOUR SUPPORT IN THE STUDY!**

**Duncan & Jurgen.**

A1 – c) good responder – her DAS28 has fallen by >1.2 and has fallen below 3.2 (and so is a good responder)

A2 – c) no change – just review in 1 month – patient is a good responder

A3 – a) >3.2 – if the patient's DAS28 rises higher than 3.2; then another course of Rituximab should be arranged.