

Real-world effectiveness of abobotulinumtoxinA (Dysport®) in adults with upper limb spasticity in routine clinical practice: an observational study

Supplementary materials

Supplementary methods

Data collection

The following characteristics were recorded during the baseline enrollment visit (visit 1 [V1]) and during V2 and V3: gender, age, height, weight, blood pressure, heart rate, stroke (date and type), spasticity history (pattern (1) (2), onset date of arm spasticity, and laterality), significant medical history/comorbidities (previous/other cerebrovascular disease, chronic lung disease, congestive heart failure, dementia, diabetes, gastric ulcer, kidney disease, liver disease, myocardial infarction, peripheral vascular disease, and cancer), prior and concomitant medications (vasodilator, botulinum toxin, hypotensive drugs, acetylsalicylic acid, nitrate, diuretic drugs, and oral antispastic and thrombolytic drugs), prior and concomitant rehabilitation (physical) therapy, and abobotulinumtoxinA (aboBoNT-A) administration (muscles location, dose, and date of injection).

Neurological examination and assessment were performed during qualification to the drug program using the Modified Ashworth Scale (MAS) and Medical Research Council (MRC, modified) scale. Mini Mental State Examination (MMSE) was obligatory in patients without aphasia. Investigators did not perform the MMSE in patients who had aphasia, due to the condition having a known impact on the outcome of MMSE (3).

References

1. Jost WH, Hefter H, Reissig A, Kollwe K, Wissel J. Efficacy and safety of botulinum toxin type A (Dysport) for the treatment of post-stroke arm spasticity: results of the German-Austrian open-label post-marketing surveillance prospective study. *J Neurol Sci.* 2014;337(1-2):86–90.
2. Hefter H, Jost WH, Reissig A, Zakine B, Bakheit AM, Wissel J. Classification of posture in poststroke upper limb spasticity: a potential decision tool for botulinum toxin A treatment? *Int J Rehabil Res.* 2012;35(3):227-33.
3. Osher JE, Wicklund AH, Rademaker A, Johnson N, Weintraub S. The mini-mental state examination in behavioral variant frontotemporal dementia and primary progressive aphasia. *Am J Alzheimers Dis Other Demen.* 2007;22(6):468–73.

Supplementary Tables

Table S1. Planned sequence of study events and the schedule of assessments performed at each visit.

	Enrolment visit (V1) Day 1	Follow-up visits (V2/V3) every 3–4 months
Written informed consent	✓	
Eligibility check	✓	
Demographic details	✓	
Stroke and spasticity history	✓	
Medical history/comorbidities	✓	
Prior and concomitant medications	✓	
Neurological examination and assessment in scales performed during qualification to drug program (MAS, MRC, MMSE)	✓	
AboBoNT-A dose and injection points (muscles) according to drug program and injector's clinical experience	✓	✓
CGI-I performed during the controlled visits: 2 between V1 and V2 2 between V2 and V3		✓**
<i>Pharmacodynamic data:</i> Total aboBoNT-A dose, interval between injections Healthcare resources: needles, syringes, identification techniques of the muscles (EMS, EMG, USG)	✓	✓
Reporting of serious and non-serious treatment-related AEs (via AE form)	✓	✓
Monitoring of treatment 1. Assessment of response to treatment in MAS (shoulder, wrist, finger, thumbs) 2. Assessment of effect of treatment by patient and physician by CGI-I		✓ ✓ ✓

<p>3. Measurement of upper limb muscle weakness by MRC scale (shoulder, elbow, wrist, fingers, thumbs)</p> <p>4. Information about rehabilitation</p>		<p style="text-align: center;">✓</p>
<p>Visit status</p>	<p style="text-align: center;">✓</p>	<p style="text-align: center;">✓</p>

*AboBoNT-A injected dose was collected for muscles moving the elbow, carpal joint and fingers.

** CGI data were collected from patient medical charts (assessments were performed according to drug programme requirements) and reported in the CRF during V1 and V2.

AboBoNT-A, abobotulinumtoxinA; AE, adverse event; CGI-I, Clinical Global Impression-Improvement; EMS, electrical muscle stimulation; EMG, electromyography; MAS, Modified Ashworth Scale; MRC, Medical Research Council; MMSE, Mini-Mental State Examination; USG, ultrasonography; V, visit.

Table S2. AboBoNT-A injection doses administered at each visit.

