Birmingham Clinical Trials Unit
Parkinson's Disease Newsletter

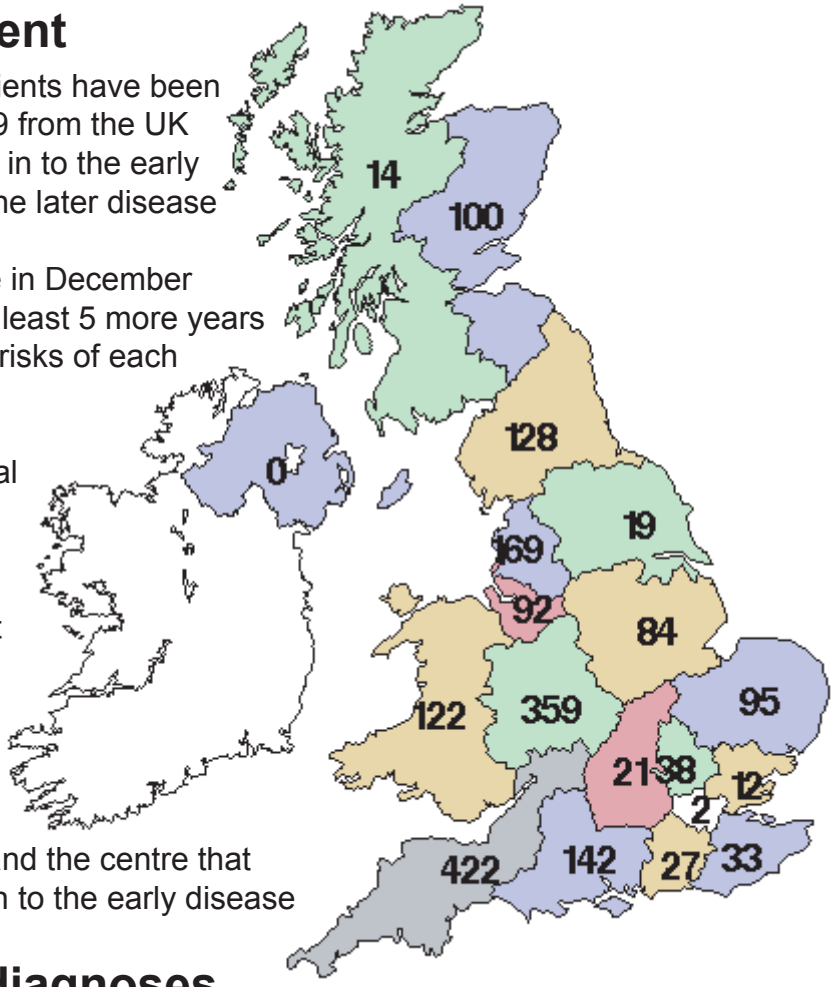
PD MED News

May 2009

PD MED is a large, simple, 'real life' trial that aims to determine more reliably which class of drug provides the most effective control, with the fewest side-effects, for both early and later Parkinson's Disease.

PD MED Recruitment

As of the end of April 2009, 1,924 patients have been recruited into the PD MED Trial (1,879 from the UK and 45 from overseas):1,481 patients in to the early disease randomisation and 443 into the later disease randomisation.
Recruitment of new patients will close in December 2009 but follow up will continue for at least 5 more years to monitor the long term benefits and risks of each treatment.



With recruitment in to the PD MED trial open for just 8 more months, please ensure that you consider all suitable patients for the trial as the more participants there are the more robust the findings will be.

PRIZES

As per tradition, we will be offering prizes to the centre that recruits our 2,000th participant and the centre that recruits our 1,500th participant in to the early disease randomisation.

Rediagnoses

As you are aware, misdiagnoses of PD are quite common due to the complex nature of the disease. There appears to be some confusion when this occurs in PD MED trial patients and some are withdrawing from the trial. We would still like to follow up these participants in the normal way so that they can be included in the intention to treat analysis.
It would be helpful if you could explain to participants whose disgnosis changes that we would like them to continue in the trial. We understand that the questionnaires that the participants receive ask questions referring to their PD, this should be understood as referring to their PD-like condition, for example in the PDQ39 where it states: Due to having Parkinson's disease,how often during the last month have you.... so in the case of a participant rediagnosed with vascular Parkinson's disease, the question should refer to that condition.

PD Collaborators' Meeting
18 - 19th May 2009

The meeting will again be held at the Jurys Inn and Botanical Gardens in Birmingham. The programme will include updates on PD SURG and the launch of PD REHAB (our new trial investigating the potential benefits of physiotherapy and occupational therapy for PD patients). If you wish to attend, but have not yet registered, please contact the PD team

PD team: Cally Rick / Neil Winkles/ Francis Dowling / Ryan Ottridge / Dani ScottTel: (0121) 415 9129 / 9128 / 9127 / 9125 or email pd-trials@bham.ac.uk

PD MED is funded by the NHS through its Health Technology Assessment Research Programme. It is supported by the Parkinson's Disease Society, the European Parkinson's Disease Association and the Parkinson's Disease Specialist Nurse Association

PD GEN - A DNA Bank

PD GEN–First use of the samples in genetic research!

The exciting news is that we have recently begun genetic research using several hundred of the PD GEN samples. These samples represented the main part of the DNA samples which were screened in a Genome Wide Association Study, GWAS, co-ordinated by Professor Nick Wood's group in London. This GWAS in Parkinson's disease was one of several funded by the Wellcome Trust, aiming to identify genetic markers that are associated with each of several common diseases.

