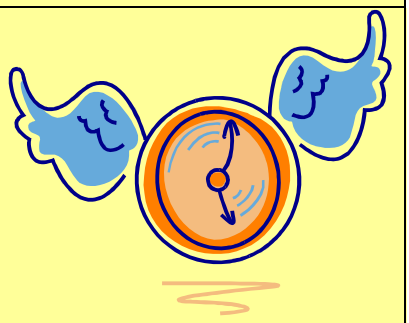
ORBIT STUDY – NEWSLETTER
10TH EDITION

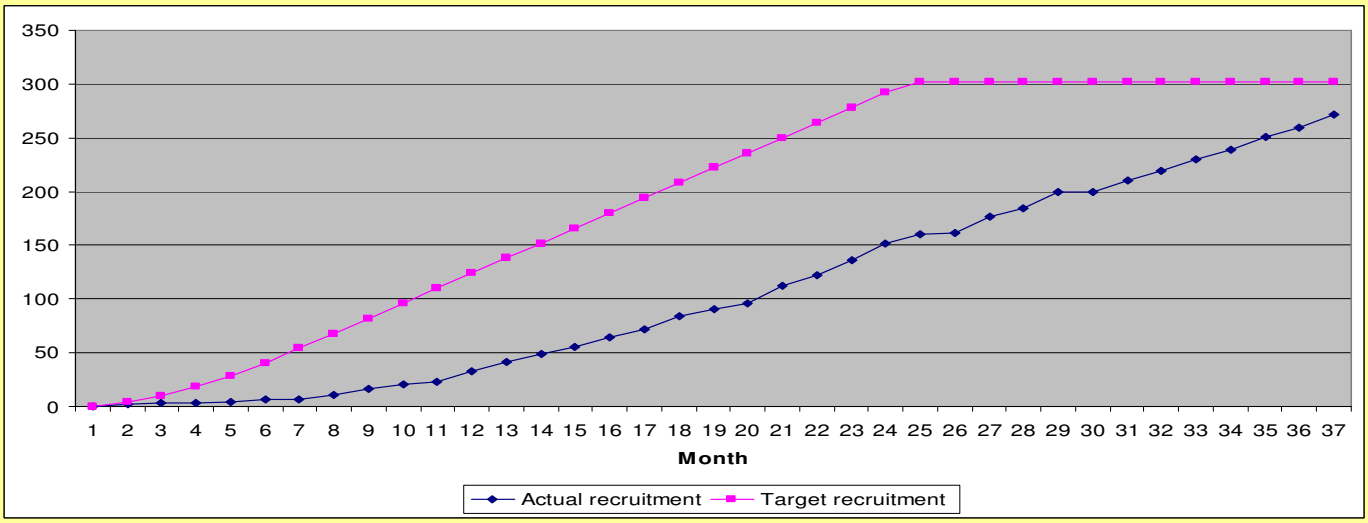
Recruitment.



Dear ORBIT colleagues
We have recruited 286 participants. Of this 25 patients withdrew prior to receiving treatment, **meaning that we require another 41 participants** to reach our target of 302 patients treated with at least one dose of study drug.
The clock is now ticking on recruitment for ORBIT – we have less than four months to recruit another 41 patients. We are urging all participating sites to make the most of this time by recruiting as many new patients as possible!

For the success and statistical power of the trial **we must meet our overall recruitment target (n=302) before end October 2013**. Please discuss and plan recruitment over the remaining four months with your site. The study management team is on hand to assist in this in any way we can. Please contact us.

Recruitment per month



Extension to the study
Many thanks to the funder – ARUK – for granting an extension to the study. The study extension amendment has been passed on to all governing bodies. This means that we can keep recruiting until end October 2013. Thank you for the sites that have recruited to target! Please don't stop there though – we are urging those sites who are "on track" to join us in one final push to help reach our target. We are hoping that some sites will be able to recruit beyond their targets. If you are falling behind, please don't lose motivation, we value your efforts – please keep looking for and approaching potential participants. Every patient enrolled moves us closer to success!

IF EVERY ACTIVE SITE RECRUITED ONE (YES, JUST ONE!!) MORE PATIENT WE WOULD BE OVER THE LINE IN A JIFFY. CAN YOU MANAGE ONE MORE PATIENT IN YOUR CENTRE?

THANK YOU FOR ALL YOUR HARD WORK AND SUPPORT!

Recruitment per site.

