Effect of Age on Effectiveness and Discontinuation of Subcutaneous Interferon β-1a, and Healthcare Utilization, in Patients with Multiple Sclerosis

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Disclosures

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- **M. Sabidó, A. Allignol**, and **E. Boutmy** are employees of Merck KGaA, Darmstadt, Germany.
- **K. Marhardt** is an employee of Merck Gesellschaft mbH, Vienna, Austria, an affiliate of Merck KGaA, Darmstadt, Germany.
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INTRODUCTION

- Subcutaneous IFN β-1a is a well-established MS therapy with a cumulative exposure of 1,766,525 patient-years across more than 100 countries worldwide.
- Previous clinical trials have shown that patient age does not impact the efficacy of subcutaneous IFN β-1a therapy for MS.[1]
  - However, there is a paucity of real-world data on this topic.

1. Traboulsee A, et al. *BMC Neurol.* 2018;18:143.
IFN, interferon; **MS**, multiple sclerosis

OBJECTIVES

To evaluate the effect of age on:

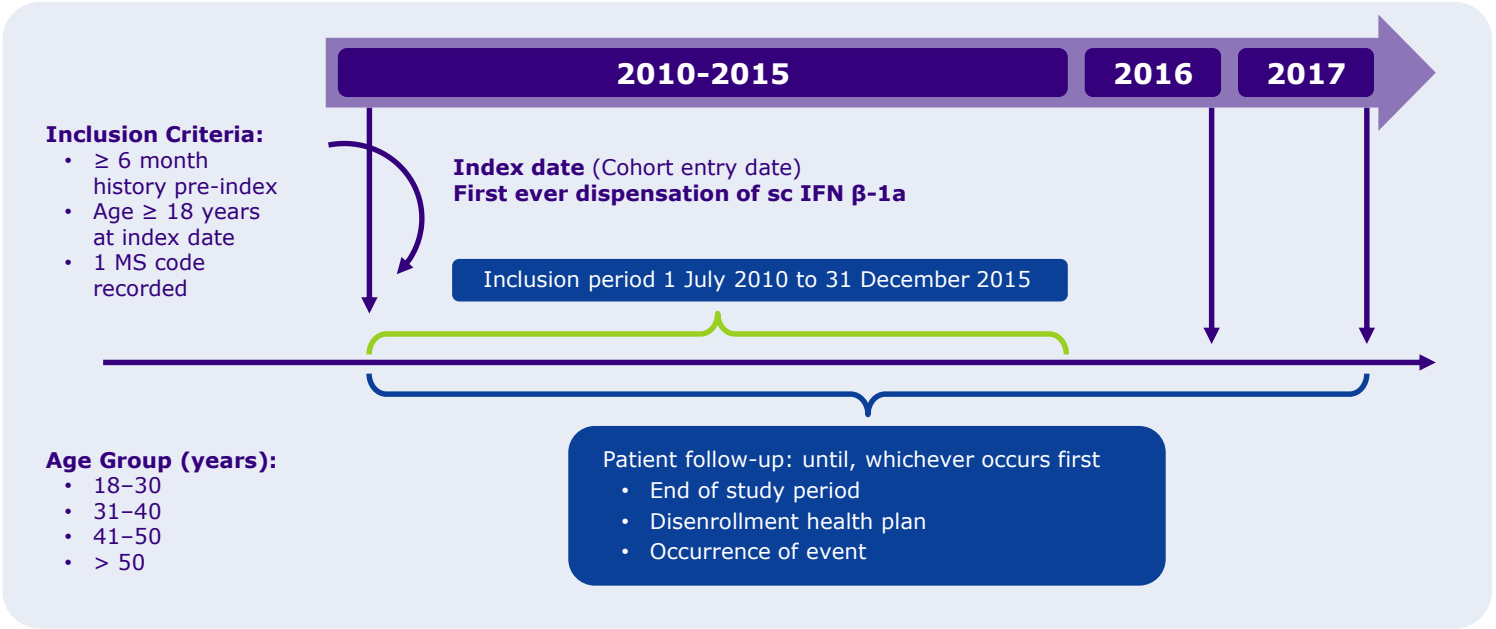
- **Treatment effectiveness and discontinuation.**
- **Healthcare resource utilization.**