AboBoNT-A dose, U	V1 n = 108	V2 n = 98	V3 n = 92	Total dose n = 108
Mean (SD)	853.4 (231.4)	838.9 (248.4)	813.8 (264.1)	2307.8 (798.0)
Median	1000.0	1000.0	1000.0	2500.0
Range	200–1100	200–1100	200–1100	600–3300

AboBoNT-A, abobotulinumtoxinA; SD, standard deviation; V, visit.

Table S3. CGI-I scale at V2 and V3 for the FAS and PP populations.

Parameter	FAS population						PP population					
	V2 (n = 98)			V3 (n = 92)			V2 (n = 57)			V3 (n = 57)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
CGI-I investigators	83			69			57			57		
Very much improved	9	10.8	4.2, 17.5	9	13.0	5.1, 21.0	8	14.0	5.0, 23.1	9	15.8	6.3, 25.3
Much improved	43	51.8	41.1, 62.6	39	56.5	44.8, 68.2	32	56.1	43.3, 69.0	29	50.9	37.9, 63.9
Minimally improved	28	33.7	23.6, 43.9	20	29.0	18.3, 39.7	14	24.6	13.4, 35.7	18	31.6	19.5, 43.6
No change	3	3.6	0.0, 7.6	1	1.4	0.0, 4.3	3	5.3	0.0, 11.1	1	1.8	0.0, 5.2
Improvement*	80	96.4	92.4, 100.0	68	98.6	95.7, 100.0	54	94.7	88.9, 100.0	56	98.2	94.8, 100.0
No change or worsening*	3	3.6	0.0, 7.6	1	1.4	0.0, 4.3	3	5.3	0.0, 11.1	1	1.8	0.0, 5.2
CGI-I patients	83			69			57			57		
Very much improved	16	19.3	10.8, 27.8	14	20.3	10.8, 29.8	12	21.1	10.5, 31.6	12	21.1	10.5, 31.6
Much improved	39	47.0	36.3, 57.7	38	55.1	43.3, 66.8	30	52.6	39.7, 65.6	30	52.6	39.7, 65.6
Minimally improved	22	26.5	17.0, 36.0	16	23.2	13.2, 33.1	11	19.3	9.1, 29.5	14	24.6	13.4, 35.7
No change	6	7.2	1.7, 12.8	1	1.4	0.0, 4.3	4	7.0	0.4, 13.6	1	1.8	0.0, 5.2
Improvement*	77	92.8	87.2, 98.3	68	98.6	95.7, 100.0	53	93.0	86.4, 99.6	56	98.2	94.8, 100.0
No change or worsening*	6	7.2	1.7, 12.8	1	1.4	0.0, 4.3	4	7.0	0.4, 13.6	1	1.8	0.0, 5.2

*Overall rating (cumulative different grades of improvement vs. no change or worsening).

CGI-I, Clinical Global Impression-Improvement scale; FAS, full analysis set; PP, per protocol; V, visit.

Table S4. Global assessment of spasticity (MAS) by joint in A) the FAS and B) the PP population.

A

		Elbow			Wrist			Finger			Thumb		
		V1 n = 108	V2 n = 98	V3 n = 92	V1 n = 108	V2 n = 98	V3 n = 92	V1 n = 108	V2 n = 98	V3 n = 92	V1 n = 108	V2 n = 90	V3 n = 90
MAS score	n (%)	0	1 (1.0)	1 (1.1)	3 (2.8)	2 (2.0)	2 (2.2)	0	0	0	7 (6.5)	2 (2.2)	3 (3.3)
1		1 (0.9)	4 (4.1)	2 (2.2)	13 (12.0)	14 (14.3)	13 (14.1)	3 (2.8)	5 (5.1)	3 (3.3)	10 (9.3)	15 (16.7)	14 (15.6)
1+		7 (6.5)	12 (12.2)	10 (10.9)	12 (11.1)	12 (12.2)	12 (13.0)	2 (1.9)	1 (1.0)	2 (2.2)	12 (11.1)	14 (15.6)	8 (8.9)
2		57 (52.8)	55 (56.1)	49 (53.3)	37 (34.3)	48 (49.0)	46 (50.0)	40 (37.0)	58 (59.2)	66 (71.7)	38 (35.2)	45 (50.0)	53 (58.9)
3		42 (38.9)	26 (26.5)	30 (32.6)	42 (38.9)	22 (22.4)	18 (19.6)	61 (56.5)	32 (32.7)	18 (19.6)	37 (34.3)	10 (11.1)	7 (7.8)
4		0	0	0	1 (0.9)	0	0	2 (1.9)	2 (2.0)	3 (3.3)	4 (3.7)	4 (4.4)	5 (5.6)
Mean (SD) MAS score		2.3 (0.6)	2.1 (0.6)	2.2 (0.6)	2.2 (0.8)	2.0 (0.7)	2.0 (0.7)	2.6 (0.6)	2.3 (0.6)	2.2 (0.6)	2.1 (0.9)	1.9 (0.8)	1.9 (0.8)
Mean change			-0.2	-0.2		-0.2	-0.3		-0.3	-0.4		-0.3	-0.3
95% CI			-0.3;-0.1	-0.3;-0.0		-0.4;-0.1	-0.4;-0.1		-0.4;-0.2	-0.5;-0.2		-0.4;-0.1	-0.4;-0.1
P-value* (vs. V1)			0.0009	0.0077		0.0009	<0.0001		<0.0001	<0.0001		0.0012	0.0023

