Autoinjector ease-of-use in patients with multiple sclerosis treated with interferon beta-1a subcutaneously: preliminary data from REDEFINE

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2016 Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC); June 1–4, 2016; National Harbor, MD, USA; Poster PO04

Introduction

- Various injection devices are available for patients with multiple sclerosis (MS) to self-inject disease-modifying drugs, but information regarding the usability and patient satisfaction with different devices is limited.
- For patients taking interferon beta-1a subcutaneously three times weekly (IFN β-1a SC tiw), options include a pre-assembled, single-use autoinjector and a reusable autoinjector with an adjustable injection-depth feature (**Table 1**).
- Understanding patient perspective with relation to the ease-of-use of each device, as well as overall patient satisfaction with each device, may help healthcare providers identify the most suitable device for the injection of IFN β-1a SC tiw for their patients with relapsing forms of MS (RMS).
- The REDEFINE (REbif® Rebidose® vs Rebiject II® autoinjector trial DEFINing patient reported Ease-of-use) study is a crossover study designed to compare relative ease-of-use of the two autoinjector devices, as well as the impact of previous experience.

Table 1. Comparison of single-use and reusable autoinjectors.

	Single-use autoinjector	Reusable autoinjector
Pre-assembled?	✓	✗
Assembly/injection procedure	3 steps	12 steps
Single use?	✓[a]	✗
Suitable for titration?	✓	✓
Training needs	Minimal	Moderate
Adjustable injection depth?	✗	✓
Inspection of contents?	Transparent window enables 360° inspection	✗
Needle shield	Shielded	Shield before and during injection; exposed during disposal
Safety lock?	✓	✓

The images of single-use and reusable autoinjectors are not shown as actual size or to scale. Single-use autoinjector is the Rebif® Rebidose® device; reusable autoinjector is the Rebiject II® device.
[a]Single use autoinjector is recycled via the Rebif® Rebidose® sharps disposal program.

Objective

- To compare patient-assessed relative ease-of-use of two autoinjectors for administration of IFN β-1a SC tiw in preliminary results from a crossover study.

Methods

Study overview

- This was a Phase IV, randomized, prospective, US-based, multicenter, crossover study (ClinicalTrials.gov identifier: NCT02019550) evaluating patient ease-of-use with Rebif® Rebidose® (single-use) versus Rebiject II® (reusable) autoinjectors in patients with RMS treated with IFN β-1a 44 µg SC tiw (study completed in March 2016).

Patients

- Eligible patients had to have been receiving IFN β-1a SC tiw by manual injection for at least 5 weeks before the screening assessment.
  - Patients with current or previous use of either the single-use or the reusable device were included.
- Patients who received any MS therapy other than IFN β-1a 44 µg SC tiw within the 12 weeks before screening or at any time during the study were excluded.

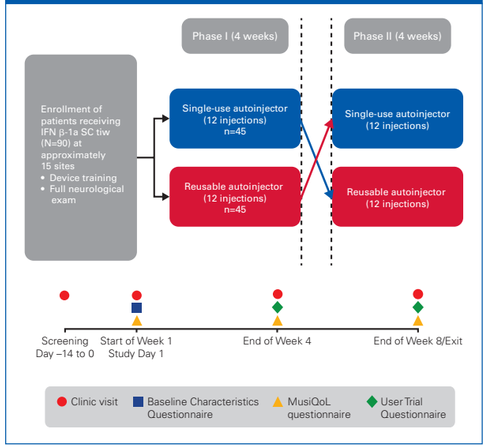
Study design and assessments

- Patients self-injected IFN β-1a 44 µg SC tiw and received training to perform a total of 24 injections over the 8-week treatment period in a crossover design (12 injections via the single-use autoinjector during the first 4 weeks, crossing over to 12 injections via the reusable autoinjector during the second 4 weeks in one study sequence, and vice versa in the other study sequence; **Figure 1**).

Endpoints

- The primary endpoint was the proportion of patients rating each device as easy to use (response categories of "easy" or "very easy") following a 4-week period using each device, with or without regard to previous experience.
  - This endpoint was determined by patients' responses to User Trial Questionnaire (UTQ) Question 14, which asks "Overall, how do you rate your experience with using the injection device?"
- Secondary endpoints included how patients rated each device on the other questions of the UTQ, which assessed topics such as:
  - Level of satisfaction with using the device while traveling
  - Amount of time needed to complete the injection
  - Level of convenience of using the device
  - Amount of needle anxiety while using the device
  - Overall satisfaction with the injection device.
- Change in quality of life as assessed by the Multiple Sclerosis International Quality of Life (MusiQoL [© MusiQoL 2008][1]) questionnaire was also a secondary endpoint.

Figure 1. Study design.



