ARTemis: Avastin® Randomised Trial with neo-adjuvant chemotherapy for patients with early breast cancer

ARTemis Newsletter
Issue 8
September 2011

Welcome to this eighth edition which will tell you about Amendment 13, recruitment, data collection, translational sub studies and GCP/ Monitoring.

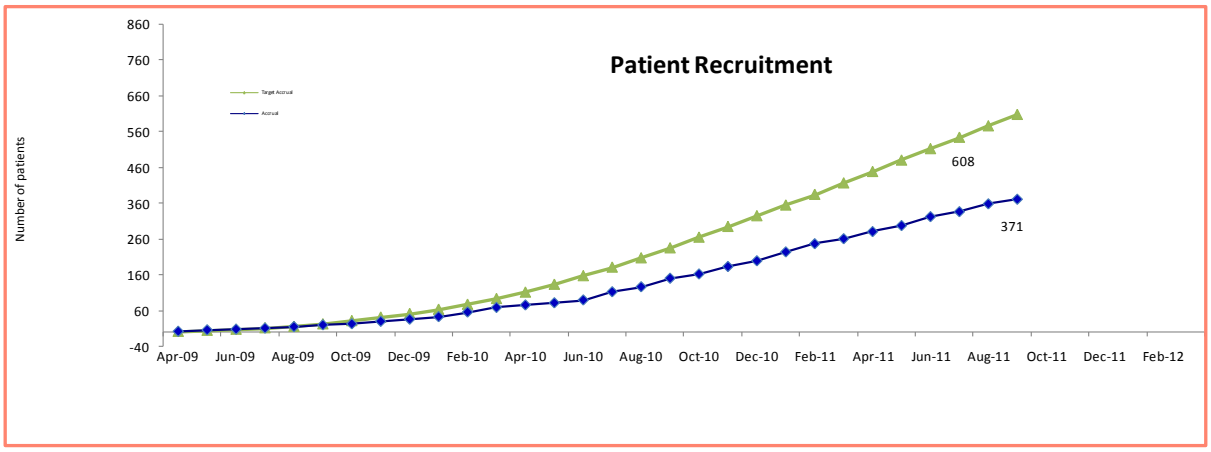
AMENDMENT 13

The Protocol, Patient Information Sheets 1, 3 & 4 have been submitted for amendment to clarify various translational aspects of the trial and tumour measurements and also to extend patient follow-up from 5 to 10 years. We hope to send the Amendment out to you as soon as we receive approval, hopefully in the next couple of weeks.

Please note that active sites can only use the new versions of the documents after their local R&D department's approval, however please remember that you may continue to recruit and use the current versions of the documents until R&D approval is gained for the new versions.

PATIENT RECRUITMENT: Number of Patients Recruited: 371

(as of 23rd Sept 2011)



With 22 patients recruited, August was a good month. However, the recruitment remains steady below target and we encourage you all to screen as many patients as possible. Please provide feedback to the Warwick Trial Office by sending your recruitment/screening logs or answering the questionnaire sent early this summer if you have not done so.

Very well done to the Addenbrooke's Hospital team: Dr Luke Hughes-Davies, Dr Karen McAdam, Ilene Cannon and Emily Barker, and for recruiting our 350th patient, and for recruiting a patient every week through July and August.

HAMPER FOR THE 400th PATIENT

We are almost halfway to our recruitment target. A hamper will be sent to the Site that recruits the 400th patient. Please help us to reach this important target and continue screening ARTemis patients.

RECRUITMENT SURVEY

At the end of July we sent you site specific recruitment information, and tips on what to mention when introducing the trial to patients. We have received feedback on recruitment from 30 sites and it has been reassuring to hear that all your neoadjuvant patients are being considered for the trial, but that unfortunately you are seeing fewer patients than expected at present.

We are pleased that the randomisation time extension is working well for you and makes it easier for HER2 testing.

A big THANK YOU for all your hard work, and we really appreciate your prompt and helpful responses.

If you wish for us to visit your site to talk about recruitment, bevacizumab, sub-studies or any other aspect of the trial please contact the Warwick team.

PETERBOROUGH PUSH FOR PATIENTS

"Here at Peterborough City Hospital our physicians and research nurse team are all very passionate about research, which makes recruitment an easier task. Our physicians always discuss from their first meetings with potential patients studies in recruitment stages that they might be eligible for. We also make full use of our MDT meetings: potential trial patients are identified during these. What really works for us is having trial recruitment packs; these are tailored around each patient's care pathway. No task is too big or too small for us: such is the dedication and commitment of our team and we endeavour to ensure that all the behind the scenes legwork is carried out prior to the patients coming in for their appointments; thus enabling us to provide a smooth transition into clinical trials."

