

Supplementary information on Composite clinical score and PROMs.

Table 1 Changes in clinical characteristics and PROMs from baseline to 3- and 12-month follow-ups

	Baseline	3 months	12 months	p ^a	p ^b
Composite Clinical Score, n= 93					
Total score, median (IQR)	20 (15-25)	5 (2-10)	3 (0-8)	<0.001	<0.001
Symptom score, median (IQR)	15 (12-18)	4 (2-7)	2 (0-7)	<0.001	<0.001
Objective findings, median (IQR)	4 (1-8)	0 (0-2)	0 (0-1)	<0.001	<0.001
≥1 any variable scored 2	91	48	38	-	-
≥1 objective variable scored 2	58	21	7	-	-
≥1 symptom variable scored 2	91	47	36	-	-
Clinical characteristics, n= 93					
Balance, positive test	61 (65.6)	20 (20.5)	15 (16.1)	-	-
Tremor	35 (37.3)	15 (16.1)	10 (10.8)	-	-
Central findings affecting extremities ^c	42 (45.2)	8 (8.6)	6 (6.5)	-	-
Ataxia	27 (29.3)	3 (3.2)	2 (2.1)	-	-
Paresis, extremities ^d	7 (7.5)	7 (7.5)	6 (6.5)	-	-
Facial palsy (all central)	2 (2.2)	1 (1.2)	1 (1.2)	-	-
PROMs					
RAND-36	n= 68	n= 81	n= 82		
summary scores, median IQR					
PCS mean (SD)	29.9 (9.0)	44.4 (10.9)	46.9 (11.1)	<0.001	0.004
MCS mean (SD)	42.3 (11.5)	47.9 (11.5)	51.0 (10.5)	0.001	0.004
Fatigue severity scale, (FSS)	n= 68	n= 82	n= 82		
FSS, median (range)	6.4 (1.9-7)	3.7 (1-7)	3.2 (1-7)	<0.001	0.218
FSS ≥4 n (%)	58 (85.3)	38 (46.3)	33 (40.2)	<0.001	0.225

Higher CSS indicates more symptoms and/or objective findings

^a Change in scores from baseline to 3 months

^b Change in scores from 3 months to 12 months

^c Including a positive plantar reflex, hyperreflexia, spasticity/hypertonia, slower speed or impaired coordination

^d Lumbar, cervical or non-radicular paresis

Table 2 Composite Clinical Score of TBE patients over time across various characteristics (n=93). Median, IQR

Characteristics	Clinical composite score (CCS)			p-value	p-value
	Median (IQR)			(baseline vs	(3 vs 12)
	baseline	3 months	12 months	3)	
CCS N= 93	20 (15-25)	5 (2-10)	3 (0-8)	<0.001	<0.001
Age group					
16-30	22 (20-24)	4 (0-9)	1 (0-3)	0.016	0.125
31-45	20 (17-26)	6 (1-13)	4 (0-10)	<0.001	0.063
46-60	19 (13-25)	4 (2-11)	3 (0-9)	<0.001	0.074
>60	20 (15-24)	5 (2-9)	3 (1-7)	<0.001	0.001
p-value	0.729	0.753	0.410		
Gender					
Male	21 (15-25)	4 (1-10)	2 (0-6)	<0.001	0.003
Female	20 (15-24)	6 (3-11)	3 (1-9)	<0.001	0.013
p-value	0.970	0.098	0.241		
Education					
Education ≤ 12/13 years	20 (15-25)	5 (1-10)	3 (1-7)	<0.001	0.005
Education > 12/13 years	20 (15-25)	5 (2-10)	3 (0-9)	<0.001	0.003
p-value	0.789	0.624	0.638		
Living alone					
Yes	19 (14-26)	5 (2-11)	6 (1-12)	<0.001	1.000
No	20 (15-24)	5 (2-10)	3 (0-7)	<0.001	<0.001
p-value	0.652	0.994	0.310		
Any comorbidity					
Yes	21 (15-24)	6 (3-10)	4 (1-9)	<0.001	0.003
No	19 (15-25)	5 (0-9)	1 (0-6)	<0.001	0.008
p-value	0.944	0.048	0.015		
Hyponatremia					
Yes	21 (15-28)	5 (2-10)	3 (0-9)	<0.001	<0.001
No	19 (13-23)	6 (1-10)	3 (0-8)	<0.001	0.043

