



PD-MED Clinical Trial & PD-GEN

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PD MED

A large, simple, pragmatic, “real life”, randomised assessment of the relative cost-effectiveness of different classes of drugs for Parkinson’s disease.

Funding: NHS Health Technology Assessment Programme

www.pdmed.bham.ac.uk



Rationale

Early PD:

- LD alone, DAs and MAOBIs are all effective (pros and cons with each)
- Lack of conclusive evidence on the comparative benefit, or harm, of each class

Later PD:

- Evidence that DAs, MAOBIs and COMTIs effective
- Little reliable evidence on their comparative efficacy

The aim of PD MED is to obtain reliable evidence on these issues.

Why is there a choice of treatment?

- Ehringer & Hornykiewicz 1960 showed basal ganglia dopamine deficiency in Parkinson's disease
- Barbeau 1961 showed a response to levodopa (precursor of dopamine)
- Birkmayer 1962 showed response to deprenyl (selegiline) MAOB inhibitor
- Calne 1974 Bromocriptine (dopamine agonist) effective
- 1960s first generation COMT inhibitors shown to be effective



Previous trials of drug therapy for PD

Many trials have:

- Been too small to give reliable answers
- Used endpoints of uncertain relevance to patients
- Had inadequate length of follow-up



Uncertainty Principle

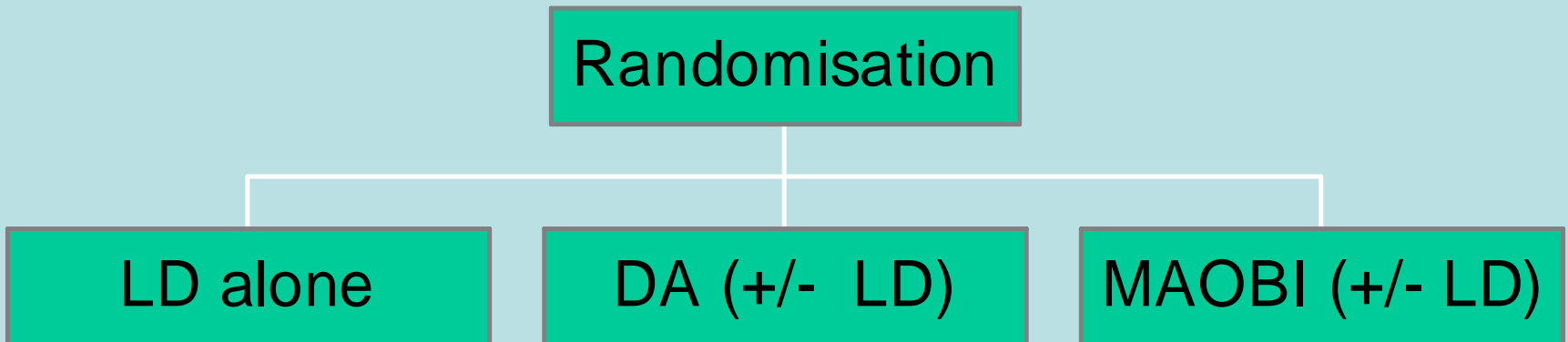
PD MED adopts a pragmatic approach and eligibility is based on “Uncertainty Principle”

If there is a definite indication for or a definite contraindication against a certain class of drug then the patient is not eligible for a randomisation including this option



Randomisation Options

Early disease
n=1500- 3000





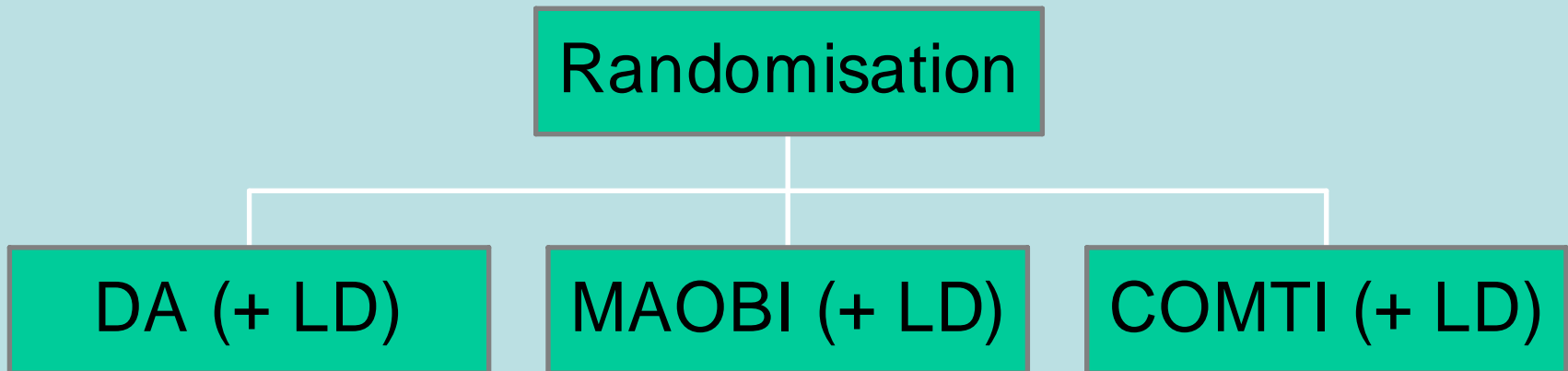
Early PD - Objectives

1. Does initial treatment with LD-sparing therapy (either DA or MAOBI) delay the progress of disability compared to LD alone?
2. If so, which class of LD-sparing treatment is preferable (DA or MAOBI)?



Randomisation Options

Advanced disease
n=1000- 2000





Advanced PD - Objectives

1. For patients with motor fluctuations uncontrolled by LD (\pm DA or MAOBI), should DA or DDI be added to LD?
2. Which class of DDI (MAOBI or COMTI) is the most cost-effective?



Diagnosis

- Use UK Brain Bank criteria
 - Summary in protocol
- Important to diagnose correctly
 - All randomised patients will be included in intention-to-treat analysis



Eligibility – Early Disease

- Newly or recently diagnosed PD
 - Previously untreated for PD
 - Or
 - Less than 3mth L-dopa
- Functional disability requiring drug therapy



Eligibility – Advanced Disease

- Identification of eligible patients
 - Patients who develop motor complications uncontrolled by LD alone and require additional drugs
 - If already receiving either DA or MAOBI, not eligible for randomisation into that arm



Eligibility – General

- Not demented
- Capable of giving written, informed consent
- Able to complete questionnaires, with assistance from carer if necessary.



Annual Assessments

- To be completed before randomisation
- To be completed by patient/ carer
 - PDQ-39
 - EuroQol EQ-5D
 - SF-36 to carer
- To be completed by clinician
 - Hoehn and Yahr stage
 - MMSE
 - Current therapy and reasons for changes



Prescription of Drugs

- Open label- all patients get active drug
- Repeat prescriptions by hospital clinician and/or GP
- Within drug class, clinician can choose which drug
- Dosage as per normal practice
- Clinician free to change therapy



Follow-Up

- LONG TERM FOLLOW UP
 - At annual intervals (for 5 years)
 - Longer follow-up planned
 - Mortality follow up by “flagging” with Office of National Statistics



Primary Endpoint

- Patient's self-evaluation of functional status (PDQ-39)



Secondary Endpoints

- Quality of life (EuroQol)
- Cognitive function (MMSE)
- Burden on carers (SF36, plus other)
- Toxicity and side-effects
- Health economics
- Time to onset of motor complications (early PD only) or time to surgical intervention or start of apomorphine (advanced PD only)
- “On-off” time in a subset of patients (advanced PD only)



Differences to be measurable

The approximate number of patients needed in each arm to detect a 6 point difference in PDQ-39 mobility scale (baseline 42, SD 32) is:

2p-value	Power	Patients per arm
0.01	95%	1000
0.01	90%	840
0.05	90%	600
0.05	80%	440



Subgroup analysis

Two prespecified hypothesis in early PD randomisations:

1. LD-sparing therapy more effective in younger patients
2. LD-sparing therapy more effective in LD naive patients

In advanced PD, time from initial diagnosis of PD to entry will be investigated.