Single-use autoinjector is the Rebif® Rebidose® device; reusable autoinjector is the Rebiject II® device.
IFN β-1a, interferon beta-1a; MusiQoL, Multiple Sclerosis International Quality of Life; SC, subcutaneously; tiw, three times weekly.

Results

- Preliminary data, as of November 9, 2015, were available from 60 subjects: 28 randomized to use the single-use autoinjector followed by the reusable autoinjector and 32 to the reusable autoinjector followed by the single-use device.
- Demographic and baseline characteristics are shown in **Table 2**.
  - 82.1% of patients in the initial single-use autoinjector and 53.1% in the initial reusable autoinjector groups were female.
  - 26 (43.3%) had previous device use with the reusable autoinjector, 23 (38.3%) with manual injection, and 11 (18.3%) with the single-use autoinjector.
- Disability level per questionnaire was similar between groups: overall, 26.7% had no disability while 20.0% had a moderate level of disability (**Table 3**).

Primary endpoint: Response to "Overall experience with using injection device"

- Overall, 64.7% of patients found the single-use autoinjector very easy or easy to use, versus 74.5% for the reusable autoinjector (difference –9.8%; p=0.3125); 45.1% felt both were easy or very easy to use (**Figure 2**).
- Five (9.8%) patients found the single-use autoinjector very difficult or difficult to use, and 4 (7.8%) patients found the reusable autoinjector very difficult or difficult to use.

Secondary endpoints

- Among those with previous device use, no significant differences were seen in the proportion identifying either device as very easy or easy to use (**Table 4**).
- 84.3% of patients felt that both devices completed injections in a satisfactory amount of time (**Table 5**).
- 98.0% felt the single-use device required a satisfactory number of steps and 82.4% felt this way for the reusable autoinjector (p=0.007; **Table 5**).
- 60.8% and 94.1% found storage of the single-use and reusable autoinjectors, respectively, to be convenient (p<0.001; **Table 5**).
- Two MusiQoL dimensions (symptoms [Spearman's correlation 0.3279; p=0.0155] and coping [0.2750; p=0.0484]) were correlated with ease-of-use after 4 weeks, but not 8 weeks.

Table 2. Demographics and baseline characteristics.

		Single-use > reusable autoinjector (n=28)	Reusable > single-use autoinjector (n=32)	Total (N=60)
Age at randomization, years				
	n	28	32	60
	Mean (SD)	50.0 (9.45)	46.9 (11.32)	48.4 (10.52)
Sex, n (%)				
	Male	5 (17.9)	15 (46.9)	20 (33.3)
	Female	23 (82.1)	17 (53.1)	40 (66.7)
Race, n (%)				
	White	24 (85.7)	30 (93.8)	54 (90.0)
	Black/African American	4 (14.3)	0 (0.0)	4 (6.7)
	Other	0 (0.0)	2 (6.3)	2 (3.3)
Type of previous device use, n (%)				
	Manual	10 (35.7)	13 (40.6)	23 (38.3)
	Single-use	4 (14.3)	7 (21.9)	11 (18.3)
	Reusable	14 (50.0)	12 (37.5)	26 (43.3)
Symbol Digit Modalities Test (oral score)				
	n	24	30	54
	Mean (SD)	45.2 (14.46)	51.1 (15.63)	48.5 (15.28)
	Median	46.5	52.0	49.0
	Min, max	(10, 75)	(17, 95)	(10, 95)
Symbol Digit Modalities Test (written score)				
	n	28	32	60
	Mean (SD)	44.1 (11.55)	47.5 (11.81)	45.9 (11.71)
	Median	44.0	48.5	46.0
	Min, max	(23, 68)	(22, 68)	(22, 68)

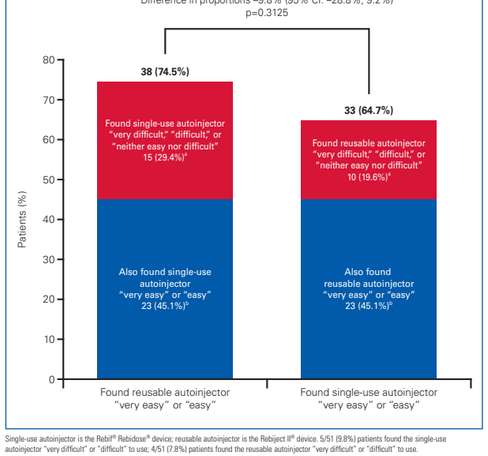
Single-use autoinjector is the Rebif® Rebidose® device; reusable autoinjector is the Rebiject II® device.
SD, standard deviation.

Table 3. Baseline questionnaire.

