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Disease-modifying therapies use in primary progressive multiple sclerosis patients in France: data from the OFSEP cohort over the 1996-2017 period

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Background: Up to now, treatment options were poor for primary progressive multiple sclerosis (PPMS) patients, as disease-modifying therapies (DMTs) approved for relapsing-remitting multiple sclerosis (MS) did not show any efficacy in this form. However, many DMTs are proposed off-label, in an attempt to reduce disability progression and answer patients' expectations.

Objective: **To describe the use of DMTs in real-life settings in a large cohort of PPMS patients from the French OFSEP cohort ('Observatoire Français de la Sclérose en Plaques') over 1996-2017 period.**

Methods: All OFSEP patients with PPMS and alive on 1996, Jan 1st (to get a chance to be treated with a DMT approved in MS) were included, i.e. **6,507 patients among a total of 54,000 MS patients**. All DMT were considered, without any minimal duration.

Periods were defined according to specific therapeutic milestones in France: **<1st Jan 1996** (approval of interferon), **1st Jan 1996 to 1st Apr 2007** (approval of natalizumab), **1st Apr 2007 to 1st Jan 2014** (approval of dimethyl fumarate), and **>= 1st Jan 2014**. In each period was considered the cohort of MS incident cases in the period, as well as the follow-up period of MS cases whose disease has started in the previous period(s).

Results: **Overall, 56.6% of PPMS patients received at least one DMT over follow-up period**, started at a mean age of 47.4 ± 10.9 years, after a mean MS duration of 6.0 ± 5.7 years, and for a cumulative duration of 4.3 ± 4.4 years, i.e. 32% of follow-up duration**.**

Table: Initial characteristics of the overall population and of incident cases in each period

	Overall N=6,507	<1996 n=2,328	1996-2007 n=2,848	2007-2014 n=1,195	>=2014 n=136
Sex ratio F:M	1.3 (3656:2851)	1.3 (1338:990)	1.3 (1602:1246)	1.2 (642:553)	1.2 (74:62)
Age at MS clinical onset (y)	42.4 ± 10.9	38.0 ± 10.1	43.9 ± 10.4	46.9 ± 10.5	46.4 ± 10.2
Follow-up (F/U) duration from MS clinical onset (y)	13.2 ± 9.0	21.0 ± 9.3	10.7 ± 5.0	5.3 ± 2.4	1.9 ± 0.8
Received at least one DMT over F/U period	3683 (56.6 %)	1380 (59.3%)	1664 (58.4%)	591 (49.5%)	48 (35.3%)

Figure 1: Distribution of DMTs use over time 1990-2017; A. including untreated patients, B. excluding untreated patients

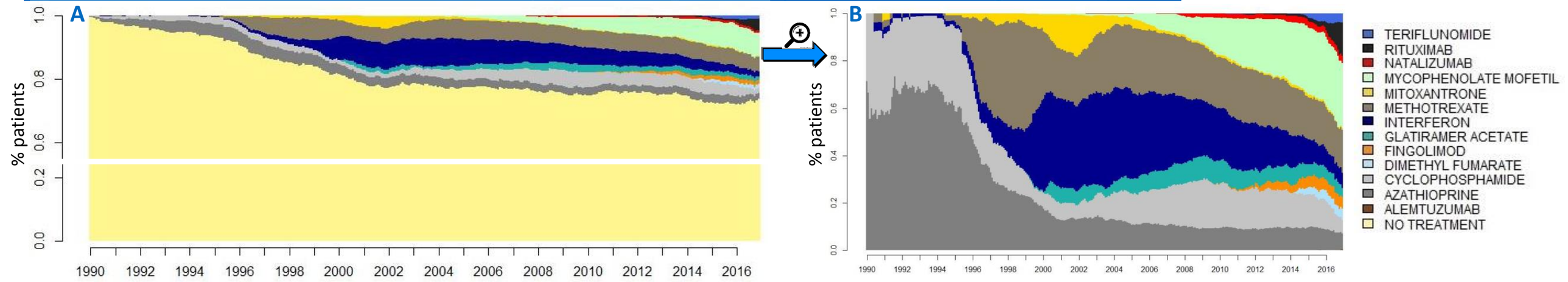

Figure 2: Proportion of treated patients, age and disease duration (DD) at first DMT initiation over F/U period in the four incident cohorts