B

		Elbow			Wrist			Finger			Thumb		
		V1 n = 57	V2 n = 57	V3 n = 57	V1 n = 57	V2 n = 57	V3 n = 57	V1 n = 57	V2 n = 57	V3 n = 57	V1 n = 57	V2 n = 57	V3 n = 57
MAS score	n (%)												
0		1 (1.8)	1 (1.8)	1 (1.8)	3 (5.3)	2 (3.5)	2 (3.5)	0	0	0	3 (5.3)	2 (3.5)	3 (5.3)
1		0	2 (3.5)	1 (1.8)	0	2 (3.5)	2 (3.5)	2 (3.5)	3 (5.3)	2 (3.5)	5 (8.8)	9 (15.8)	9 (15.8)
1+		1 (1.8)	3 (5.3)	2 (3.5)	2 (3.5)	5 (8.8)	4 (7.0)	1 (1.8)	1 (1.8)	2 (3.5)	3 (5.3)	3 (5.3)	2 (3.5)
2		21 (36.8)	29 (50.9)	27 (47.4)	18 (31.6)	29 (50.9)	32 (56.1)	16 (28.1)	36 (63.2)	39 (68.4)	17 (29.8)	36 (63.2)	36 (63.2)
3		34 (59.6)	22 (38.6)	26 (45.6)	33 (57.9)	19 (33.3)	16 (28.1)	36 (63.2)	15 (26.3)	12 (21.1)	27 (47.4)	4 (7.0)	5 (8.8)
4	0	0	0	1 (1.8)	0	1 (1.8)	2 (3.5)	2 (3.5)	2 (3.5)	2 (3.5)	3 (5.3)	2 (3.5)	
Mean (SD) MAS score		2.6 (0.6)	2.3 (0.7)	2.4 (0.6)	2.5 (0.8)	2.2 (0.7)	2.2 (0.7)	2.7 (0.6)	2.3 (0.6)	2.2 (0.6)	2.3 (0.9)	1.9 (0.8)	1.9 (0.8)
Mean change			-0.3	-0.2		-0.3	-0.3		-0.4	-0.4		-0.4	-0.4
95% CI			-0.4;-0.1	-0.3;0.0		-0.5;-0.1	-0.5;-0.1		-0.5;-0.3	-0.6;-0.3		-0.6;-0.2	-0.7;-0.2
P-value* (vs. V1)			0.0007	0.0185		0.0019	0.0009		<0.0001	<0.0001		0.0004	<0.0001

*Wilcoxon signed rank test.

CI, confidence interval; FAS, full analysis set; MAS, Modified Ashworth Scale; PP, per protocol; SD, standard deviation; V, visit.

Table S5. Cumulative MAS score for the FAS and PP populations.

	FAS			PP population		
	V1 n = 108	V2 n = 80	V3 n = 82	V1 n = 57	V2 n = 57	V3 n = 57
Mean (SD) MAS score	11.1 (2.5)	10.2 (2.2)	10.2 (2.5)	11.9 (2.6)	10.4 (2.4)	10.5 (2.5)
Mean change		-1.2	-1.2		-1.5	-1.4
95% CI		-1.7;-0.8	-1.7;-0.7		-2.0;-0.9	-1.9;-0.8
P-value† (vs. V1)		<0.0001	<0.0001		<0.0001	<0.0001

†Paired *t*-test.

CI, confidence interval; FAS, full analysis set; MAS, Modified Ashworth Scale; PP, per protocol; SD, standard deviation; V, visit.

Table S6. Measurement of upper limb muscle weakness by MRC for A) the FAS population and B) the PP population.