p-value	0.053	0.578	0.620		
Biphasic course					
Yes	20 (15-25)	5 (2-10)	2 (0-8)	<0.001	<0.001
No	20 (15-24)	4 (2-10)	3 (1-9)	<0.001	0.029
p-value	0.776	0.812	0.676		
Pleocytosis					
Yes	21 (15-25)	5 (1-10)	3 (0-8)	<0.001	<0.001
No	18 (6-20)	10 (2-12)	3 (2-10)	0.141	0.250
p-value	0.203	0.286	0.464		
Severity of diseases					
Mild	15 (8-19)	3 (0-6)	2 (0-7)	<0.001	0.329
Moderate	21 (16-25)	5 (1-9)	2 (0-6)	<0.001	<0.001
Severe	28 (22-34)	10 (10-12)	10 (5-11)	0.001	0.043
p-value*	<0.001	0.001	0.007		

IQR=interquartile range

*Comparison test with Bonferroni correction: Severity of diseases: **at baseline**, mild vs moderate, adjusted p-value <0.001; mild vs severe, adjusted p-value<0.001; moderate vs severe, adjusted p-value = 0.031; **at 3 months**, mild vs moderate, adjusted p-value =0.269; mild vs severe, adjusted p-value<0.001; moderate vs severe, adjusted p-value = 0.002; **at 12 months**, mild vs moderate, adjusted p-value >0.999; mild vs severe, adjusted p-value = 0.008; moderate vs severe, adjusted p-value =0.003.

Confidence Interval

Characteristics	Clinical composite score (CCS),			Change %	(95% CI)	Change %	(95% CI)
	Mean, (SD)			CCS ^a		CCS ^b	
	baseline	3 months	12 months				
CCS, n= 93	20.0 (7.6)	6.3 (6.1)	4.6 (5.4)	68.4%	(63-74)	77.2%	(72– 82)
By age group, years							
16-30, n= 7	21.6 (3.0)	4.4 (4.3)	2.0 (3.3)	79.5%	(68- 92)	90.7%	(80– 99)
31-45, n= 19	20.9 (6.5)	8.0 (9.0)	5.9 (7.7)	61.8%	(43– 77)	71.6%	(55– 85)
46-60, n= 35	19.5 (8.6)	6.0 (5.0)	4.9 (4.8)	69.2%	(61– 77)	75.1%	(68 – 82)
>60, n= 32	19.7 (7.9)	6.1 (5.5)	4.0 (4.5)	69.1%	(61– 77)	79.9%	(73– 86)
By gender							
Male, n=56	20.0 (8.1)	5.7 (6.3)	4.1 (5.5)	71.4%	(63– 78)	79.2%	(72– 85)
Female, n=37	20.1 (6.9)	7.2 (5.7)	5.1 (5.1)	68.4%	(63– 74)	74.2%	(67– 81)
By education							
n=91							
Education ≤ 12/13 y, n=44	20.2 (8.1)	6.0 (5.6)	4.2 (4.7)	70.1%	(63- 77)	79.2%	(73– 85)
Education > 12/13 y, n=47	20.3 (6.9)	6.7 (6.6)	5.0 (6.0)	66.8%	(58- 75)	75.2%	(69- 82)
By living alone							
Yes, n= 12	18.8 (6.9)	5.8 (4.7)	6.2 (5.8)	68.9%	(55- 82)	67.1%	(52- 82)
No, n= 81	20.2 (7.7)	56.4 (6.3)	4.3 (5.3)	68.4%	(62- 74)	78.6%	(73- 83)
By comorbidity							
Yes, n=47	19.9 (8.1)	7.0 (5.0)	5.2 (4.7)	65.0%	(59- 71)	73.4%	(68- 79)
No, n=46	20.1 (7.1)	5.6 (7.1)	3.8 (5.9)	71.9%	(62- 80)	81.1%	(73- 88)
By biphasic course							
n=92							

