Effectiveness of Dimethylfumarate in multiple sclerosis, a French cohort within SNDS nationwide claims database

Pauline Bosco-Lévy1,2, Patrick Blin1, Séverine Lignot-Maleyran1, Régis Lassalle1, Abdellah Abouelfath1, Pauline Diez-Andreu1, Marc Debouverie1, Bruno Brochet1, Francis Guillemin2, Nicholas Moore1,4, Cecile Droz-Pepoteau1

1 Bordeaux PharmacoEpi, Univ. Bordeaux-INSERM CIC4601, Bordeaux, France, 2 Bordeaux Population Health Research Centre, INSERM UMR 1219, Univ. Bordeaux, Bordeaux, France, 3 Département de neurologie, CHU Nancy, F 54005 Nancy, France; Université de Lorraine, EA 4360 APEMAC, F 54500 Vandœuvre-Lès-Nancy, France, 4 CRC SEP, service de Neurologie, CHU de Bordeaux, 1 CHRU de Nancy, INSERM CIC 1433 Épidémiologie clinique, Nancy, Université de Lorraine, EA 4360 APEMAC, F 54500 Vandœuvre-Lès-Nancy, France, 5 CHU de Bordeaux, Bordeaux, France.

Background

Cohort using the SNDS nationwide claims database.

Objectives

To assess the effectiveness of dimethylfumarate in multiple sclerosis compared to other oral drugs (teriflunomide and fingolimod) and injectable immunomodulators, in real life settings.

Methods

Study Design

Cohort study using SNDS (Système National des Données de Santé) nationwide French claims database including all patients with:

- a first reimbursed dispensing of a MS drug from 2015 to 2016,
- a follow-up from 1 to 2.5 years after index date (ID),
- at least 4.5-year database history.

Data source

The SNDS database contains individual pseudonymised information from 68 million persons on:

- Gender, date of birth, area of residence, date of death;
- Long-term disease registration with associated ICD-10 codes for full insurance coverage (with start and end dates);
- Outpatient reimbursed healthcare expenditures: visits, medical procedures, lab tests, drugs ...
- Hospital discharge summaries with ICD-10 codes for diagnosis (primary, linked and associated diagnoses) for all private and public medical, obstetric and surgery hospitalisations, with the date and duration of hospitalisation, medical procedures.

Outcomes

The primary outcome was the annual rate of relapses (ARR) during the index treatment period.

Relapses were identified through a complex algorithm that included dispensing of high dose of corticosteroids for outpatient and hospitalisations with MS relapse diagnosis potentially combined with high dose of corticosteroids dispensing (positive and negative predictive value: 95.2% and 100 % respectively) of [Abstract # 3874].

Data analyses

Descriptive analyses

Baseline characteristics of patients by treatment group.

Comparative analyses

Head-to-head comparisons: DMF vs IMM, DMF vs TFR or DMF vs FTY.

After high-dimensional propensity scores (hdPS) trimming analysis and 1:1 matching

Sensitivity analysis including hdPS adjustment and weighting

A negative binomial regression model was used to estimate the relative risk (RR z [95% CI]).

Results

Study population

Dimethylfumarate treated vs TFR (varied) or IMM drugs during 01/07/15 and 31/12/17 and affiliated to main scheme

Population restricted to the inclusion period between 01/07/15 and 31/12/16 and a follow-up from 1 to 2.5 years after

N = 34 620

Table 1. Description of treatment groups in naïve population

<table>
<thead>
<tr>
<th>Treatment groups</th>
<th>% Rather than 4.5-year database</th>
<th>% Rather than 4.5-year database</th>
<th>% Rather than 4.5-year database</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMF (n=1777)</td>
<td>39.6 (11.8)</td>
<td>36.0 (11.4)</td>
<td>37.8 (12.3)</td>
</tr>
<tr>
<td>Teriflunomide (TFR)</td>
<td>3190 (32.2)</td>
<td>3190 (32.2)</td>
<td>3190 (32.2)</td>
</tr>
<tr>
<td>Fingolimod (FTY)</td>
<td>255 (5.3)</td>
<td>255 (5.3)</td>
<td>255 (5.3)</td>
</tr>
<tr>
<td>Injectable Immunomodulator</td>
<td>1801 (31.0)</td>
<td>1801 (31.0)</td>
<td>1801 (31.0)</td>
</tr>
<tr>
<td>Corticosteroids &amp; Peptide therapy</td>
<td>355 (10.7)</td>
<td>355 (10.7)</td>
<td>355 (10.7)</td>
</tr>
<tr>
<td>Interferon beta1a</td>
<td>312 (9.0)</td>
<td>312 (9.0)</td>
<td>312 (9.0)</td>
</tr>
<tr>
<td>Interferon beta1b</td>
<td>32 (0.9)</td>
<td>32 (0.9)</td>
<td>32 (0.9)</td>
</tr>
<tr>
<td>Interferon beta2</td>
<td>7 (0.1)</td>
<td>7 (0.1)</td>
<td>7 (0.1)</td>
</tr>
</tbody>
</table>

Figure 2. Probability of discontinuation or a switch of index treatment during the follow-up period, according to treatment groups, in the naïve population (Kaplan-Meier curve).

Annuallyal relapse rates

Dimethylfumarate vs Teriflunomide

95% CI ARR

Cox's (n=1153 vs n=1246)

[0.67 - 0.96] 0.13 0.16

hdPS matching (n=1153 vs n=1246)

[0.83 - 1.00] 0.14 0.17

hdPS adjustment (n=1153 vs n=1246)

[0.60 - 0.96] 0.13 0.16

FTY n=1246

[0.90 - 0.97] 0.13 0.16

Dimethylfumarate vs Immunomodulators

Cox's (n=1153 vs n=1246)

[0.54 - 0.81] 0.13 0.19

hdPS matching (n=1059 vs n=1019)

[0.56 - 0.90] 0.14 0.18

hdPS adjustment (n=1144 vs n=1364)

[0.57 - 0.87] 0.13 0.19

FTY n=1144

[0.55 - 0.82] 0.13 0.19

Conclusion

This real-life nationwide study showed:

- A significantly lower risk of relapses with dimethylfumarate than teriflunomide and IFN in real conditions of use
- The specific profile of fingolimod patients makes the comparison with dimethylfumarate patients difficult.

Declaration of Interest Statement: The EVIDEMS study is carried out by the Bordeaux PharmacoEpi platform in collaboration with Biogen. This work was supported by Biogen and supervised by an independent scientific committee.

Figure 3. Relapse incidence rate (TFR vs TFR, TMR vs IM)

Negative binomial regression model