



Usage trend of oral drugs for multiple sclerosis in Argentina.

Ricardo Alonso^{1,8}, Maria Barbara Eizaguirre¹, Federico Man², Abril Lopez Bizzo², Cohen Leila¹, Juan Ignacio Rojas³, Liliana Patrucco³, Edgardo Cristiano³, Cecilia Pita¹, Veronica Tkachuk⁴, Maria Eugenia Balbuena⁴, Edgar Carnero Contentti⁵, Pablo Lopez⁵, Juan Pablo Pettinichi⁵, Norma Deri⁶, Jimena Miguez⁷, Agustín Pappolla⁷, Nora Fernandez Liguori⁸, Jorge Correale⁹, Adriana Carrá^{10,11}, Orlando Garcea¹, Berenice Silva¹

1-Centro Universitario de Esclerosis Múltiple. Hospital Ramos Mejía

2-Servicio de Neurología. Hospital Ramos Mejía.

3- Centro de esclerosis múltiple de Buenos Aires, CABA

4- Sección de Esclerosis Múltiple y Enfermedades Desmielinizantes, Servicio de Neurología - Hospital de Clínicas José de San Martín, CABA

5- Neuroimmunology Unit, Department of Neuroscience, Hospital Aleman, Buenos Aires

6- Centro de Investigaciones Diabaid, CABA

7- Servicio de Neurología, Hospital Italiano de Buenos Aires, Buenos Aires

8-Servicio de Neurología. Sanatorio Guemes

9-Departamento de Neurología - FLENI, CABA.

10- Sección de Enfermedades Desmielinizantes - Hospital Británico, CABA.

11-Instituto de Neurociencias - Fundación Favaloro/INECO, CABA

CONFLICT OF INTEREST



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INTRODUCTION



Oral drugs modified treatments (oDMTs) for relapsing remitting multiple sclerosis (RRMS) have substantially increased over the past decade with four approved oral compounds now available: *fingolimod*, *dimethyl fumarate*, *teriflunomide*, and *cladribine*.

Recently, was presented the first nation-wide MS registry in Argentina (Clinical Trials registry number NCT NCT03375177), providing an updated information on epidemiological features, disease characteristic and treatment of MS and NMOSD in Argentina Real-world observational studies of large populations of MS patients are invaluable for capturing the trend of the use of treatments.

To know this information, also could enable design studies comparisons of effectiveness and safety among DMTs and the characterization of prognostic subgroups of patients.

Our aim was to describe the usage trend of oral DMTs (oDMTs), as first treatment option or after switch, regarding its approval in Argentina.

METHODS



A retrospective study was conducted in a cohort of MS patients follow-uped in five MS centers of Buenos Aires and incorporated in RelevareM: Hospital Ramos Mejia, Hospital Alemán, Hospital Italiano de Buenos Aires / CEMBA, Hospital de Clinicas de Buenos Aires and Centro de Investigaciones Diabaid. The inclusion criteria for this study were: diagnosis of RRMS, >18 years old and started treatment since 2012.

Regarding the availability of different oDMTs in Argentina, we define three time periods (P1-3): P1: from 2012 to 2014; P2: from 2015 to 2017 and P3: from 2018 to 2020. An analysis was performed comparing between these three periods to assess the tendency of oDMTs use over time.

Related to the use of oDMTs, three scenarios were defined: initial treatment, first switch and second switch.

Statistical analysis

Data were analyzed with SPSS 21.0 statistical program. The following statistical descriptors were used: frequency, percentage, range, media, and standard deviation. For inferential analyzes the paired samples t-test was used. Statistical significance was set at $p < .05$.

RESULTS

Out of 202 RRMS patients, 58% were female, mean age 32.4 ± 11.0 years, mean disease evolution 8.0 ± 5.5 years, 46 % started with oDMTs and 64% oDMTs was the first choice after a switch. Demographic characteristics of these patients are summarized in **Table 1**.

Treatments were analyzed according each time period. The most frequent treatment at the beginning of the disease was: interferon beta 1a (40%) in P1, fingolimod (37.3%) in P2 and also fingolimod (35%) in P3. A total of 40.6% of MS patients switched the treatment at least once and the main cause for the first switching treatment was treatment failure (39%). A second change of treatment was needed in 14.4% of the patients and also the most frequent cause was also treatment failure (52.2%) (**Table 2**).



Table 1. General characteristics of patients with RRMS and their treatment

General characteristics	
N	202
Mean age at survey, (\pm SD)	40.58 (\pm 11.64)
Female No (%)	117 (57.9)
Disease Evolution, y mean \pm SD (range)	8.09 \pm 5.54 (1-44)
Most frequent beginning treatment No (%)	
Period 1 (n 79)	
Interferon	47 (59.5%)
Glatiramer acetate	13 (16.5%)
Period 2 (n 83)	
Fingolimod	31 (37.3%)
Interferon	16 (19.3%)
Period 3 (n 40)	
Fingolimod	14 (35%)
Interferon	6 (15%)

P1: from 2012 to 2014; P2: from 2015 to 2017 and P3: from 2018 to 2020

Table 2. Disease-modifying treatment used in the first and second treatment change according to period

Period	Eligible DMTs	First treatment change N:75	Second treatment change N: 31
		Frequency (%)	Frequency (%)
Period 1	Injectables	9 (19.1%)	-
	oDMTs	28 (59.6%)	14 (77.8%)
	Monoclonal antibodies	10 (21.3%)	4 (22.2%)
Period 2	Injectables	2 (7.7%)	-
	oDMTs	19 (73.1%)	10 (83.3%)
	Monoclonal antibodies	5 (19.2%)	2 (16.7%)
Period 3	Injectables	-	-
	oDMTs	1 (50%)	1 (100%)
	Monoclonal antibodies	1 (50%)	-

Abbreviations: DMTs: disease-modifying treatment. oDMTs: oral disease-modifying treatment T/A: switch frequency due to adherence or tolerance. E: switch frequency due to efficacy.

