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User trial questionnaire and quality of life responses in patients with multiple sclerosis by neurological and cognitive status: MOSAIC study

B Hughes,[1] J Calkwood,[2] B Hayward,[3] F Dangond[3]

[1]Ruan Multiple Sclerosis Center, Des Moines, IA, USA; [2]Schapiro Center for Multiple Sclerosis, Minneapolis Clinic of Neurology, Golden Valley, MN, USA; [3]EMD Serono, Inc.,* Rockland, MA, USA

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Introduction

- Multiple interferon beta-1a (IFN β-1a) formulations are approved for the treatment of multiple sclerosis (MS). A shared feature of IFN β-1a therapies is a requirement for patients to self-administer subcutaneous or intramuscular injections, although the dosage and schedule of injections varies between treatments.
- Frequently self-administering injections may impact overall patient satisfaction with IFN-based therapies.
- MOSAIC (Multicenter, Open-label, Single-use AutoInjector Convenience study; NCT00958009) was a 12-week, single-arm study designed to evaluate the ease-of-use of Rebidose® (EMD Serono, Inc.,* Rockland, MA, USA), a ready-to-use autoinjector for IFN β-1a 44 µg injected subcutaneously (SC) three times weekly (tiw).[1]
- Included patients (n=109) had relapsing forms of MS (RMS), were 18–65 years of age, and were being treated with IFN β-1a 44 µg SC tiw for ⩾12 weeks before screening.[1]
- In a user trial questionnaire (UTQ) that was given at 12 weeks, 86% of patients rated the autoinjector as 'easy' or 'very easy' to use (primary endpoint). The overall convenience of the autoinjector was the most important perceived benefit.[1]
- In this exploratory analysis, the effects of deficits in neurological and cognitive status (ie, non-normal status) on patient-reported treatment satisfaction, device acceptability, and quality of life (QoL) while using the autoinjector were investigated.

Objective

- To determine the effect of non-normal cognitive or neurological status on patient-reported satisfaction, acceptability, and QoL while using the IFN β-1a SC tiw autoinjector.

Methods

- Patients' perceptions of the autoinjector were assessed using a 32-item UTQ taken after first dose and at 6 and 12 weeks.
- Prespecified analyses compared 14 individual UTQ responses, as well as summed UTQ scores, for patients with normal or non-normal baseline status for 15 neuro-cognitive subtypes using multiple linear regression and analysis of covariance, respectively.
- Least squares means (LSM) analysis was used to generate composite summed scores from 25 preselected UTQ items assessing patient satisfaction and device functionality and convenience.
  - LSM total scores ranged from –50 to 50, with higher scores indicating greater satisfaction (–50: most negative response possible; 0: neutral; 50: most positive response possible).
- Baseline assessments included detailed neurological, mental, visual, and cognitive status exams with patients categorized as having 'normal' or 'non-normal' status for each variable.
  - Cognitive status was assessed using a validated 30-item computerized cognitive battery (MindStreams®, NeuroTrax™).[2]
- Dominant-hand abnormalities were considered relevant to self-administration of injections using the autoinjector and were assessed at baseline. Coordination, muscle tone, strength, reflex status, and sensory status of patients' dominant hand and upper extremities were all assessed as part of the dominant-hand examination.
- Patient QoL was assessed using the 36-item Short Form Health Survey (SF-36) at baseline and Week 12. Score changes from baseline were generated for eight subscales and two summary scores (mental and physical component scores).
- QoL changes from baseline were analyzed in both the intent-to-treat (ITT) population and non-normal subgroups using paired *t*-tests.
- All analyses were conducted using the ITT population (patients who received ⩾1 dose of IFN β-1a SC tiw). In the analysis of individual UTQ items, responses missing data at Week 12 were determined using worst case imputation; patients with missing data at 12 weeks were excluded from the summed LSM analysis.

