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Memory medication study: Alzheimer's Drug Duration - Impact on Functionality

Submission date	Recruitment status	[ ] Prospectively registered
19/09/2008	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
21/10/2008	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
12/10/2009	Nervous System Diseases	[ ] 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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Study information

Scientific Title
Alzheimers Drug Duration - Impact on Functionality: a pragmatic trial of continuing, stopping or switching cholinesterase inhibitors among patients with indeterminate response

Acronym
ADD-IF

Study objectives
Among patients with mild to moderate Alzheimer's disease whose functionality has neither improved nor substantially declined during the 6 to 12 months since starting treatment with a cholinesterase inhibitor (ChEI), donepezil, rivastigmine or galantamine, the following is hypothesised:
1. Continuing medication versus stopping:
1.1. Superiority hypothesis: continuing use of the ChEI is associated with better cognitive prognosis than tapering and stopping the medication
1.2. Non-inferiority hypothesis: tapering and stopping use of the medication does not increase the rate of cognitive decline in patients, compared with continuing the medications
2. Continuing current ChEI versus switching to another ChEI:
2.1. Superiority hypothesis: continuing use of the current ChEI is associated with better cognitive prognosis than switching to another ChEI
2.2. Non-inferiority hypothesis: switching to another ChEI does not increase the rate of cognitive decline in patients, compared with continuing the current ChEI

Ethics approval required
Old ethics approval format

Ethics approval(s)
University of Victoria Human Research Ethics Board granted approval on the 4th April 2008 (ref: 08-07-252-c)

Primary study design
Interventional

Study design
Pragmatic randomised-withdrawal and randomised-switching with three concurrent parallel arms

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Alzheimers Disease

Interventions
Continuation arm:
Cholinesterase inhibitor used until randomisation will be continued as prescribed by patients' physician according to the following titration pattern. Donepezil at a starting dose of 5 mg daily (2.5 mg if frail) for 4 to 6 weeks, increased by 5 mg as tolerated with an effective range of 5 to 10 mg daily, galantamine at a starting dose of 8 mg ER daily for 4 to 6 weeks, increased by 8 mg as tolerated with an effective range of 16 to 24 mg daily or rivastigmine at a starting dose of 1.5 mg daily for 2 to 4 weeks, increased by 1.5 to 3 mg as tolerated with an effective range of 6 to 12 mg daily. Treatment will be continued from 5 months to 24 months after randomisation.

Switching arm:
Cholinesterase inhibitor currently used until randomisation will be discontinued and patient will be started on one of the other two according to each physician's practice and experience, within the following guidelines: a washout period of 2 days for galantamine and rivastigmine and 5 to 7 days for donepezil; start of a new cholinersterase inhibitor using the same titration pattern as for new starts (see above).

Withdrawal arm:
Cholinesterase inhibitor currently used until randomisation will be discontinued and special authority request forms (where the outcome measures of MMSE and OPAR are reported) will continue to be recorded to facilitate restarts if there is a noticeable decline in cognition /function within 7 to 10 days of stopping. Patients will be called one week after discontinuation to detect sudden deterioration. All patients in this arm will be re-examined by their physician at one month after withdrawal.

As of 12/10/2009 this record has been updated due to major problems with physician recruitment. The randomised allocation in this trial has been temporarily eliminated and physicians and patients are only being recruited for a prospective cohort study. This will be a run-in phase to assess the feasibility of recruitment without randomised allocation, in due time the randomised element may be reinstated.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Donepezil, rivastigmine, galantamine

Primary outcome(s)
Physicians assessment of cognitive status and global assessment rating, measured at 6 months, 12 months, 18 months, 24 months.

Key secondary outcome(s)
1. Assessment of patients' cognitive status using Telephone Interview of Cognitive Status
2. Differences in caregiver assessments of the medications effectiveness
3. Incidence rates of health services use and use of other drugs using Ministry of Health Services central administrative databases
4. Net cost of health services using Ministry of Health Services central administrative databases and private expenses reported by caregivers in telephone interviews

Measured at 6 months, 12 months, 18 months, 24 months.

Completion date
31/03/2011

Eligibility

Key inclusion criteria
1. Policy criteria:
The patient is approved at least once for insurance coverage of ChEIs by British Columbia PharmaCare (the publicly financed drug benefit plan), meaning:
1.1. They are residents of British Columbia eligible for PharmaCare coverage
1.2. They are not in a hospital or long-term care institution (because drugs of such patients are mostly covered by the Health Authorities)
1.3. A physician has reported on a Special-Authority Request (insurance coverage application)

form that the patient has a diagnosis involving Alzheimer's disease, and the severity of dementia was mild-to-moderate (scoring greater than 10 but less than 26 on the Standardised Mini-Mental Status Examination [SMMSE]) when they were first covered by PharmaCare

2. Clinical criteria:
At enrolment:
2.1. The patient has taken ChEIs for no longer than 12 months and has not used them for at least 12 months prior to that 12 months
2.2. The patient has tolerated ChEIs for at least 5 months but may have switched within that time due to intolerance of one type of ChEI
2.3. A physician has reported on a Special-Authority Request (insurance coverage application) form that the patient's Overall Patient Assessment Rating (OPAR), including assessments of cognition, function and behaviour, has neither improved nor seriously declined (i.e. 'indeterminate response', which means the difference in OPAR score is 0 or -1) by 6 to 12 months after starting the medications
2.4. Males and females included with no set age

3. Social-logistical criteria:
The personal caregiver (e.g. spouse or guardian) must be informed and consent as well as the patient. Therefore, the patient and caregiver:
3.1. Must speak English
3.2. Must be available by telephone
3.3. Must be willing to communicate by telephone with the Centre on Ageing. The patient's physician must also agree to their prescribing decisions being directed by a study protocol.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Non-Alzheimer-related dementia (for Special-Authority coverage, the diagnosis must be Alzheimer's disease, Alzheimer's disease with a vascular component, Alzheimer's disease with Lewy bodies or mixed dementia with predominant Alzheimer's disease)
2. Delay in recruitment of patients or their follow-up visit to their physician, so that they have taken ChEIs continuously for longer than 12 months prior to their availability to be randomised
3. Any use of ChEIs, even if brief, during the 12 months prior to the patient's most recent start of continuous use. However, patients who have used and stopped ChEIs more than 12 months before their most recent start of continuous use may be included.

Date of first enrolment
01/10/2008

Date of final enrolment

31/03/2011

Locations

Countries of recruitment
Canada

Study participating centre
Centre on Aging
Victoria, BC
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Sponsor information

Organisation
British Columbia Ministry of Health Services (Canada)

ROR
https://ror.org/05smbmp94

Funder(s)

Funder type
Government

Funder Name
British Columbia Ministry of Health Services (Canada)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration