Manuscript title: MD1003 (high dose Pharmaceutical grade Biotin) for the treatment of chronic visual loss related to optic neuritis in multiple sclerosis: A randomized, double-blind, placebo-controlled study

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Online Resources 4. Secondary and exploratory endpoints in the total cohort (double-blind, placebo-controlled phase)

Endpoint	MD1003 (n=65)	Placebo (n=28)	*P* value
Patients with improvement of VA of ≥0.3 logMAR of the selected eye at 100% contrast, n (%)	6 (9.2)	2 (7.1)	0.99
Patients with improvement of binocular VA from <70 to ≥70/100 at 100% contrast, n (%)	2 (9.5)	0 (0.0)	0.99
Eyes with reappearance of P100 waves or improvement of P100 latencies ≥10 ms, n (%)			
Selected eye	14 (21.5)	8 (28.6)	0.50
Non-selected eye	11 (16.9)	5 (17.9)	(for all eyes)
Mean (SD) change from baseline in latencies (all eyes)	-2.49 (9.05)	-0.39 (4.13)	0.46
Mean (SD) change from baseline in amplitudes (all eyes)	-0.276 (2.383)	0.438 (2.827)	0.14
Mean (SD) CGI	3.77 (0.82)	3.92 (0.69)	0.53
Mean (SD) SGI	3.76 (0.88)	3.73 (0.67)	0.90
Mean (SD) change from baseline in composite NEIVFQ-25	4.53 (12.66)	2.99 (8.85)	0.55
Mean (SD) change from baseline in MSQOL-54			
Physical health composite endpoint	0.12 (13.73)	-0.93 (12.58)	0.38
Mental health composite endpoint	-1.21 (16.77)	-7.69 (14.36)	0.09
Cognitive function	0.67 (18.75)	-2.14 (12.35)	0.32
Change in health	5.77 (27.87)	-5.36 (31.44)	0.17
Emotional well-being	-1.55 (14.75)	-5.82 (18.61)	0.25

Energy	0.66 (14.84)	0.43 (16.34)	0.90
Health distress	2.69 (20.12)	-7.14 (17.29)	**0.0153**
Health perceptions	-0.08 (15.23)	-3.57 (14.65)	0.24
Overall quality of life	-0.72 (14.73)	-6.93 (10.66)	**0.0538**
Pain	-1.38 (18.09)	-2.38 (20.23)	0.70
Physical health	-1.23 (28.07)	-1.29 (21.21)	0.28
Role limitations due to physical problems	0.77 (46.76)	6.25 (45.96)	0.64
Role limitations due to emotional problems	-4.62 (45.98)	-14.29 (39.99)	0.40
Satisfaction with sexual function	2.50 (25.08)	0.00 (28.87)	0.80
Sexual function	1.61 (22.45)	-1.49 (23.15)	0.65
Social function	-2.31 (17.77)	-1.19 (19.60)	0.55
Exploratory analyses			
Mean (SD) change from baseline in logMAR at 100% contrast of non-selected eyes, all eyes and binocular vision			
Non-selected eye	-0.002 (0.113)	-0.012 (0.120)	0.73
All eyes	-0.031 (0.168)	-0.024 (0.154)	0.90
Binocular vision	-0.015 (0.141)	-0.024 (0.150)	0.80
Mean (SD) change from baseline in logMAR at 5% contrast			
Selected eye	-0.052 (0.182)	-0.086 (0.218)	0.44
All eyes	-0.051 (0.170)	-0.078 (0.223)	0.50
Patients with improvement of VA in at least one eye at 5% contrast of at least: n (%)			
≥0.3 logMAR	6 (9.2)	4 (14.3)	0.48
≥0.2 logMAR	12 (18.5)	7 (25.0)	0.58
≥0.1 logMAR	30 (46.2)	14 (50.0)	0.82
Mean (SD) change from baseline in mean deviation visual field defects			
Selected eye	0.288 (2.916)	0.526 (2.824)	0.79
All eyes	0.049 (2.819)	0.272 (2.337)	0.53
Mean (SD) change from baseline in RNFL thickness (all eyes)	-0.5 (2.6)	-0.3 (2.7)	0.51
Mean (SD) change from baseline in temporal RNFL (all eyes)	0.1 (4.5)	-0.1 (2.2)	0.80
Mean (SD) change from baseline in macular volume (all eyes)	0.002 (0.141)	0.024 (0.102)	0.35

P values indicating a significant difference are highlighted in bold. *CGI* clinical global impression scale evaluated by the clinician, *MSQOL-54* Multiple Sclerosis Quality of Life-54, *NEIVFQ-25*, National Eye Institute 25-Item Visual Function Questionnaire, *RNFL* retinal nerve fiber layer, *SD* standard deviation, *SGI* clinical global impression scale evaluated by the subject, *VA* visual acuity.