REVISTA NEUROCIÊNCIAS

Disease-modifying treatment patterns among multiple sclerosis patients: a Brazilian descriptive study

Padrões de tratamento modificadores da doença em pacientes com esclerose múltipla: um estudo descritivo sobre o Brasil

Patrones de tratamiento modificadores de la enfermedad en pacientes con esclerosis múltiple: un estudio descriptivo brasileño

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Resumo

Introdução. A esclerose múltipla (EM) é uma doença autoimune que leva à desmielinização do sistema nervoso central, comprometendo suas funções. Embora o curso da EM seja variável, esta é uma doença naturalmente progressiva, que apresenta uma deterioração neurológica acelerada na maioria dos pacientes. Estudos de padrão de tratamento são importantes para compreender a prática e os resultados clínicos do mundo real. **Objetivo**. Foi descrever os padrões de tratamento de pacientes com EM no sistema público de saúde brasileiro. **Método.** Foi realizado um estudo de coorte retrospectivo por meio da análise de dados secundários entre os anos 2008 e 2020. Com a finalidade de comparar a prática clínica com o recomendado pelos Protocolos Clínicos e Diretrizes Terapêuticas (PCDT) ao longo dos anos, as análises de tratamento foram fragmentadas em 2008–2014, 2015–2017 e 2018-2020. Os dados foram obtidos do Sistema Único de Saúde, de um banco de dados anônimo (DataSus). **Resultados**. Os pacientes com EM foram identificados pelo código G35 na Classificação Internacional das Doenças (10ª edição) e 340 (9ª edição). As taxas epidemiológicas foram calculadas por anos, em 2020 a taxa de incidência era de 1,7 por 100.000 habitantes. **Conclusão**. Em relação aos padrões de tratamento, o interferon beta foi o medicamento de primeira linha prescrito para EM mais comum nos três períodos analisados, seguido do acetato de glatiramer. O glatiramer foi o tratamento de segunda linha mais prescrito apenas no primeiro período extraído (2008-2014).

Unitermos. Esclerose múltipla; Padrões de tratamento; Sistema Único de Saúde

Abstract

Introduction. Multiple sclerosis (MS) is an autoimmune disease that leads to demyelination of the central nervous system, compromising its functions. Although the course of MS is variable, it is a naturally progressive disease, which has accelerated neurological deterioration in most patients. Treatment pattern studies are important to understand the real-world practice and clinical outcomes. **Objective.** The aim of this study was to describe treatment patterns among patients with MS in the Brazilian public healthcare system. **Method.** A retrospective cohort study was carried out through the analysis of secondary data from 2008 to 2020. To compare the clinical practice with that recommended by the Clinical Protocols and Therapeutic Guidelines (PCDT) over the years, the treatment analyzes were fragmented into 2008-2014, 2015-2017, and 2018-2020. The data was obtained from Brazilian National Health System, which is a real-world anonymized database. **Results.** MS patients were identified by the G35 code on International Classification of the Diseases 10th edition and with code 340 on 9th edition. The incidence and prevalence rates were calculated by years, in 2020 the incidence rate was 1.7 per 100,000 population. **Conclusions.** Regarding the treatment patterns, beta-

interferon was the most common first-line prescribed medication for MS in all the three analyzed periods, followed by glatiramer acetate. Glatiramer was the most frequently prescribed second-line treatment only in the first extracted period (2008–2014).
Keywords. Multiple sclerosis; Treatment patterns; Brazilian healthcare system

