G.7.4.2 Behavioural variant frontotemporal dementia

Cholinesterase inhibitors versus placebo

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	AChEI	Placebo	Summary of results	
Cognitive outcomes – global cognition									
MMSE (higher values = better score)									
1 (Kerstesz 2008)	RCT	Not serious	Not serious	Not serious	Very serious[1]	17	17	MD 4.40 (-1.02, 9.82)	Low
Dementia Rating Scale (higher values = better score)									
1 (Kerstesz 2008)	RCT	Not serious	Not serious	Not serious	Very serious[1]	17	17	MD 22.00 (-3.37,47.37)	Low

Quality assessment						No of patients		Effect estimate		Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	AChEI	Placebo	Summary of results		
Neuropsychiatric symptoms										
NPI (lower values = better score)										
1 (Kerstesz 2008)	RCT	Not serious	Not serious	Not serious	Very serious[1]	17	17	MD 5.80 (-7.25, 18.85)		Low
Functional ability										
Functional Assessment Battery (higher values = better score)										
1 (Kerstesz 2008)	RCT	Not serious	Not serious	Not serious	Very serious[1]	17	17	MD 2.50 (-0.99, 5.99)		Low
ADCS-ADL (higher value = better score)										
1 (Kerstesz 2008)	RCT	Not serious	Not serious	Not serious	Very serious[1]	17	17	MD 7.00 (-7.55, 21.55)		Low
Adverse events										
Any adverse events (lower values = better score)										
1 (Kerstesz 2008)	RCT	Not serious	Not serious	Not serious	Very serious[1]	4/18	5/18	RR 0.80 (0.26, 2.50)		Low
Discontinuation due to adverse events (lower values = better score)										
1 (Kerstesz 2008)	RCT	Not serious	Not serious	Not serious	Very serious[1]	1/18	1/18	RR 1.00 (0.07, 14.79)		Low

1. Small sample size and non-significant result.
2. 95% CI crosses two lines 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)										
2 (Boxer 2013, Vercelletto 2011)	RCT	Not serious	Not serious	Not serious	Serious[1]	50	55	MD 0.26 (-1.43, 1.95)		Moderate
Mattis Dementia Rating Scale (lower values = better score)										
1 (Vercelletto 2011)	RCT	Not serious	Not serious	N/A	Very serious[2]	18	23	MD 6.30 (-9.55, 22.15)		Low
EXIT-25 (lower values = better score)										
1 (Boxer 2013)	RCT	Not serious	Not serious	N/A	Serious[1]	31	33	MD 1.20 (-1.86, 4.26)		Moderate

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Memantine	Placebo	Summary of results	
Neuropsychiatric symptoms									
NPI (lower values = better score)									
2 (Boxer 2013, Vercelletto 2011)	RCT	Not serious	Not serious	Not serious	Serious[1]	48	55	MD -3.61 (-8.79, 1.57)	Moderate
Global assessment									
Clinician's Interview based Impression of Change (lower values = better score)									
1 (Vercelletto 2011)	RCT	Not serious	Not serious	N/A	Very serious[2]	18	23	MD -0.80 (-1.82, 0.22)	Low
Clinician's Global Impression of Change (lower values = better score)									
1 (Boxer 2013)	RCT	Not serious	Not serious	N/A	Serious[1]	31	33	MD -0.50 (-1.35, 0.35)	Moderate
Clinical Dementia Rating Sum of Boxes (lower values = better score)									
1 (Boxer 2013)	RCT	Not serious	Not serious	N/A	Serious[1]	31	33	MD -0.10 (-2.22, 2.02)	Moderate
Motor function									
Unified Parkinson's disease rating scale (lower values = better score)									
1 (Boxer 2013)	RCT	Not serious	Not serious	N/A	Serious[1]	31	33	MD -0.30 (-3.46, 2.86)	Moderate
Carer burden									
ZBI (lower values = better score)									
1 (Vercelletto 2011)	RCT	Not serious	Not serious	N/A	Very serious[2]	16	23	MD -5.40 (-14.52, 3.72)	Low
Adverse events									
Any adverse events (lower values = better score)									
1 (Vercelletto 2011)	RCT	Not serious	Not serious	N/A	Very serious[4]	8/23	10/26	RR 0.90 (0.43, 1.90)	Low
Serious adverse events (lower values = better score)									
2 (Boxer 2013, Vercelletto 2011)	RCT	Not serious	Not serious	Not serious	Very serious[4]	7/54	12/59	RR 0.65 (0.29,1.48)	Very low
Discontinuation due to adverse events (lower values = better score)									
1 (Vercelletto 2011)	RCT	Not serious	Not serious	N/A	Very serious[4]	3/23	3/26	RR 1.13 (0.25, 5.06)	Low
Mortality (lower values = better scores)									
1 (Vercelletto 2011)	RCT	Not serious	Not serious	N/A	Very serious[2]	2/23	0/26	RR 5.63 (0.28, 111.43)	Low

1. Non-significant result
2. Small sample size and non-significant result.
3. i²>40%.
4. *95% CI crosses two lines of a defined MID interval*

Network meta-analyses

No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Active	Placebo	Summary of results	Quality
Quality assessment						**No of patients**		**Effect estimate**	**Quality**
Cognitive outcomes – global cognition									
MMSE (higher values = better score)									
3 (Boxer 2013, Kertesz 2008, Vercelletto 2011)	RCT	Not serious	Not serious	Not serious	Serious[1]	67	72	See appendix H	Moderate
Neuropsychiatric symptoms									
NPI (lower values = better score)									
3 (Boxer 2013, Kertesz 2008, Vercelletto 2011)	RCT	Not serious	Not serious	Not serious	Serious[1]	65	72	See appendix H	Moderate
Adverse events									
Any adverse events (lower values = better score)									
2 (Kertesz 2008, Vercelletto 2011)	RCT	Not serious	Not serious	N/A	Serious[1]	41	44	See appendix H	Moderate
Discontinuation due to adverse events (lower values = better score)									
2 (Kertesz 2008, Vercelletto 2011)	RCT	Not serious	Not serious	N/A	Serious[1]	41	44	See appendix H	Moderate

1. Analysis could not differentiate any treatment groups.
2. $i^2>40\%$.