

Supplementary material - Tables

Online supplementary table 1. Baseline clinical and demographic data by centre.			
Variable	London	Oxford	Newcastle
<i>Number of patients</i>	110 (60.8)	46 (25.4)	25 (13.8)
<i>Sex</i>			
Male	81 (73.6)	29 (63.0)	12 (48.0)
Female	29 (26.4)	17 (37.0)	13 (52.0)
<i>Age at enrolment (years)</i>	(<i>n</i> = 110) 66.1 (42.0, 86.3; 10.0) / 66.9 (59.6 – 74.1)	(<i>n</i> = 41) 67.6 (51.0, 80.0; 7.8) / 69.0 (63.0 – 74.0)	(<i>n</i> = 25) 69.3 (48.8, 85.0; 8.4) / 70.4 (64.6 – 74.8)
<i>Time of follow-up (years)</i>	(<i>n</i> = 110) 1.6 (0.0, 7.3; 1.9) / 1.0 (0.0 – 2.6)	(<i>n</i> = 46) 3.2 (0.0, 5.4; 1.7) / 3.9 (1.8 – 4.5)	(<i>n</i> = 25) 1.3 (0.0, 3.7; 1.1) / 1.1 (0.4 – 2.0)
<i>Age of onset (years)</i>	(<i>n</i> = 107) 58.4 (16.4, 82.4; 11.0) / 59.4 (50.2 – 66.5)	(<i>n</i> = 39) 57.1 (36.0, 74.0; 9.8) / 59.0 (50.0 – 65.0)	(<i>n</i> = 24) 60.8 (41.7, 82.1; 9.6) / 59.7 (57.5 – 65.0)
<i>Disease duration (years)</i>	(<i>n</i> = 107) 8.0 (1.2, 30.6; 4.9) / 7.2 (4.5 – 9.8)	(<i>n</i> = 39) 10.9 (1.9, 27.1; 6.0) / 9.9 (6.2 – 15.0)	(<i>n</i> = 24) 8.4 (2.9, 17.3; 3.7) / 7.5 (6.1 – 10.9)
<i>Diagnostic delay (years)</i>	(<i>n</i> = 105) 4.6 (0.0, 18.1; 3.7) / 3.5 (2.0 – 6.4)	(<i>n</i> = 39) 6.5 (1.5, 19.0; 4.0) / 5.3 (3.9 – 6.8)	(<i>n</i> = 21) 6.9 (2.0, 14.0; 3.4) / 6.0 (5.0 – 7.5)
<i>Site of onset*</i>	(<i>n</i> = 106)	(<i>n</i> = 41)	(<i>n</i> = 24)
Proximal muscles of lower limbs	70 (66.0)	27 (65.9)	16 (66.7)
Distal muscles of lower limbs	13 (12.3)	5 (12.2)	1 (4.2)
Proximal muscles of upper limbs	2 (1.9)	0 (0.0)	0 (0.0)
Distal muscles of upper limbs	26 (24.5)	9 (22.0)	3 (12.5)
Bulbar muscles	8 (7.5)	1 (2.4)	4 (16.6)
Other	1 (0.9)	0 (0.0)	0 (0.0)
<i>Nature of onset*</i>	(<i>n</i> = 106)	(<i>n</i> = 41)	NA
Weakness	87 (82.1)	35 (85.4)	
Pain	7 (6.6)	0 (0.0)	
Falls	23 (21.7)	7 (17.1)	

