Effectiveness of peginterferon beta-1a versus non-pegylated interferons and glatiramer acetate in a real-world setting using propensity score matching

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Objective

- To compare real-world clinical effectiveness in German outpatient populations using subcutaneous (SC) peginterferon beta-1a with populations using interferons (IFN) including SC IFN beta-1a, intramuscular (IM) IFN beta-1a, SC IFN beta-1b, or SC glatiramer acetate (GA).

Conclusions

- Peginterferon beta-1a demonstrated statistically significant reduced time to 12weeks-confirmed disability worsening (CDW) compared to other IFNs and GA.
- The current analysis is based on sample sizes of 147 patients per group (peginterferon beta-1a vs. IFN group) and 121 patients per group (peginterferon beta-1a vs. GA) and a meaningful follow-up time of two years, which can impact validity of the results.
- As data collection is ongoing, future re-analyses with include larger sample sizes and longer follow-up time to reevaluate differences in clinical effectiveness between these injectables.

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Disclosures

- SB received honoraria from Kassenärztliche Vereinigung Bayerns and health maintenance organisations for patient care, and from Biogen, MedDay, NeuroTransData, Novartis, and Roche for consulting, project management, clinical studies, and lectures; he also received honoraria and expense compensation as a board member of NeuroTransData.
- AB received honoraria from NeuroTransData for project management, clinical studies, and travel expenses from Novartis and Servier; he also received honoraria and expense compensation as a board member of NeuroTransData.
- FR is an employee of NeuroTransData.
- KT, FP, TK and KRW are employees of Biogen.

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Introduction

Peginterferon beta-1a

- Peginterferon beta-1a is an approved therapy for treatment of relapsing-remitting MS (RRMS) based on the results of the pivotal ADVANCE clinical trial.[1-3]
- Peginterferon beta-1a with a prolonged half-life and increased systemic exposure was developed to improve the therapeutic potency with less frequent dosing intervals for the treatment of relapsing-remitting multiple sclerosis (RRMS) without attenuating the biological or pharmacodynamic properties associated with existing interferon (IFN) treatments.[5,6]
- Compared to non-pegylated interferons, peginterferon beta-1a is characterized by longer half-life with less frequent dosing, increased bioavailability, and slower renal clearance, however with the known IFN beta safety profile.[5-7]
- Sustained clinical and paraclinical activity has been demonstrated in randomized clinical trials;[1-4,8] however, data on real-world experience is limited.

NeuroTransData (NTD)

- NeuroTransData GmbH (NTD) is a Germany-wide network of neurologists and psychiatrists founded in 2008.
  - Currently, 78 neurologists in 153 offices work in NTD practices serving about 600,000 outpatients per year.
  - Each practice is certified according to network-specific and ISO 9001 criteria.
- The NTD MS registry is a database capturing demographic, clinical history, and clinical variables from MS patients in a real-world setting.
- The NTD MS registry includes about 25,000 patients with MS.

[1]Calabresi PA et al. Lancet Neurol 2014; 13: 657-665; [2]Kieseier BC et al. Mult Scler. 2015;21:1025-1035; [3]Newsome SD, et al. J Neurol. 2016 263: 1778-1787; [4]Newsome SD et al. Ther Adv Neurol Disord. 2017, Vol. 10(1) 41–50; [5]Baker DP et al. J Interferon Cytokine Res 2010; 30: 777-785; [6]Hu X et al. J Clin Pharmacol 2012; 52: 798-808; [7]Hu X, et al. Br J Clin Pharmacol. 2016; 82 380–388 [8]Newsome SD, et al. Ther Adv Neurol Disord. 2018 11: 1756286418791143.

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Methods

Design

- Retrospective analysis of data from the NTD registry between 01.01.2014 and 01.04.2019.

