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AVONEX® Assessment in Multiple Sclerosis-Therapy (ASSET) – an observational study in 1354 patients

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INTRODUCTION

Efficacy and safety of the disease modifying treatments (DMT), interferon (IFN) beta and glatirameracetate, have been demonstrated in pivotal clinical trials and follow-up studies in the treatment of relapsing remitting multiple sclerosis (RRMS). However, the parenteral application mode as well as undesirable effects of the treatment, e.g. local injection site reactions, can negatively affect the Quality of life (QoL) and thus might negatively influence adherence and efficacy. Valid comparative studies which provide comparative information on cutaneous side reactions of all DMTs under daily practice conditions are limited. Thus, a comparative study investigating the available DMTs in a real-life setting in a high number of patients is of major interest.

OBJECTIVES

To prospectively assess treatment efficacy, safety and tolerability (with a particular focus on skin tolerability) as well as the patients` QoL under a stable parenteral DMT.

STUDY DESIGN AND METHODS

- This was an open-label, multicenter, prospective, observational study conducted in Germany.
- Patients with MS undergoing treatment with an approved DMT (IM Interferon beta 1a, SC Interferon beta 1a, SC Interferon beta 1b, SC Glatirameracetate) were observed for 12 months.
- Course of disease (EDSS and relapses), injection site reactions, overall tolerability, general health status and QoL were documented every 3 months.
- Primary endpoint: efficacy of the different DMTs (relapse activity); secondary endpoints: disability progression (EDSS), MRI findings, tolerability, overall health status and QoL (EQ5D).

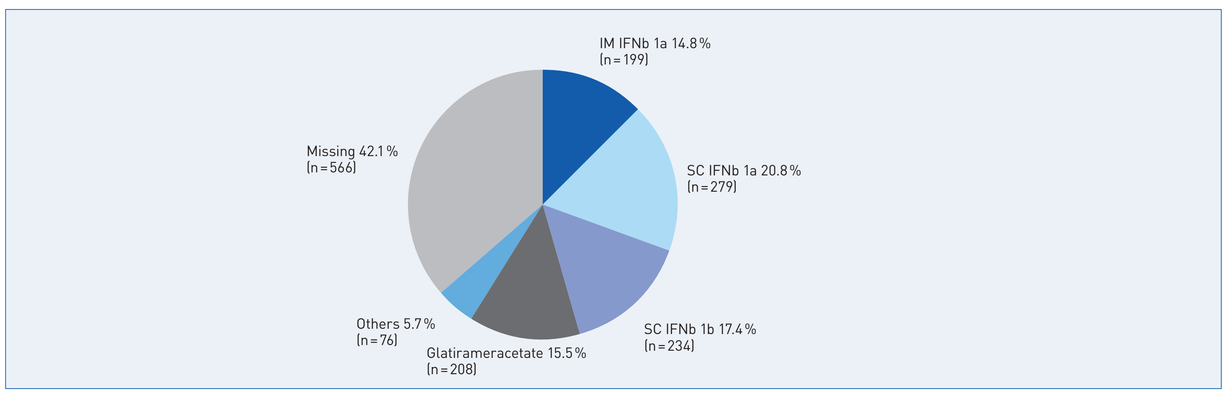
RESULTS

Demographics and disease characteristics

- Data from 1343 patients in 76 sites were evaluated (26.9 % male, 71 % female).
- Mean duration from first MS diagnosis until start of a specific MS-treatment was 30.8 (0.0 – 475.5) months.
- Mean duration from first MS symptoms until inclusion into the study was 115.9 (0.6 – 530.3) months.
- Mean baseline EDSS was 2.3 (± 1.6).
- Mean relapse rate within the 12 months period before study entry was 0.6 (± 0.9).
- Mean relapse rate within the 12 months period before start of the recent MS-treatment was 1.3 (± 1.0).
- Mean observation time was 10.3 (± 3.8) months.

Previous MS-treatments before enrolment

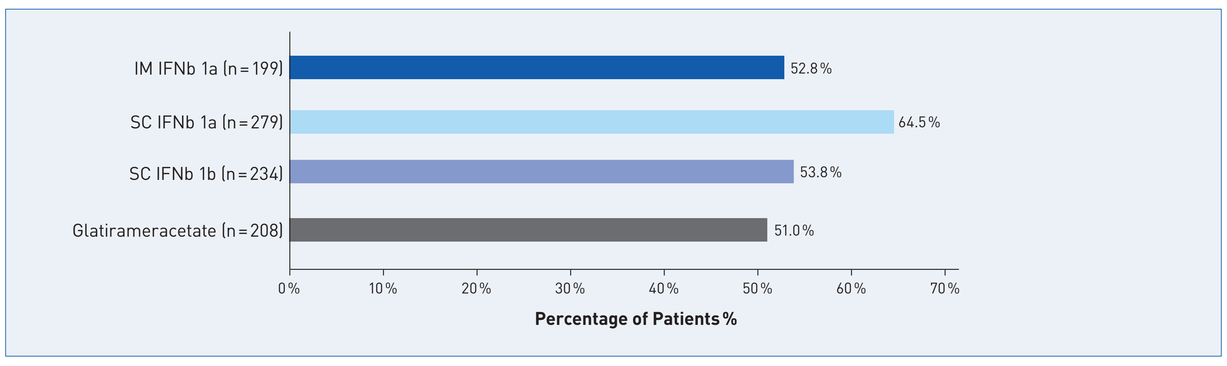
Figure 1: Percentages of previous MS-treatments (multiple nominations possible), n = 1343.



Percentage of patients who stopped previous MS-treatment

- Approximately 50 % of the patients stopped previous MS-treatment (range: 51.0 % – 64.5 %; depending on the treatment).
- Previous treatment with SC Interferon beta 1a was stopped by 64.5 % of the patients.
- Mean duration between beginning of current MS-treatment and visit 1 was 45.7 months (all treatments).

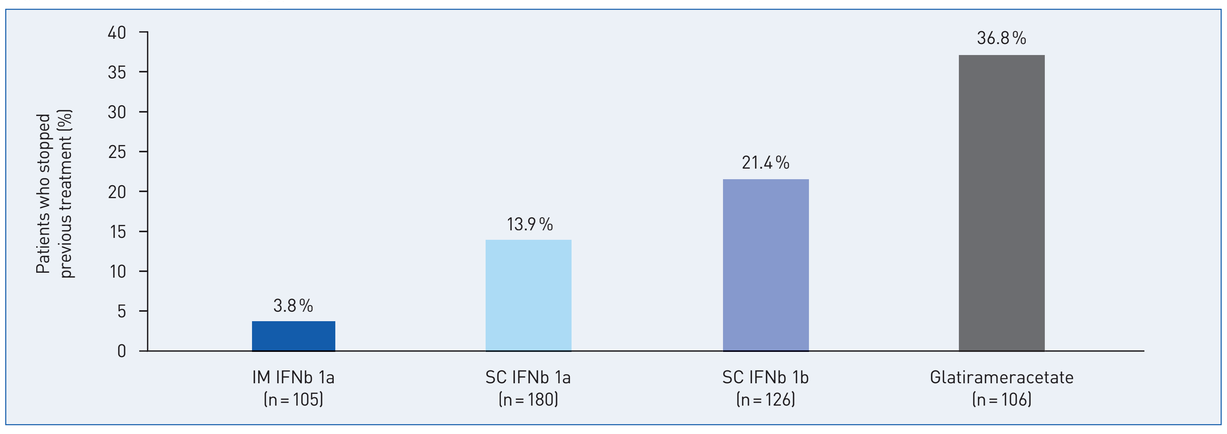
Figure 2: Nearly half of patients stopped previous treatment before study entry.



