

Recruitment Brochure

The PERSEPHONE Trial is now in it's final 7 months of recruitment. We are trying to boost recruitment as much as possible so bring you this special Recruitment Brochure featuring a recruitment update with plans for the next 7 months, important key facts about the trial, photos and tips from our lucky Sites who received gifts and many more exciting features.....please read on and enjoy!

PERSEPHONE has been a challenging trial for well versed reasons. Nonetheless, with your continued support and efforts we have accrued 90% of the recruitment target and recruitment continues at a steady pace. We are now getting even closer to the finish line with just under 400 patients more to recruit to reach our total target of 4000 patients. So we take this opportunity to say.....



Recruitment update and Trial status

Recruitment to date (26.11.14): 3626 patients

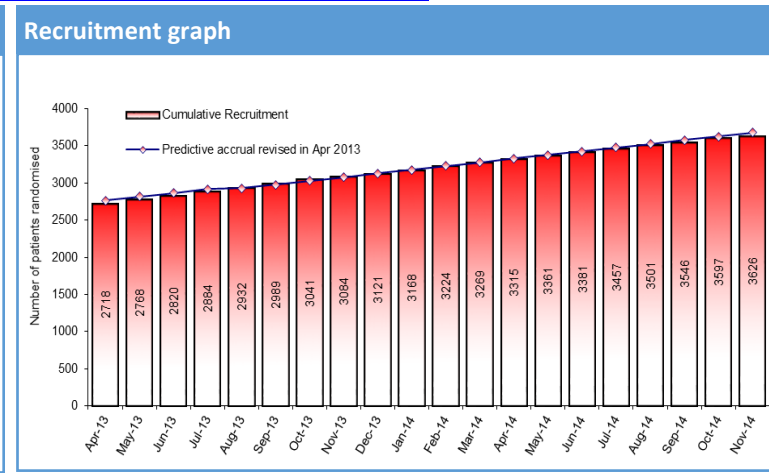
- In October we recruited a fantastic 51 patients! Please help us to keep recruitment up at this rate!
- In September we recruited 45 patients
- Average monthly recruitment 2014: 48 pts.**
- Target monthly recruitment: 50+ patients

Sites recently opened:

- Milton Keynes– entered 2 pts. so far!
- Royal Berkshire Hospital - actively screening!

Sites in set-up:

- Leighton Hospital
- Ashford Hospital



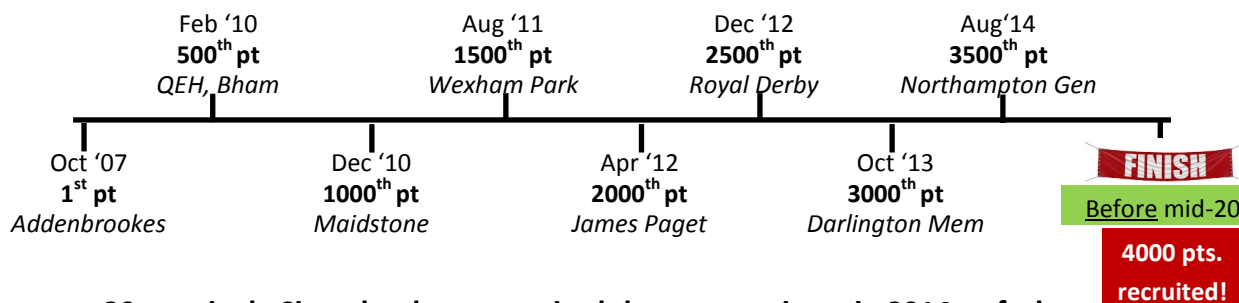
Recruitment.....the next 7 months!

We are pushing to finish recruitment before mid-2015. We are very excited and optimistic and believe that with your help this CAN be achieved! We ask all our 156 participating Sites to come together in a national joint effort to **recruit 3 patients each in the coming months.....any more than 3 patients would be a bonus!** So if you haven't entered a patient yet there is still time to make your final contribution to the trial before we reach the recruitment finish line....hopefully early next year!