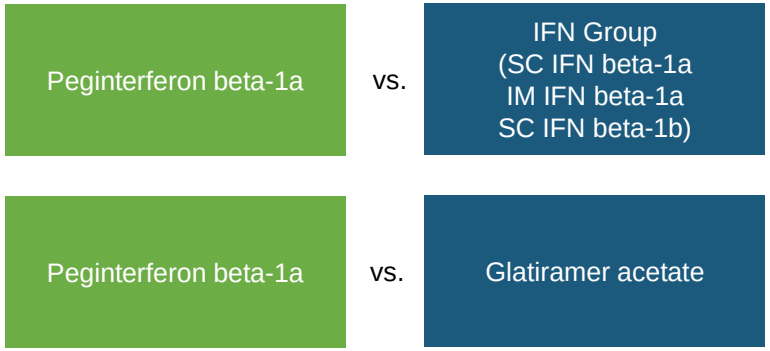
Patients

- Adult patients with RRMS who
  - received one of the following treatment options:
    - peginterferon beta-1a, SC IFN beta-1a, IM IFN beta-1a, SC IFN beta-1b, or glatiramer acetate
  - initiated treatment no earlier than 2014
  - had ≥12 months of treatment exposure
  - A valid EDSS measurement and/or a relapse after index therapy initiation.

Endpoints

- Primary endpoints were annualized relapse rate (ARR) and time to first relapse.
- The secondary endpoint was time to confirmed (after 12 weeks) disability worsening (CDW), defined as at least 0.5-point EDSS score increases for patients with baseline EDSS score greater than 5.5, and at least 1.0-point EDSS score increases for patients with baseline EDSS score 0–5.5.

Figure 1. Treatment groups compared by PSM



Statistics

- 1:1 propensity score matching (PSM, %:1 greedy matching algorithm) with non-pairwise censoring was used to match measured baseline characteristics of peginterferon populations to comparator populations for each treatment comparison (Figure 1).

ARR = Annualized relapse rate; CDW = Confirmed disability worsening, defined as progression (at least 0.5-point EDSS score increases for patients with baseline EDSS score greater than 5.5, and at least 1.0-point EDSS score increases for patients with baseline EDSS score 0–5.5) confirmed after 12 weeks; EDSS = Expanded Disability Status Scale; IFN = Interferon; IM = intramuscular; NTD = NeuroTransData; PSM = Propensity score matching; RRMS = Relapsing-remitting multiple sclerosis; SC = subcutaneous
IFN group: SC IFN beta-1a, IM IFN beta-1a, SC IFN beta-1b

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Results (1 of 6)

Patient disposition

- In total, 175 patients treated with peginterferon beta-1a, 308 from the IFN group (SC IFN beta-1a, IM IFN beta-1a, SC IFN beta-1b), and 287 GA patients were included in the analysis set (Table 1).

Table 1. Baseline characteristics after PSM

Parameter	Peginterferon beta-1a	IFN group	Peginterferon beta-1a	GA
N	147	147	121	121
Age at index therapy initiation (years), Mean ± SD	40.4 ± 11.6	39.2 ± 11.2	39.5 ± 12.2	39.2 ± 11.6
Female, N (%)	114 (77.6)	111 (75.5)	93 (76.9)	94 (77.7)
Years since diagnosis at therapy initiation, Mean ± SD	6.4 ± 6.3	5.8 ± 5.8	5.7 ± 6.3	5.0 ± 6.5
Diagnosed less than 6 months before therapy initiation, N (%)	38 (25.9)	35 (23.8)	37 (30.6)	37 (30.6)
Number of prior therapies, N (%)				
0	49 (33.3)	54 (36.7)	49 (40.5)	47 (38.8)
1	68 (46.3)	64 (43.5)	46 (38.0)	49 (40.5)
2	23 (15.6)	23 (15.6)	19 (15.7)	16 (13.2)
3	3 (2.0)	3 (2.0)	3 (2.5)	4 (3.3)
4	3 (2.0)	3 (2.0)	3 (2.5)	4 (3.3)
5	1 (0.7)	0 (0.0)	1 (0.8)	1 (0.8)
EDSS at therapy initiation, Mean ± SD	1.6 ± 1.3	1.5 ± 1.5	1.6 ± 1.3	1.5 ± 1.4
Number of relapses 12 months prior to therapy initiation, N (%)	100 (68.0)	100 (68.0)	79 (65.3)	72 (59.5)
0	41 (27.9)	42 (28.6)	37 (30.6)	41 (33.9)
1	6 (4.1)	5 (3.4)	5 (4.1)	7 (5.8)
2	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)