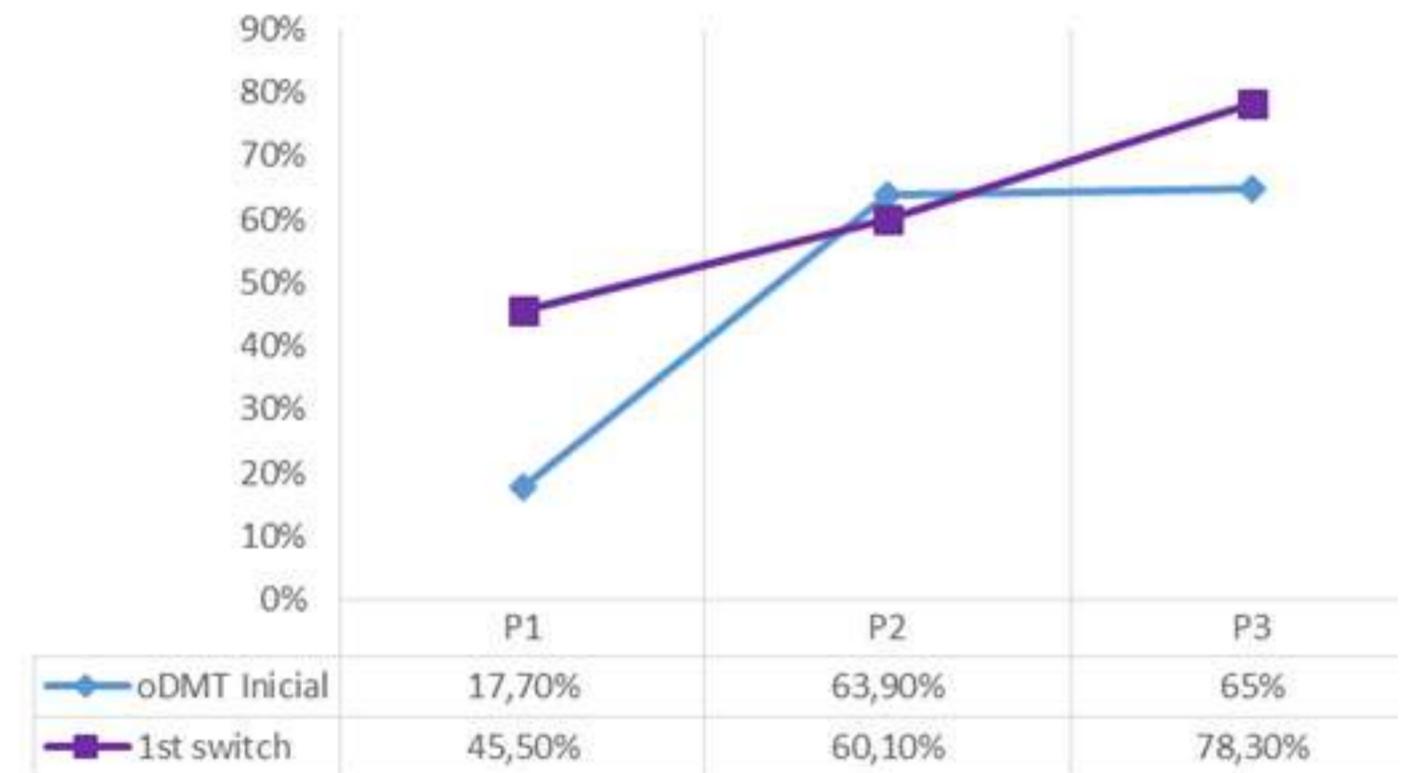
RESULTS

The tendency among the patients who switched due to therapeutic failure was for a more effective treatment to be chosen. Injectable therapies were the most frequently withdrawn in relation to oDMTs and monoclonal antibodies (Chi-square = 23.6; $p < 0.01$). We found an increase in the use of oDMTs as initial treatment over time (P1: 17.7%, P2: 63.9% and P3: 65.0%; Chi-square = 41.9 $p < 0.01$). We also found a tendency in increasing use of oDMTs after a first switch (P1: 45.5%, P2: 60.1% and P3 78.3%) (Figure 1).

Multivariate analysis showed that disease evolution (OR=1.06, $p=0.04$), and year of starting treatment (OR=1.00, $p < 0.01$) were independently associated with choice of oDMTs.



Figure 1 Usa trend of oDMTs relatad to time period



CONCLUSION

To date, reports regarding the use of oDMTs in patients with MS are scarce in our country.

We have identified an increasing tendency in the use of oDMTs as initial treatment of RMS regarding its approval in Argentina.

More studies with a greater number of patients are necessary to corroborate the results found in our research.