Reasons for stopping previous MS treatment were documented (all treatments):

- Additional relapses (25.7 %), patient's wish (24.6 %), other side effects (22.1 %), skin reactions (18.3 %), other reasons (13.3 %), physician´s wish (8.7 %), pregnancy (2.1 %) and non-compliance (1.7 %).
- Particularly, skin reactions were a frequent cause for stopping previous treatment with Glatirameracetate and Interferon beta 1b (36.9 % and 21.4 %), with IM Interferon beta 1a only 3.8 %.

Figure 3: Reasons for stopping previous MS-treatment – local skin reactions, n = 517 (p < 0.0001).



Current MS-treatment

- 1013 of enrolled patients (75.4 %) did not change MS-treatment within the observational period.
- IM Interferon beta 1a was the most frequently applied MS-treatment within the observational period (range: 24.6 % – 27.5 %) followed by Glatirameracetate (range: 22.6 % – 26.6 %) and Interferon beta 1b (range: 16.5 % – 20.8 %).

Figure 4: Percentages of current MS-treatments.

Efficacy

Similar efficacy in all DMTs.

EDSS

- Mean EDSS was stable for all treatments within the observational period (range: 1.8 – 2.6 [total: 2.3; 95 % CI: 2.2 – 2.4]).

Relapses

- Mean annual relapse rate within the observational period (visit 1 to 5) was markedly reduced compared to the 12 month period previous to the current MS-treatment (0.3 [95 % CI: 0.3 – 0.4] vs. 1.2 [95 % CI: 1.1 – 1.3], p < 0.0001, n = 754, with consistent medication within the observational period and with complete observation).
- There were no significant differences between current MS-treatments.

Safety and tolerability

Systemic adverse reactions

- 43.1 % of patients experienced systemic adverse reactions (all treatments), most of them flu-like symptoms (73.1 %) and sleep disturbances (20.6 %).
- Only 0.7 % of patients experienced severe adverse events; without causal relation to the MS-treatment.

Table 1: Adverse events (at baseline visit; without local skin reactions).

Adverse event	Total (n = 579)	IM Interferon beta 1a (n = 232)	SC Interferon beta 1a 22 µg (n = 61)	SC Interferon beta 1a 44 µg (n = 85)	SC Interferon beta 1a not spec. (n = 6)	SC Interferon beta 1b (n = 105)	Glatiramer-acetate (n = 82)
Flu-like symptoms	423 (73.1 %)	201 (86.6 %)	49 (80.3 %)	69 (81.2 %)	5 (83.3 %)	80 (76.2 %)	15 (18.3 %)
Sleep disturbances	119 (20.6 %)	47 (20.3 %)	11 (18.0 %)	19 (22.4 %)	1 (16.7 %)	21 (20.0 %)	18 (22.0 %)
Itching	101 (17.4 %)	8 (3.4 %)	7 (11.5 %)	17 (20.0 %)	1 (16.7 %)	17 (16.2 %)	49 (59.8 %)
Depression	75 (13.6 %)	22 (9.5 %)	12 (19.7 %)	14 (16.5 %)	1 (16.7 %)	16 (15.2 %)	9 (11.0 %)
Elevation of liver enzymes	16 (2.8 %)	3 (1.3 %)	3 (4.9 %)	3 (3.5 %)	0 (0.0 %)	5 (4.8 %)	2 (2.4 %)
Others	105 (18.1 %)	41 (17.7 %)	9 (14.8 %)	15 (17.6 %)	3 (50.0 %)	16 (15.2 %)	19 (23.2 %)

Local skin reactions

- Approx. 50 % of the patients experienced local skin reactions (over all treatments).
- IM Interferon beta 1a showed a significantly better skin tolerability than the SC applied MS-treatments:
  - Reddening, swelling, skin defects, open lesions, indurations and dents of the skin occurred significantly more frequently in SC injections as compared to IM injection.