Resumen

Introducción. Esclerosis múltiple (EM) es una enfermedad autoinmune que conduce a la desmielinización del sistema nervioso central, comprometiendo sus funciones. Aunque el curso de la EM es variable, es una enfermedad naturalmente progresiva que ha acelerado el deterioro neurológico en la mayoría de los pacientes. Los estudios de patrones de tratamiento son importantes para comprender la práctica del mundo real y los resultados clínicos. **Objetivo.** El objetivo de este estudio es describir los patrones de tratamiento de los pacientes con EM en el sistema público de salud brasileño. **Método.** Se realizó un estudio de cohorte retrospectivo mediante el análisis de datos secundarios entre los años 2008 y 2020. Con el fin de comparar la práctica clínica con la recomendada por los Protocolos Clínicos y Guías Terapéuticas (PCDT) a lo largo de los años, los análisis de tratamiento se fragmentaron en 2008-2014, 2015-2017 y 2018-2020. Los datos se obtuvieron del Sistema Nacional de Salud de Brasil, que es una base de datos anónima del mundo real. **Resultados**. Los pacientes con EM fueron identificados por el código G35 en la 10ª edición de la Clasificación Internacional de Enfermedades y con el código 340 en la 9ª edición. Las tasas de incidencia y prevalencia se calcularon por años, en 2020 la tasa de incidencia fue de 1,7 por 100.000 habitantes. **Conclusión**. En cuanto a los patrones de tratamiento, se prescribió interferón beta corresponde a 60,5% dos pacientes de primera línea. En cuanto a los patrones de tratamiento, el interferón beta fue el fármaco prescrito de primera línea más común para la EM en los tres períodos analizados, seguido del acetato de glatiramer. Glatiramer fue el tratamiento de segunda línea prescrito con más frecuencia solo en el primer período extraído (2008-2014).
Palabras clave. Esclerosis múltiple; Patrones de tratamiento; Sistema de salud brasileño

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INTRODUCTION

Multiple sclerosis (MS) is an autoimmune disease that leads to demyelination of the central nervous system (CNS) compromising its functions. In 2016, the prevalence of MS was 30.1 cases per 1,000,000 population worldwid[1-5]. In Brazil, the overall prevalence is estimated to be 8.69 (95% CI: 6.0–12.6) per 100,000 inhabitants[2].

Although the course of MS is variable, it is a naturally progressive disease. Initially, patients normally experience relapses, followed by partial or total recovery[3,4]. This stage

is called the relapsing-remitting form of multiple sclerosis (RRMS). Over time, some patients can experience the transition to secondary progressive (SPMS) diseas e, in which there is a progressive worsening of neurologic function (accumulation of disability) over time[3].

In 15% of the cases, patients have a progressive disease from onset, which is called primary progressive multiple sclerosis (PPMS). The clinical course of PPMS is characterized by progression over time, with symptoms being more noticeable slowly but progressively over time[3].

MS directly affects qualify of life (QoL) due to its impacts in weakness, movement ability and cognitive functions[4]. Mental comorbidities, including depression, are more frequent in these patients than in the overall population. The depressive disorders affect not only QoL, but also impacts adherence to treatments, increasing the risk of progression due to poor control of the disease[4-9]. Considering the complex scenario of progression and comorbidities, MS imposes substantial economic burdens.

Since the beginning of the 1990s, several DMTs became available for MS patients. Normally, these therapies are related with the reduction of neurological inflammation, and some treatments may influence neurodegeneration. Interferons and Glatiramer Acetate were the first treatments used and remain as the main recommendation of the first line of therapy according to Brazilian Clinical Protocol and Therapeutic Guidelines (PCDT)[5–7]. In case of disease progression, PCDT recommends further treatments based on

their proven safety and efficacy. Also, the PCDT excluded patients with PPMS[10-12].

Real-world studies play key roles in generating information, helping to determine disease characteristics and treatment patterns. This information is essential to subsidize the planning of public health programs and resource allocation, considered important in a country with a heterogeneous socioeconomic profile and scarce data such as Brazil. This way, the study aims to describe the treatment patterns of patients with MS in the Brazilian public health system, including the most common medications and their combinations in a real-world Brazilian scenario.

METHOD

Study design

A retrospective cohort study was carried out through the analysis of secondary data between 2008 and 2020. To compare the clinical practice with that recommended by the Clinical Protocols and Therapeutic Guidelines (PCDT) over the years, the treatment analyzes were fragmented into 2008-2014, 2015-2017, and 2018–2020. This subgroup analysis encompassed both (I) patients who started their first line of treatment and (II) the drug switches that occurred within each year range. The incidence and prevalence rates were calculated by years, in the time frame from 2008 to 2020.

Study population

Demographics and treatment information were collected for all eligible patients according to the inclusion criteria, which included: (i) At least one registration in the database between January 01, 2008, and December 31, 2020; and (ii) 18 years or older on the first registration. Subjects with inconsistent and missing data that could impact the study analysis were not included in the study.

Datasource

Outpatient data was collected from Outpatient Information System ("Sistema de Informação Ambulatorial" - SIA/SUS) from the Department of Informatics of the Brazilian Unified Health System (DATASUS) MS patients were identified by the G35 code on International Classification of the Diseases 10th edition (ICD-10) and with the code 340 on 9th edition (ICD-9).