EDSS = Expanded Disability Status Scale; GA = Glatiramer acetate; IFN = Interferon; IM = intramuscular; PSM = Propensity score matching; SC = subcutaneous; SD = standard deviation
IFN group: SC IFN beta-1a, IM IFN beta-1a, SC IFN beta-1b

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Results (2 of 6)

Figure 2. Propensities distribution before and after PSM

GA = Glatiramer acetate; IFN = Interferon; IM = intramuscular; PSM = Propensity score matching; SC = subcutaneous
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Results (3 of 6)

Annualized relapse rate

- After PSM, no difference was found in the ARR between peginterferon beta-1a patients and patients from the IFN group (Table 2) or the GA group (Table 3).

Table 2. Peginterferon beta-1a vs. IFN group: ARR

Parameter	Peginterferon beta-1a	IFN group
N after PSM	147	147
ARR	0.136	0.113
Estimated ARR ratio (95% CI)	1.2 (0.79, 1.81)	
Treatment effect p-value	0.3857	

Table 3. Peginterferon beta-1a vs. GA: ARR

Parameter	Peginterferon beta-1a	GA
N after PSM	121	121
ARR	0.140	0.190
Estimated ARR ratio (95% CI)	0.74 (0.45, 1.24)	
Treatment effect p-value	0.2608	

ARR = Annualized relapse rate; CI = Confidence interval; GA = Glatiramer acetate; IFN = Interferon; IM = intramuscular; PSM = Propensity score matching; SC = subcutaneous
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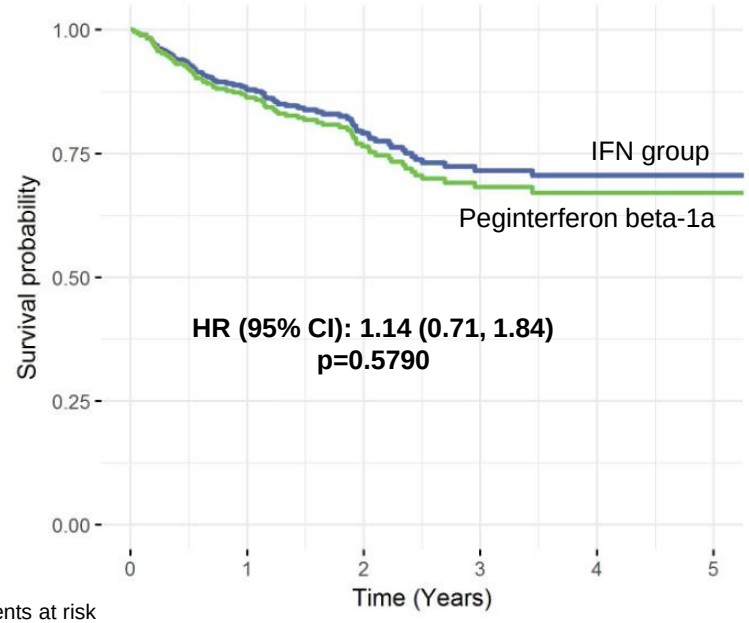
Results (4 of 6)

Time to first relapse

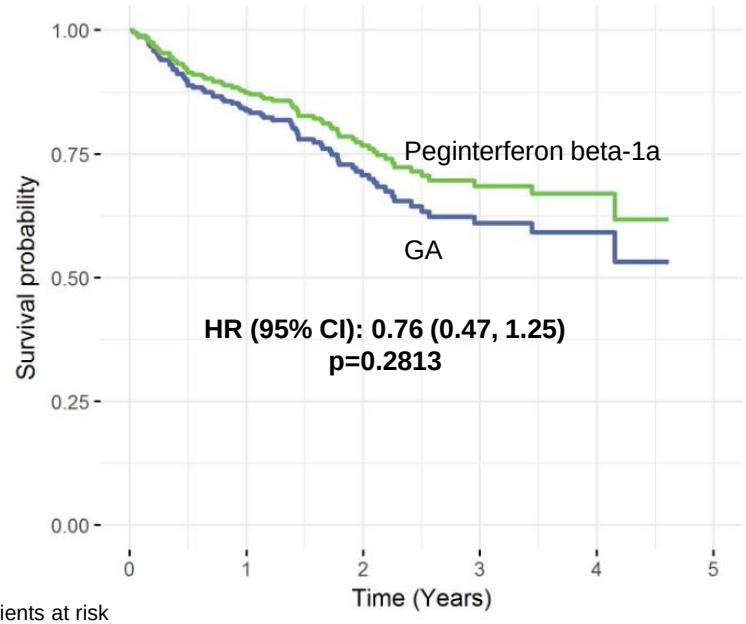
- After PSM, no difference was found in the time to first relapse between peginterferon beta-1a patients and patients from the IFN group (Figure 2) or the GA group (Figure 3).

Figure 2. Peginterferon beta-1a vs. IFN group: Time to first relapse



Patients at risk											
IFN	147	140	130	96	78	59	45	35	22	14	6
Peginterferon beta-1a	147	132	126	90	65	45	36	26	14	3	0

Figure 3. Peginterferon beta-1a vs. GA: Time to first relapse



Patients at risk											
GA	121	109	102	74	54	29	21	16	5	1	0
Peginterferon beta-1a	121	109	105	76	56	39	31	22	13	1	0

CI = Confidence interval; GA = Glatiramer acetate; HR = Hazard ratio; IFN = Interferon; IM = intramuscular; PSM = Propensity score matching; SC = subcutaneous
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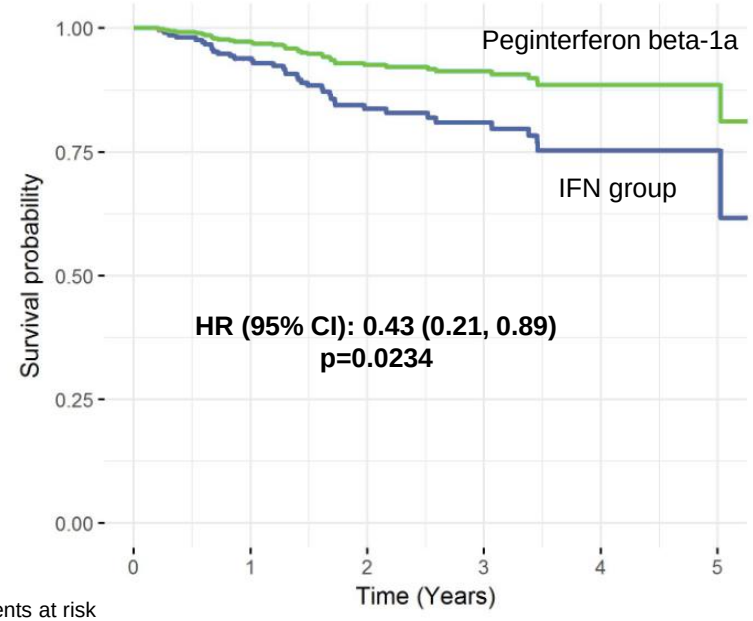
Results (5 of 6)

