Supplementary Table S2. Primary and secondary endpoint measurements used in clinical trials of FTD spectrum disorders

Study	Primary Endpoint Measures	Secondary Endpoint Measures	Main Findings
Behavioural variant FTD			
Pardini *et al.* (2015) [41]	NPI (total score); FAB (total score); Reading the Mind in the Eyes Test (total score); CGI-S (total score); Frequency, Intensity, and Burden of Side Effects Rating Scale.		Significant reduction of behavioural symptoms and an increase in Theory of Mind skills with Souvenaid^{TM}.
Hughes *et al.* (2015) [42]	Go and NoGo task (reaction times and response accuracy).	ACE-r; MMSE; Hayling and Brixton Task; Graded Naming Test; revised Beck Depression Inventory (BDI-II); Kirby Temporal Discounting Test; Visual Analogy Scale; Cambridge Behavioural Inventory.	Citalopram restored the P3 and enhanced cortical response of the right inferior frontal gyrus during NoGo inhibition.
Finger *et al.* (2015) [43]	Safety and tolerability (adverse effects).	NPI; FBI; CGI-C; CDR – FTLD; Interpersonal Reactivity Index; Multi-faceted Empathy Test.	No serious adverse events with Oxytocin. Possible trends of improvement of apathy (NPI and FBI) and IRI empathic concern scale.
Boxer *et al.* (2013) [47]	NPI (total score); CGI-C.	CDR-FTD; MMSE; FAQ; TFLS; EXIT25; CVLT; Verbal fluency; Modified BNT; Backward digit span; Digit Symbol test; Modified Trails B; Modified UPDRS; need for antipsychotic therapy.	No significant differences between groups on the primary and secondary endpoints. Worst neuropsychological performance in the Memantine group on the BNT and for processing speed.
Jesso et al. (2011) [48]	Facial expression recognition task and intensity task; Vocal affect recognition task; Mind in the Eyes task.	NPI; FBI.	Significant improvement in scores on the NPI and reduced recognition of angry facial expressions by patients following oxytocin administration.
Vercelletto *et al.* (2011) [49]	Clinician's Interview-Based Impression of Change Plus Caregiver Input.	NPI; FBI; Mattis Dementia Rating Scale; MMSE; Disability Assessment for Dementia; Zarit Burden Inventory.	No significant differences between the groups on primary and secondary endpoints, except for lower FBI score for the Memantine group.
Kertesz *et al.* (2007) [52]	FBI; Aphasia Quotient of the Western Aphasia Battery; and the Clinical Global Impressions of Improvement and of Severity.	MMSE; Mattis Dementia Rating Scale; FAB; NPI; AD cooperative study – ADL scale; subscales of the WAB and the FBI.	No significant improvement on Galantamine.
Rahman *et al.* (2006) [53]	CANTAB battery: pattern recognition memory, spatial recognition, spatial span, spatial working memory, and attentional set-shifting. Tower of London test of spatial planning; Cambridge Gamble Task.		Methylphenidate was effective in normalizing the decision-making behaviour.
Deakin *et al.* (2004) [54]	Verbal fluency (Benton 1968); Forward and backward digit span; CANTAB and CANTAB extensions; immediate and delayed pattern recognition; spatial recognition; spatial span; spatial working memory; visual discrimination learning/attentional set shifting; Decision-making "Gamble"; Paired-associates learning; NPI; Cambridge Behavioural Inventory.		No significant improvement of scores on Paroxetine.
Moretti *et al.* (2004) [55]	NPI; Cornell Scale for Depression in dementia; Behavioural Pathology in AD rating Scale; Relative Stress Scale; Clinical insight rating scale; MMSE; Ten Point Clock test; Proverb Interpretation Tasks.		Reduction of behavioural symptoms and of caregiver burden with Rivastigmine.
Lebert *et al.* (2004) [56]	NPI (total score).	Clinical Global Impression of Improvement; MMSE.	Significant reduction of the NPI total score with Trazodone. No significant change on secondary endpoints.
Moretti *et al.* (2003) [57]	MMSE; Ten Point Clock test; Proverb interpretation Tasks; Stroop Test; NPI, Clinical Insight Rating Scale; Cornell Scale for depression in dementia; Behavioural Pathology in AD Rating Scale; Relative Stress Scale.		Significant reduction of caregiver stress with Paroxetine.