		Single-use > reusable autoinjector (n=28)	Reusable > single-use autoinjector (n=32)	Total (N=60)
n (missing)		28 (0)	28 (4)	56 (4)
Average no. of nights/month spent traveling away from home	Mean (SD)	2.82 (3.345)	1.25 (2.717)	2.04 (3.122)
	Median	2.00	0.00	0.00
	Min, max	(0.0, 14.0)	(0.0, 13.0)	(0.0, 14.0)
Highest education completed, n (%)	High school/GED	7 (25.0)	13 (40.6)	20 (33.3)
	Associate's degree	3 (10.7)	4 (12.5)	7 (11.7)
	Bachelor's degree	10 (35.7)	9 (28.1)	19 (31.7)
	Postgraduate (master's, doctorate)	6 (21.4)	2 (6.3)	8 (13.3)
	Other	2 (7.1)	0 (0.0)	2 (3.3)
Difficulty dressing, n (%)	No difficulty	20 (71.4)	19 (59.4)	39 (65.0)
	A little difficulty	7 (25.0)	7 (21.9)	14 (23.3)
	Moderate difficulty	1 (3.6)	2 (6.3)	3 (5.0)
	A great deal of difficulty	0 (0.0)	0 (0.0)	0 (0.0)
Difficulty lifting full cup/glass to mouth, n (%)	No difficulty	23 (82.1)	21 (65.6)	44 (73.3)
	A little difficulty	3 (10.7)	7 (21.9)	10 (16.7)
	Moderate difficulty	2 (7.1)	0 (0.0)	2 (3.3)
	A great deal of difficulty	0 (0.0)	0 (0.0)	0 (0.0)
Level of disability, n (%)	None	8 (28.6)	8 (25.0)	16 (26.7)
	Mild	14 (50.0)	13 (40.6)	27 (45.0)
	Moderate	5 (17.9)	7 (21.9)	12 (20.0)
	Severe	1 (3.6)	0 (0.0)	1 (1.7)
Difficulty distinguishing colors, n (%)	No difficulty	26 (92.9)	24 (75.0)	50 (83.3)
	A little difficulty	2 (7.1)	2 (6.3)	4 (6.7)
	Moderate difficulty	0 (0.0)	1 (3.1)	1 (1.7)
	A great deal of difficulty	0 (0.0)	1 (3.1)	1 (1.7)
Difficulty reading newspaper (with glasses if needed), n (%)	No difficulty	14 (50.0)	15 (46.9)	29 (48.3)
	A little difficulty	8 (28.6)	10 (31.3)	18 (30.0)
	Moderate difficulty	6 (21.4)	2 (6.3)	8 (13.3)
	A great deal of difficulty	0 (0.0)	1 (3.1)	1 (1.7)
Anxiety about giving self-injection, n (%)	Not at all anxious	7 (25.0)	18 (56.3)	25 (41.7)
	A little anxious	15 (53.6)	8 (25.0)	23 (38.3)
	Moderately anxious	3 (10.7)	1 (3.1)	4 (6.7)
	Very anxious	3 (10.7)	1 (3.1)	4 (6.7)
	Extremely anxious	0 (0.0)	0 (0.0)	0 (0.0)
Generally afraid of needles, n (%)	Not at all	10 (35.7)	15 (46.9)	25 (41.7)
	A little	12 (42.9)	8 (25.0)	20 (33.3)
	Moderately	2 (7.1)	1 (3.1)	3 (5.0)
	Very	3 (10.7)	3 (9.4)	6 (10.0)
	Extremely	1 (3.6)	1 (3.1)	2 (3.3)

Single-use autoinjector is the Rebif® Rebidose® device; reusable autoinjector is the Rebiject II® device.
SD, standard deviation.

Figure 2. Response to "Overall experience with using injection device."



Single-use autoinjector is the Rebif® Rebidose® device; reusable autoinjector is the Rebiject II® device. 5/51 (9.8%) patients found the single-use autoinjector "very difficult" or "difficult" to use; 4/51 (7.8%) patients found the reusable autoinjector "very difficult" or "difficult" to use.
CI, confidence interval.
[a]Patients with discordant responses. [b]Patients with concordant responses.

Table 4. Response to "Overall experience with using injection device" by previous device use.

Type of previous device use	Single-use autoinjector	Reusable autoinjector	Both devices[a]	p value[b]	Difference[c] (95% CI)
Manual (n=18)					
Very easy/easy	13 (72.2%)	12 (66.7%)	8 (44.4%)	1.000	5.6% (–27.0%, 38.1%)
Very difficult/difficult/neither	5 (27.8%)	6 (33.3%)	1 (5.6%)		
Rebif® Rebidose® (n=10)					
Very easy/easy	7 (70.0%)	7 (70.0%)	4 (40.0%)	1.000	0.0% (–48.0%, 48.0%)
Very difficult/difficult/neither	3 (30.0%)	3 (30.0%)	0 (0.0%)		
Rebiject II® (n=22)					
Very easy/easy	12 (54.5%)	18 (81.8%)	10 (45.5%)	0.109	–27.3% (–53.0%, –1.5%)
Very difficult/difficult/neither	10 (45.5%)	4 (18.2%)	2 (9.1%)		

Single-use autoinjector is the Rebif® Rebidose® device; reusable autoinjector is the Rebiject II® device.
CI, confidence interval.
[a]Patients with concordant responses. [b]Based on exact sign test of equality of paired proportions. [c]Difference of proportions.