- Peterborough Trials Team

SITE SET UP

We currently have **52 sites open**. Welcome to Royal Free Hospital, Prince Charles Hospital and Queens Hospital, Romford who opened recently.

Congratulations to Queens Hospital, Romford, for recruiting their first patient 6 days after site activation!

DATA COLLECTION

Tumour measurements

Ultrasound measurements are mandatory for completion of trial CRFs. If, for randomisation purposes, a more accurate radiological test (MRI, spiral CT) is performed which confirms a tumour of >20mm (where the US is ≤20mm), please contact Warwick Trials Office for confirmation of eligibility.

Sentinel Lymph Node Biopsies

Please allow 7-10 days between a SLNB and chemotherapy start date, regardless of the treatment arm.

Pharmacovigilance

There is no need to report grade 3 toxicities or Adverse Events of Special Interest as SAEs anymore, unless the event meets the usual definition of an SAE (hospitalisation, life-threatening, death, etc).

Tumour Blocks

We'll be requesting tumour blocks shortly, so please send in outstanding On-Study and Surgery Forms for patients 101-150 as soon as possible.

Pathology Report

It would be enormously helpful if you could write the patient trial number on the front of all pathology reports, having blacked out all other ID.

Centres open:
sorted by date of activation

Addenbrooke's Hospital	69
Western General Hospital	32
Peterborough District Hospital	19
Royal Surrey County Hospital	15
St Bartholomew's Hospital	10
Guy's Hospital	1
St Mary's London	8
Torbay District General Hospital	9
Charing Cross Hospital	15
St James's University Hospital	12
Queen's Hospital Burton	4
Newham Hospital	3
West Middlesex Hospital	24
Christie Hospital	8
Southampton General Hospital	3
Essex County Hospital	4
Aberdeen Royal Infirmary	10
Royal Hampshire County	4
Maidstone Hospital	9
Bedford Hospital	3
Glan Clwyd Hospital	5
City Hospital (Sandwell)	7
Clatterbridge Centre for Oncology	0
St John's Hospital	1
Royal Liverpool & Broadgreen	2
Royal Glamorgan Hospital	2
Southport Hospital	2
UCLH (London)	6
UHCW	6
New Cross Hospital	7
North Middlesex Hospital	2
Royal Bournemouth Hospital	18
Warrington & Halton Hospitals	1
Dorset County Hospital	1
King's College Hospital	3
Nottingham University Hospital	11
Southend University	7
Gloucestershire Royal Hospital	0
Cheltenham General Hospital	3
Royal Gwent Hospital	0
Macclesfield District Hospital	4
Poole Hospital	4
St Helen's Hospital	8
Sandwell Hospital	1
Worcestershire Royal	0
Weston Park Hospital	1
Ysbyty Gwynedd	1
Leicester Royal Infirmary	4
Blackpool Victoria Hospital	1
Royal Free Hospital	0
Prince Charles Hospital	0
Queens Hospital, Romford	1

Centres to be open soon

Barking, Havering & Redbridge Hospital
Basingstoke & North Hampshire Hospital
Kidderminster
Medway Maritime Hospital
Queen Elizabeth Hospital, Birmingham
Royal Derby Hospital
Stafford Hospital
Velindre Hospital

Thank you to all centres for your continued efforts on setting up sites.

DATA COLLECTION CONTINUED

CRFs

Asha, ARTemis Administrator at Warwick, says thank you for your prompt responses to her query letters. It's really good to have such enthusiasm for good quality data, which will aid the success of the trial. If you are using the CRF booklets version 4.0, remember to use the Withdrawal Form V4.1 in conjunction with the booklets.

Thank you in advance for returning your SAE query responses back to Louise in Cambridge.

TRANSLATIONAL

Sub-studies

Please re-discuss the sub-studies with your wider team and ensure that your patients are not consented to sub-studies in which your site is not participating. If you change your mind and wish to sign up for any of the sub-studies, please contact the Warwick Trial Office. These sub-studies are very important for determining the healthcare for future patients, therefore please keep approaching your patients for these important sub-studies. Every sample is **important and very gratefully received!**

Mandatory blood samples

At the moment, the number of blood samples is slightly slower than expected. Please ensure that all your patients have been sampled. In case of doubt or for an up to date list of samples due please contact Louise Grybowicz.