A

	n (%)	Elbow flexors			Elbow extensors			Forearm supinators			Forearm pronators		
		V1 n = 108	V2 n = 98	V3 n = 92	V1 n = 108	V2 n = 98	V3 n = 92	V1 n = 108	V2 n = 91	V3 n = 88	V1 n = 108	V2 n = 92	V3 n = 88
MRC score													
0 (no contraction)		8 (7.4)	3 (3.1)	3 (3.3)	14 (13.0)	11 (11.2)	8 (8.7)	31 (28.7)	24 (26.4)	23 (26.1)	25 (23.1)	21 (22.8)	21 (23.9)
1		11 (10.2)	8 (8.2)	9 (9.8)	25 (23.1)	16 (16.3)	15 (16.3)	17 (15.7)	17 (18.7)	19 (21.6)	22 (20.4)	20 (21.7)	17 (19.3)
2		23 (21.3)	18 (18.4)	12 (13.0)	17 (15.7)	17 (17.3)	17 (18.5)	15 (13.9)	15 (16.5)	13 (14.8)	9 (8.3)	10 (10.9)	13 (14.8)
3		29 (26.9)	33 (33.7)	39 (42.4)	16 (14.8)	21 (21.4)	23 (25.0)	18 (16.7)	14 (15.4)	12 (13.6)	24 (22.2)	18 (19.6)	12 (13.6)
4		36 (33.3)	35 (35.7)	28 (30.4)	35 (32.4)	32 (32.7)	28 (30.4)	26 (24.1)	20 (22.0)	21 (23.9)	27 (25.0)	22 (23.9)	25 (28.4)
5 (full strength)		1 (0.9)	1 (1.0)	1 (1.1)	1 (0.9)	1 (1.0)	1 (1.1)	1 (0.9)	1 (1.1)	0	1 (0.9)	1 (1.1)	0
Mean (SD) MRC score		2.7 (1.3)	2.9 (1.1)	2.9 (1.1)	2.3 (1.5)	2.5 (1.4)	2.6 (1.3)	1.9 (1.6)	1.9 (1.5)	1.9 (1.5)	2.1 (1.6)	2.0 (1.6)	2.0 (1.6)
Mean change			0.2	0.1		0.1	0.2		0.0	-0.0		0.0	0.0
95% CI			0.1;0.4	-0.0;0.3		-0.0;0.3	0.0;0.3		-0.1;0.2	-0.2;0.1		-0.1;0.2	-0.1;0.2
P-value* (vs. V1)			0.0094	0.1278		0.0699	0.0373		0.7128	0.6819		0.5013	0.6729

		Wrist flexors			Wrist extensors			Finger flexors			Thumb adductor		
		V1 n = 108	V2 n = 98	V3 n = 92	V1 n = 108	V2 n = 98	V3 n = 92	V1 n = 108	V2 n = 98	V3 n = 92	V1 n = 108	V2 n = 90	V3 n = 88
MRC score	n (%)	28 (25.9)	19 (19.4)	16 (17.4)	38 (35.2)	32 (32.7)	26 (28.3)	19 (17.6)	14 (14.3)	13 (14.1)	19 (17.6)	17 (18.9)	17 (19.3)
0 (no contraction)		30 (27.8)	31 (31.6)	27 (29.3)	23 (21.3)	21 (21.4)	20 (21.7)	17 (15.7)	9 (9.2)	9 (9.8)	25 (23.1)	15 (16.7)	14 (15.9)
1		14 (13.0)	17 (17.3)	16 (17.4)	9 (8.3)	9 (9.2)	11 (12.0)	14 (13.0)	19 (19.4)	17 (18.5)	16 (14.8)	15 (16.7)	16 (18.2)
2		16 (14.8)	14 (14.3)	16 (17.4)	15 (13.9)	14 (14.3)	14 (15.2)	27 (25.0)	26 (26.5)	26 (28.3)	20 (18.5)	18 (20.0)	17 (19.3)
3		20 (18.5)	17 (17.3)	17 (18.5)	22 (20.4)	21 (21.4)	20 (21.7)	30 (27.8)	29 (29.6)	26 (28.3)	27 (25.0)	24 (26.7)	23 (26.1)
4		0	0	0	1 (0.9)	1 (1.0)	1 (1.1)	1 (0.9)	1 (1.0)	1 (1.1)	1 (0.9)	1 (1.1)	1 (1.1)
5 (full strength)													
Mean (SD) MRC score		1.7 (1.5)	1.8 (1.4)	1.9 (1.4)	1.7 (1.6)	1.7 (1.6)	1.8 (1.6)	2.3 (1.5)	2.5 (1.4)	2.5 (1.4)	2.1 (1.5)	2.2 (1.5)	2.2 (1.5)
Mean change			0.1	0.2		0.1	0.2		0.1	0.1		0.0	0.0
95% CI			-0.1;0.2	0.0;0.3		-0.0;0.2	0.0;0.3		-0.0;0.3	-0.1;0.3		-0.1;0.2	-0.2;0.2
P-value* (vs. V1)			0.3044	0.0337		0.1547	0.0075		0.0484	0.3019		0.4601	0.8427