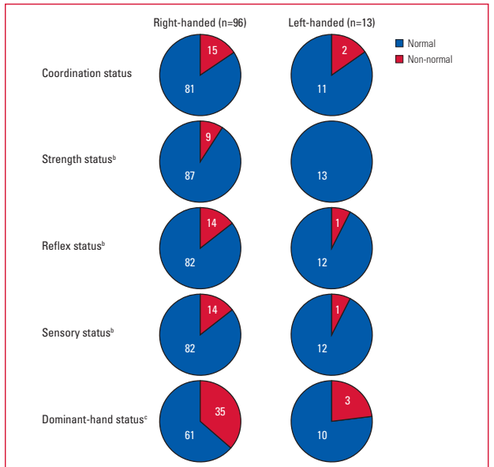
Results

- Baseline patient demographics for the 109 patients included in the ITT populations are shown in **Table 1**. Thirty-eight patients had neurologically abnormal dominant-hand status (**Figure 1**).
  - Ten right-handed patients experienced tremor/dysmetria and 13 had abnormal rapid alternating movements.
  - One left-handed patient experienced mild tremor/dysmetria, while two patients had abnormal rapid alternating movements.
- Summed UTQ response scores (n=95) showed significant differences between normal and non-normal status for three neuro-cognitive subtypes (**Figure 2**).
  - Patients with impaired extra-ocular movements (n=10) and dominant-hand abnormality (n=38) gave less positive summed UTQ responses (LSM scores [normal/non-normal] of 46.7/25.5 and 44.4/27.8, respectively).
  - Patients with non-normal upper extremity sensory status (n=15) considered the autoinjector more positively: LSM scores were 23.0 for normal status and 49.2 for non-normal status.
- Further neuro-cognitive subtypes, including global cognition, executive function, coordination, and visual status, did not significantly affect patients' summed UTQ responses, which remained positive in all cases (**Figure 2**).

Table 1. Baseline patient characteristics, ITT population.

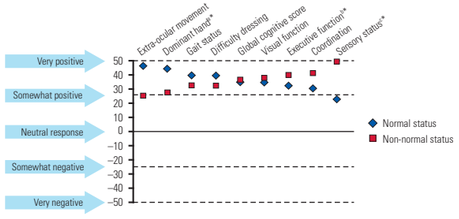
Characteristic	Patients (N=109)
Age, years, mean (SD)	46.00 (9.32)
Sex, n (%)	
Male	33 (30.3)
Female	76 (69.7)
Race, n (%)	
White	94 (86.2)
Black	8 (7.3)
Other	7 (6.4)
Employment status, n (%)	
Employed	66 (60.6)
Unemployed	26 (23.9)
Other	17 (15.6)
Overall neurological status, n (%)	
Neurological normal[a]	14 (12.8)
Neurological abnormal	95 (87.2)
Global cognitive score, n (%)	
Abnormal/probable abnormal	48 (44.0)
Normal/probable normal	48 (44.0)
Insufficient data	13 (11.9)
SF-36 score,[b] mean (SD)	
Physical health component	45.05 (9.7)
Mental health component	52.00 (9.6)

ITT, intent-to-treat; SD, standard deviation; SF-36, 36-item Short Form Health Survey.
[a]Neurological normal patients had normal score on all 72 items assessed.
[b]N=108. Mean SF-36 score in the US population is approximately 50, with an SD of 13–17 depending on the subdomain assessed.[3]



[a]Upper extremity assessments were completed for patients' dominant side (right- or left-handed) only, due to the likelihood that this hand/arm would be used during injection.
[b]Derived from dominant upper extremity assessments.
[c]Derived from tone status (not shown; all patients normal), strength status, reflex status, sensory status, and coordination status for the dominant hand.

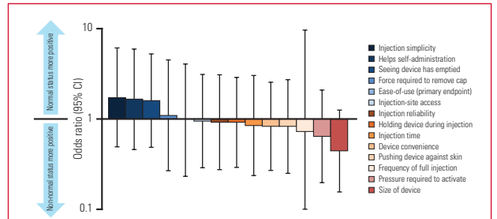
Figure 1. Dominant upper extremity neurological assessments.[a]



Responses to 25 summed UTQ questions (as calculated using LSM, possible score range: –50 to 50) by non-normal and normal status on selected neuro-cognitive assessments at baseline are shown. Statistical comparisons between groups were achieved using analysis of covariance. Only patients with complete data (n=95) are included in this analysis.
LSM, least squares means; UTQ, user trial questionnaire.
[a]Derived from tone status (not shown; all patients normal), strength status, reflex status, sensory status, and coordination status for the dominant hand.
[b]Derived from a subscale of the computerized global cognitive assessment battery.
[c]Derived from dominant upper extremity assessments.
*Denotes statistical significance in response between normal and non-normal patients.

