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

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Background

➢ **Multiple sclerosis (MS)**
- Incapacitating, progressive, chronic neurological disorder that involves a selective, chronic inflammation and demyelination of the central nervous system
- Relapsing-remitting MS form (RRMS) is the most common, and are characterized by the presence of relapses without disability progression between relapses
- In France, prevalence in 2015: 135 per 100 000 inhabitants and 87 000 cases in 2017

➢ **Current therapeutic strategy of RRMS**
- The first-line generation of medications approved were the Injectable ImmunoModulators (**IMM**)
- Treatment options have broadened to include the orally administered: dimethylfumarate (**DMF**), teriflunomide (**TERI**) and fingolimod (**FTY**).

➢**In this context a project was designed** to assess the benefit of DMF to other drugs in current practice, and especially to the two other oral drugs, TERI and FTY.

➢**Cohort using the SNDS** nationwide claims and hospital database.

Objectives

➢ **To assess the effectiveness of dimethylfuarate 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 66 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 outpatients and hospitalizations with MS relapse diagnosis potentially combined with high dose of corticosteroids dispensing (positive and negative predictive value: 95.2% and 100 %, respectively) ***cf [Abstract # 3874].***

➢ **Data analyses**
- **Descriptive analyses**
  - ✓ Baseline characteristics of patients by treatment group.
  - ✓ Probability of discontinuation or switch of the index treatment (i.e. no dispensing of the index drug during 60 days after the end of the last dispensing) using Kaplan-Meier survival analysis.
- **Comparative analyses**
  - ✓ Head-to-head comparisons: DMF vs IMMs, DMF vs TERI or DMF vs FTY.
  - ✓ After high-dimensional propensity scores (hdPS) trimming and 1:1 matching
  - ✓ Sensitivity analysis including hdPS adjustment and weighting
  - ✓ A negative binomial regression model was used to estimate the relative risk (RR ± [95% CI]).

Results

➢ **Study population**

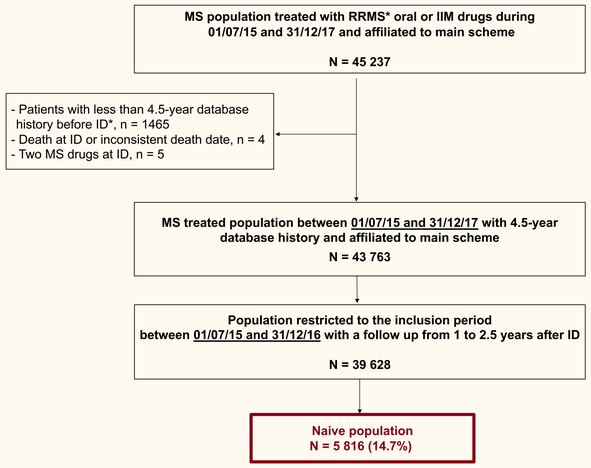

Figure 1. Identification and selection of patients for data analysis (SNDS data)

➢ **Description of treatment groups at baseline in the selected MS treated population**

Table 1. Description of treatment groups in naive population

	Naive population N = 5816
Treatment groups, n (%)	
Dimethylfumarate (DMF)	1777 (30.6)
Teriflunomide (TERI)	1930 (33.2)
Fingolimod (FTY)	308 (5.3)
Injectable Immunomodulator (IIM)	1801 (31.0)
Glatiramere acetate	623 (10.7)
Peginterferon bêta-1a	512 (8.8)
Interferon beta 1a (Avonex®)	392 (6.7)
Interferon beta 1a (Rebif®)	235 (4.0)
Interferon beta 1b (Betaferon®)	32 (0.6)
Interferon beta 1b (Extavia®)	7 (0.1)

➢ **Description of initial characteristics at inclusion and within 2 years years preceding the ID**

Table 2. Description of initial characteristics in naive population

	DMF n = 1777	TERI n = 1930	FTY n = 308	IIM n = 1801	Total n = 5816
Age, mean (± SD)	39.6 (11.6)	43.0 (11.4)	39.0 (12.1)	37.6 (12.3)	40.1 (12.0)
Female, n (%)	1326 (74.6)	1309 (67.8)	201 (65.3)	1395 (77.5)	4231 (72.7)
History of clinical characteristics					
Nb of relapses, mean (± SD)	0.14 (0.28)	0.13 (0.27)	0.17 (0.32)	0.13 (0.26)	0.14 (0.27)
MS relapse hospitalisations, n (%) (excluding relapses)	752 (42.3)	758 (39.3)	226 (73.4)	751 (41.7)	2487 (42.8)
Neurologist visit, n (%)	1570 (88.4)	1696 (87.9)	237 (76.9)	1529 (84.9)	5032 (86.5)
Cerebral or spinal cord MRI , n (%)	1656 (93.2)	1822 (94.4)	266 (86.4)	1657 (92.0)	5401 (92.9)

➢ **Discontinuation and switch of index treatment during the follow-up period**

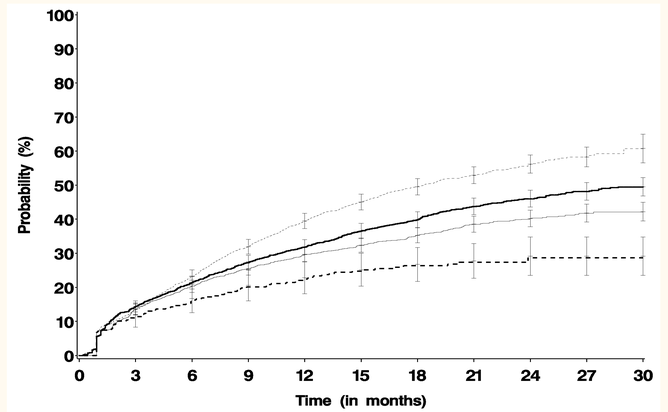

Figure 2. Probability of discontinuation or switch of index treatment during the follow-up period, according to treatment groups, in the naive population (Kaplan-Meier curve)

➢ **Annualized relapses rate**

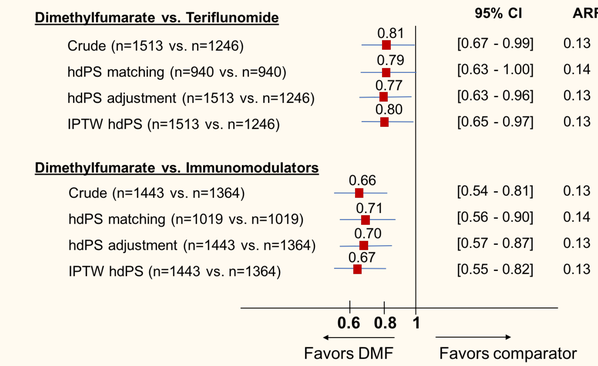

Figure 3. Relapse incidence rate (TMF vs TERI, TMF vs IIM) Negative binomial regression model

Conclusion

➢ This real-life nationwide study showed:
- **A significantly lower risk of relapses with dimethylfumarate** than teriflunomide and IIM in real conditions of use
- The **specific profile** of **fingolimod** patients makes the **comparison with dimethyl fumarate** 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.

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