THE LANCET Neurology

Supplementary webappendix

Supplementary Material

Supplementary Figure 1 Kaplan Meier analysis of time from baseline visit to death stratified by median baseline UMSARS score
Legend: Group "Baseline UMSARS scores below median" – UMSARS scores 0 – 48·9, Group "Baseline UMSARS scores above median" UMSARS scores above 49.

Supplementary Table 1. Progression of clinical scales (complete-case per protocol analysis; sensitivity analysis to linear interpolation approach)

			6-month follow-up		12-month follow-up		18-month follow-up		24-month follow-up	
	N	**Baseline**, mean (SD)	Score, mean (SD)	Difference, mean (SD) (compared to baseline)	Score, mean (SD)	Difference, mean (SD) (compared to baseline)	Score, mean (SD)	Difference, mean (SD) (compared to baseline)	Score, mean (SD)	Difference, mean (SD) (compared to baseline)
UMSARS	22	44·4 (16·5)	52·2 (17·8)	7·8 (7·3)	58·4 (18·5)	14 (11·1)	62·9 (18·2)	18·5 (10·4)	67·4 (17·9)	23 (9·9)
Activities of daily living	22	22 (7·9)	25·3 (8·8)	3·3 (4·3)	29 (9·7)	7 (6)	30·8 (9·2)	8·8 (5·2)	32·2 (9·4)	10.2 (5.6)
Motor examination	22	22·4 (9·3)	26·9 (9·6)	4·5 (4·0)	29·4 (9·3)	7 (5·9)	32·1 (9·9)	9·7 (5·9)	35·2 (9·1)	12.8 (5.2)
Global Disability Scale	22	2·1 (0·7)	2·1 (0·7)	0 (0·5)	2·5 (0·5)	0·4 (0·5)	2·7 (0·5)	0·6 (0·5)	2·7 (0·5)	0·6 (0·6)
Hoehn & Yahr staging	22	3·6 (0·7)	3·8 (0·8)	0·2 (0·6)	4·1 (0·8)	0·5 (0·6)	4·3 (0·8)	0·7 (0·8)	4·2 (1·2)	0·6 (1·1)
Schwab & England ADL	22	5·9 (1·7)	5 (2·3)	-0·9 (1·4)	4·3 (2)	-1·6 (1·3)	3·6 (2·1)	-2·3 (1·3)	3·1 (2·1)	-2·7 (1·4)

The present table presents data from the complete-case per protocol analysis that constrains evaluation to patients having a complete data-set (no missing value at any of the time points). This analysis was performed as sensitivity analysis to the linear interpolation approach.

Abbreviations: UMSARS … unified MSA rating scale, SD … standard deviation

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Supplementary Table 2. Quality of Life in MSA Patients

	Baseline	6-Month Follow-Up	12-Month Follow-Up	18-Month Follow-Up	24-Month Follow-Up
EQ-5D					
EQ-5D Index Score, mean (n, median, SD, 95%CI)	0·35 (78; 0·52; 0·33; 0·27 - 0·42)	0·28 (80; 0·26; 0·34; 0·2 - 0·35)	0·21 (55; 0·15; 0·34; 0·12 - 0·31)	0·17 (45; 0·14; 0·37; 0·06 - 0·28)	0·16 (32; 0·15; 0·31; 0·05 - 0·27)
SF-36 Summary Scores					
Physical Functioning, mean (n, median, SD, 95%CI)	16·99 (73; 10; 19·79; 12·45 - 21·53)	16·78 (74; 5; 24·05; 11·3 - 22·26)	12·04 (55; 0; 23·08; 5·94 - 18·14)	8·04 (37; 0; 12·33; 4·07 - 12·01)	7·83 (24; 0; 13·04; 2·61 - 13·04)
Role-Physical, mean (n, median, SD, 95%CI)	23·36 (73; 0; 33·24; 15·73 - 30·98)	13·21 (74; 0; 24·35; 7·67 - 18·76)	14·9 (55; 0; 24·38; 8·46 - 21·35)	13·24 (37; 0; 25·55; 5 - 21·47)	13·1 (24; 0; 26·95; 2·31 - 23·88)
Bodily Pain, mean (n, median, SD, 95%CI)	44·95 (73; 52; 26·87; 38·78 - 51·11)	55·43 (74; 52; 30·8; 48·41 - 62·45)	61·06 (55; 51; 31·9; 52·63 - 69·49)	67·52 (37; 72; 32·14; 57·16 - 77·87)	59·09 (24; 51; 32; 46·29 - 71·89)
General Health, mean (n, median, SD, 95%CI)	68·75 (73; 70; 13·07; 65·75 - 71·75)	60·59 (74; 68·75; 21·62; 55·66 - 65·51)	61·25 (55; 60; 21·52; 55·56 - 66·94)	63·57 (37; 60; 21; 56·81 - 70·34)	67·88 (24; 68·75; 17·88; 60·73 - 75·04)
Vitality, mean (n, median, SD, 95%CI)	59·12 (73; 60; 12·99; 56·14 - 62·1)	43·15 (74; 37·5; 31·74; 35·92 - 50·38)	34·28 (55; 30; 24·73; 27·74 - 40·82)	40·57 (37; 40; 23·38; 33·04 - 48·11)	29·02 (24; 22·5; 22·34; 20·08 - 37·95)
Social Functioning, mean (n, median, SD, 95%CI)	56·07 (73; 50; 14·57; 52·72 - 59·41)	41·18 (74; 37·5; 28·12; 34·77 - 47·58)	44·32 (55; 50; 28·83; 36·7 - 51·94)	39·67 (37; 37·5; 30·54; 29·83 - 49·51)	43·38 (24; 25; 31·9; 30·62 - 56·15)
Role-Emotional, mean (n, median, SD, 95%CI)	52·82 (73; 33·33; 45·6; 42·36 - 63·28)	56·86 (74; 66·67; 44·26; 46·78 - 66·95)	48·72 (55; 33·33; 44·02; 37·09 - 60·35)	59·8 (37; 100; 46·26; 44·9 - 74·71)	53·97 (24; 66·67; 48·85; 34·42 - 73·51)
Mental Health, mean (n, median, SD, 95%CI)	64·06 (73; 65; 9·85; 61·8 - 66·32)	56·58 (74; 60; 20·47; 51·92 - 61·25)	59·04 (55; 60; 21·49; 53·36 - 64·72)	57·03 (37; 64; 21·83; 49·99 - 64·06)	56·91 (24; 58; 22·09; 48·07 - 65·75)