Your contribution will make a difference in helping change practice for future breast cancer patients.

We need all our Sites to continue screening all HER2+ patients and offering the trial to those that are fully eligible. Remember, each and every patient you recruit into the PERSEPHONE Trial brings us even closer to answering the ever more important, long awaited Trastuzumab duration question.
See next page for important key points that you can mention to your patients!

PERSEPHONE Recruitment Milestones



20 top single Sites that have recruited the most patients in 2014 so far!

Charing Cross Hospital.....	14	Royal Lancaster Infirmary.....	11	Luton and Dunstable Hospital.....	8	Southend Hospital.....	8
City Hospital.....	12	Addenbrooke's Hospital.....	10	Medway Maritime Hospital.....	8	Staffordshire General Hospital.....	8
Royal Sussex County Hospital...	12	Norfolk & Norwich University Hospital	9	Musgrove Park Hospital.....	8	Great Western Hospital.....	7
Peterborough City Hospital.....	11	Conquest Hospital.....	8	Northampton General Hospital....	8	Staffordshire General Hospital.....	7
Queen's Hospital (Romford).....	11	Guy's Hospital.....	8	Queen's Hospital (Burton).....	8	Southampton General Hospital.....	7

Important key facts about the PERSEPHONE Trial

Screening Logs

Thank You to all Sites that returned their most recent Screening Log. We can see that our Sites, even those that haven't entered a patient this year are working really hard offering the trial to eligible patients. Some Sites have asked the following questions:

What do Screening Logs tell us about patient acceptance?

- 1 in 5 patients are consented to the trial, that's a 20% acceptance rate.

What is the main reason for patient decline in the trial?

- Patients want the standard 12 months treatment.

What are the key points that can be mentioned when offering PERSEPHONE to patients:

- ◆ PERSEPHONE is a big trial targeting 4,000 patients. Even before reaching the 4,000 patient target PERSEPHONE is now the largest UK academic led Herceptin duration trial.
- ◆ 12 months is usually the duration for a new drug and is not evidence based. Clinicians need to refine this so that patients achieve minimal toxicity with maximum benefit.
- ◆ The duration question remains ever more important and has not been answered definitively.
- ◆ PERSEPHONE will answer the duration question to prevent future patients receiving unnecessary treatment.
- ◆ Results from the PHARE trial remain inconclusive and immature. PERSEPHONE is therefore in a very strong position making it the only Herceptin trial that can answer the Trastuzumab duration question definitively. This further supports the importance and need to complete PERSEPHONE recruitment and report results.
- ◆ Another 14,000 European patients were recruited into similar trials of shorter duration of Herceptin, some receiving only 9 weeks of treatment (FinHer).
- ◆ FinHER has shown that a shorter duration of 9 weeks of Herceptin has a similar sized benefit to 12 months Herceptin when given concurrently with taxane based chemotherapy.
- ◆ HERA has shown that 24 months is not superior to 12 months so longer treatment is not necessarily better treatment.
- ◆ Cardiac monitoring data in the PERSEPHONE Trial has shown patients in the 6 month arm have a more rapid recovery of cardiac function compared to those in the 12 month arm.
- ◆ From 6-12 months, the 12 month patients have cumulative cardiotoxicity, treatment delays and discontinuation compared to the 6 month arm.

Other supportive statements about PERSEPHONE:

- ◆ The DSMC and the TSC review the trial on an annual basis. At the most recent meetings, the PERSEPHONE team have been congratulated on their tenacity regarding excellent CRF return rate and were encouraged to continue their efforts with recruitment.
- ◆ Prof. Clark, Chair NICE Technology Appraisal Committee said "PERSEPHONE addresses an important question and one to which the world is waiting for an answer"
- ◆ Prof. Piccart (HERA PI, BIG) voiced her support agreeing that the current data on Herceptin duration trials are inconclusive and lack power to address the non-inferiority duration question, so it's of "vital importance" that PERSEPHONE continues as planned.

