Subjective and objective adherence in patients with multiple sclerosis using RebiSmart®: The CORE study

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Introduction

- Given the chronic nature of multiple sclerosis (MS), the need for long-term treatment makes adherence particularly challenging.
- MS patients with poor levels of adherence to disease-modifying treatments have a higher risk of relapse[1,2] and hospitalization, and incur higher MS-related medical costs.[1] Factors that influence poor adherence include forgetfulness,[3] treatment-related adverse events (including injection site reactions and pain)[3] and anxiety about self-injection.[4]
- RebiSmart® is an electronic, multidose, mechanical autoinjector for subcutaneous (sc) injection of interferon (IFN) β-1a. The electronic log-file records objective adherence data and enables patients to avoid missed injections leading to poor adherence.[5-7]
- Few Swiss-derived data are available regarding MS therapy adherence.

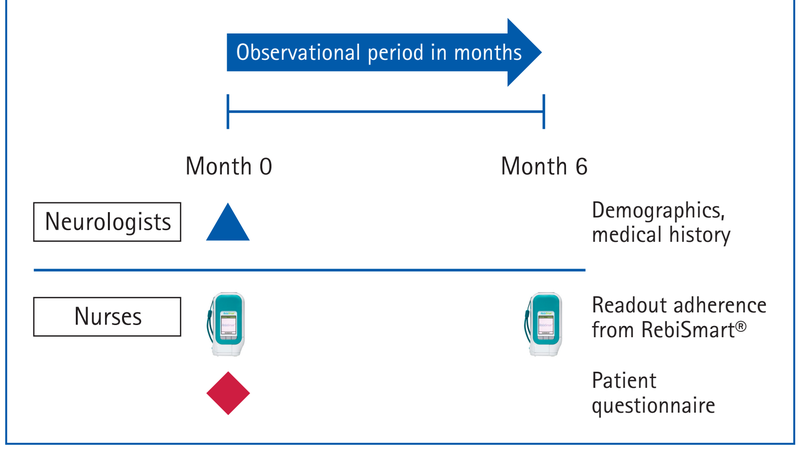
Objectives

- To compare objectively recorded dosing history using RebiSmart® with subjectively patient-reported adherence, and to identify demographic, clinical and RebiSmart® features associated with therapy adherence in Swiss MS patients.

Methods

- CORE (**C**omparison **O**f subjective patient-reported adherence with the objective adherence in **R**ebif patients using RebiSmart® **E**lectronic device): a Swiss, multicenter, observational practice survey (**Figure 1**).
- Patients were treated according to the clinical and paraclinical course and laboratory findings as routinely evaluated by the physician (i.e. no practice survey-specific clinical interventions).
- Inclusion criteria:
  - Patients with relapsing remitting MS (RRMS)
  - Use of sc IFN β-1a 44/22 µg using RebiSmart® for ≥9 months
  - Patients capable of self-injections using RebiSmart®
  - Signed informed consent.
- Primary aim:
  - Difference between objective adherence (measured using the RebiSmart® log-file), and self-reported adherence (based on a patient questionnaire).
  - Self-reported adherence and non-adherence were defined as missing 0 and ≥1 injections, respectively, during 9 months before baseline.
- Secondary aims:
  - Difference between objective adherence 9 months before baseline (retrospective) and 6 months after baseline (prospective)
  - Identification of factors, using patient and neurologist questionnaires, associated with objective adherence level (i.e. low [<90%], medium [90–99.9%], and high [>99.9%]).
- Statistical analysis:
  - The difference between objective and self-reported adherence was analyzed using one-way analysis of variance (ANOVA).
  - Wilcoxon matched pairs test was used to analyze the difference between retrospective and prospective objective adherence.
  - Ordinal regression models were used to investigate factors associated with greater objective adherence.

Figure 1. CORE study design



Results

Patient demographics

- A total of 56 patients completed baseline questionnaires, of which 53 had been on sc IFN β-1a 44/22 µg using RebiSmart® for >9 months and provided data for analysis (for 2 patients the form was not evaluable; 1 patient was on treatment for <9 months).
- Baseline characteristics and demographics are shown in **Table 1**.

Table 1. Baseline characteristics and demographics

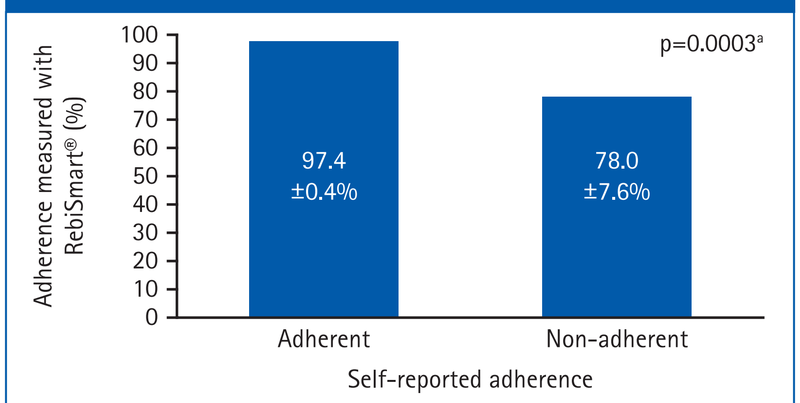
Characteristic	N=53
Mean (SD) age, years	48.2 (12.1)
Female, n (%)	41 (77.4)
Median (range) last known EDSS[a]	2.0 (0.0–4.5)
Median (range) time since diagnosis, years[b]	6.5 (1.0–22.0)
Median (range) duration of therapy, months[c]	47.0 (2.0–240.0)
Median (range) duration of therapy with sc IFN β-1a, months	24.0 (10.0–144.0)
Patients with relapse during past 9 months, n (%)	8 (15.1)

[a]Data missing for 2 patients; [b]Data missing for 1 patient; [c]Data missing for 5 patients
EDSS, Expanded Disability Status Scale; IFN, interferon; sc, subcutaneous; SD, standard deviation.

Objective adherence vs subjective adherence

- Mean (SD) objective adherence in the self-reported adherent group (n=33) was 97.4 (0.4)%.
- Mean (SD) objective adherence with RebiSmart® in the self-reported non-adherent group (n=20) was 78.0 (7.6)%.
- Objective adherence was significantly different between self-reported adherent and non-adherent patients (p=0.0003; **Figure 2**).

Figure 2. Difference between objective adherence measured with RebiSmart® between self-reported adherent and non-adherent patients



[a]p-value is for self-reported adherent vs non-adherent groups, analyzed using ANOVA.

Retrospective adherence vs prospective adherence

- Mean (SD) retrospective objective adherence (9 months before baseline, n=53) was 90.1 (3.9)%.
- Mean (SD) prospective objective adherence (6 months after baseline, n=53) was 90.7 (3.5)%.
- The difference between objective retrospective and prospective adherence was not statistically significant (p=0.75).

Factors associated with objective adherence

- 15 (28.3%), 18 (34.0%) and 20 (37.7%) patients had low (<90%), medium (90-99.9%) and high (>99.9%) objective adherence, respectively.
- Variables that were significantly associated with greater objective adherence were **(Table 2)**:
  - Older age;
  - Greater EDSS;
  - Higher subjective estimates of adherence provided by the treating neurologists.
- Characteristics of RebiSmart® (scored from 1 = not at all important, to 10 = extremely important) that were significantly associated with greater objective adherence were **(Table 2)**:
  - Perceived importance of ease of administration with RebiSmart®;
  - Perceived importance of ease of storage of RebiSmart®.
- Greater objective adherence was significantly associated with being more informed about features of RebiSmart® (scored from 1 = do not agree at all, to 10 = totally agree) **(Table 2)**.

Table 2. Factors impacting adherence

Factor	Adherence group: Low (<90%) n=15	Medium (90–99.9%) n=18	High (>99.9%) n=20	p-value[a]
Patient's age, years	42.3 (12.0)	47.6 (11.5)	53.1 (11.0)	0.006
Patient's last known EDSS[b]	1.6 (0.9)	2.2 (1.1)	2.7 (1.2)	0.006
Neurologists' estimations of adherence	8.5 (2.3)	8.9 (1.2)	9.6 (0.7)	0.023
Patient's previous MS therapy	0.2 (0.4)	0.3 (0.5)	0.0 (0.0)	0.090
Importance of ease of administration with RebiSmart®	8.3 (1.5)	9.1 (1.7)	9.7 (0.9)	0.01
Importance of storage of RebiSmart®	6.9 (2.6)	7.3 (2.8)	8.7 (1.7)	0.032
Being well informed about features of RebiSmart®	9.5 (0.7)	9.7 (0.6)	10 (0.0)	0.009
Importance of treatment in delaying progression of disease	8.6 (1.9)	9.7 (0.6)	8.3 (2.1)	0.830
Importance of frequency of administration	7.8 (1.8)	8.2 (2.0)	7.9 (2.8)	0.943

[a]p-value is for linear relationship between each factor and adherence group levels
[b]Data missing for 2 patients
Data are reported as mean (SD)
EDSS, Expanded Disability Status Scale; IFN, interferon; sc, subcutaneous; SD, standard deviation.

Conclusions

- **In this Swiss patient population, objectively-measured adherence to sc IFN β-1a administered by RebiSmart® is very high and largely consistent with subjective self-reported adherence using questionnaires. There was no substantial change in objective adherence after patients initiated the study and became aware of the future adherence controls.**
- **Older age and greater disability were associated with greater objective adherence to RebiSmart®.**
- **The subjective estimate of adherence provided by the treating neurologists was generally in line with objective adherence to RebiSmart®.**
- **Patients with greater adherence to RebiSmart® considered ease of administration and storage to be important and were well informed about RebiSmart® features.**

References

1. Steinberg S.C., et al. Clin Drug Investig. 2010;30:89–100.
2. Al-Sabbagh A, et al. J Neurol. 2008;255(Suppl 2):S79.
3. Treadaway K, et al. J Neurol. 2009;256:568–76.
4. Mohr D.C., et al. Ann Behav Med. 2001;23:125–32.
5. Devonshire V.A., et al. Ther Deliv. 2011;2:1455–65.
6. Bayas A, et al. Expert Opin Drug Deliv. 2015;12:1239–50.
7. Lugaresi A, et al. BMC Neurol. 2012;12:7.

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