Other	7 (6.6)	0 (0.0)	
<i>Asymmetry</i>			
At onset	71 (70.3) (<i>n</i> = 101)	18 (46.2) (<i>n</i> = 39)	NA
At anytime	80 (80.8) (<i>n</i> = 99)	28 (73.7) (<i>n</i> = 38)	
<i>Initial alternative diagnosis</i>	(<i>n</i> = 101)	(<i>n</i> = 39)	NA
None	68 (67.3)	18 (46.1)	
Polymyositis or other inflammatory myopathy	18 (17.8)	13 (33.3)	
Other myopathy	7 (6.9)	1 (2.6)	
Other neurological disease	5 (5.0)	6 (15.4)	
Other disease	3 (3.0)	1 (2.6)	
<i>Baseline MMT composite score</i> (<i>n</i> = 155)	(<i>n</i> = 109, <i>max</i> = 115) 96.2 (53.1, 112.5; 12.3) / 99.2 (91.5 – 104.3) M: 96.8 (53.1, 112.6; 12.9) / 100.3 (91.2 – 105.1) F: 94.5 (66.8, 111.8; 10.5) / 95.4 (91.9 – 100.8)	(<i>n</i> = 46, <i>max</i> = 75) 62.8 (31.5, 74.4; 8.9) / 65.0 (60.5 – 69.0) M: 64.1 (41.0, 74.4; 8.0) / 65.3 (60.5 – 70.3) F: 60.8 (31.5, 72.0; 10.3) / 63.5 (59.0 – 68.0)	NA
<i>Baseline percent of maximal score (%)</i>	83.6 (46.1, 97.9; 10.7) / 86.2 (79.6 – 90.7) M: 84.1 (46.1, 97.9; 11.2) / 87.2 (79.3 – 91.4) F: 82.2 (58.0, 97.2; 9.1) / 82.9 (79.9 – 87.6)	83.8 (42.0, 99.1; 11.9) / 86.7 (80.7 – 92.0) M: 85.4 (54.7, 99.1; 10.6) / 87.0 (80.7 – 93.7) F: 81.1 (42.0, 96.0; 13.7) / 84.7 (78.7 – 90.7)	
<i>Baseline composite percent predicted MVICT score (%)</i>	(<i>n</i> 82) 32.6 (13.0, 89.0; 14.0) / 30.6 (22.3 – 40.9) M: 31.7 (13.0, 89.0; 14.0) / 29.4 (22.0 – 39.0) F: 35.2 (13.7, 64.8; 14.1) / 34.6 (24.9 – 43.0)	NA	NA
<i>Baseline composite IBMFRS score</i> (<i>max</i> = 40)	(<i>n</i> = 110) 27.1 (10.0, 39.0; 6.2) / 28.5 (23.0 – 32.0) M: 27.8 (10.0, 39.0; 6.1) / 29.0 (24.0 – 32.0) F: 25.2 (10.0, 36.0; 6.3) / 25.0 (22.0 – 30.0)	(<i>n</i> = 46) 26.1 (5.0, 40.0; 7.9) / 27.0 (20.0 – 32.0) M: 26.8 (13.0, 40.0; 7.6) / 27.0 (20.0 – 32.0) F: 25.0 (5.0, 35.0; 8.4) / 26.0 (19.0 – 31.0)	(<i>n</i> = 25) 28.9 (20.0, 36.0; 5.4) / 29.0 (23.0 – 34.0) M: 30.3 (21.0, 36.0; 5.0) / 31.5 (28.0 – 33.5): F: 27.7 (20.0, 35.0; 5.7) / 29.0 (22.0 – 34.0)

<i>Baseline percent of maximal score (%)</i>	67.8 (25.0, 97.5; 15.5) / 71.3 (57.5 – 80.0) M: 69.5 (25.0, 97.5; 15.2) / 72.5 (60.0 – 80.0) F: 63.1 (25.0, 90.0; 15.7) / 62.5 (55.0 – 75.0)	65.3 (12.5, 100.0; 19.6) / 67.5 (50.0 – 80.0) M: 67.0 (32.5, 100.0; 19.0) / 67.5 (50.0 – 80.0) F: 62.5 (12.5, 87.5; 21.0) / 65.0 (47.5 – 77.5)	72.3 (50.0, 90.0; 13.6) / 72.5 (57.5 – 85.0) M: 75.6 (52.5, 90.0; 12.5) / 78.8 (70.0 – 83.8) F: 69.2 (50.0, 87.5; 14.2) / 72.5 (55.0 – 85.0)
Data are expressed as number (n) and (%) for categorical variables and mean (minimum, maximum; standard deviation)/median (interquartile range) for continuous variables. * Participants may have presented with multiple sites or symptoms at onset. F, females; IBMFRS, Inclusion Body Myositis Functional Rating Scale; M, males; MMT, manual muscle testing; MVICT, Maximum Voluntary Isometric Contraction Testing.			