Time to confirmed disability worsening

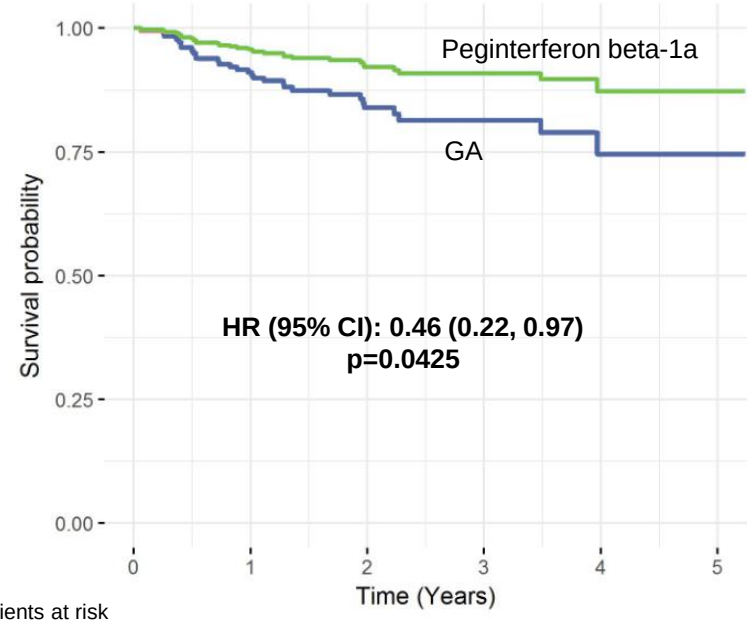
- For time to 12-week CDW, a significantly higher estimated treatment effect in favor of peginterferon beta-1a was found compared to both, the IFN group (Figure 4) and the GA group (Figure 5).

Figure 4. Peginterferon beta-1a vs. IFN group: Time to 12-week CDW



Patients at risk											
IFN	147	145	130	102	79	63	48	34	23	12	6
Peginterferon beta-1a	147	145	142	100	78	55	45	34	18	5	0

Figure 5. Peginterferon beta-1a vs. GA: Time to 12-week CDW



Patients at risk											
GA	121	115	110	83	60	34	26	19	8	4	2
Peginterferon beta-1a	121	119	116	83	67	47	39	28	16	3	0

CDW = Confirmed disability worsening, defined as progression (at least 0.5-point EDSS score increases for patients with baseline EDSS score greater than 5.5, and at least 1.0-point EDSS score increases for patients with baseline EDSS score 0–5.5) confirmed after 12 weeks; CI = Confidence interval; GA = Glatiramer acetate; HR = Hazard ratio; IFN = Interferon; IM = intramuscular; SC = subcutaneous
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Results (6 of 6)

Overview of matched samples comparisons

- There was a numerical tendency towards favoring peginterferon beta-1a vs. GA regarding ARR and TTR. The comparative effectiveness of peginterferon beta-1a with the IFN group and GA reached statistical significance for the secondary endpoint time to CDW (TTW, Table 4).
- To reevaluate comparative clinical effectiveness with larger sample sizes and longer observation periods, re-analyses will be done with database lock September 2020.

Table 4. Overview of cohort comparisons based on PSM baseline characteristics

Comparator	IFN group			GA		
Treatment arms' size	147			121		
Endpoint	**ARR**	**TTR**	**TTW**	**ARR**	**TTR**	**TTW**
Higher estimated treatment effect for peginterferon beta-1a	X	X	✓	✓	✓	✓
Statistical significance	X	X	✓	X	X	✓

ARR = Annualized relapse rate; CDW = Confirmed disability worsening, defined as progression confirmed after 12 weeks; CI = Confidence interval; GA = Glatiramer acetate; HR = Hazard ratio; IFN = Interferon; IM = intramuscular; SC = subcutaneous; TTW = Time to confirmed disability worsening; TTR = Time to relapse
IFN group: SC IFN beta-1a, IM IFN beta-1a, SC IFN beta-1b