It was considered the treatment regimens for all lines of MS therapy, either monotherapy or combination of drugs. Other variables assessed gender, age, race/ethnicity, age at diagnosis and comorbidities (anxiety/depression).

The study was conducted according to the guidelines of the Declaration of Helsinki[13]. All activities were conducted according to the applicable Brazilian federal laws. Based on the resolution 510/2016 from the National Brazilian Ethical Committee, studies using secondary anonymized databases do not require ethical approval[14].

RESULTS

A total of 67,095 MS patients were identified in the SIA/SUS database from 01/01/2008 to 12/31/2020. Of them, 40,449 met the eligibility criteria and were included for the analysis. **Erro! Fonte de referência não e ncontrada.** shows the patients selection flow.

Demographic and clinical characteristics are described in

. Most patients were women (73.3%) and did not report their race/ethnicity (49.3%). The median age at diagnosis was 37.0 years (18 - 71 years) with a median body mass index of 24.2 (22.1 – 27.6, minimum and maximum respectively).

Only 3,613 (8.9%) of the selected patients had a mental or neurological comorbidity registered in their records. The most prevalent mental disorder was Schizophrenia, presented in 1.2% of the patients, followed by bipolar affective disorder (0.3%) and schizoaffective disorders (0.1%).

The incidence and prevalence rates were calculated by years. In 2020 the incidence rate was 1.7 per 100,000 population and the prevalence rate was 11.0 per 100,000 population. **Erro! Fonte de referência não encontrada.** s hows the incidence and prevalence by year.

Table 1. Demographic and clinical characteristics.

Variables	n (40,449)	%	
Gender			
Female	29,636	73.3	
Male	10,813	26.7	
Race/ Ethnicity			
White	13,624	33.6	
Black	779	2.0	
Indian	4	0.0	
Others	6,105	15.1	
Not reported	19,937	49.3	
Region			
Southeast	23,240	57.4	
South	3,076	7.6	
Northeast	5,372	13.3	
Central-West	7,699	19.0	
North	654	1.6	
Mental disorders			
Schizophrenia	492	1.2	
Bipolar affective disorder	135	0.3	
Schizoaffective disorders	19	0.1	
Diseases of the nervous system			
Epilepsy	882	2.2	
Parkinson's disease	790	2.0	
Paraplegia and quadriplegia	421	1.0	
Others	874	2.2	
		Median (1st - 3rd quartile)	**Mean±SD**
Weight (kg)	37,136	67.0 (60.0 – 78.0)	70.2±17.6
Height (cm)	36,848	165.0 (160.0 – 170.0)	165.7±11.2
Body mass index	36,446	24.2 (22.1 – 27.6)	25.3±7.0
Age at diagnosis	40,449	37.0 (18.0 – 71.0)	38.2±12.2

The treatment patterns and treatment duration by line are described in **Erro! Fonte de referência não e ncontrada.**, considering the specific periods. The analysis of the 2015-2017 period showed betainterferon as the most used drug in first line, with 30.6 months of duration, one of the highest between all the evaluated drugs, nearly 2 months lower than natalizumab (32.4 months), and 1.2 months

higher than glatiramer (29.4 months). For the second line, fingolimod demonstrated 41.9 months of duration, the higher between all the evaluated DMT, 6.6 months higher than natalizumab (35.3 months), and 17.6 months higher than beta interferons (24.3 months). In the third line, fingolimod presented 39.8 months of duration, natalizumab 33.2 months and beta interferons 23.8 months. In the analysis from 2018-2020, the first line fingolimod showed no major differences between DMTs. Since the period, once includes only 24 months, it was not possible to reach the period where differences can be identified (24-40 months after start of treatment).

Table 2. Incidence and prevalence of MS in public healthcare system during the year.

	Incidence rate (per 100 000 population)	**Prevalence rate (per 100 000 population)**
2008	4.7*	4.7*
2009	1.0	5.2
2010	1.1	5.7
2011	1.3	6.4
2012	1.3	7.0
2013	1.3	7.4
2014	1.3	7.5
2015	1.7	8.0
2016	1.7	8.7
2017	1.7	9.2
2018	1.8	9.7
2019	2.1	10.5
2020	1.7	11.0

*Note: it was considered that all cases in the first year of data collection (2008) were new. In this sense, incidence and prevalence are the same.

