

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



ARTEMIS Newsletter Issue 9 December 2011

Welcome to this ninth edition which will tell you about Amendment 13, recruitment, site setup, data collection, holiday closures, translational sub-studies, FDA news and error protocol version 4.

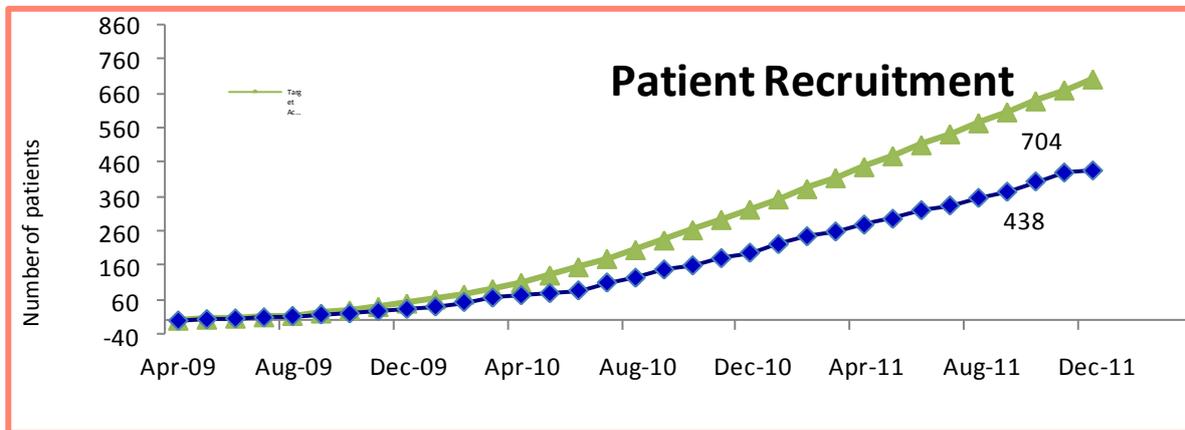
AMENDMENT 13

All sites should have submitted Amendment 13 to their R&D departments for approval and 16 sites have already had their approvals through. Once we have authorised implementation, please send to Warwick CTU copies of the new versions of Patient Information Sheets 1, 3 and 4 printed on your Trust headed notepaper.

Please note that previous patients do not need to be re-consented to the new versions of the Patient Information Sheets / Informed Consent Forms as the extension of the follow-up period is covered by the initial consent to The Office for National Statistics flagging (see point 8 in previous versions of PIS1).

PATIENT RECRUITMENT: Number of Patients Recruited: 438

(as of 9th Dec 2011)



HAMPER FOR THE 400th PATIENT : WEST MIDDLESEX HOSPITAL

Congratulations to West Middlesex Hospital for randomising the 400th ARTEMIS patient!

A small clinical team operates out of West Middlesex, headed up by Dr Riz Ahmad as the hardworking PI at three sites: West Middlesex, Charing Cross and St Mary's. She is ably supported by Dr Pippa Riddle as Co-I, Tina Henry as RN and Sagal Kullane as Data Manager. West Middlesex is a recruiting base using Charing Cross as the treating Hospital. The site are our third highest recruiters and to date they have randomised a massive 27 patients for ARTEMIS, so the hamper was well deserved.



For Tina Henry who started in Feb 2010, this is her first ever post in research. She started recruiting into ARTEMIS in May 2010 and works across 2 sites. Tina says: "Patient information is patient friendly; Trial is easy to explain to patients; the Flowchart is useful for patients to understand where they are in terms of the treatment and timeline to surgery. Clinical oncologists Riz Ahmad and Pippa Riddle are very keen on clinical trials, which is a big plus to me. There is excellent team work from the ARTEMIS team, namely Clare and Louise in assisting with all clinical queries and prompt replies from Louise for authorisations (even at very short notice!). Everyone in ARTEMIS is pleasant and helpful, which makes all the difference." Sagal agrees with Tina and adds that "we are fortunate to have two clinical oncologists who are driven towards research which makes it easier for us to recruit patients into ARTEMIS. Also having supportive, friendly staff (Asha, Clare and Louise) who reply all queries promptly and are ready to help make it that much easier to recruit into ARTEMIS trial."

Their hot top tips to recruitment:

- attend the breast MDT;
- engage with Breast Care nurses;
- and meet the patient at the very first oncology appointment.