Abbreviations: UMSARS … unified MSA rating scale, SD … standard deviation, EQ-5D ... EuroQoL 5 Dimensions, SF-36 ... Short Form (36) Health Survey, CI ... confidence interval

Supplementary Table 3. Dynamics of characteristic features

	Baseline	6-Month Follow-up	12-Month Follow-Up	18-Month Follow-Up	24-Month Follow-Up
N	141	94	84	49	43
Autonomic symptoms, n (%)	136 (96·5)	86 (91·5)	81 (96·4)	45 (91·8)	41 (95·3)
Urinary incontinence, n (%)	103 (73)	67 (71·3)	65 (77·4)	37 (75·5)	35 (81·4)
Orthostatic hypotension, n (%)	80 (56·7)	47 (50)	35 (41·7)	13 (26·5)	17 (39·5)
Incomplete bladder emptying, n (%)	72 (51·1)	57 (60·6)	42 (50)	31 (63·3)	22 (51·2)
Constipation, n (%)	82 (58·2)	58 (61·7)	59 (70·2)	33 (67·3)	32 (74·4)
Parkinsonism, n (%)	128 (90,8)	90 (95·7)	74 (88·1)	45 (91·8)	38 (88·4)
Bradykinesia, n (%)	128 (90·8)	90 (95·7)	75 (89·3)	45 (91·8)	38 (88·4)
Rigidity, n (%)	117 (83)	77 (81·9)	71 (84·5)	40 (81·6)	35 (81·4)
Postural instability, n (%)	115 (81·6)	82 (87·2)	70 (83·3)	42 (85·7)	38 (88·4)
Postural tremor, n (%)	79 (56)	60 (63·8)	56 (66·7)	32 (65·3)	27 (62·8)
Rest tremor, n (%)	50 (35·5)	40 (42·6)	29 (34·5)	20 (40·8)	18 (41·9)
Gait freezing, n (%)	56 (39·7)	47 (50)	46 (54·8)	25 (51)	22 (51·2)
Cereballar symptoms, n (%)	101 (71,6)	70 (74·5)	62 (73·8)	37 (75·5)	33 (76·7)
Gait ataxia, n (%)	87 (61·7)	56 (59·6)	50 (59·5)	31 (63·3)	23 (53·5)
Limb ataxia, n (%)	79 (56)	57 (60·6)	49 (58·3)	33 (67·3)	27 (62·8)
Ataxic dysarthria, n (%)	77 (54·6)	64 (68·1)	54 (64·3)	30 (61·2)	25 (58·1)
Pyramidal involvement, n (%)	70 (49,6)	51 (54·3)	46 (54·8)	27 (55·1)	23 (53·5)
Babinski sign, n (%)	38 (27)	31 (33)	31 (36·9)	22 (44·9)	21 (48·8)
Hyperreflexia, n (%)	58 (41·1)	42 (44·7)	37 (44)	16 (32·7)	15 (34·9)

Supplementary Table 4. Progression of COMPASS change scale scores.

	Baseline to 6-months follow-up		6 to 12-months follow-up		12 to 18-months follow-up		18 to 24-months follow-up	
	n of Patients	Score, mean (SD, % of maximum score)	n of Patients	Score, mean (SD, % of maximum score)	n of Patients	Score, mean (SD, % of maximum score)	n of Patients	Score, mean (SD, % of maximum score)
Orthostatic Intolerance (0-60)	28	33 (20•2, 54•9)	25	36•3 (21•8, 60•5)	12	42•9 (11•3, 71•5)	14	28•7 (21•9, 47•9)
Sexual Failure (0-10, males only)	18	6•7 (5•1, 66•7)	18	6•7 (4•2, 66•7)	10	6•5 (4•7, 65)	9	3•3 (5, 33•3)
Bladder Disorder (0-30)	28	9•8 (10•6, 32•7)	25	6•4 (8•2, 21•3)	12	9•6 (8•1, 31•9)	14	5•7 (9•8, 19)
Secretomotor (0-25)	28	3•5 (5•1, 14•1)	25	3•7 (5•7, 14•7)	12	4•8 (7•4, 19)	14	3•1 (5•7, 12•6)
Constipation (0-10)	28	2 (4•6, 19•6)	25	3 (4•1, 30)	12	2•5 (4, 25)	14	1•1 (4•9, 10•7)
Sleep Disorder (0-25)	28	4•4 (8•6, 17•4)	25	5•4 (8•4, 21•6)	12	4•6 (5•8, 18•3)	14	2•9 (6•7, 11•4)
CSS Total Score (0-150/160)	28	56•9 (31, 35•6)	25	54•4 (32•6, 34)	12	69•7 (29•1, 43•5)	14	43•6 (43•7, 27•2)

Abbreviations: SD ... standard deviation, COMPASS … Composite autonomic symptom scale, CSS … COMPASS change scale

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