Online supplementary table 2 Baseline composite MMT and QMT scores for each muscle group		
	Mean (standard deviation)	Median (interquartile range)
<i>Composite MMT score (average score)</i>		
Facial muscles	4.6 (0.6)	5.0 (4.3 – 5.0)
Neck extensors	4.9 (0.2)	5.0 (5.0 – 5.0)
Neck flexors	4.4 (0.6)	4.3 (4.0 – 5.0)
Shoulder abductors	4.5 (0.7)	4.8 (4.0 – 5.0)
Elbow extensors	4.2 (0.7)	4.2 (3.9 – 4.7)
Elbow flexors	4.3 (0.7)	4.3 (4.0 – 4.9)
Wrist extensors	4.4 (0.8)	4.7 (4.0 – 5.0)
Wrist flexors	3.9 (0.8)	4.0 (3.5 – 4.5)
Finger extensors	4.1 (0.9)	4.2 (3.9 – 4.7)
First dorsal interosseous	4.2 (0.8)	4.3 (4.0 – 4.7)
Abductor digiti minimi	3.8 (1.0)	4.0 (3.5 – 4.3)
Long finger flexors	2.9 (1.4)	3.3 (2.0 – 4.0)
Short finger flexors	3.7 (1.0)	3.9 (3.0 – 4.5)
Abductor pollicis brevis	4.2 (0.6)	4.3 (4.0 – 4.7)
Hip extensors	4.6 (0.6)	5.0 (4.3 – 5.0)
Hip flexors	4.0 (1.0)	4.2 (3.7 – 4.9)
Knee extensors	3.2 (1.3)	3.5 (2.4 – 4.2)
Knee flexors	4.4 (0.8)	4.7 (4.0 – 5.0)
Ankle plantarflexors	4.7 (0.9)	5.0 (5.0 – 5.0)
Ankle dorsiflexors	4.0 (1.3)	4.5 (4.0 – 5.0)
Ankle inverters	4.4 (1.2)	5.0 (4.3 – 5.0)
Ankle everters	4.2 (1.3)	5.0 (4.0 – 5.0)
Extensor hallucis longus	4.1 (1.4)	4.7 (4.0 – 5.0)
<i>Composite MVICT score (percentage of predicted score, %)</i>		
Elbow extensors	29.9 (18.3)	25.3 (19.5 – 35.7)
Elbow flexors	40.8 (19.4)	39.1 (29.8 – 50.6)
Knee extensors	19.5 (13.3)	17.3 (10.0 – 28.1)
Knee flexors	39.7 (20.7)	38.2 (23.6 – 54.5)
Ankle dorsiflexors	32.8 (19.2)	32.3 (17.3 – 44.0)
Grip	32.7 (22.0)	27.5 (18.7 – 39.5)
MMT, manual muscle testing; MVICT, Maximum Voluntary Isometric Contraction Testing.		

Online supplementary table 3 Output from multilevel models for MMT, MVICT and IBMFRS score over time from onset of disease. Age of onset and gender as covariates.