Site	Green For Go	Randomised
Gartnavel General Hospital, Glasgow	02/04/2010	33
Haywood Hospital, Stoke On Trent	23/02/2011	17
Wishaw General Hospital, Wishaw	07/09/2010	19
Raigmore Hospital, Inverness	16/08/2010	14
Glasgow Royal Infirmary, Glasgow	09/06/2010	15
Barts and the London NHS Trust; London	04/11/2010	13
Nuffield Orthopaedic Centre, Oxford	04/04/2012	13
Poole Hospital NHS Trust, Poole, Dorset	15/06/2011	10
Western General Hospital, Edinburgh	07/07/2010	10
Royal Cornwall Hospitals NHS Trust, Truro	07/10/2011	10
Stobhill General Hospital, Glasgow	10/06/2010	9
Derriford Hospital, Derriford, Plymouth	24/08/2011	9
Cannock Chase Hospital, Cannock	16/08/2012	9
Leicester Royal Infirmary, Leicester	10/02/2012	9
Torbay Hospital, Torquay	01/08/2011	8
Royal Victoria Infirmary, Newcastle	11/03/2010	8
Basildon and Thurrock Hospitals	26/07/2011	8
James Cook University Hospital; Middlesborough	13/05/2011	7
King George Hospital, Essex	02/10/2012	7
University of Birmingham, Birmingham	01/02/2011	6
Aberdeen Royal Infirmary, Aberdeen	23/09/2010	6
Borders General Hospital, Borders	08/10/2010	6
Salisbury NHS Foundation Trust	26/01/2012	5
Ipswich Hospital, Ipswich	11/07/2011	5
Whytemans Brae Hospital, Fife	08/11/2010	4
South London Healthcare NHS Trust, London	13/07/2011	4
Queens Hospital, Essex, Romford	31/10/2011	4
Countess of Chester Hospital, Chester	31/01/2012	4
University of Cardiff, Cardiff	18/01/2012	4
Inverclyde Royal Hospital, Greenock	05/08/2010	3
Ninewells Hospital, Dundee	04/06/2010	3
Royal Devon and Exeter NHS Trust, Exeter	27/07/2011	2
Coventry University Hospitals, Coventry	06/01/2012	1
Llandudno Hospital, Llandudno	21/02/2012	1
West Suffolk Hospital, Bury St Edmonds	21/02/2012	0
West Herts Hospital NHS Trust, Hertfordshire	04/04/2012	0
North Manchester General Hospital	20/08/2012	0
New Cross Hospital, Wolverhampton	29/08/2012	0
Royal Lancaster Infirmary, Lancaster	22/11/2012	0

Kettering General Hospital	13/11/2012	0
Southend Hospital, Dr Dasgupta	28/01/2013	0
Trafford General Hospital, Dr McKenna	05/06/2013	0
TOTAL		**286**

STAR site – CONGRATULATIONS to Leicester Royal Infirmary for recruiting the highest number of patients in the last three months. Well done, and THANK YOU!

Amendments.
A summary sheet detailing all amendments will be forwarded to the study teams. Can we ask to insert this summary sheet in your study site file – Section 3, amendments.

Time window between visits.

A quick reminder ☺ - study visits should take place as close as possible to the same calendar date each month (e.g. baseline is on 7th Feb, then follow up visits should aim for 7th of each month thereafter). You have a leeway of +/- 7 days; if the patient is unable to attend (e.g. holidays) this can be extended to +/- 14 days as long as you make a note in the Study Visit Booklet. If a visit cannot be made within this window, omit the visit and complete a file note to explain why. If you are still confused, then e-mail Jurgen for further guidance/explanation!

Changes to the eCRF.

A new release of the eCRF will be available in the near future, it will contain the following changes:

IV Rituximab log. Administration of the IMP is currently documented via the IV Rituximab log. The log will shortly be available on the eCRF. Can we ask to retrospectively complete the "Rituximab infusion log" column on the eCRF; and this for all patients who had IV Rituximab administered throughout the study. The log can be accessed via the last column on the patient timeline in the eCRF. An entry should be made for each drug administered

CRP results. By selecting the "Under Treshold" radio button it will be possible to record a value of "<3" or "<5". If applicable; can we ask to retrospectively amend said results.

RF results. It will be possible to record values of more then 999. If applicable: can we ask to retrospectively amend said results.

