# 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 yea

#### Plain English summary of protocol

Not provided at time of registration

#### Contact information

#### Type(s)

Scientific

#### Contact name

Dr Neena Chappell

#### Contact details

Centre on Aging University of Victoria PO BOX 1700, STN CSC Victoria, BC Canada V8W 2Y2 senage@uvic.ca

### Additional identifiers

**Protocol serial number** N/A

# 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 ChEl versus switching to another ChEl:
- 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)

#### Study design

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

#### Primary study design

Interventional

#### 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 runin 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

# Date of final enrolment 31/03/2011

#### Locations

Countries of recruitment

Canada

Study participating centre Centre on Aging Victoria, BC Canada V8W 2Y2

# 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