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A phase III, seven-day randomised, double-blind, placebo-controlled, parallel group study to assess efficacy of Donepezil for reducing the incidence and severity of Post-Operative Delirium after an elective total hip or knee replacement in patients over 65 years old

Submission date
01/06/2007

Recruitment status
Stopped

Registration date
12/06/2007

Overall study status
Stopped

Last Edited
12/09/2008

Condition category
Surgery

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
DPOD III

Study information

Scientific Title

Acronym
DPOD III

Study objectives
Patients who are treated with 5 mg of Donepezil (DPZ) for seven days after an elective total hip or knee replacement will show a reduced incidence of delirium.

Please note that this trial record was updated on 12/09/2008. As of this update date, the start date of the trial was updated (initial anticipated start date: 09/07/2007); due to several changes of sponsor, the study has been delayed and is currently on temporary hold. Estimated completion date is now December 2009 (initial anticipated end date: 30/06/2008). The initial sponsor was University College London Clinical Research Management Centre (UCL CRMC) (UK) and the sponsorship is currently being transferred to Imperial College London.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Charing Cross Research Ethics Committee granted approval on the 25th July 2007 (ref: 07/Q0411/61)

Study design
Double-blind, parallel group, single-centre study of seven days of post-operative donepezil or placebo after an elective total hip or knee replacement in patients over 65 years old

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Post-operative delirium

Interventions
5 mg of donepezil (DPZ) or matched placebo once daily for seven days.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Donepezil

Primary outcome measure
The primary endpoint of the study will be the incidence of post-operative delirium. Patients will be considered as a case of delirium if at any point during the course of follow up (to Day seven) they develop an episode of delirium. A risk ratio will be calculated.

Delirium will be diagnosed using the Confusion Assessment Method (CAM) as the primary outcome variable. This is the most widely used instrument for the detection of delirium in the acute hospital setting. It has a sensitivity of 94-100% and a specificity of 90-95% and generates a Diagnostic and Statistical Manual of mental disorders - Fourth Edition (DSM IV) diagnosis of delirium.

Secondary outcome measures
1. The severity of delirium: severity of delirium will be measured by the Delirium Symptom Index (DSI) post- operatively twice a day (morning and afternoon) up to day six. The DSI is a seven item clinician rated scale which measures the severity of delirium and is sensitive to change. It has good internal consistency and inter-rater reliability
2. Length of delirium: this will be measured as the total number of days on which a patient achieves DSM IV caseness for delirium using the CAM. It will be considered that the patient has had delirium that day if either of the two assessments in a 24-hour period were positive for delirium
3. Presence of subsyndromal delirium and behavioural symptoms: this will be measured using the CAM and be defined as any symptoms of new disorientation, disturbance of attention or perceptual or behavioural disturbance that do not meet the full criteria for delirium
4. Changes in cognition: the Mini-Mental State Examination (MMSE) will be used post-operatively once a day (morning up to day six). This is the most widely used screening test for cognitive impairment. It has a maximum score of 30 and assesses a range of cognitive skills. The MMSE has high inter-rater reliability (0.8)
5. Length of hospital stay: this outcome will indicate whether delirium prophylaxis using DPZ may have health economic benefits. Length of hospital stay will be measured in days

Overall study start date
20/03/2008

Completion date

01/12/2009

Reason abandoned (if study stopped)
This trial is currently on temporary hold due to changes with the sponsor.

Eligibility

Key inclusion criteria
1. Awaiting elective total hip or knee replacement
2. 65 years old or over
3. Valid written informed consent

Participant type(s)
Patient

Age group
Senior

Sex
Not Specified

Target number of participants
300 randomised

Key exclusion criteria
1. Subjects with delirium as defined by the Confusion Assessment Method (CAM)
2. Subjects undergoing revision/complex hip/knee surgery
3. Subjects who are deaf, visually impaired or have insufficient English to the extent where they cannot complete the study assessments
4. Subjects with moderately severe cognitive impairment at baseline (i.e. Mini Mental State Examination [MMSE] less than 20)
5. Subjects with alcohol dependence syndrome (International Classification of Diseases [ICD-10] definition)
6. Subjects with severe nausea and vomiting precluding the use of DPZ
7. Subjects currently taking cholinesterase inhibitors
8. Subjects taking antipsychotic/neuroleptic medication that may mask symptoms of delirium
9. Hypnotics or anxiolytics initiated less than a month ago
10. Subjects with a known hypersensitivity to DPZ (piperidine derivatives or any excipients used in its formulation or that of the placebo)
11. Severe bladder outflow obstruction
12. Spinal anaesthesia during surgery
13. Subjects with cardiac problems that contraindicate the prescription of cholinesterase inhibitors:
13.1. Sick sinus syndrome
13.2. Resting pulse of less than 50
13.3. Supraventricular conduction defects

Date of first enrolment
20/03/2008

Date of final enrolment
01/12/2009

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Department of Psychological Medicine
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W6 8RP

Sponsor information

Organisation
Imperial College London (UK)

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Sponsor type
University/education

Website
http://www.imperial.ac.uk

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Industry

Funder Name
Eisai Europe Ltd (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration