

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

<b>Submission date</b> 19/09/2008	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 21/10/2008	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 12/10/2009	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

**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

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
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 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)

## Study design

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

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Not specified

## Study type(s)

Treatment

## Participant information sheet

## 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 cholinesterase 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 measure

Physicians assessment of cognitive status and global assessment rating, measured at 6 months, 12 months, 18 months, 24 months.

### Secondary outcome measures

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.

**Overall study start date**

01/10/2008

**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

**Age group**

Adult

**Sex**

Both

**Target number of participants**

Minimum of 300, with 100 per arm with a target of 1000

**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

Canada

V8W 2Y2

**Sponsor information****Organisation**

British Columbia Ministry of Health Services (Canada)

**Sponsor details**

Pharmaceutical Services Division

1515 Blanshard Street

Victoria

Canada

V8W 3C8

EnquiryBC@gov.bc.ca

**Sponsor type**

Government

**Website**

<http://www.gov.bc.ca/>

**ROR**

<https://ror.org/05smbmp94>

**Funder(s)****Funder type**

Government

**Funder Name**

British Columbia Ministry of Health Services (Canada)

**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