

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

## ARTemis Newsletter Issue 4 July 2010

Welcome to our fourth edition. This newsletter will keep you updated on trial progress, safety updates, translational studies, the Medical Liaison Team from Roche and new document versions.

### PATIENT RECRUITMENT

Total Number of Patients Recruited: 88

Thanks to everyone for your support & efforts in screening and recruiting patients for ARTemis trial. We are doing well with opening sites and currently have 24 open, of whom 15 are actively recruiting patients. We are however 50 patients under our target. Feedback from active sites reports mainly logistical challenges due to:

- The time window from core biopsy to treatment including the HER2 results
- Screening and/or treatment at different sites.

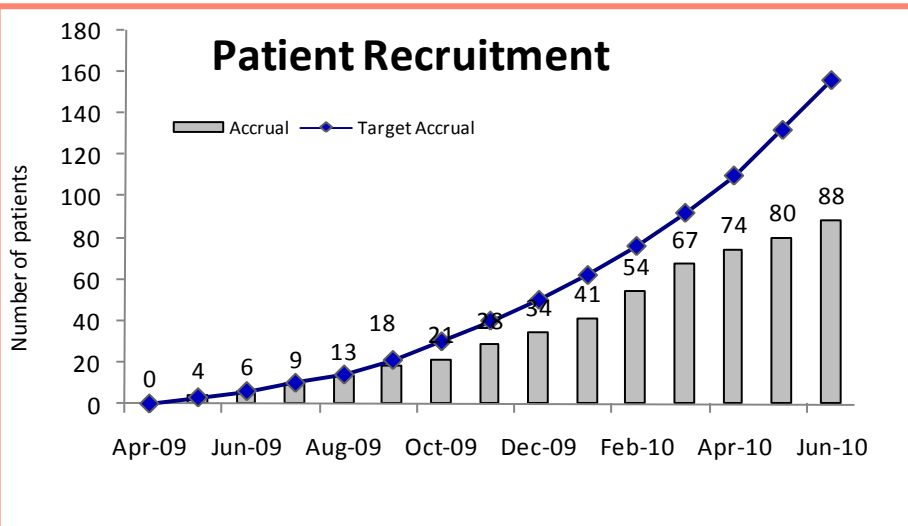
Some sites suggest that it would be easier if patients are aware of the trial sooner rather than later, and some also find that approaching patients before the HER2 status is known has improved patient recruitment. Please do not hesitate to approach patients even before the HER2 status results (85% chance of the patient being negative) and possibly offer another trial like PERSEPHONE neo-adjuvant if the patient is HER2+.

Below are some facts to encourage your patients to have neo-adjuvant chemotherapy as part of this trial:

- They get the chance to receive a new drug which is known to be very effective for other cancers
- They are going to get some extra investigations and more monitoring
- They can start your treatment and fight against the disease straightaway
- They will give their surgeons (plastic team and surgery team) more time to get organised
- With neo-adjuvant treatment they may get less invasive surgery
- They can still have their surgery privately
- They are going to help to find out if this new drug makes a real difference. That will help future patients.

### Please keep trying hard, remember each patient counts

All data correct as on 30 June 2010



#### Centres open

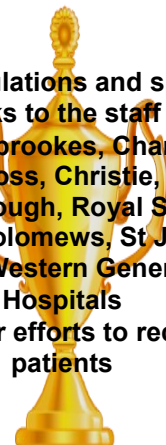
|                                   |    |
|-----------------------------------|----|
| Addenbrookes Hopspital            | 39 |
| Western General Hospital          | 10 |
| Charing Cross Hospital            | 6  |
| St Bartholomew's Hospital         | 6  |
| Royal Surrey County Hospital      | 5  |
| Christie Hospital                 | 5  |
| Peterborough District Hospital    | 4  |
| St James's University Hospital    | 3  |
| St Mary's Hospital, London        | 2  |
| West Middlesex Hospital           | 2  |
| Guy's Hospital                    | 1  |
| Queen's Hospital, Burton on Trent | 1  |
| Newham Hospital                   | 1  |
| Essex County Hospital             | 1  |
| Aberdeen Royal Infirmary          | 1  |
| Royal Hampshire County Hospital   | 1  |
| Torbay District General Hospital  | 0  |
| Southampton General Hospital      | 0  |
| Maidstone & Tunbridge Wells       | 0  |
| Bedford Hospital NHS Trust        | 0  |
| Glan Clwyd Hospital               | 0  |
| City Hospital                     | 0  |
| Clatterbridge Centre for Oncology | 0  |
| St John's Hospital                | 0  |
| Royal Liverpool Hospital          | 0  |