Two years after subcutaneous IFN β-1a initiation for the treatment of MS using the IBM MarketScan© databases.*

* The IBM MarketScan® Commercial and the Medicare© Supplemental databases.
IFN, interferon; **MS**, multiple sclerosis

METHODS

Study Design



IFN, interferon; **MS**, multiple sclerosis; **sc**, subcutaneous

METHODS

Eligibility

- Adult patients newly initiated with sc IFN β-1a between Jul 2010-Dec 2015, regardless of prior treatment with DMD.
- ≥6 months' patient history before initiation (index date).
- Recorded diagnosis of MS over the 6 months before or at initiation.

Statistical Analysis

- Incidence rate per 100 person-years was used to estimate discontinuation risk.
- HR and 95% CI were calculated using Cox proportional methods to estimate time to first relapse and time to discontinuation.
- Healthcare resource utilization* was reported on a per patient per month basis over 2 years and according to age groups.
- Patients were censored at treatment discontinuation.

* For each patient, monthly healthcare resource utilisation (HRU) was calculated by dividing the total HRU over the total period exposed to sc INF beta-1a (with maximum of 12 and 24 months).
CI, confidence interval; **DMD,** disease-modifying drug; **HR**, hazard ratio; **IFN**, interferon; **MS**, multiple sclerosis; **sc**, subcutaneous

RESULTS

Patients Meeting All Inclusion Criteria

Inclusion criteria	Number (proportion)
Have a first dispensation of sc IFN β-1a between 01 July 2010 and 31 December 2015	19,693
Age ≥ 18 years at the time of index date	19,553 (99.3%)
With at least 6 months of patient history prior to the index date (baseline period)	5,789 (29.4%)
Recorded diagnosis of MS over the 6 months prior to the index date or at the index date	5,340 (27.1%)

IFN, interferon; **sc**, subcutaneous

Baseline Characteristics

	Age group, years			
	18–30 (N=773, 14.5%) n (%)	31–40 (N=1468, 27.5%) n (%)	41–50 (N=1630, 30.5%) n (%)	>50 (N=1469, 27.5%) n (%)
Female	576 (74.5)	1118 (76.2)	1247 (76.5)	1148 (78.2)
DMD*				
Treatment-naïve	585 (75.7)	1073 (73.1)	1136 (69.7)	947 (64.5)
Use of IM	162 (21.0)	333 (22.7)	422 (25.9)	430 (29.3)
Use of IS	30 (3.9)	66 (4.5)	85 (5.2)	113 (7.7)
Use of IM and IS	1 (0.1)	1 (0.1)	4 (0.3)	9 (0.6)
Glucocorticoid† during baseline (≥6 months)	406 (52.5)	650 (44.3)	702 (43.1)	549 (37.4)
Number of patients with at least one relapse during baseline (≥6 months)	154 (19.9)	216 (14.7)	204 (12.5)	139 (9.5)

* DMDs included: Avonex® (IFN β-1a), Betaferon® (IFN β-1b), Copaxone® (glatiramer acetate), Extavia® (IFN β-1b), Glatopa™ (glatiramer acetate, generic equivalent of Copaxone 20 mg), Plegridy® (pegylated IFN β-1a), Rebif® (IFN β-1a), Aubagio® (teriflunomide), Gilenya® (fingolimod), Tecfidera® (dimethyl fumarate), Lemtrada® (alemtuzumab), Tysabri® (natalizumab), methotrexate, mitoxantrone, cyclophosphamide, mycophenolate mofetil, Imuran® (azathioprine), rituximab, and tacrolimus; †Glucocorticoids included: betamethasone, cortisone, dexamethasone, fludrocortisone, hydrocortisone, methylprednisolone, prednisolone, and triamcinolone. **DMD**, disease-modifying drug; **IFN**, interferon; **IM**, immunomodulator; **IS**, immunosuppressant; **SD**, standard deviation

Baseline Characteristics

- In total, 5340 patients were included in the study.
- At baseline, the proportion of patients who were treatment-naïve or received glucocorticoid therapy decreased with age.
- The proportion of patients with at least one relapse during baseline was lower in older versus younger patients.