		Shoulder adductors			Shoulder internal rotators		
		V1 n = 108	V2 n = 79	V3 n = 76	V1 n = 108	V2 n = 79	V3 n = 76
MRC score	n (%)						
0 (no contraction)		5 (4.9)	2 (2.5)	3 (3.8)	9 (8.8)	4 (5.1)	4 (5.1)
1		7 (6.9)	2 (2.5)	2 (2.6)	11 (10.8)	10 (12.7)	7 (9.0)
2		20 (19.6)	20 (25.3)	15 (19.2)	23 (22.5)	18 (22.8)	16 (20.5)
3		24 (23.5)	21 (26.6)	23 (29.5)	27 (26.5)	22 (27.8)	22 (28.2)
4		45 (44.1)	34 (43.0)	35 (44.9)	31 (30.4)	25 (31.6)	29 (37.2)
5 (full strength)	1 (1.0)	0	0	1 (1.0)	0	0	
Mean (SD) MRC score		3.0 (1.2)	3.1 (1.0)	3.1 (1.0)	2.6 (1.3)	2.7 (1.2)	2.8 (1.2)
Mean change			-0.0	0.0		0.1	0.2
95% CI			-0.2;0.1	-0.2;0.2		-0.1;0.3	-0.0;0.5
P-value* (vs V1)			0.8783	0.9860		0.3481	0.1051

B

		Elbow flexors			Elbow extensors			Forearm supinators			Forearm pronators		
		V1	V2	V3	V1	V2	V3	V1	V2	V3	V1	V2	V3
		n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57
MRC score	n (%)												
0 (no contraction)		6 (10.5)	3 (5.3)	3 (5.3)	9 (15.8)	8 (14.0)	6 (10.5)	20 (35.1)	19 (33.3)	17 (29.8)	18 (31.6)	18 (31.6)	15 (26.3)
1		5 (8.8)	3 (5.3)	3 (5.3)	11 (19.3)	9 (15.8)	8 (14.0)	7 (12.3)	8 (14.0)	10 (17.5)	8 (14.0)	8 (14.0)	9 (15.8)
2		7 (12.3)	10 (17.5)	7 (12.3)	6 (10.5)	7 (12.3)	9 (15.8)	4 (7.0)	5 (8.8)	5 (8.8)	2 (3.5)	2 (3.5)	4 (7.0)
3		12 (21.1)	17 (29.8)	22 (38.6)	8 (14.0)	11 (19.3)	12 (21.1)	8 (14.0)	7 (12.3)	7 (12.3)	8 (14.0)	8 (14.0)	6 (10.5)
4		27 (47.4)	24 (42.1)	22 (38.6)	23 (40.4)	22 (38.6)	22 (38.6)	18 (31.6)	18 (31.6)	18 (31.6)	21 (36.8)	21 (36.8)	23 (40.4)
5 (full strength)	0	0	0	0	0	0	0	0	0	0	0	0	
Mean (SD) MRC score		2.9 (1.4)	3.0 (1.1)	3.0 (1.1)	2.4 (1.6)	2.5 (1.5)	2.6 (1.4)	1.9 (1.7)	1.9 (1.7)	2.0 (1.7)	2.1 (1.7)	2.1 (1.7)	2.2 (1.7)
Mean change			0.1	0.1		0.1	0.2		0.0	0.0		0.0	0.1
95% CI			-0.1;0.3	-0.1;0.3		-0.2;0.3	0.0;0.4		-0.2;0.2	-0.1;0.2		-0.1;0.1	-0.0;0.3
P-value* (vs. V1)			0.3169	0.2183		0.4705	0.0418		1.0000	0.8258		1.0000	0.2263
		Wrist flexors			Wrist extensors			Finger flexors			Thumb adductor		
		V1	V2	V3	V1	V2	V3	V1	V2	V3	V1	V2	V3
		n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57	n = 57

