

G.7.4 Cholinesterase inhibitors and memantine for types of dementia other than typical Alzheimer's disease

- How effective are cholinesterase inhibitors and memantine for types of dementia other than typical Alzheimer's disease?

G.7.4.1 Vascular dementia

Cholinesterase inhibitors versus placebo

No of studies	Quality assessment					No of patients		Effect estimate	Quality
	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	AChEI	Placebo	Summary of results	
Cognitive outcomes – global cognition									
MMSE (higher values = better score)									
4 (Ballard 2008, Black 2003, Mok 2007, Roman 2010)	RCT	Not serious	Not serious	Not serious	Not serious	1,417	884	MD 0.58 (0.30, 0.86)	High
ADAS-cog (lower values = better score)									
4 (Ballard 2008, Black 2003, Roman 2010, Wilkinson 2003)	RCT	Not serious	Not serious	Serious ¹	Not serious	1,719	1,015	MD -1.36 (-2.03, -0.70)	Moderate
ADAS-cog-11 (lower values = better score)									
2 (Auchus 2007, Small 2003)	RCT	Not serious	Not serious	Not serious	Not serious	486	440	MD -1.59 (-2.39, -0.78)	High
Vascular Dementia Assessment Scale – cognitive subscale (lower values = better score)									
1 (Roman 2010)	RCT	Not serious	Not serious	N/A	Not serious	535	283	MD -1.15 (-1.99, -0.31)	High
EXIT-25 (lower values = better score)									
2 (Auchus 2007, Roman 2010)	RCT	Not serious	Not serious	Serious ¹	Serious ²	991	692	MD -0.57 (-1.40, 0.25)	Low
Neuropsychiatric symptoms									
NPI (lower values = better score)									
2 (Auchus 2007, Mok 2007)	RCT	Not serious	Not serious	Not serious	Not serious	376	381	MD 1.76 (0.28, 3.24)	High
NPI-12 (lower values = better score)									

No of studies	Quality assessment					No of patients		Effect estimate	Quality
	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	AChEI	Placebo	Summary of results	
1 (Ballard 2008)	RCT	Not serious	Not serious	N/A	Serious ²	364	342	MD 0.40 (-1.36, 2.16)	Moderate
Global assessment									
Clinician's Global Impression of Change (lower values = better score)									
1 (Ballard 2008)	RCT	Not serious	Not serious	N/A	Not serious	329	320	MD -0.10 (-3.68, -3.48)	High
Vascular Dementia Assessment Scale (lower values = better score)									
1 (Ballard 2008)	RCT	Not serious	Not serious	N/A	Serious ²	355	327	MD -1.03 (-2.62, 0.02)	Moderate
Global deterioration scale									
1 (Ballard 2008)	RCT	Not serious	Not serious	N/A	Serious ²	365	345	MD -0.10 (-2.25, 2.05)	Moderate
Clinical Dementia Rating Sum of Boxes (lower values = better score)									
4 (Black 2003, Mok 2007, Roman 2010, Wilkinson 2003)	RCT	Serious ³	Not serious	Not serious	Not serious	1,379	696	MD -0.17 (-0.33, -0.00)	Moderate
Functional ability									
ADCS-ADL (higher values = better score)									
2 (Auchus 2007, Ballard 2008)	RCT	Not serious	Not serious	Not serious	Serious ²	728	716	MD -0.13 (-1.16, 0.90)	Moderate
Instrumental Activities of Daily Living (lower values = better score)									
3 (Black 2003, Mok 2007, Wilkinson 2003)	RCT	Very serious ⁴	Not serious	Serious ¹	Serious ²	751	375	MD -0.38 (-1.04, 0.27)	Very low
Alzheimer's Disease Functional Assessment and Change Scale (lower values = better score)									
2 (Black 2003, Wilkinson 2003)	RCT	Not serious	Not serious	Not serious	Not serious	570	356	MD -0.95 (-1.73, -0.18)	High
Functional Assessment Battery (higher values = better score)									
1 (Mok 2007)	RCT	Not serious	Not serious	N/A	Very serious ⁵	20	19	MD -0.40 (-2.13, 1.33)	Low
Disability assessment for Dementia									
1 (Roman 2010)	RCT	Not serious	Not serious	N/A	Serious ²	628	321	MD 1.77 (-0.10, 3.64)	Moderate
Adverse events									
Any adverse events (lower values = better score)									
5 (Auchus 2007, Black 2003, Mok 2007, Roman 2010, Wilkinson 2003)	RCT	Not serious	Not serious	Not serious	Not serious	1592/1891	884/1128	RR 1.05 (1.01, 1.09)	High
Serious adverse events (lower values = better score)									