Table 3. Treatment pattern per line of therapy.

	2008 to 2014				2015 to 2017				2018 to 2020			
	First line	Second line	Third line	Fourth Line	First line	Second line	Third line	Fourth Line	First line	Second line	Third line	Fourth Line
Treatment patterns	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total patient	**21,170**	**2,741**	**1,680**	**426**	**7683**	**2989**	**1764**	**673**	**8935**	**4541**	**2620**	**952**
Betainterferon	16,415 (77,5)	543 (19,8)	483 (28,7)	111 (26,1)	4,438 (57,8)	261 (8,7)	205 (11,6)	48 (7,1)	3,556 (39.7)	131 (2.9)	151 (5,8)	44 (4.6)
duration months (mean±SD)	60.2±45.1	43.4±36.6	34.9±33.6	39.1±34.6	30.6±19.8	24.3±19.2	23.8±19.1	25.7±21.0	14.0±9.5	14.2±10.0	10.1±9.5	10.4±9.3
Glatiramer	4,484 (21,2)	1,602 (58,4)	785 (46,7)	112 (26,3)	2,090 (27,2)	1,069 (35,8)	429 (24,3)	44 (6,5)	2,017 (22.5)	439(9,7)	244 (9,3)	48 (5.0)
duration months (mean±SD)	56.0±43.9	41.3±35.5	39.5±34.2	36.7±35.6	29.4±19.5	23.2±18.8	25.5±20.0	23.1±20.7	13.3±9.7	13.2±9.8	11.8±9.7	11.4±9.4
Natalizumab	271 (1,3)	596 (21,7)	413 (24,6)	203 (47,7)	518 (6,7)	628 (21,0)	507 (28,7)	254 (37,7)	754 (8,4)	545 (12,0)	433 (16,5)	195 (20,5)
duration months (mean±SD)	43.1±28.9	47.2±30.6	48.2±29.2	44.7±28.3	32.4±18.8	35.3±18.4	33.2±17.9	34.7±18.4	13.4±9.6	16.3±9.8	15.6±10.4	15.8±11.0
Fingolimode					637 (8,3)	1031 (34,5)	623 (35,3)	327 (48,6)	763 (8,5)	1,392 (30,7)	909(34,7)	348 (36,6)
duration months (mean±SD)					40.4±19.6	41.9±19.7	39.8±18.4	38.5±20.3	15.1±9.5	16.1±9.6	16.3±9.4	16.2±9.7
Dimetyl Fumarate									1207 (13,5)	1,629 35,9)	706 (26,9)	256 (26,9)
duration months (mean±SD)									9.7±6.2	12.3±6.3	10.9±6.1	11.1±6.4
Teriflunomide									638 (7,1)	405 (8,9)	177 (6,8)	61 (6,4)
duration months (mean±SD)									10.8±6.6	12.1±6.4	11.2±6.5	10.5±6.5

DISCUSSION

In this study, we described real-world prescribing patterns for MS patients over a 13-year period using the database from the Department of Informatics of the Brazilian Unified Health System (DATASUS). Our results provide insight into the characteristics of the patients and the current state of MS treatment in Brazil.

The characteristics of the DATASUS MS population is comparable with the MS populations from previously published literature, with the majority of subjects being female (73.3%) and receiving a first diagnosis in the third decade of life (mean age of 38 years)[15–17]. The delayed

diagnosis and, consequently, the late treatment present a negative impact: the MS patients that had early treatment reduce the relapse rate and disease progression, improving treatment efficacy and patient outcomes[18]. Regarding the geographic distribution of MS cases throughout Brazil, the observed differences may reflect the population density as well as the number of neurologists in each region, which are highest in the South and Southeast region[19].

Our study found a prevalence rate ranged from 6.9 to 11.0 cases per 100,000 persons during 2008-2020, which was lower than the median estimated global prevalence reported by the WHO Atlas of MS: 30 cases per 100,000 person[20], but it is aligned to the Brazilian estimates (8.69 cases per 100,000)[2]. Although incidence rates remained quite stable over the study period, prevalence rates almost doubled, this could potentially be attributed to improved patient survival[5]. A systematic review about MS prevalence in Brazil considers that the main contributors of this increase throughout the years are the progress in diagnosis and treatment, and the good development of other reference centers for MS in public hospitals[2]. In this scenario, it is important to consider the implications of the increasing number of patients with MS for the health systems.