In a GWAS, hundreds of thousands of variable DNA markers that are distributed throughout the entire genome are typed in large numbers of DNA samples from patients, and from control individuals without the disease. Complex statistical analysis is then used to determine which, if any, of the markers are more frequently found in people with the disease compared to control individuals. With so many markers being typed, some will be found to be associated with the disease purely by chance. Using large numbers of samples, we can reduce the likelihood of finding such spurious associations, and instead detect DNA variants that represent true associations with the disease. The project is now at the stage where all the sample typing has been performed, and the statistical analysis is underway. The next phase is to screen variants that have been found to be associated with the disease in a large set of DNA samples from further patients. The samples that we have collected since last autumn, and those collected from now on, will be used in this so-called 'replication analysis'. Once we have identified DNA variants that are confirmed to associate with PD in this replication set, the proteins which are encoded or regulated by these DNA variants will be investigated to determine their function and the biochemical pathways in which they are involved. It is anticipated that this will lead to increased knowledge about the abnormal mechanisms in the disease, a first step towards identifying effective therapies.

For more information or PD GEN packs, please contact the PD Trial team.

PD SURG NEWS

May 2009

The first draft of the PD SURG paper is currently being reviewed by PIs at all the participating sites. It should be submitted by the end of May.

A report of the PD SURG 1-year results is currently being reviewed by the PIs at all the participating sites for comment prior to submission to the New England Journal of Medicine - we plan to submit the document by the end of the month.
Following the submission of the first report, a series of more in depth papers will be written, focussing on the neuropsychiatric data, carer data, surgery, SAEs, apomorphine usage and health economic analyses.
We are also discussing the possibility of performing an individual patient data meta-analysis in collaboration with the Veterans, German and French groups that have performed (smaller) trials of a similar design.

Follow Up Data

We are continuing to collect data from the later time points in the trial. The later follow up will provide a unique understanding of the longer term effects of DBS surgery. Longer term costs and benefits are particularly important for the health economic analyses as unlike medication, most of the costs of DBS are incurred in the first year - so to get a fair comparison of the relative costs, events over a number of years must be included.
Every participant has now passed the 2 - year time point and the data are being analysed - these data do not form the same clean comparison as the 1st year as participants in the medical arm were able to have DBS surgery after 1 year. To date 130 participants in the medical arm have had surgery (12 before the 1 year time point due to medical need), more than 100 of them between 12 - 18 months post randomisation.

Chasing data

If an assessment is missed, it is particularly important for the statistical analyses to obtain data from the next assessment. If you are unable to see a patient in clinic at the annual follow up time point, can you please let us know so that we can send the questionnaires to the participants directly?
We will be sending out questionnaires to all participants who should have completed a form within the last 12 - 18 months. We will also be sending the corresponding annual follow up forms to the sites, as they can be partially completed retrospectively.
We will be performing longitudinal repeated measures analysis - so even if you miss one time point, please keep filling out the forms as the data will be used.

GP Packs

The PD SURG Nurses group has written an information pack for GPs about DBS surgery and the care of patients who have undergone the procedure. This document will soon be available (Medtronic has agreed to cover the printing costs).

For more information please contact: Cally Rick (0121) 415 9129 or c.e.rick@bham.ac.uk

PD REHAB News

May 2009

A Randomised Controlled Trial to Assess the Clinical- and Cost-Effectiveness of Physiotherapy and Occupational therapy in Parkinson's Disease.

The PD REHAB trial is progressing well in its 'start-up' phase. NRES approval was secured in December 2008 and final amendments to the protocol before launch has been submitted to NRES in April 2009. These amendments reflect the input from the specialist groups and Patient and Public Involvement members and should aid the smooth running and relevance of the trial.

Changes to the running of the trial :

1. Exclusion criterion has been changed to having received PT or OT within 1 year
2. Age and sex of carers joining the trial has been added to the randomisation notepad along with patient height.
3. Weight has been added to the exit form
4. The extra leaflet for control arm patients explaining about the importance of controls has been removed - it was felt that it might deter patients from seeking PT or OT who needed it, and from previous experience in rehabilitation trials was thought not to be neccessary for general compliance.
5. The intervention sites for OT and PT have been relaxed so that the rehab interventions can take place in day hospital setting, not just at home/"community".

Trial Sites

⇨Although we hope to get a large number of centres starting the trial in July 2009, City Hospital, Birmingham is on track to test the trial systems by randomising the first patients in May.

⇨The PD Trials Team is currently progressing R & D approvals for 13 centres and another 45 centres are actively discussing the trial with their teams. However, not all of the latter group will join the trial, so there is still room for enthusiastic centres to get involved, even if we have not contacted you directly (please see contact details below).

⇨Site Specific Assessment is now performed by investigator's own Research and Development (R & D) departments, rather than LRECs which should speed the approvals process.

Meetings

⇨The PD REHAB Launch Meeting has been arranged for Monday 18th May 2009 and there are a few places still available. The meeting will present the background to the trial, details of the trial protocol, and how patients will be recruited, treated and monitored throughout the trial. There will be a breakout session in the afternoon, so that the physiotherapists and occupational therapists can have an orientation session about the content of the therapies administered in the trial.

⇨The Patient and Public Involvement (PPI) team has been established by Dr Sandy Herron-Marx. She will be leading a study day for the team on 23rd April. The PPI team has already provided useful input to the protocol.

BCTU

The IT Department at University of Birmingham Clinical Trials Unit have developed the online system for entering baseline demographics which leads on to the randomisation software. This is particularly easy to use and will speed up the randomisation process and produce better quality data.

The PD Trials Team at University of Birmingham Clinical Trials Unit has been re-organised to accommodate PD REHAB. This has included the appointment of a new data manager, Dani Scott.

If you would like any further information about this trial, please contact:
Carl Clarke - c.e.clarke@bham.ac.uk, Cath Sackley - c.m.sackley@bham.ac.uk
Cally Rick - c.e.rick@bham.ac.uk