	Age group, years			
	18–30	31–40	41–50	>50
Glucocorticoid[†] during baseline (≥6 months)	406 (52.5)	650 (44.3)	702 (43.1)	549 (37.4)
Number of patients with at least one relapse during baseline (≥6 months)	154 (19.9)	216 (14.7)	204 (12.5)	139 (9.5)

[*] DMDs included: Avonex® (IFN β-1a), Betaferon® (IFN β-1b), Copaxone® (glatiramer acetate), Extavia® (IFN β-1b), Glatopa™ (glatiramer acetate, generic equivalent of Copaxone 20 mg), Plegridy® (pegylated IFN β-1a), Rebif® (IFN β-1a), Aubagio® (teriflunomide), Gilenya® (fingolimod), Tecfidera® (dimethyl fumarate), Lemtrada® (alemtuzumab), Tysabri® (natalizumab), methotrexate, mitoxantrone, cyclophosphamide, mycophenolate mofetil, Imuran® (azathioprine), rituximab, and tacrolimus; [†]Glucocorticoids included: betamethasone, cortisone, dexamethasone, fludrocortisone, hydrocortisone, methylprednisolone, prednisolone, and triamcinolone. **DMD**, disease-modifying drug; **IFN**, interferon; **IM**, immunomodulator; **IS**, immunosuppressant; **SD**, standard deviation

RESULTS

Treatment Discontinuation at 2 Years After sc IFN β-1a Initiation

Age group, years	Number of events	Discontinuation IR (95% CI)	Unadjusted HR* (95% CI)
18–30 (N=773, 14.5%)	395	72.06 (65.12; 79.52)	-
31–40 (N=1468, 27.5%)	707	62.11 (57.62; 66.86)	0.89 (0.79; 1.01)
41–50 (N=1630, 30.5%)	790	58.25 (54.26; 62.46)	0.86 (0.76; 0.97)
>50 (N=1469, 27.5%)	708	57.95 (53.76; 62.38)	0.86 (0.76; 0.97)

Normal approximation CIs were used. *HRs were calculated using a Cox proportion hazards model.
CI, confidence interval; **IFN**, interferon; **IR**, incidence rate (per 100 person-years); **HR**, hazard ratio; **sc**, subcutaneous

RESULTS

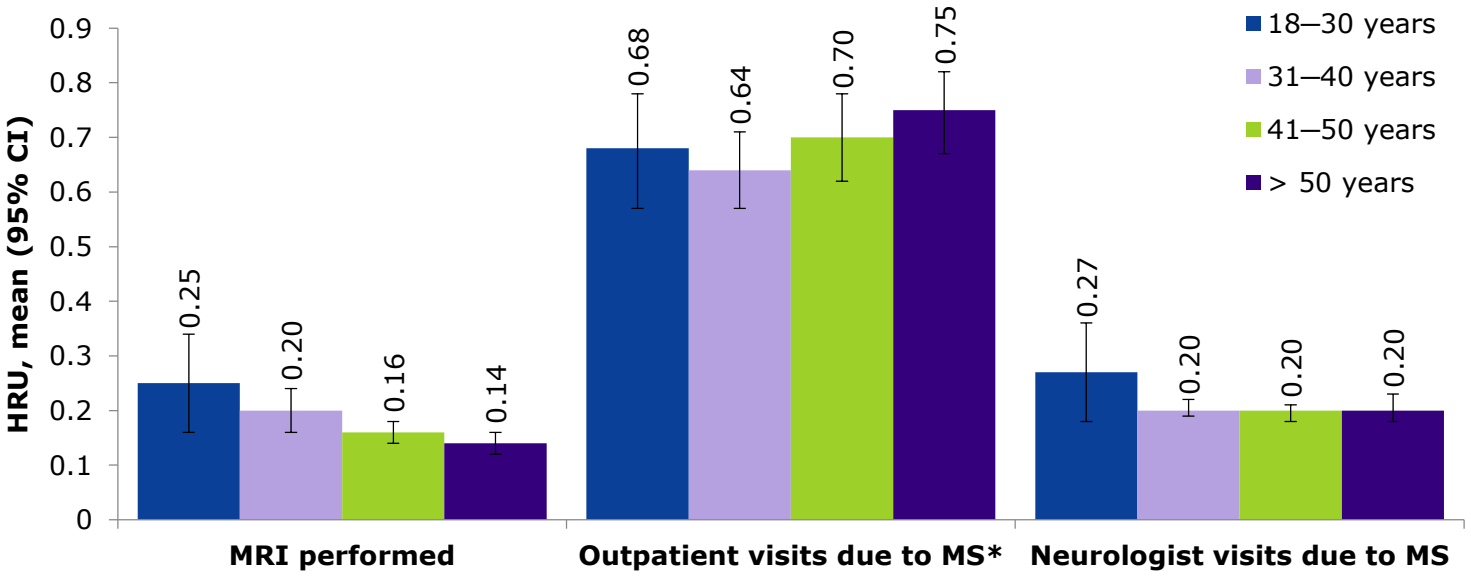
Patients Being Relapse-free 2 years After sc IFN β-1a Initiation According to Age