Comorbidities were reported for a very small proportion of individuals with MS. Although it is well established that the presence of comorbidities is common in this population[21], a previous retrospective study also using DATASUS identified a low rate (10%) of co-existing conditions in MS[22]. A possible

explanation for these results may be explained by the fact that the registry of comorbidities in the SUS databases is not mandatory to release the prescription of medicines for the treatment of MS. Therefore, MS comorbidities in our study might be underestimated. Particularly to the coexistence of chronic disease and depression, this comorbidity leads to an increased burden of disease compared to having one or the other[23]. Disability also impacts the burden of disease, specifically the QoL, followed by depression and anxiety. In this sense, interventions to reduce incapacity are expected to improve the QoL.

The choice of DMT depends on several clinical factors, such as progression status and disease activity, prognostic, patient and disease phenotype, severity, comorbidities, safety profile, tolerability. On the other hand, physicians also consider patient preference, convenience, cost, and treatment availability in the health system.

Considering the availability of DMTs in the public health system and the analysis only for this cohort, interferon-beta was the most common first-line prescribed medication for MS in all the three analyzed periods, followed by glatiramer acetate. Glatiramer was the most frequently prescribed second-line treatment only in the first extracted period (2008–2014), being replaced by fingolimod after 2015. Interferon-beta and glatiramer were the only alternatives for first-line treatment of patients with MS until 2015 in the Brazilian public health system, according to the clinical guidelines for MS at that time[24,25]. These results match those

observed in earlier studies with retrospective data in Brazil[22], United States[25], and Canada[26]. Fingolimod, natalizumab, and azathioprine were also prescribed for MS treatment in the public system.

Currently and according to Brazilian PCDT, DMT options at SUS are distributed into three different lines (for patients without high disease activity): (i) first line: beta-interferon, glatiramer, teriflunomide, and dimethyl fumarate; (ii) second line: fingolimod or other first line drug; (iii) third line: natalizumab[10]. Switching is allowed when patients present intolerance, adverse reactions, therapeutic failure, or lack of adherence. Discontinuation rates of the first DMTs among MS patients are usually high, ranging from 39% to 65.7%[27-30]. Aligned to the MS Brazilian guideline, the second line most used treatments were glatiramer and fingolimod. The prescription behavior of the DMTs analyzed in this study show the use of DMT in the first or second line were compliant on the PCDTs publish from 2014 to 2015, 2018-2019-2021[31-34].

In this study the time to treatment failure for each DMT could also be estimated using the comparison of mean duration of treatment. The period between 2008-2014 represents the start of the data research. Since all first data for DMT per patient was considered the first line of treatment the analysis and comparisons for this period will have a high level of deviation. Due to this reason, this was not included in this analysis.

The analysis of duration of treatment per each line reveals the use of different therapies in first and second lines than the ones established in PCDT, demonstrating the preference from physicians to anticipate lines of treatment following international guidelines due the possible clinical factors observed in the patient at the time of DMT treatment introduction. On the past years there was not common knowledge the importance of early treatment in MS patients[35]. However, the improvement of the early treatment awareness consolidates the importance of treat MS patients during the window of opportunity in order to guarantee the best outcomes.

This study explored data from a public data bank (DATASUS) and the analysis of this data can present some limitations. DATA-SUS do not differentiate the types of MS in RRMS or other manifestations, however the literature prevalence of RRMS (80-85%)[36] in the MS patients suggest that <85% of the patients are in RRMS stage. Corroborating with this hypothesis PCDT exclude the treatment for PPMS manifestation which could reflect that all patients found at DATA-SUS are treating the RRMS form. Other point that needs to be aware is the high number in First line 2008-2014: once we do not have data previous 2008, all treatments collected in the first period (2008–2014) was considered as first line of treatment. It is important to highlight that this number is probably overestimated.

The limitation of this study was the medication data that was obtained from prescriptions by physicians inserted in the

databases. It is not possible therefore to confirm that the patient indeed took the medication. Despite these limitations, the large sample size of the databases allowed for description of treatment patterns in a large sample size of patients with MS as compared with other study designs (clinical trials or prospective cohort studies). Furthermore, the databases provide an opportunity to assess treatment of patients with MS under real-world conditions.