Figure 5: Patients with skin reactions of patients with consistent medication over all visits within the observational period (n = 403 of 759 [53.1 %] at visit 5).

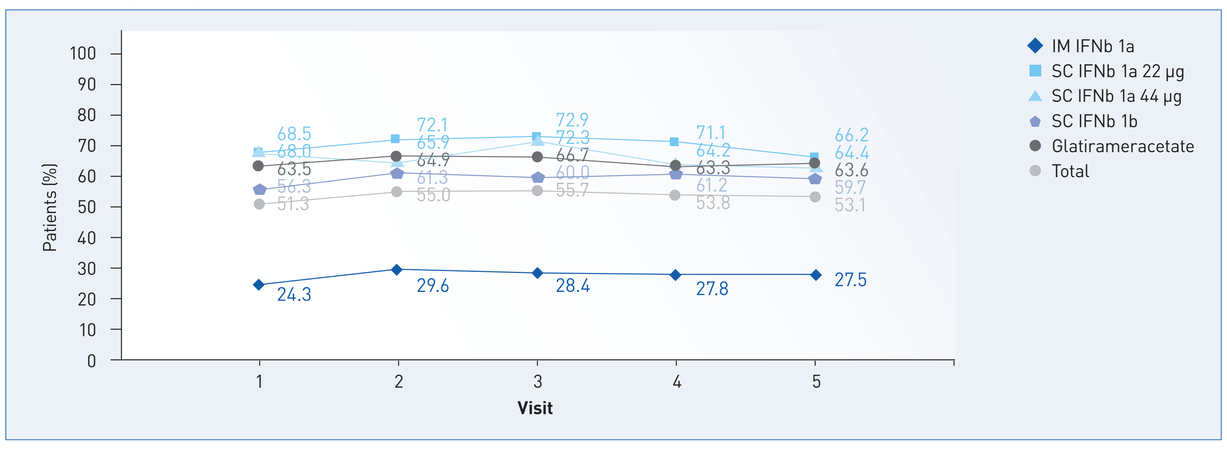


Figure 6: Patients with reddened skin (same treatment over all visits, n = 400 [41.2 %] at visit 5), p < 0.0001 visit 1 – 5.