Thank you to the following sites who have sent in blood samples for <u>all</u> of their patients so far: Southend, Glan Clwyd, Poole, Bedford, Cheltenham, Kings, Macclesfield, Southampton, and Dorset.

And a gold star to the following sites for continuing to catch up on blood samples despite having <u>lots</u> of patients to collect from: Addenbrookes, Peterborough, Edinburgh, and West Middlesex.

Sequential blood samples

To date 74 patients have consented and ideally we would like 200 patients. For this sub-study we will investigate markers in the blood which may help us, in the future, to understand which patients will benefit most from bevacizumab treatment. The blood tests which are to be taken will be examined for levels of the molecules with which bevacizumab interacts, and other markers that may be affected by bevacizumab or chemotherapy treatment. With the blood samples taken in this sub-study we will isolate cells and also measure DNA, RNA or proteins. This information will be matched with the clinical information, including the response to treatment, side effects, and whether the cancer recurs in the future. We can use this information to try to identify markers predicting whether patients are likely to benefit from therapies such as bevacizumab, ultimately working towards a way to 'tailored' treatment for individual breast cancer patients in the future.

To facilitate the collection of bloods for the sequential blood study, the team in Edinburgh keeps track of the sampling dates for the ARTemis patients and, when a patient has completed her sampling schedule (post cycle 6 / pre-surgery), will contact you to arrange courier collection. The email will ask for contact details and a full postal address. <u>Please reply to these collection prompts</u> as it is important the bloods are stored centrally, plus it has the added benefit of freeing room up in your freezers!

Fresh tissue samples

In order to get more detailed protein and genetic information about breast cancer, we are collecting extra biopsies of <u>fresh</u> tissue from 200-300 patients participating in the *ARTemis* trial. To date 101 patients have consented. Please continue (if applicable) to approach your ARTemis patients for the **fresh tissue sub-study**, and remember to collect tissue at baseline, midway through treatment, and at surgery where possible.

TRANSLATIONAL CONTINUED

Quality of Life Questionnaires

Please check that all completed questionnaires have been sent in, and that you are collecting at the relevant time points – baseline, post cycles 3 and 6, on completion of surgery/radiotherapy, 12 and 24 months post surgery.

GCP / MONITORING

Site Signature & Delegation Logs

Have you updated your site signature & delegation log recently? Is your PI on the log? If not, please send in an updated log (ask your PI to initial and date amends, and sign and date at the bottom) and/or new log (version 3.0 05 July 2011) for new trial staff.

Consent

A protocol amendment is a good time to go back a step and in-house monitor some of the key GCP processes. Please use the checklist which will be sent with the amendment and ensure that patients' consent is documented properly (i.e. initialled each box of the consent, signed and dated on the same day as the clinician, original document file in site file, copy in the notes) but also that your site file is complete and in order. For guidelines do not hesitate to contact the team.

AOB

Other cancer trials

There is no problem with ARTemis patients going into the SUPREMO (Selective Use of Postoperative Radiotherapy After Mastectomy) trial. If ARTemis patients go into the REACT (Randomised European Celecoxib Trial) trial, they must be on follow-up, need permission from the REACT team and the follow-up CRF must record trial participation.

Your thoughts are appreciated!

Please do not hesitate to contact us if you would like us to feature a specific topic in future Newsletters.

PERSEPHONE

Please be aware that **neo-adjuvant HER-2+** patients can be entered into *PERSEPHONE*.
Herceptin® can be administered either concomitantly or sequentially for 6 or 12 months in conjunction with chemotherapy. For more details, please contact anne-laure.vallier@addenbrookes.nhs.uk

Persephone

CONTACTS:

Phase III Trial

Warwick Clinical Trials Unit, University of Warwick, Gibbet Hill Road, Coventry CV4 7AL

Clare Blenkinsop 💻: c.blenkinsop@warwick.ac.uk ☎: 024 7615 1057
ARTemis Fax: 024 7615 1586 Randomisation Fax: 024 7615 0549

Pharmacovigilance, Pharmacy and Translational Studies

Cambridge Cancer Trials Centre, (S4) Box 279, Addenbrookes Hospital, Hills Road, Cambridge CB2 0QQ

Louise Grybowicz 💻: louise.grybowicz@addenbrookes.nhs.uk ☎: 01223 348447
Anne-Laure Vallier 💻: anne-laure.vallier@addenbrookes.nhs.uk ☎: 01223 348086