Table 5. User Trial Questionnaire responses.[a]

	Single-use autoinjector strongly agree/ agree	Reusable autoinjector strongly agree/agree	p value[b]	Difference in proportions (95% CI)	Strongly agree/ agree for both devices
Satisfied with amount of time it took to complete injection, n (%)	46 (90.2)	47 (92.2)	0.705	–2.0% (–12.1%, 8.2%)	43 (84.3)
Satisfied with number of steps it took to complete injection, n (%)	50 (98.0)	42 (82.4)	0.007	15.6% (4.3%, 27.1%)	41 (80.4)
Overall experience with holding device, n (%)[c]	34 (66.7)	38 (74.5)	0.341	–7.8% (–24.0%, 8.3%)	27 (52.9)
Convenience of using the device, n (%)[c]	43 (84.3)	37 (72.5)	0.150	11.8% (–4.2%, 27.7%)	31 (60.8)
Convenient to store the injection device, n (%)	31 (60.8)	48 (94.1)	<0.001	–33.3% (–48.4%, –18.3%)	29 (56.9)
Device features help minimize safety hazards, n (%)	31 (60.8)	37 (72.5)	0.362	–8.8% (–29.2%, 11.5%)	19 (37.3)
Trainer provided easily understandable, unbiased and practical information about proper injection, n (%)	51 (100.0)	51 (100.0)	–	–0.1% (–5.2%, 5.1%)	51 (100.0)
Recommend injection device to others needing this therapy, n (%)[c]	31 (60.8)	38 (74.5)	0.248	–14.4% (–33.5%, 4.7%)	21 (41.2)
Overall, satisfied with injection device, n (%)	32 (62.7)	41 (80.4)	0.093	–18.0% (–35.3%, –0.7%)	25 (49.0)
Anxiety giving yourself an injection with device, n (%)[c]	9 (17.6)	4 (7.8)	0.180	9.9% (–1.0%, 20.8%)	2 (3.9)
Device allows easy access to various injection sites, n (%)	35 (68.6)	42 (82.4)	0.167	–16.0% (–32.1%, 0.0%)	29 (56.9)

Single-use autoinjector is the Rebif® Rebidose® device; reusable autoinjector is the Rebiject II® device.
CI, confidence interval.
[a]The number of respondents to the questionnaire was 51. [b]Based on exact sign test of equality of paired proportions. [c]Responses were "very easy" or "easy." [d]Responses were "extremely convenient" or "somewhat convenient." [e]Responses were "very likely" or "likely." [f]Responses were "extremely anxious" or "very anxious."

Conclusions

- **This study's preliminary results suggest potential differences in the satisfaction of relative ease-of-use of two autoinjectors for administration of IFN β-1a SC tiw.**
- **The majority of patients found each device to be either easy or very easy to use.**

Reference

1. Simeoni M, *et al. Mult Scler* 2008;14:219–30.

Acknowledgments

MusiQoL contact information and permission to use: Mapi Research Trust, Lyon, France. E-mail: PROinformation@Mapi-trust.org – Internet: www.Mapi-trust.org or karine.baumstarck@univ-amu.fr or pascal.auquier@univmed.fr.

The authors thank Stacey Reeber, PhD, of Caudex, New York, NY (supported by EMD Serono, Inc.,* Rockland, MA, USA) for editorial assistance in drafting the poster, collating the comments of authors, and assembling tables and figures.

Study supported by EMD Serono, Inc.,* Rockland, MA, USA and Pfizer Inc, New York, NY, USA.
Poster development supported by EMD Serono, Inc.,* Rockland, MA, USA.

Disclosures

SW acted as a consultant for Biogen, Genzyme, and Teva, and received research funding from Alkermes, Biogen, EMD Serono, Inc.,* Genzyme, Novartis, Receptos, and Roche/Genentech. **BS** acted as a consultant and/or speaker for Acorda, Bayer, Biogen, EMD Serono, Inc.,* Genzyme, Pfizer, Novartis, and Teva, and has received research funding from Acorda, Biogen, Genzyme, MedImmune, Novartis, and Roche. **BH** and **CC** are employees of EMD Serono, Inc.,* Rockland, MA, USA.

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