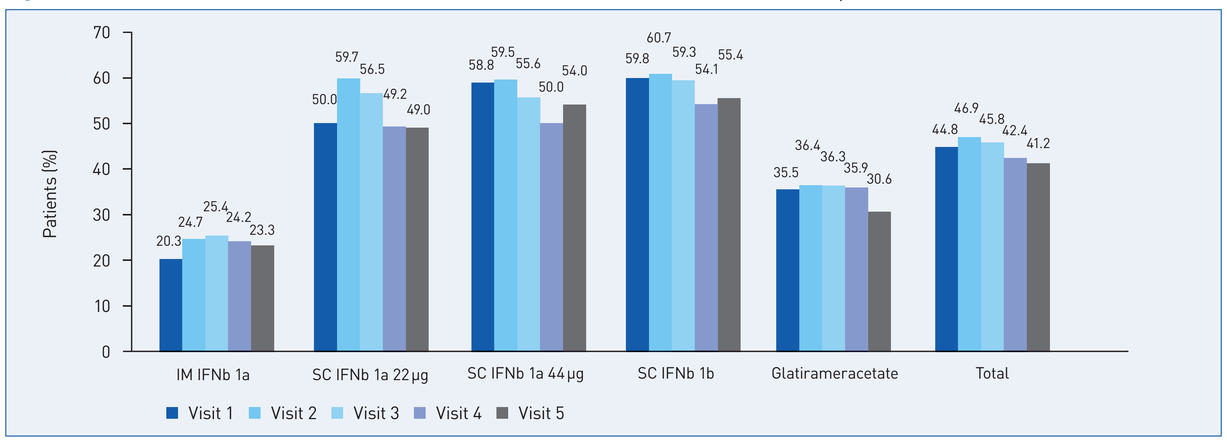
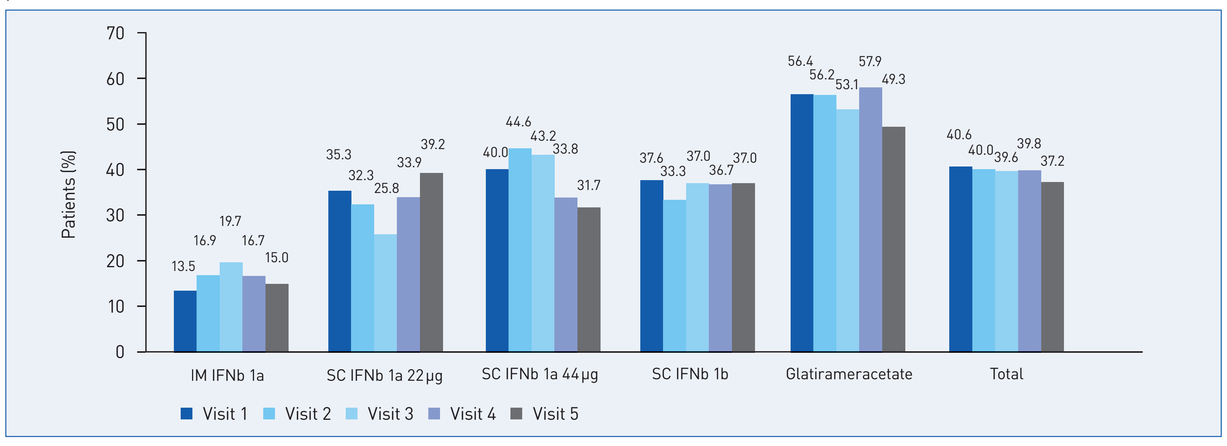


Figure 7: Patients with indurations of skin (patients with skin reactions and the same treatment over all visits, n = 400 [37.2 %] at visit 5), p < 0.0001 visit 1 – 5.



General health status and quality of live

- QoL (assessed every 3 months [EQ5D consists of two parts, a descriptive part (utility) and a visual analogue scale (VAS, health states ranges from 0.0 (death) to 1.0 (full health)]: no difference in QoL between the different DMTs with an increasing trend over study duration.
- Generally, most relevant alterations due to MS were documented for the domains pain/ physical discomfort and anxiety/depressiveness (approx. 40 – 50 % of patients were affected [all treatments]).

CONCLUSIONS

- The results of this observation in a real life setting underline the good efficacy and safety of DMTs : stable EDDS and reduction of relapse rates.
- Whereas the DMTs showed comparable efficacy, cutaneous adverse reactions remain a significant concern of the SC applied DMTs. In contrast, IM Interferon beta 1a provides a significantly better skin tolerability.
  - Patients treated with IM Interferon beta 1a experienced fewer injection site reactions.
- Skin reactions were a frequent cause for stopping previous treatment with SC applied DMTs
  - Particularly, previous treatment with Glatirameracetate and Interferon beta 1b (36.9 % and 21.4 %).
- There was no difference in QoL between the different DMTs with an increasing trend over study duration.

The results showed similar treatment efficacy in all applied DMTs but differences in nature and frequency of injection site reaction. This underlines the relevance of a good skin tolerability of DMTs, particularly regarding the treatment-related impairment of the patients' daily life and QoL.

DISCLOSURE

MM: received lecture fees and travel grants from the following companies: Bayer Health Care AG, Beiersdorf AG, Biogen Idec GmbH, Merck KGaAO, Novartis, Pharma GmbH, Pfizer Pharma GmbH, Sanofi-Aventis, Teva. TG: Honoraria, research support, speaking honoraria and travel expenses for scientific meetings from Biogen Idec GmbH. GN, KRW, CW: Employees of Biogen Idec GmbH. Study, medical writing assistance and editorial support was funded by Biogen Idec GmbH.