Yes, n=52	20.0 (7.4)	6.4 (6.5)	4.5 (5.6)	67.9%	(59- 75)	77.4%	(69- 84)
No, n=40	19.9 (7.9)	6.0 (5.5)	4.7 (5.0)	70.1%	(62- 77)	76.2%	(70- 83)
By pleocytosis							
n=89							
Yes, n= 82	20.4 (7.4)	6.2 (6.3)	4.5 (5.4)	70.0%	(64- 75)	78.0%	(73- 83)
No n= 7	17.5 (7.5)	6.2 (3.3)	4.8 (5.7)	51.1%	(17- 74)	70.4%	(43- 88)
By severity							
Mild, n=23	14.1 (6.9)	4.1 (4.0)	3.9 (4.4)	70.8%	(58- 81)	73.2%	(61- 84)
Moderate, n=59	20.9 (6.3)	6.2 (6.5)	4.1 (5.3)	70.5%	(63- 77)	80.4%	(74- 86)
Severe, n=11	27.3 (7.1)	11.6 (4.7)	8.6 (4.8)	57.5%	(47- 66)	68.4%	(58- 78)

CI=confidence interval

SD=standard deviation

^a Change in CCS from baseline to 3 months

^b Change in CCS baseline to 12 months

Note: Percent change is calculated from baseline to 3 months and from baseline to 12 months. Confidence interval and Percent change is based on bootstrap estimation (10,000 repetitions)

Table 4 RAND-36 scale-scores for the TBE patients at 12-months follow-up and the normal controls

Scales	TBE patients n=89	Normative controls n= 2214	p-value ^a
SF-36 summary scores, mean (SD)			
PCS	47.0 (11.0)	na	-
MCS	50.5 (10.9)	na	-
SF-36 norm-based scales, mean (SD)			
Physical functioning	81.5 (24.0)	88.4 (17.4)	0.008
Role limitations, physical	63.5 (43.0)	79.7 (34.4)	<0.001
Role limitations, emotional	78.3 (36.6)	82.5 (31.8)	0.282
Vitality	57.2 (24.8)	60.3 (20.7)	0.242
Mental health	76.7 (19.8)	78.8 (16.4)	0.343
Social functioning	77.1 (25.5)	86.1 (21.8)	0.001
Bodily pain	75.5 (26.4)	75.7 (25.6)	0.943
General health	67.2 (23.2)	77.4 (21.8)	<0.001

^ap-value for differences between the TBE patients at 12 months follow-up and the reference group
Higher score indicates greater Quality of life

Table 5: SF- 36 scores in all participants and grouped by FSS $\geq$ 4 vs FSS<4 at 12-month follow-up

RAND-36 domaine	All participants n=89 Median, IQR	FSS $\geq$ 4 n=37 Median, IQR	FSS < 4 n=52 Median, IQR	p-value ^a
Physical function	95 (75-100)	70 (50-95)	100 (93-100)	<0.001
Role Physical	100 (25-100)	25 (0-50)	100 (100-100)	<0.001
Role emotional	100 (67-100)	67 (0-100)	100 (100-100)	<0.001
Vitality	60 (35-80)	35 (20-45)	78 (65-83)	<0.001
Mental health	84 (68-92)	64 (52-76)	88 (84-92)	<0.001
Social function	88 (63-100)	50 (50-63)	100 (88-100)	<0.001
Body pain	90 (55-100)	45 (35-78)	100 (90-100)	<0.001
General health	70 (50-85)	50 (35-60)	83 (70-95)	<0.001

^ap-value calculated for comparison between FSS $\geq$ 4 vs FSS<4 (Mann–Whitney U test)