Recruitment procedures from our Sites that we've shared in the past!

- Adopt a team approach to consenting patients- the Surgeons, Oncologists, Cardiologists, Clinical Research staff and RNs communicating with each other to support the trial.
- Keep track of the potential patients in a database until the patient makes their decision.
- As soon as patients have been highlighted as eligible, put a flyer which lists key eligibility at the front of that patients' case notes to highlight "this is a potential PERSEPHONE patient".
- Put CRUK flyers into patient information packs and place posters within the unit to de-mystify trials, helping the patient to get used to the idea of them.
- Post-surgery results, the patient meets with the Oncologist where all treatments are discussed (including Herceptin® and the trial)
- Mention the trial first during chemo sessions and answer any questions. It is important to mention the trial to patients early so that they know they may not receive 12 months and they familiarise themselves with the study over a long period of time.
- Mention the trial briefly to the patient at every clinical appointment.
- When discussing the trial in detail, mention that 1 year of Herceptin® is an arbitrary figure and put the trial into the context of the wider world, highlighting the reduced cardiac toxicity risk and time spent at hospital.
- Tell patients that trials are a normal part of your unit and that you actively participate in several trials as part of patients treatment. It is good to mention it, however briefly, at each clinical appointment to plant the seed of the trial.

Congratulations to all 3 Sites! ★

3500th patient recruited

Northampton General Hospital



Left to right: Sharon Ryan (Cancer Research Assistant), Malgorzata Kaczmarczyk (Research Nurse), Liz Tee (Senior Research Nurse) and Caroline Duncombe (Research Nurse).

Northampton General Hospital opened to recruitment in November 2011. The Site have since recruited a tremendous 15 patients. Congratulations and well-done to Dr Craig McMillian (PI) and the team for all their hard work and continued support with PERSEPHONE.

Liz's perspective of Persephone:

It appears self perpetuating. The more people on the trial, the more embedded it is as a normal part of the treatment options.

Patient discussion:

The trial is more likely to be discussed now fairly early in the treatment pathway. Therefore, when it is appropriate to give the patient information leaflet, the patients are usually expecting it. Plus, the patients talk to each other, so the more patients recruited to the trial, the more the word is spreading and receptiveness to having less than standard treatment seems to have increased.

"receptiveness to having less than standard treatment seems to have increased"

3501st patient recruited

Southend Hospital



Left to right: Anne Mcpherson (Research Nurse) and Eugene Mphansi (Research Nurse)

Southend Hospital opened to recruitment in April 2009. The Site has since recruited a fantastic 58 patients. Thank You and well-done to Dr Hafiz Algurafi (PI) and the team for all their hard work and continued support with PERSEPHONE.

Anne's perspective of Persephone:

Patient identification:

Like most of the other Hospital's recruiting into the PERSEPHONE Trial, we too identify the majority of our patients at the MDT meeting. However we have a very flexible approach as to when to introduce the trial to the patients that are eligible.

Trial introduction:

Introduction could be in the clinic after the diagnosis when explaining the patients treatment plan or once they have started their Chemotherapy. The emphasis is always that it is the patients decision to participate in the trial and we make sure that we allow them plenty of time to take home the PIS and discuss it with family members or their GP explaining that they have up to their 9th treatment to be entered into the Trial. My contact details are also given to the patients as some patients make their minds up very quickly to enter the Trial so have the opportunity to contact me themselves. Good communication skills and giving much needed time to the patients, answering their questions and reassuring them helps with our recruitment.

"Good communication skills and giving much needed time to the patients, answering their questions and reassuring them helps with our recruitment."

3499th patient recruited

Royal Liverpool University

Royal Liverpool University Hospital opened to recruitment in November 2007. The Site has since recruited a magnificent 53 patients and currently overall are our second best recruiters. Thank you and well-done to Dr Susan O'Reilly (PI) and the team for all their hard work and continued support with PERSEPHONE.

Pam Brereton (Research Nurse) and Maria Horton (Data Co-ordinator) were very pleased to receive the gifts.