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	AChEI	Placebo	Summary of results	
5 (Auchus 2007, Ballard 2008, Black 2003, Roman 2010, Wilkinson 2003)	RCT	Not serious	Not serious	Not serious	Serious ⁶	337/2019	220/1452	RR 1.11 (0.95, 1.30)	Moderate
Discontinuation due to adverse events (lower values = better score)									
3 (Auchus 2007, Ballard 2008, Mok 2007)	RCT	Not serious	Not serious	Not serious	Not serious	76/779	31/754	RR 2.40 (1.61, 3.59)	High
Mortality (lower values = better scores)									
6 (Auchus 2007, Ballard 2008, Black 2003, Mok 2007, Roman 2010, Wilkinson 2003)	RCT	Not serious	Not serious	Serious ¹	Serious ²	37/2254	24/1472	RR 0.99 (0.43, 2.30)	Low
1. $i^2 > 40\%$. 2. Non-significant result. 3. Primary outcomes in some studies presented without measures of dispersion; unclear reporting of sample size in secondary outcomes at endpoint 4. Primary outcomes in some studies only presented in graphs 5. Small sample size and non-significant result. 6. 95% CI crosses one line of a defined MID interval									

Memantine versus placebo

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Memantine	Placebo	Summary of results	
Cognitive outcomes - global cognition									
MMSE (higher values = better score)									
1 (Orgogozo 2002)	RCT	Not serious	Not serious	N/A	Not serious	105	108	MD 1.23 (0.23, 2.23)	High
ADAS-cog (lower values = better score)									
2 (Orgogozo 2002, Wilcock 2002 ²)	RCT	Not serious	Not serious	Not serious	Not serious	377	375	MD -2.19 (-3.16, -1.21)	High

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Memantine	Placebo	Summary of results	
Behavioural symptoms									
Nurses' Observation Scale for Geriatric Patients (lower values = better score)									
2 (Orgogozo 2002, Wilcock 2002)	RCT	Not serious	Not serious	Not serious	Serious ¹	275	250	MD -0.92 (-2.90, 1.05)	Moderate
Global assessment									
Gottfries-Bråne-Steen scale (lower values = better score)									
2 (Orgogozo 2002, Wilcock 2002)	RCT	Not serious	Not serious	Not serious	Serious ¹	311	284	MD -1.83 (-4.22, 0.56)	Moderate
Clinician's Interview based Impression of Change (lower values = better score)									
1 (Orgogozo 2002)	RCT	Not serious	Not serious	N/A	Serious ¹	114	114	MD -0.29 (-0.66, 0.08)	Moderate
Adverse events									
Any adverse events (lower values = better score)									
1 (Wilcock 2002)	RCT	Not serious	Not serious	N/A	Not serious	226/295	212/284	RR 1.03 (0.94, 1.13)	High
Serious adverse events (lower values = better score)									
1 (Orgogozo 2002)	RCT	Not serious	Not serious	Not serious	Very serious ³	38/93	40/95	RR 0.97 (0.69, 1.36)	Low
<ol style="list-style-type: none"> 1. Non-significant result. 2. Corrected an error in published results 3. 95% CI crosses two lines of a defined MID interval 									

Network meta-analyses

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Active	Placebo	Summary of results	
Cognitive outcomes – global cognition									
MMSE (higher values = better score)									

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Active	Placebo	Summary of results	
5 (Ballard 2008, Black 2003, Mok 2007, Orgogozo 2002, Roman 2010)	RCT	Not serious	Not serious	Not serious	Not serious	1,522	992	See appendix H	High
ADAS-cog (lower values = better score)									
6 (Ballard 2008, Black 2003, Orgogozo 2002, Roman 2010, Wilcock 2002, Wilkinson 2003)	RCT	Not serious	Not serious	Serious ¹	Not serious	2,096	1,390	See appendix H	Moderate
Adverse events									
Any adverse events (lower values = better score)									
6 (Auchus 2007, Black 2003, Mok 2007, Roman 2010, Wilcock 2002, Wilkinson 2003)	RCT	Not serious	Not serious	Not serious	Not serious	2,186	1,412	See appendix H	High
Serious adverse events (lower values = better score)									
5 (Auchus 2007, Ballard 2008, Black 2003, Orgogozo 2002, Roman 2010, Wilkinson 2003)	RCT	Not serious	Not serious	Not serious	Serious ²	2,112	1,547	See appendix H	Moderate
¹ >40%. ² Analysis could not differentiate any treatment groups.									