CONCLUSION

Despite the limitations, the present study demonstrates that the prescription pattern of DMTs for MS treatment in Brazil, especially related to lines of treatment, follow Brazilian and international guidelines where mostly of the DMTs are susceptible to be prescribe in any line of treatment.

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SUPPLEMENTS

Supplement 1. Switch treatment pattern per line of therapy (2008–2014).

From first line to second line treatment			
First line (n=21,170)	**Second line**	**n**	**%**
Betainterferon	Glatiramer	2283	59.3
	Natalizumab	584	15.2
Glatiramer	Betainterferon	697	18.1
	Azatioprine	58	1.5
	Natalizumab	222	5.8
Natalizumab	Betainterferon	4	0.1
	Glatiramer	5	0.1
Second line (n=2,741)	**Third line**	**n**	**%**
Betainterferon	Glatiramer	28	7.9
	Natalizumab	43	12.1
Glatiramer	Betainterferon	118	33.3
	Natalizumab	149	42.1
Natalizumab	Betainterferon	5	1.4
	Glatiramer	11	3.1

Supplement 2. Switch treatment pattern per line of therapy (2015–2017).

From first line to seconds line			
First line (n=7,683)	**Second line**	**n**	**%**
Betainterferon	Glatiramer	398	36.2
	Natalizumab	155	14.1
	Fingolimode	130	11.8
Glatiramer	Betainterferon	151	13.7
	Natalizumab	92	8.4
	Fingolimode	68	6.2
Natalizumab	Betainterferon	1	0.1
	Glatiramer	7	0.7
	Fingolimode	30	2.7
Fingolimode	Betainterferon	5	0.5
	Natalizumab	19	1.7
From second line to third line			
Second line (n=2,989)	**Third line**	**n**	**%**
Betainterferon	Natalizumab	9	11.5
	Fingolimode	4	5.1
Glatiramer	Betainterferon	5	6.4
	Natalizumab	35	44.9
	Fingolimode	18	23.1
Natalizumab	Fingolimode	4	5.1
	Glatiramer	1	1.3
Fingolimode	Natalizumab	1	1.3
	Betainterferon	1	1.3

Supplement 3. Switch treatment pattern per line of therapy (2018–2020).

From first line to seconds line			
First line (n=8,935)	**Second line**	**n**	**%**
Betainterferon	Glatiramer	145	8.3
	Natalizumab	120	6.9
	Teriflunomide	87	5.0
	Dimethyl Fumarate	448	25.8
	Fingolimode	295	17.0
Glatiramer	Betainterferon	45	2.6
	Natalizumab	69	4.0
	Teriflunomide	34	2.0
	Dimethyl Fumarate	202	11.6
	Fingolimode	183	10.5
Natalizumab	Betainterferon	1	0.1
	Glatiramer	3	0.2
	Teriflunomide	1	0.1
	Dimethyl Fumarate	10	0.6
	Fingolimode	41	2.4
Fingolimode	Betainterferon	4	0.2
	Glatiramer	3	0.2
	Teriflunomide	1	0.1
	Dimethyl Fumarate	13	0.7
	Natalizumab	32	1.8
From second line to third line			
Second line (n=4,541)	**Third line**	**n**	**%**
Betainterferon	Glatiramer	1	1.1
	Natalizumab	3	3.2
	Dimethyl Fumarate	2	2.2
	Fingolimode	4	4.3
Glatiramer	Dimethyl Fumarate	12	12.9
	Betainterferon	1	1.1
	Natalizumab	4	4.3
	Fingolimode	5	5.4
Dimethyl Fumarate	Betainterferon	3	3.2
	Glatiramer	3	3,2
	Natalizumab	9	9.7
	Teriflunomide	2	2.2
	Fingolimode	8	8.6
Natalizumab	Betainterferon	1	1.1
	Dimethyl Fumarate	1	1.1
	Glatiramer	1	1.1
	Fingolimode	2	2.2
Fingolimode	Dimethyl Fumarate	1	1.1
	Natalizumab	10	10.8
Teriflunomide	Betainterferon	3	3.2
	Fingolimode	7	7.5

Dimethyl Fumarate	8	8.6
Natalizumab	1	1.1
Glatiramer	1	1.1