Composite score	Covariate	Coefficient	95% confidence interval	p value
MMT (%)	Log (time + 1)	-15.44	-17.88 - -12.99	<0.001
	Log (age + 1)	-2.15	-11.1 - 6.8	0.639
	Gender	1.41	-2.35 - 5.16	0.463
MVICT (%)	Log (time + 1)	-15.80	-20.32 - -11.28	<0.001
	Log (age + 1)	0.05	-17.12 – 17.24	0.995
	Gender	4.86	-2.22 – 11.94	0.182
IBMFRS (%)	Log (time + 1)	-26.47	-30.12 - -22.83	<0.001
	Log (age + 1)	-17.05	-29.33 - -4.77	0.007
	Gender	-1.20	-6.14 to 3.74	0.633

IBMFRS, Inclusion Body Myositis Functional Rating Scale; MMT, manual muscle testing; MVICT, Maximum Voluntary Isometric Contraction Testing.

Online supplementary table 4 Output of the adaptive LASSO regression for MMT and QMT model, regressing log(Time+1) against all other covariates, with shrinkage parameter λ less than one standard error from the minimum Mean-Squared Error.

Model	Covariate	Coefficient	
MMT	Intercept	6.280703593	
	Gender	0.051886162	
	log(Age+1)	-0.748227010	
	Facial muscles	0	
	Neck extensors	-0.010156287	
	Neck flexors	0	
	Shoulder abductors	0	
	Elbow extensors	0	
	Elbow flexors	-0.150067586	
	Wrist extensors	0	
	Wrist flexors	0	
	Finger extensors	0	
	First dorsal interosseous	0	
	Abductor digiti minimi	0	
	Long finger flexors	-0.001779063	
	Short finger flexors	0	
	Abductor pollicis brevis	-0.068863433	
	Hip extensors	0	
	Hip flexors	0	
	Knee extensors	-0.028257228	
	Knee flexors	0	
	Ankle plantarflexors	0	
	Ankle dorsiflexors	0	
	Ankle inverters	0	
	Ankle everters	0	
	Extensor hallucis longus	0	
	QMT	Intercept	5.919478278
		Gender	0.145829341
		log(Age+1)	-0.844180486
		Elbow extensors	0
Elbow flexors		0	
Knee extensors		0	
Knee flexors		0	
Ankle dorsiflexors		-0.005628840	
Grip	-0.004556293		

MMT, manual muscle testing; QMT, Quantitative Muscle Testing.

Online supplementary table 5 Output from linear mixed effects models for MMT Factor (mfac), QMT Factor (qfac) and IBMFRS total score over time from onset of disease. Age of onset and gender as covariates.

Composite score	Covariate	Coefficient	Standard Error	p value
Mfac (max = 5)	Intercept	5.605	0.6603	<0.001
Residual = 0.1739	Gender	-0.09225	0.06888	0.1827
	log(Age+1)	-0.06563	0.1504	0.6632
	log(Time+1)	-0.4232	0.05288	<0.001
Qfac (max = 100)	Intercept	82.18	43.97	0.0654
Residual = 6.468	Gender	7.632	4.160	0.0704
	log(Age+1)	-4.870	10.18	0.6340
	log(Time+1)	-14.91	3.054	<0.001
IBMFRS (max = 40)	Intercept	74.42	10.92	<0.001
Residual = 2.787	log(Time+1)	-10.43	0.732	<0.001
	log(Age+1)	-6.194	2.524	0.0147

IBMFRS, Inclusion Body Myositis Functional Rating Scale; MMT, manual muscle testing; QMT, Quantitative Muscle Testing.

Online supplementary table 6 Sample size calculation for a double-blind placebo-controlled trial (1:1 ratio) based on the models developed for each outcome measure and for different trial assumptions.

Disease duration assumption at the start of the trial	1 year disease duration			3 years disease duration			6 years disease duration		
Relative percentage difference in the rate of decline between active and placebo groups	20%	30%	40%	20%	30%	40%	20%	30%	40%
IBMFRS (age and gender perfectly matched between placebo and active groups)									
Power and trial follow-up period	N per treatment arm (N for combined placebo and treatment arms)								
70% power, 1-year follow-up	143 (286)	64 (128)	36 (72)	473 (946)	210 (420)	118 (236)	1321 (2642)	587 (1174)	330 (660)
70% power, 2-year follow-up	49 (98)	22 (44)	12 (24)	143 (286)	64 (128)	36 (72)	373 (746)	166 (332)	93 (186)
70% power, 3-year follow-up	28 (56)	12 (24)	7 (14)	75 (150)	33 (66)	19 (38)	185 (370)	82 (164)	46 (92)
80% power, 1-year follow-up	182 (364)	81 (162)	46 (92)	602 (1204)	267 (534)	150 (300)	1680 (3360)	747 (1494)	420 (840)
80% power, 2-year follow-up	62 (124)	28 (56)	16 (32)	182 (364)	81 (162)	46 (92)	474 (948)	211 (422)	119 (238)
80% power, 3-year follow-up	36 (72)	16 (32)	9 (18)	96 (192)	43 (86)	24 (48)	236 (472)	105 (210)	59 (118)

IBMFRS (no consideration for age and gender)									
Power and trial follow-up period	N per treatment arm (N for combined placebo and treatment arms)								
70% power, 1-year follow-up	253 (506)	113 (226)	63 (126)	836 (1672)	372 (744)	209 (418)	2335 (4770)	1038 (2076)	584 (1168)
70% power, 2-year follow-up	87 (174)	39 (78)	22 (44)	253 (506)	113 (226)	63 (126)	659 (1318)	293 (586)	165 (330)
70% power, 3-year follow-up	50 (100)	22 (44)	12 (24)	133 (266)	59 (118)	33 (66)	327 (654)	145 (290)	82 (164)
80% power, 1-year follow-up	322 (644)	143 (286)	81 (162)	1063 (2126)	473 (946)	266 (532)	2970 (5940)	1320 (2640)	742 (1484)
80% power, 2-year follow-up	110 (220)	49 (98)	28 (56)	322 (644)	143 (286)	81 (162)	838 (1676)	373 (746)	210 (420)
80% power, 3-year follow-up	63 (126)	28 (56)	16 (32)	169 (338)	75 (150)	42 (84)	416 (832)	185 (370)	104 (208)
MMT-5 (age and gender perfectly matched between placebo and active groups)									
Power and trial follow-up period	N per treatment arm (N for combined placebo and treatment arms)								
70% power, 1-year follow-up	346 (692)	154 (308)	87 (174)	1143 (2286)	508 (1016)	286 (572)	3193 (6386)	1419 (2838)	798 (1596)
70% power, 2-year follow-up	118 (236)	53 (106)	30 (60)	346 (692)	154 (308)	87 (174)	901 (1802)	401 (802)	225 (450)
70% power, 3-year follow-up	68 (136)	30 (60)	17 (34)	182 (364)	81 (162)	45 (90)	447 (894)	199 (398)	112 (224)
80% power, 1-year follow-up	440 (880)	196 (392)	110 (220)	1454 (2908)	646 (1292)	363 (726)	4060 (8120)	1804 (3608)	1015 (2030)