HAMPER FOR 500TH PATIENT

We are over halfway to our recruitment target. Another hamper will be sent to the Site that recruits the 500th patient. Please help us to reach this important target and continue screening ARTemis patients.



SITE SET UP

We currently have **56 sites open**. Welcome to Kidderminster, Velindre, Medway Maritime Hospitals and Beatson West of Scotland Cancer Centre. We also have a further 11 sites in active set-up.

Congratulations to Velindre, Kidderminster and Medway on randomising their first patient so soon after site activation!



DATA COLLECTION

Radiology Forms

In order to reduce the number of queries you receive, please double-check your calculations that the tumour bulk measurement = total of the tumour size measurements (minus axilla) in boxes S1 to S5! Please also ensure that the tumour site relates consistently to the S1-S5 boxes across all three radiology forms.

Sequential Blood Tips

We are always looking at new ways to help sites with the sequential blood samples sub-study. We asked you for tips for remembering blood sample timepoints, and this is what you have said:

- Enter dates of patients' sub-study blood collections in the breast cancer diary.
- Print off patient schedule of timepoints and file with the patient CRFs.
- Use the Tracking Form in the CRF booklet.
- Prime colleagues to get the bloods at surgery.
- Run weekly query on trials' database to show the week's appointments and timepoints.
- Pin lists of appointment dates and timepoints in office when seeing the patients.
- Staple laboratory requisition form blue slip to inside of CRF which is used at pre-chemo clinic appointment and double check timepoints against PIS4. RN gives blood bottles to phlebotomists who take the bloods, and if they fail to take blood at this time, the chemo girls take it when cannulating. And the patients are very good at prompting!
- Write out a schedule of appointments and put a star or whatever against those where sub-study bloods are required. Put at the front of the CRF so you don't have a problem remembering. If just one RN dealing with this and s/he is not there, s/he could write in the diary and ask a colleague to deal with it to make sure it isn't missed.
- Patients can be a useful tool! If they know when their blood samples are due to be taken they usually can remind you, so keep them informed.

If you have any other ideas that you would be willing to share, please let us know.

Quality of Life

With 53 sites participating in this most popular sub-study, we are achieving a high consent rate of 82% of patients. However we notice that some sites are failing to collect the post cycle 3 questionnaire, so please can you diary this into the schedule, along with the baseline, post cycle 6, on completion of surgery/radiotherapy, 12 and 24 months post surgery.

Centres open: sorted by date of activation



Addenbrooke's Hospital.....	75
Western General Hospital	34
Peterborough District Hospital	24
Royal Surrey County Hospital.....	20
St Bartholomew's Hospital	12
Guy's Hospital	1
St Mary's London	8
Torbay District General Hospital ..	12
Charing Cross Hospital.....	16
St James's University Hospital.....	12
Queen's Hospital Burton.....	5
Newham Hospital	4
West Middlesex Hospital	27
Christie Hospital	12
Southampton General Hospital.....	3
Essex County Hospital	4
Aberdeen Royal Infirmary	11
Royal Hampshire County	5
Maidstone Hospital.....	12
Bedford Hospital	3
Glan Clwyd Hospital	6
City Hospital (Sandwell)	8
Clatterbridge Centre for Oncology .	0
St John's Hospital.....	1
Royal Liverpool & Broadgreen	3
Royal Glamorgan Hospital.....	2
Southport Hospital.....	2
UCLH (London)	8
UHCW.....	7
New Cross Hospital.....	9
North Middlesex Hospital.....	2
Royal Bournemouth Hospital	20
Warrington & Halton Hospitals	1
Dorset County Hospital.....	1
King's College Hospital	3
Nottingham University Hospital....	14
Southend University	7
Gloucestershire Royal Hospital.....	0
Cheltenham General Hospital.....	3
Royal Gwent Hospital	1
Macclesfield District Hospital	4
Poole Hospital	5
St Helen's Hospital.....	12
Sandwell Hospital.....	2
Worcestershire Royal	0
Leicester Royal Infirmary.....	6
Weston Park Hospital	1
Ysbyty Gwynedd	2
Weston Park Hospital.....	1
Blackpool Victoria Hospital	1
Royal Free Hospital.....	1
Prince Charles Hospital.....	0
Queens Hospital, Romford	3
Kidderminster Hospital.....	1
Velindre Hospital.....	1
Medway Maritime.....	1
Beatson West of Scotland.....	0

Centres to be open soon

Basingstoke & North Hampshire
Castle Hill, Hull
Crosshouse, Ayrshire & Aran
Diana Princess of Wales, Grimsby
Forth Valley
Hereford
Hinchinbrooke, Huntingdon
Queen Elizabeth Hospital, B'ham
Royal Devon & Exeter
Russells Hall
University Hospitals Morecambe Bay
Thank you to all centres for your continued efforts on setting up sites.