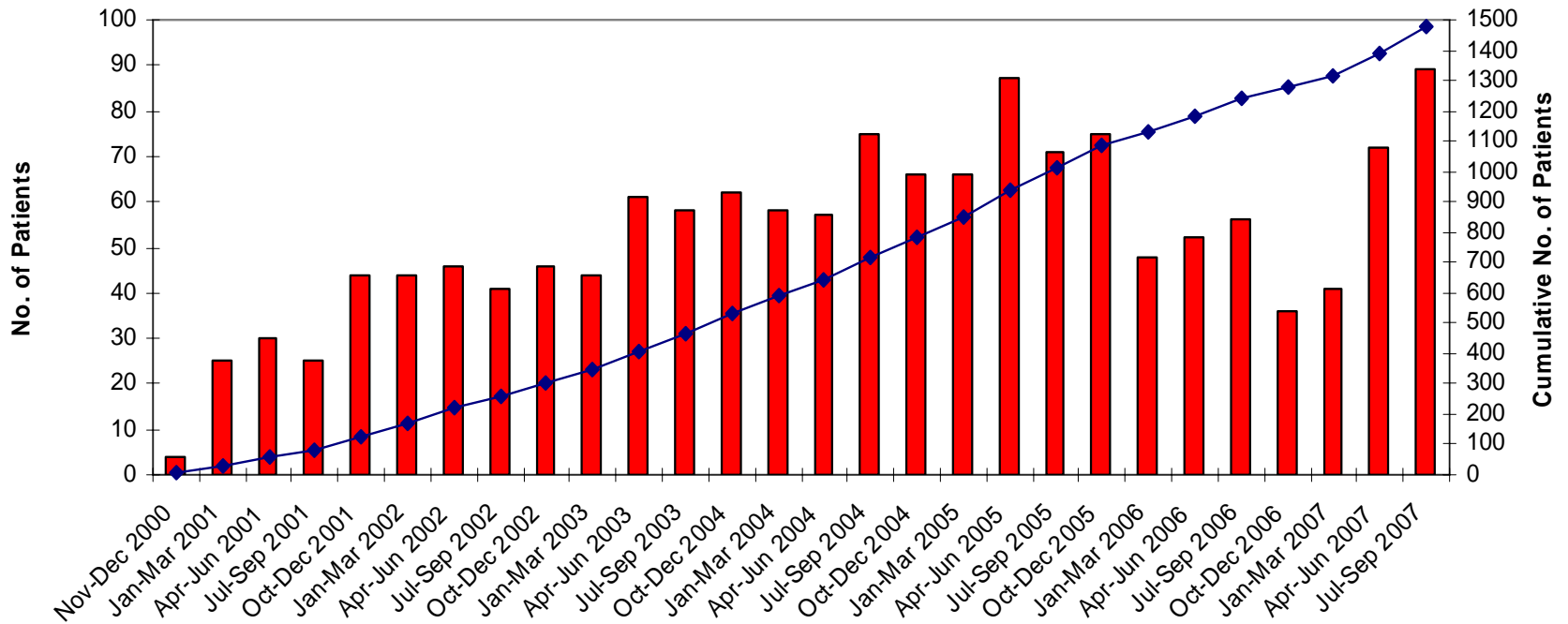
All subgroup analyses will be interpreted cautiously.



Recruitment

Quarterly Recruitment into PD MED

■ No. of Patients Per Quarter ◆ Cumulative No. of Patients





Local Recruitment

- Arrowe Park 36 (11th highest recruiter)
- Walton 23 (21st highest recruiter)
- Victoria Central 2

Recruitment is open until end of December 2008



PD GEN

Parkinson's Disease DNA Database

Funded by the Medical Research Council

www.pdgen.bham.ac.uk



What is PD GEN?

- PD GEN is a sub-study linked to PD MED and PD SURG.
- Blood samples are taken from Patients taking part in PD MED or PD SURG and their Carers’.
- Patients and Carers also complete an epidemiology questionnaire to gather some background information about themselves.
- These samples are then stored in a ‘DNA bank’ for future genetics research into Parkinson’s Disease.
- This will give future researchers both DNA samples and data on the samples from both the questionnaire and the patients PD MED & PD SURG records to study.
- This will lead to the largest collection of DNA from patients with Parkinson’s disease worldwide.



How many samples have been collected to date?

- We have currently collected 697 samples for PD GEN, these samples have been collected from 43 centres around the UK.
- 418 of these are from Patients with PD whilst 279 are from their Carers. (The carer samples will be used as control samples to compare the PD samples against).
- Samples can be collected in regular clinic appointments by a PD Nurse or Consultant.



Local Results

- Arrowe Park / Victoria Central
34 samples (21 from patients)
- Walton
7 samples (5 from patients)

DeNDRoN

DeNDRoN support should be available for these trials via their North West LRN. For details,

Please contact:

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Further information

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