MRC score													
0 (no contraction)	n (%)	15 (26.3)	11 (19.3)	10 (17.5)	23 (40.4)	21 (36.8)	19 (33.3)	12 (21.1)	9 (15.8)	10 (17.5)	12 (21.1)	11 (19.3)	13 (22.8)
1		12 (21.1)	15 (26.3)	15 (26.3)	5 (8.8)	6 (10.5)	7 (12.3)	5 (8.8)	4 (7.0)	3 (5.3)	6 (10.5)	7 (12.3)	6 (10.5)
2		7 (12.3)	8 (14.0)	8 (14.0)	6 (10.5)	5 (8.8)	6 (10.5)	7 (12.3)	11 (19.3)	10 (17.5)	9 (15.8)	8 (14.0)	9 (15.8)
3		6 (10.5)	7 (12.3)	8 (14.0)	5 (8.8)	6 (10.5)	7 (12.3)	11 (19.3)	11 (19.3)	13 (22.8)	9 (15.8)	9 (15.8)	8 (14.0)
4		17 (29.8)	16 (28.1)	16 (28.1)	17 (29.8)	18 (31.6)	17 (29.8)	21 (36.8)	21 (36.8)	20 (35.1)	20 (35.1)	21 (36.8)	20 (35.1)
5 (full strength)		0	0	0	1 (1.8)	1 (1.8)	1 (1.8)	1 (1.8)	1 (1.8)	1 (1.8)	1 (1.8)	1 (1.8)	1 (1.8)
Mean (SD) MRC score		2.0 (1.6)	2.0 (1.5)	2.1 (1.5)	1.8 (1.8)	1.9 (1.8)	2.0 (1.7)	2.5 (1.6)	2.6 (1.5)	2.6 (1.5)	2.4 (1.6)	2.4 (1.6)	2.3 (1.6)
Mean change			0.1	0.1		0.1	0.1		0.1	0.1		0.1	-0.1
95% CI			-0.1;0.3	-0.1;0.3		-0.0;0.2	-0.0;0.3		-0.0;0.3	-0.1;0.3		-0.2;0.3	-0.3;0.2
P-value* (vs. V1)			0.5692	0.2424		0.2432	0.1162		0.1447	0.4258		0.5521	0.8723

		Shoulder adductors			Shoulder internal rotators		
		V1 n = 57	V2 n = 57	V3 n = 57	V1 n = 57	V2 n = 57	V3 n = 57
MRC score	n (%)						
0 (no contraction)		3 (5.3)	1 (1.8)	2 (3.5)	7 (12.3)	3 (5.3)	3 (5.3)
1		2 (3.5)	1 (1.8)	0	5 (8.8)	7 (12.3)	4 (7.0)
2		8 (14.0)	12 (21.1)	9 (15.8)	9 (15.8)	11 (19.3)	10 (17.5)
3		10 (17.5)	11 (19.3)	15 (26.3)	12 (21.1)	12 (21.1)	13 (22.8)
4		33 (57.9)	32 (56.1)	31 (54.4)	23 (40.4)	24 (42.1)	27 (47.4)
5 (full strength)	1 (1.8)	0	0	1 (1.8)	0	0	
Mean (SD) MRC score		3.2 (1.2)	3.3 (1.0)	3.3 (1.0)	2.7 (1.4)	2.8 (1.3)	3.0 (1.2)
Mean change			0.0	0.0		0.1	0.3
95% CI			-0.1;0.2	-0.2;0.2		-0.2;0.3	-0.0;0.6
P-value* (vs. V1)			0.8724	0.7435		0.6750	0.0874

*Wilcoxon signed rank test.

CI, confidence interval; FAS, full analysis set; MRC, medical research council; PP, per protocol; SD, standard deviation; V, visit.

Table S7. Cumulative MRC score for FAS and PP population.

	FAS population			PP population		
	V1 n = 108	V2 n = 79	V3 n = 76	V1 n = 57	V2 n = 57	V3 n = 57
Mean (SD) MRC score	22.2 (12.1)	23.0 (12.0)	23.8 (11.9)	24.0 (13.3)	24.7 (12.9)	25.1 (12.4)
Mean change		0.8	1.0		0.7	1.1
95% CI		-0.0;1.7	0.0;1.9		-0.2;1.6	0.0;2.2
P-value* (vs. V1)		0.0566	0.0282		0.1178	0.0242

*Wilcoxon signed rank test.

CI, confidence interval; FAS, full analysis set; MRC, Medical Research Council; PP, per protocol; SD, standard deviation; V, visit.