Data querying

Data is an integral part of the trial so we need your co-operation and support in returning to us as much complete data as possible. CRFs are often returned to us with missing data or anomalies. In such instances our Persephone Data Input Clerks, Lisa Poulton and Peter Bell, will contact you with data queries. We would appreciate it if you could confirm receipt of the data queries via e-mail and promptly return the amended CRFs in the post.

CRFs with missing data:

1. Refer to all highlighted sections on the CRF
2. Complete the missing boxes on the highlighted page only, remembering to initial and date each box amendment.
3. Photocopy the form for your files and send the original highlighted form to the PERSEPHONE office.

CRFs with data clarification required:

1. Refer to the highlighted section on the CRF and the accompanying DCF.
2. Provide clarification on the DCF, remembering to sign and date the DCF.
3. Amend the CRF according to the clarification provided on the DCF, remembering to initial and date each amendment .
4. Photocopy the DCF and the CRF for your files.
5. Ensure the DCF and CRF are attached together and send the original highlighted forms and the DCF to the PERSEPHONE office.

To avoid data queries being sent back to you please ensure all boxes are provided with a response. Where information is not known or not available please use the N/K or N/A boxes to indicate this.

CRF specific common data errors to avoid

Eligibility form - All boxes must be ticked and the form must be signed by a clinician who has registered to the trial and has undergone GCP training.

Randomisation form - If any doses have been given just before randomisation please indicate this on the form providing the date for the next dose.

Following randomisation, please remember to send the original signed and dated Eligibility and Randomisation Form to us. On the Randomisation Form please clearly state the TNO and treatment allocation as given at randomisation.

Treatment form - For dose reduced don't indicate 'yes' dose reduced for subsequent maintenance doses. This is not an actual dose reduction.

- For treatment discontinued don't indicate 'yes' when treatment has actually been completed as per treatment allocation at randomisation.
- Complete toxicity information at least 3 weeks after the dose was administered.
- Do not transcribe toxicities from the patient completed Patient Diary Sheet onto the CRF. The toxicities should be discussed with the patient and interpreted onto the CRF. We often come across Grade 4 toxicities transcribed from the Patient Diary Sheet. A Grade 4 toxicity would constitute as an SAE.
- If 'N/K' is ticked to all toxicity data please provide a note to state why this information is unavailable to prevent data queries.

Treatment Summary Form- Complete details for all chemotherapy cycles administered. Please don't provide details of the Trastuzumab doses as this is recorded on the Trastuzumab Form, however do state how many Trastuzumab doses were actually administered.

Any personnel completing PERSEPHONE CRFs at Site must be registered to do so by means of signing the Site Signature and Delegation Log and indicating their responsibilities within the trial on the log. Please remember to return the updated log to us so that we can register you on the trial.

AOBs

- We'll be posting out a small Christmas gift to all our Sites! If your address details have changed please let us know so we can be sure to mail the gift out to the correct address.

In the New Year we will be:

- Sending detailed guidelines on form completion to all admin staff
- Reviewing our Sites for best data returners and sending out certificates...look out for these!
- Sending the next annual Investigator Site File and Pharmacy Site File Monitoring Checklist

PERSEPHONE team		
Trial Coordination (Warwick)	Mrs Shrushma Loi	Persephone@warwick.ac.uk Phone: 0247 615 0492
Clinical Trial Administration (Warwick)	Miss Donna Howe	Persephone@warwick.ac.uk Phone: 0247 615 0600
Data Management (Warwick)	Miss Lisa Poulton Mr Peter Bell	Persephone@warwick.ac.uk Phone: 0247 615 1665 Persephone@warwick.ac.uk Phone: 0247 615 1665
Pharmacovigilance & Pharmacy (Cambridge)	Mrs Anne-Laure Vallier	anne-laure.vallier@addenbrookes.nhs.uk Phone: 01223 348086
Translational Studies (Cambridge)	Miss Louise Grybowicz	louise.grybowicz@addenbrookes.nhs.uk Phone: 01223 348083