#### Centres to be open soon

|   |
|---|
| King's College Hospital                                 |
| New Cross Hospital                                      |
| Newcastle Hospitals NHS trust                           |
| Royal Glamorgan Hospital                                |
| Southport and Ormskirk Hospitals NHS Trust              |
| UCLH Hospital NHS Foundation Trust                      |
| University Hospital Coventry and Warwickshire NHS Trust |
| Warrington and Halton Hospitals NHS Foundation Trust    |
| Poole Hospital NHS Foundation Trust                     |

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

**Congratulations and special thanks to the staff at Addenbrookes, Charing Cross, Christie, Peterborough, Royal Surrey, St Bartholomews, St James and Western General Hospitals for their efforts to recruit patients**



## ADVERSE EVENTS OF SPECIAL INTEREST

Please keep an eye out for these Adverse Events of Special Interest and report them to Cambridge as SAEs:

|   |  |
|---|--|
| <b>Hypertension:</b> <i>Grade 2 or 3</i>                                | <b>GI perforations:</b> <i>Any Grade</i>                           |
| <b>Reversible leukoencephalopathy:</b> <i>Any grade</i>                 | <b>Proteinuria:</b> <i>Grade 2, 3 or 4</i>                         |
| <b>Wound complications:</b> <i>Any grade</i>                            | <b>DVT / embolism:</b> <i>Grade 3 or 4</i>                         |
| <b>Arterial thrombosis/embolism:</b> <i>Any grade</i>                   | <b>Angina or MI:</b> <i>Any grade</i>                              |
| <b>Haemorrhage:</b> <i>Grade 3 or 4 (pulmonary or CNS inc. grade 2)</i> | <b>Allergy:</b> <i>Any grade</i>                                   |
| <b>Cerebrovascular ischemia:</b> <i>Any grade</i>                       | <b>LV systolic dysfunction:</b> <i>asymptomatic or symptomatic</i> |
| <b>Fistula or Intra-abdominal abscess formation:</b> <i>Any grade</i>   |  |

To date we have received: one Hypertension SAE (Grade 2) and two Haemorrhage (GI) SAEs (Grade 2, one with hospitalisation).

## ARTEMIS SCIENCE:

### Tumour block collection:

This autumn, diagnosis and surgery blocks (tumour and healthy tissue) and surgery slides will be collected prospectively by Cambridge directly via the named Pathology contact. Material will only be taken from the blocks if there is a sufficient amount and after gaining permission from the nominated Pathologist at site. Slides and diagnosis blocks will be returned to Pathology departments still containing a sufficient amount of diagnostic material for a representative sample of the disease (at least six 0.6mm cores). Pathology departments will receive a per-patient fee for supplying the requested materials for the trial.

### Sequential blood sub-study:

Currently open only in Addenbrookes as a pilot study. We will open the sub-study to other sites in a few months if it goes well.

## MEDICAL LIAISON TEAM AT ROCHE

A regional team of Roche Medical Liaison Managers (MLMs) are able to travel to sites to provide additional training on Avastin (bevacizumab) either 1:1 or as a group. They will specifically focus on the mode of action, safety and tolerability of Avastin, and the ARTEMIS protocol. If you would like to arrange a training date or discuss this further please contact the ARTEMIS Team and we will arrange this for your site.

## CRFS

Please make sure your site is now using Version 3.0 of the CRF dated 31 March 2010.

### What's changed?

**Booklets:** Most of the CRFs are in self-replicating (NCR) booklets, although the Transfer Form, Withdrawal Form, SAE Form, SAE Continuation Form and Additional Information Form are completed on an *ad-hoc* basis and so are supplied as paper copies.

**Eligibility Form:** Deadline for screening LVEF measurement has been extended to 6 weeks prior to randomisation.

**Radiology Forms:** There are 2 fundamental differences between version 2 and 3 of the radiological forms, specifically:

- 1) Tumour bulk definition: Axillary nodes are no longer included in tumour bulk measurement
- 2) Radiological response criteria: Response criteria (CR, PR, SD, PD) has been changed.

Radiological response is an important endpoint of the trial and we need consistent and thus comparable data on all patients randomised into the trial. Therefore **for all your patients, including patients randomised in 2009**, sites must complete version 3 of the radiological forms (pre, mid and end treatment radiology forms).

### How to complete V3.0 CRFs?

- **Please use CRF version 3 for all new data to be reported.**
- **For all newly randomised patients going forwards, please use the NCR booklets.**
- **For patients currently on the trial either complete paper photocopies of the new V3.0 CRF or use a booklet.**
- Do not transpose any data already reported onto the new forms.
- On completion of each form please post the top white copy to Warwick ARTEMIS trial office, retaining the green copy for your records.

### Phase III Trial

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