Supplementary Table S2. *Continued*

Study	Primary Endpoint Measures	Secondary Endpoint Measures	Main Findings
Primary progressive aphasia			
Finger *et al.* (2015) [43]	Safety and tolerability (adverse effects).	NPI; FBI; CGI-C; CDR – FTLD; Interpersonal Reactivity Index; Multi-faceted Empathy Test.	No serious adverse events with Oxytocin. Possible trends of improvement of apathy (NPI and FBI) and IRI empathic concern scale.
Boxer *et al.* (2013) [47]	NPI (total score); CGI-C.	CDR-FTD; MMSE; FAQ; TFLS; EXIT25; CVLT; Verbal fluency; Modified BNT; Backward digit span; Digit Symbol test; Modified Trails B; Modified UPDRS; need for antipsychotic therapy.	No significant differences between groups on the primary and secondary endpoints. Worst neuropsychological performance in the Memantine group on the BNT and for processing speed.
Kertesz *et al.* (2007) [52]	FBI; Aphasia Quotient of the Western Aphasia Battery; and the Clinical Global Impressions of Improvement and of Severity.	MMSE; Mattis Dementia Rating Scale; FAB; NPI; AD cooperative study – ADL scale; subscales of the WAB and the FBI.	Clinical improvement on CGI-S for Galantamine (not significant when the Bonferroni correction was applied).
Progressive supranuclear palsy syndrome			
Leclair-Visonneau *et al.* (2016) [38]	PSPRS score at 12 and 24 months.	Cognitive and behavioural status: MMSE; MDRS; Wisconsin Card Sorting Test; verbal fluency; Gröber and Buschke test; Oral Denomination 80 tests; NPI; FAB; Tolerability and compliance.	Similar PSPRS score at 24 months. No significant differences between VPA and placebo groups for the secondary endpoints.
Nuebling *et al.* (2016) [39]	PSPRS and requirement for L-dopa rescue medication.	MMSE; FAB; Schwab and England Activities of Daily Living; Montgomery-Asberg Depression Rating Scale; posturographic measurements.	No effect on the primary and secondary endpoint was detected.
Apetauerova *et al.* (2016) [40]	PSPRS; UPDRS.	ADL; MMSE; PDQ-39; SF-36.	No effect on the primary and secondary endpoint was detected.
Tolosa *et al.* (2014) [44]	PSPRS change from baseline.	Adverse effects; Modified Schwab and England Scale; Timed Up and Go Test; Dementia Rating Scale-2; FAB; category and letter verbal fluency; Starkstein Apathy Scale; UPDRS part II and European Quality of Life Questionnaire; CGI-C; CGI-S.	No effect of Tideglusib over placebo on clinical results.
Höglinger *et al.* (2014) [45]	Global and regional brain atrophy rates on MRI.	Adverse effects; Modified Schwab and England Scale; Timed Up and Go Test; Dementia Rating Scale-2; FAB; category and letter verbal fluency; Starkstein Apathy Scale; UPDRS part II and European Quality of Life Questionnaire; CGI-C; CGI-S.	Progression of atrophy was significantly lower in the active group than in the placebo group for the whole brain, cerebrum, parietal lobe, and occipital lobe.
Boxer *et al.* (2014) [46]	PSPRS and Schwab and England ADL Scale. Occurrence of adverse events.	Clinical Global Impression of Disease Severity or Change, brain ventricular volume on T1-weighted MRI images; Repeatable Battery for the Assessment of Neuropsychological Status; color trails; phonemic fluency (FAS); letter-number sequencing. Geriatric Depression Scale.	There were no group differences on the primary and secondary endpoints.

Supplementary Table S2. *Continued*

Study	Primary Endpoint Measures	Secondary Endpoint Measures	Main Findings
Progressive supranuclear palsy syndrome			
Bensimon *et al.* (2009) [50]	Death of any cause.	Hoehn and Yahr staging scale; Schwab and England ADL; Clinical Global Impression for Severity; CGI-dysautonomia; MMSE; Short Motor Disability Scale.	No significant difference in survival between groups. No statistically significant difference between groups in progression rate with any of the scales.
Stamelou *et al.* (2008) [51]	PSPRS; UPDRS part II and III; modified H&Y stage; MMSE; FAB; MADRS; Schwab and England. Occurrence of adverse effects.	Cerebral energy metabolites (^{31}P- and ^{1}H-MRS).	Statistically significant improvement on PSPRS and FAB with CoQ10. Significant reduction of low-energy phosphate concentration in occipital lobes.
Litvan *et al.* (2001) [58]	Parkinson's disease quality of life – mobility; MMSE; NPI; California Card sorting Test; Selective reminding test; Sternberg Paradigm; PSPRS.	UPDRS-Quality of life; Apathy Evaluation; Hamilton Depression Scale; Double Memory Test; Go No-Go; Tapping, no tapped.	Significant deterioration of motor function with Donepezil. No significant changes in any of the primary outcome measures. Slight improvement in memory was observed.
Frattali *et al.* (1999) [59]	Oral Motor Scale; duration of swallowing phases.		No statistically significant change on swallow duration or oral motor function with Physostigmine.
Rascol *et al.* (1998) [60]	UPDRS-Part III.	UPDRS motor subscores; stand-walk-sit test; MADRS; CGI.	No significant changes between groups on primary and secondary endpoints.