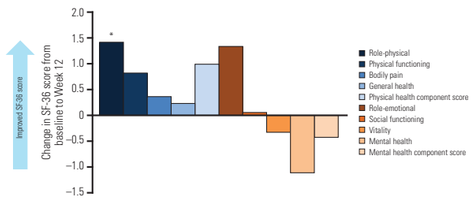
Figure 2. Summed UTQ total scores by normal or non-normal baseline characteristics.

- Individual responses to 14 preselected individual UTQ items were not affected by baseline dominant-hand status (normal vs non-normal; **Figure 3**). Additionally, 100% of patients with non-normal dominant-hand status indicated that they would continue to use the autoinjector after the study ended, while 58.6% of patients with normal dominant-hand status would continue.
  - 84.2% of patients with non-normal dominant-hand status, compared with 87.3% with normal status, rated the autoinjector as either 'easy' or 'very easy' to use (primary endpoint).
- Of the further 14 neuro-cognitive subtypes assessed at baseline, non-normal status for global cognitive score was associated with a significantly greater likelihood of considering the autoinjector reliable (p=0.021), and non-normal gait status was significantly associated with dissatisfaction with the device size (p=0.009). No other UTQ responses were affected by baseline neuro-cognitive status.
- At 12 weeks, QoL (as measured using the SF-36 questionnaire) had improved significantly for the domain assessing physical health ('role-physical') in the ITT population (p=0.04; **Figure 4**).
- QoL increases for physical health ('role-physical') were not seen in the subgroup of patients with non-normal dominant-hand status (mean [standard deviation (SD)] change from baseline: –1.22 [6.827]; p=0.28); however, a non-significant trend toward an increased SF-36 score for the 'general health' domain was seen in this subgroup (mean [SD] change from baseline to Week 12: 2.12 [6.694]; p=0.06; **Figure 5**).
  - Significant improvements in SF-36 domains were seen in subgroups with non-normal memory (n=83, role-physical: p=0.02; role-emotional: p=0.04) and non-normal executive function (n=82; role-physical: p=0.03; physical health component: p=0.04).



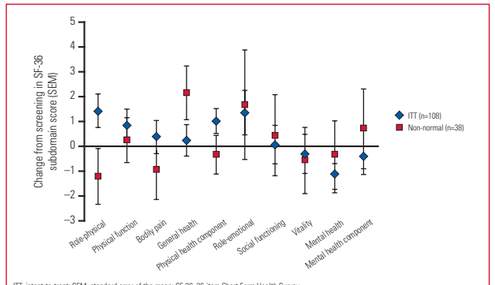
CI, confidence interval; UTQ, user trial questionnaire.

Figure 3. Effect of dominant-hand normality status on individual responses to UTQ questions.



ITT, intent-to-treat; SF-36, 36-item Short Form Health Survey.
*p=0.004.

Figure 4. Change from baseline in domains of the SF-36 questionnaire: ITT population at 12 weeks.



ITT, intent-to-treat; SEM, standard error of the mean; SF-36, 36-item Short Form Health Survey.

Figure 5. Change from baseline in domains of the SF-36 questionnaire: ITT population versus non-normal dominant-hand subgroup.

Conclusions

- After 12 weeks of using the ready-to-use autoinjector, patients' positive opinions of the device were unaffected by the majority of baseline neuro-cognitive abnormalities assessed.
- Deficits in extra-ocular movements and dominant-hand status were associated with reduced overall satisfaction with the autoinjector; however, in a separate analysis, responses to individual UTQ questions were unaffected by baseline neuro-cognitive status. Notably, 100% of patients with deficits in dominant-hand status reported that they would continue to use the autoinjector at study end.
- Patients with deficits in upper extremity status rated the autoinjector more positively than any other subgroup, suggesting that the device ergonomics may not hinder use by impaired patients. Further studies are needed to corroborate these findings.
- Increases in SF-36 QoL physical health domains were seen in both the ITT population and in patients with deficits in memory or executive function.
- Limitations of this study include the short study duration and the small sample size of some of the subgroups with neuro-cognitive deficits.
- Overall patient perceptions of the ready-to-use autoinjector were positive in all neuro-cognitive subgroups and ranged from 'somewhat satisfied' to 'very satisfied.' Overall, 96% of patients rated the device positively for the ability to deliver the full injection of IFN β-1a 44 µg SC tiw over 12 weeks.

References

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