80% power, 2-year follow-up	151 (302)	67 (134)	38 (76)	440 (880)	196 (392)	110 (220)	1146 (2292)	509 (1018)	287 (574)
80% power, 3-year follow-up	86 (172)	38 (76)	22 (44)	231 (462)	103 (206)	58 (116)	569 (1138)	253 (506)	142 (284)
MMT-5 (no consideration for age and gender)									
Power and trial follow-up period	N per treatment arm (N for combined placebo and treatment arms)								
70% power, 1-year follow-up	633 (1266)	281 (562)	158 (316)	2090 (4180)	929 (1858)	522 (1044)	5836 (11672)	2594 (5188)	1459 (2918)
70% power, 2-year follow-up	217 (434)	96 (192)	54 (108)	633 (1266)	281 (562)	158 (316)	1648 (3296)	732 (1464)	412 (824)
70% power, 3-year follow-up	124 (248)	55 (110)	31 (62)	332 (664)	148 (296)	83 (166)	818 (1636)	364 (728)	205 (410)
80% power, 1-year follow-up	805 (1610)	358 (716)	201 (402)	2658 (5316)	1181 (2362)	664 (1328)	7422 (14844)	3299 (6598)	1856 (3712)
80% power, 2-year follow-up	275 (550)	122 (244)	69 (138)	805 (1610)	358 (716)	201 (402)	2095 (4190)	931 (1862)	524 (1048)
80% power, 3-year follow-up	158 (316)	70 (140)	39 (78)	423 (846)	188 (376)	106 (212)	1040 (2080)	462 (924)	260 (520)
QMT-2 (age and gender perfectly matched between placebo and active groups)									
Power and trial follow-up period	N per treatment arm (N for combined placebo and treatment arms)								
70% power, 1-year follow-up	432 (864)	192 (384)	108 (216)	1427 (2854)	634 (1268)	357 (714)	3985 (7970)	1771 (3542)	996 (1992)
70% power, 2-year follow-up	148 (296)	66 (132)	37 (74)	432 (864)	192 (384)	108 (216)	1125 (2250)	500 (1000)	281 (562)

70% power, 3-year follow-up	85 (170)	38 (76)	21 (42)	227 (454)	101 (202)	57 (114)	558 (1116)	248 (496)	140 (280)
80% power, 1-year follow-up	550 (1100)	244 (488)	137 (274)	1815 (3630)	806 (1612)	454 (908)	5067 (10134)	2252 (4504)	1267 (2534)
80% power, 2-year follow-up	188 (376)	84 (168)	47 (94)	550 (1100)	244 (488)	137 (274)	1431 (2862)	636 (1272)	358 (716)
80% power, 3-year follow-up	108 (216)	48 (96)	27 (54)	289 (578)	128 (256)	72 (144)	710 (1420)	316 (632)	178 (356)
QMT-2 (no consideration for age and gender)									
70% power, 1-year follow-up	1454 (2908)	646 (1292)	364 (728)	4801 (9602)	2134 (4268)	1200 (2400)	13407 (26814)	5959 (11918)	3352 (6704)
70% power, 2-year follow-up	498 (996)	221 (442)	124 (248)	1454 (2908)	646 (1292)	364 (728)	3785 (7570)	1682 (3364)	946 (1892)
70% power, 3-year follow-up	285 (570)	127 (254)	71 (142)	763 (1526)	339 (678)	191 (382)	1879 (3758)	835 (1670)	470 (940)
80% power, 1-year follow-up	1849 (3698)	822 (1644)	462 (924)	6105 (12210)	2713 (5426)	1526 (3052)	17049 (34098)	7577 (15154)	4262 (8524)
80% power, 2-year follow-up	633 (1266)	281 (562)	158 (316)	1849 (3698)	822 (1644)	462 (924)	4813 (9626)	2139 (4278)	1203 (2406)
80% power, 3-year follow-up	362 (724)	161 (322)	91 (182)	971 (1942)	431 (862)	243 (486)	2390 (4780)	1062 (2124)	597 (1194)
IBMFRS, Inclusion Body Myositis Functional Rating Scale; MMT, manual muscle testing; QMT, quantitative muscle testing.									

Online supplementary table 7 Summary output of Cox (proportional hazards) regression model.

Condition	Hazard ratio \pm 95% CI	Pr(> z)
Gender	0.98 (0.64-1.51)	0.93
Age of onset	1.06 (1.04-1.90)	5.3e-08 ***

Age of onset impacted significantly on time to use of mobility aid. CI = confidence interval. Pr(>|z|) = p value corresponding to z statistics. ***significance $p < 0.001$.