Time windows between visits. When scheduling a patient's next monthly visit an information message will be dispayed if the visit falls outwith the required +/- 7days of the recommended date. If the visit is outwith +/- 14 days of the recommended date a message will be displayed advising that the next visit should be omitted. In both cases it will be necessary to record a reason. If a visit is omitted the following visit should be scheduled via the instructions page of the omitted visit as normal

Data query forms
The data query process is now well underway and the sites have received the first batch of data query forms. Thank you for responding to the queries. If you have any queries then please contact the centre (email below)

Safety update
To date we have received 44 Serious Adverse Event reports involving 36 subjects. Of these 19 have been assessed as being possibly or probably related to a study drug (6-adalimumab, 11-rituximab, and 2-etanercept) with one of these considered being a SUSAR.

The Pharmacovigilance Office team (Dr Eleanor Dinnett – PV officer and June Allan – PV Administrator) is happy to answer any questions you may have regarding any aspect of the SAE assessment and reporting process and can be contacted by phone at 0141 330 4744 or by email at: pharmacovig@glasgowctu.org

Cumulative list of SAEs received by the Pharmacovigilance Office to 21/06/2013:

Diagnosis on SAE form	**Classification**	**Trial Drug**
Asthma	SAE	
Cerebral Infarction -left sided hemiparesis + left sided visual/sensory neglect	SAE	
Myocardial Infarction	SAE	
Investigations for increased confusion	SAE	

Left groin pain	SAE	
Admitted for analgesia assessment	SAE	
Flare of RA	SAE	
NIDDM (Type 2 Diabetes)	SAE	
(R+ TKR) Right total knee replacement	SAE	
Grade 2 cancer left breast	SAE	
Urinary tract infection + urinary retention	SAE	
Headache, diarrhoea, abdominal pain (hospitalisation)	SAE	
Pneumonitis	SAE	
Left # NOF	SAE	
Rheumatoid arthritis flare up	SAE	
Elective admission to hosp for decompression and fusion surgery for lumbar spine l4/l5	SAE	
Chest pain	SAE	
Colonic polyps	SAE	
Laminectomy	SAE	
Musculoskeletal chest pain	SAE	
Septic arthritis left 2nd DIP joint	SAE	
Pulmonary embolism	SAE	
Fracture of left femur bone	SAE	
Right hip replacement	SAE	
Admitted with lower abdominal pain and vomitting ?bowel obstruction	SAE	
Urticaria, itch	SAR	Rituximab
Chest Infection	SAR	Adalimumab
Chest Infection	SAR	Adalimumab
Neutropaenia	SAR	Rituximab
SAR Cutaneous Vasculitis	SAR	Adalimumab
New onset interstitial lung disease	SAR	Etanercept
Neutropenia	SAR	Rituximab
Non specific abdominal pain	SAR	Rituximab
Neutropenic sepsis	SAR	Rituximab
Labyrinthitis (acute)	SAR	Adalimumab
Epigastric pain, fever, vomitting	SAR	Etanercept
Chest infection	SAR	Rituximab
Gram negative sepsis	SAR	Rituximab
Urine infection	SAR	Rituximab
Parotiditis	SAR	Rituximab
Acalculic cholecystitis	SAR	Adalimumab
Chest infection	SAR	Rituximab
Probably viral tonsillitis	SAR	Adalimumab
Abnormal Liver Function Test Results	SUSAR	Rituximab

Pharmacy update

As we near the end of the recruitment period for the ORBIT study we will be continuing to keep a close eye on Rituximab supplies held at site in order to minimise wastage. We may contact you to confirm exact requirements prior to placing orders with Roche. Thank you for your patience with this.

QUERIES.

Should you have any queries then please contact:

- Data queries: ORBITsupport@glasgowctu.org
- PEAC sampling queries:
  - Dr Becky Hands: r.e.hands@qmul.ac.uk
  - Ms Rita Jones: m.r.jones@qmul.ac.uk
  - Dr Vidalba Rocher: v.rocher@qmul.ac.uk
  - Sudeh Riahi: s.riahi@qmul.ac.uk
- For Pharmacy information: please contact Elizabeth on Elizabeth.Douglas@ggc.scot.nhs.uk or R&Dimp@ggc.scot.nhs.uk
- Cost questionnaires, please contact Emma on Emma.Miller@ggc.scot.nhs.uk
- For general information / queries please contact Jurgen on: Jurgen.van-melckebeke@ggc.scot.nhs.uk or Duncan on: Duncan.Porter@glasgow.ac.uk

THANK YOU FOR YOUR SUPPORT IN THE STUDY!

Duncan & Jurgen.