Age group, years	Number of events	2-year relapse-free probability, % (95% CI)	Unadjusted HR* (95% CI)
18–30 (N=773, 14.5%)	47	91.44 (88.88; 93.99)	-
31–40 (N=1468, 27.5%)	91	91.70 (89.95; 93.45)	1.00 (0.70; 1.43)
41–50 (N=1630, 30.5%)	82	93.52 (92.13; 94.91)	0.79 (0.55; 1.12)
>50 (N=1469, 27.5%)	81	92.82 (91.27; 94.38)	0.86 (0.60; 1.24)

Normal approximation CIs were used. *HRs were calculated using a Cox proportion hazards model.
CI, confidence interval; **IFN**, interferon; **IR**, incidence rate (per 100 person-years); **HR**, hazard ratio; **sc**, subcutaneous

RESULTS

Healthcare Resource Utilization Over 2 Years of Treatment with sc IFN β-1a (Per Patient Per Month)



* Outpatient visits included: visits with a neurologist, general practitioner or nurse, hospital visits, and ER visits; however, visits with a psychologist, psychiatrist, or speech therapist, or rehabilitation were excluded.
CI, confidence interval; **ER**, emergency room; **HRU**, healthcare resource utilization; **IFN**, interferon; **MRI**, magnetic resonance imaging; **MS**, multiple sclerosis; **sc**, subcutaneous

RESULTS

Healthcare Resource Utilization Over 2 Years of Treatment with sc IFN β-1a (Per Patient Per Month)

- Healthcare resource utilization was very low with respect to hospitalizations, ER visits, and nurse visits due to MS (≤0.01 per patient per month), regardless of age.
- Mean number of outpatient visits over 2 years numerically increased with increasing age, whereas the number of MRI scans performed numerically decreased with increasing age.

* Outpatient visits included: visits with a neurologist, general practitioner or nurse, hospital visits, and ER visits; however, visits with a psychologist, psychiatrist, or speech therapist, or rehabilitation were excluded.
CI, confidence interval; **ER**, emergency room; **HRU**, healthcare resource utilization; **IFN**, interferon; **MRI**, magnetic resonance imaging; **MS**, multiple sclerosis; **sc**, subcutaneous

CONCLUSIONS

The following general trends were observed with increasing age:

- **Regarding effectiveness:**
  - **Decreased discontinuation rates.**
  - **Greater probability of being relapse-free at 2 years although not significant.**
- **Regarding healthcare resource utilization:**
  - **Increased MS-related outpatient care.**
  - **Reduced use of MRI.**

- **Therefore, older patients receiving subcutaneous IFN ß-1a appear to have less active MS disease than younger patients.**

IFN, interferon; **MS**, multiple sclerosis; **MRI**, magnetic resonance imaging