G.7.3.2 Parkinsons disease dementia – memantine

PDD – memantine vs. placebo: adverse events

Quality assessment						No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Memantine	Placebo	Relative (95% CI)	Absolute (95% CI)	

Any adverse events (probability of experiencing ≥1; follow-up 16 to 24 weeks, lower is better)										
2[1,2]	RCT	not serious	not serious	not serious	serious[3]	34/73 (46.6%)	35/72 (48.6%)	RR 0.97 (0.69 to 1.37)	15 fewer per 1000 (from 151 fewer to 180 more)	⊕⊕⊕O MODERATE
Serious adverse events (probability of experiencing ≥1; follow-up 16 to 24 weeks, lower is better)										
2[1,2]	RCT	not serious	not serious	not serious	very serious[3,4]	9/73 (12.3%)	8/72 (11.1%)	RR 1.09 (0.45 to 2.67)	10 more per 1000 (from 61 fewer to 186 more)	⊕⊕OO LOW
Adverse events requiring treatment withdrawal (probability of experiencing; follow-up 24 weeks, lower is better)										
1[1]	RCT	not serious	N/A	not serious	very serious[3,4]	6/62 (9.7%)	5/58 (8.6%)	RR 1.12 (0.36 to 3.48)	10 more per 1000 (from 55 fewer to 214 more)	⊕⊕OO LOW

[1] Emre 2010; data reported for PDD population only; study also included people with DLB
[2] Leroi 2009; not clear if adverse event data reported at end of active treatment (16 weeks) or end of drug withdrawal phase (22 weeks)
[3] At a 95% confidence level, data are consistent with appreciable harm, appreciable benefit or no difference
[4] Very small numbers of events

PDD – memantine vs. placebo: cognitive function

Quality assessment						No of patients		Effect	Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Memantine**	**Placebo**	**Mean difference (95% CI)**	
MMSE (follow-up 16 weeks; range of scores: 0-30; higher is better)									
1[1]	RCT	not serious	N/A	not serious	very serious[2,3]	10	14	1 lower (6.01 lower to 4.01 higher)	⊕⊕OO LOW
Clock drawing test (follow-up 24 weeks; range of scores: 0-10; higher is better)									
1[4]	RCT	not serious	N/A	not serious	serious[2]	57	56	3.1 higher (6.94 lower to 13.14 higher)	⊕⊕⊕O MODERATE

[1] Leroi 2009; data reported for end of drug treatment phase (16 weeks)
[2] At a 95% confidence level, data are consistent with appreciable benefit, appreciable harm or no difference
[3] Very small numbers of participants in the study
[4] Emre 2010; data reported for PDD population only; study also included people with DLB

PDD – memantine vs. placebo: global assessment

Quality assessment						No of patients		Effect (95% CI)	Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Memantine**	**Placebo**		
ADCS-CGIC (follow-up 24 weeks; range of scores: 1-7; lower is better)									
1[1]	RCT	not serious	N/A	not serious	serious[2]	60	56	MD 0.2 lower (0.69 lower to 0.29 higher)	⊕⊕⊕O MODERATE
CIBIC+ (at least minimal improvement; follow-up 16 weeks; higher is better)									
1[3]	RCT	not serious	N/A	not serious	very serious[2,4]	6/10 (60%)	6/14 (42.9%)	RR 1.4 (0.64 to 3.08) 171 more per 1000 (from 154 fewer to 891 more)	⊕⊕OO LOW

[1] Emre 2010; data reported for PDD population only; study also included people with DLB
[2] At a 95% confidence level, data are consistent with appreciable benefit, appreciable harm or no difference
[3] Leroi 2009; data reported for end of drug treatment phase (16 weeks)
[4] Data from a single very small study

PDD – memantine vs. placebo: activities of daily living

Quality assessment						No of patients		Effect	Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Memantine	Placebo	Mean difference (95% CI)	
ADCS-ADL (follow-up 24 weeks; measured with: 23-item score; higher is better)									
1[1]	RCT	not serious	N/A	not serious	serious[2]	60	56	0.8 higher (3.22 lower to 4.82 higher)	⊕⊕⊕O MODERATE

[1] Emre 2010; data reported for PDD population only; study also included people with DLB
[2] At a 95% confidence level, data are consistent with appreciable benefit, appreciable harm or no difference

PDD – memantine vs. placebo: carer-reported outcomes

Quality assessment						No of patients		Effect	Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Memantine	Placebo	Mean difference (95% CI)	
ZBI (follow-up 16 to 24 weeks; lower is better)[1]									
2[2,3]	RCT	not serious	not serious	not serious	serious[4]	71	70	3.4 lower (7.21 lower to 0.42 higher)	⊕⊕⊕O MODERATE

[1] Data from Leroi 2009 reported in a secondary publication (Leroi 2014)
[2] Leroi 2009; data reported for end of drug treatment phase (16 weeks)
[3] Emre 2010; data reported for PDD population only; study also included people with DLB
[4] At a 95% confidence level, data are consistent with appreciable benefit, appreciable harm or no difference

PDD – memantine vs. placebo: other non-cognitive outcomes

Quality assessment						No of patients		Effect	Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Memantine	Placebo	Mean difference (95% CI)	
NPI 12-item (follow-up 24 weeks; range of scores: 0-144; lower is better)									
1[1]	RCT	not serious	N/A	not serious	serious[3]	60	56	MD 1.50 lower (6.35 lower to 3.35 higher)	⊕⊕⊕O MODERATE
NPI 10-item (follow-up 16 weeks; range of scores: 0-120; lower is better)									
1[2]	RCT	not serious	N/A	not serious	very serious[3,4]	10	14	MD 2.00 lower (11.64 lower to 7.64 higher)	⊕⊕OO LOW
UPDRS III (follow-up 16 to 24 weeks; lower is better)									

2[1,2]	RCT	not serious	not serious	not serious	serious[3,5]	70	70	MD 0.88 higher (2.35 lower to 4.1 higher)	⊕⊕⊕O MODERATE

[1] Emre 2010; data reported for PDD population only; study also included people with DLB
[2] Leroi 2009; data reported for end of drug treatment phase (16 weeks)
[3] At a 95% confidence level, data are consistent with appreciable benefit, appreciable harm or no difference
[4] Data from a single very small study
[5]CI cross MID between 3.25 (Horvath et al 2015) and 5 points (Schrag et al., 2006)