Posting arrangements for the ARTemis mandatory blood samples

Blood samples should not be taken and posted to the Cambridge Trial Office between Friday 16 December 2011 and Tuesday 3 January 2012. These samples can be taken from the patient at any time while on-trial therefore please arrange for the blood to be collected at a later appointment.

Posting arrangements for the ARTemis fresh tissue samples

Please do not post fresh tissue to the Cambridge Trial Office between Friday 16 December 2011 and Tuesday 3 January 2012. If tissue is taken around this time, please store it in a fridge (2 – 8°C) until Tuesday 3 January 2012 when you should then post it to the Cambridge Trial Office.

Orders for Bevacizumab

Aptuit's last shipment date for bevacizumab will be on Wednesday 21 December 2011, and they will re-open on Tuesday 3 Jan 2012.

If you require an **emergency** delivery between these dates please contact Aptuit, however please do try to order enough stock to cover for the holiday period as there will be very minimal staff working at Aptuit over the Christmas / New Year period and an emergency order may not be processed in time.

Randomisation Service

The Randomisation Service and Warwick Clinical Trials Unit will close on Thursday 22 December 2011 at 12 noon and re-open on Tuesday 3 January 2012 at 9.00am. **Please try to arrange for your patients to be randomised according to these times.**

Sequential blood samples

The Endocrine Cancer Research Centre at Edinburgh will be closed from Friday 23 December 2011 to Tuesday 3 January 2012 inclusive.

Just for fun see if you can find Wally



The Randomisation service will close on Thursday 22nd December at 12 noon and re open on Tuesday 3rd of January 2012 at 9 am

FDA REVOKES APPROVAL FOR THE USE OF AVASTIN IN METASTATIC BREAST CANCER

In November the FDA revoked its approval for the use of Avastin in combination with Paclitaxel for first-line treatment of patients with metastatic breast cancer. We would like to take the chance to remind you of a few points to remember, in case your patients have any questions relating to this issue and ARTemis:

- ARTemis is investigating Avastin in different disease setting
- ARTemis is investigating Avastin in combination with different chemotherapies
- One of the main aims of ARTemis has been and remains the identification of subgroups in whom bevacizumab is best used, by means of the associated translational science. The neoadjuvant setting provides the best opportunity to identify molecular markers of response and benefit.

A meta-analysis of the primary endpoint of ARTemis with the equivalent study in the USA (NSABP-B40) which also remains open, should provide the necessary power to confirm (or refute) the observations found in the recent Geparquinto study, i.e. potential benefit in the triple negative subgroup.

ERROR PROTOCOL VERSION 4

There is a typo error in the Protocol Version 4, July 2011 so please amend, initial and date. The Protocol will not be re-issued.

Page 22: Section 6.6 Translational blood & tissue sample collection Optional tissue and blood samples to be collected for analyses

2. Sequential blood samples: one prior to treatment, one pre cycle 2, one pre cycle 3, and one **post cycle 5**, and one after cycle 6 / pre surgery, from 200-400 patients for circulating angiogenic markers.

This should read:

2. Sequential blood samples: one prior to treatment, one pre cycle 2, one pre cycle 3, and one **pre cycle 5**, and one after cycle 6 / pre surgery, from 200-400 patients for circulating angiogenic markers.

Unfortunately this mistake has been replicated in the **ARTemis Amendment 13 Summary of Changes dated 15 Nov 2011**. Please amend page 2, section 8 to read:

8. Clarification on the sequential blood samples sub-study: One 20ml sample should be taken at the following timepoints: prior to treatment; pre cycle 2; pre cycle 3; **pre cycle 5**; and after cycle 6 / pre surgery.

MERRY CHRISTMAS



The ARTemis Team at Warwick and Cambridge would like to thank everyone for their hard work and co-operation this year and wish you all a very Merry Christmas & Happy New Year. We look forward to your continued support in 2012.



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



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