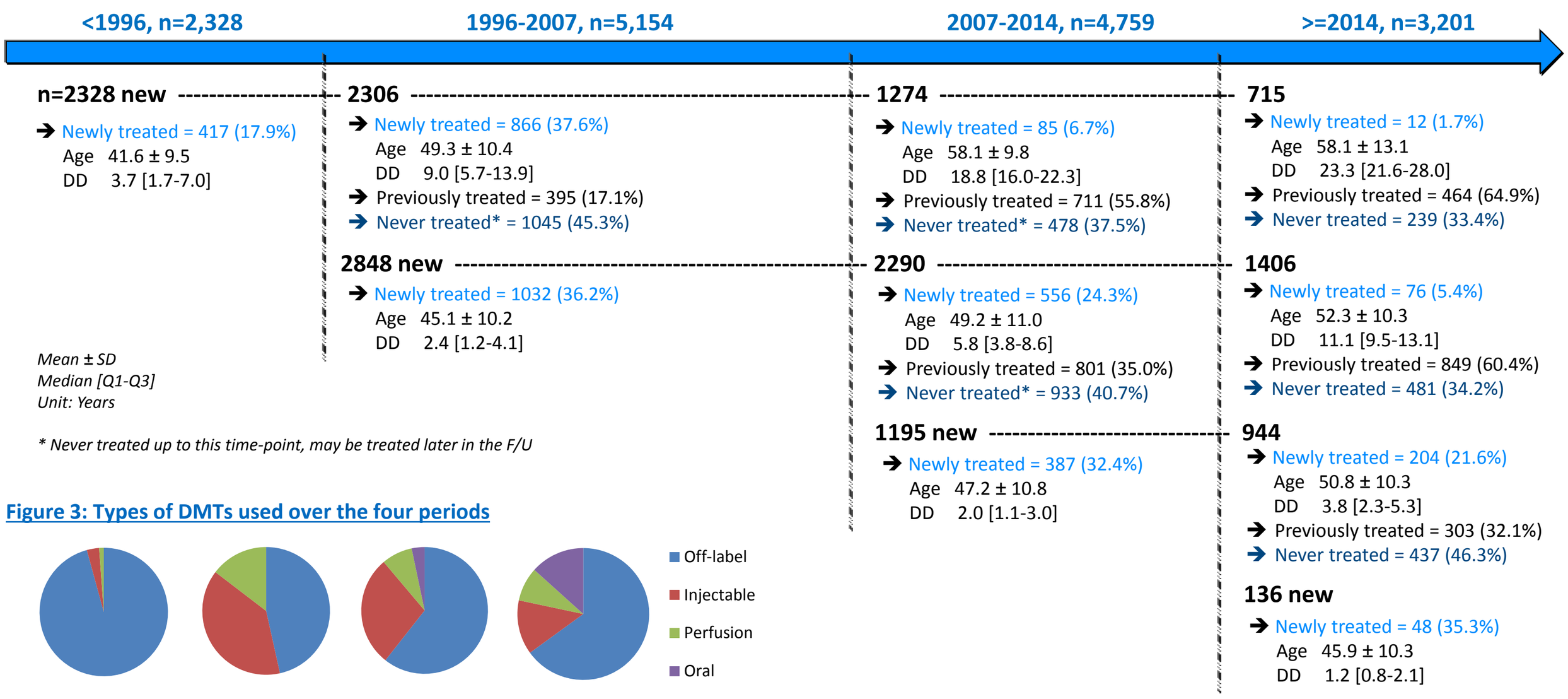

Figure 3: Types of DMTs used over the four periods

Discussion: This study highlights **the active attitude of French neurologists regarding use of DMTs in PPMS (>50% treated)** as well as the **diversity of practices**. Indeed, neurologists seem to be inclined to try all kinds of drugs, when they came available for relapsing MS, and earlier now than before. DMT is sometimes started later in the disease or at an advanced age (but level of disability was not considered here). However, the limited duration of DMTs probably reflects the fact that neurologists don't leave a patient under a drug if the expectations regarding efficacy are not met. Some patients did not receive any DMT over their whole disease duration (30 to 50% depending on F/U duration). **Gathering data from more than 20 years at a national scale offers the opportunity to assess changes in daily practice with the perspective of newly approved drugs in PPMS in the coming months or years in France.**

Disclosures: **Dr Leray** reports personal fees as speaker or consultant from Novartis and Sanofi Genzyme, outside the submitted work, and travel grants from Novartis and Roche SAS. Sources of funding in the last year came from the French ARSEP Foundation, the French National Security Agency of Medicines and Health Products, the EDMUS Foundation, and donation from Roche SAS. **F. Rollot** has nothing to disclose. **R. Casey** has nothing to disclose. **Dr de Sèze** received personal fees as speaker or consultant from Biogen, Merck Serono, Bayer, LFB, Sanofi-aventis, Teva, Genzyme, Almiral, and Alergan. **Dr Laplaud** received honoraria and consulting fees from Biogen, Merck, Novartis, Sanofi-Genzyme and Roche, and grants from Biogen, Medday, Novartis, Roche and Sanofi-Genzyme. **Dr Vukusic** received consultancy fees, speaker fees, research grants (non-personal) or honoraria from Biogen, Geneuro, Genzyme-Sanofi, Medday, Merck-Serono, Novartis, Roche and Teva.

Acknowledgements: J. Roux (EHESP)

This work has been supported by a grant provided by the French State and handled by the "Agence Nationale de la Recherche," within the framework of the "Investments for the Future" programme, under the reference ANR-10-COHO-002 Observatoire Français de la Sclérose en plaques (OFSEP).
It also received support from the ARSEP Foundation and the Eugène Devic EDMUS Foundation against multiple sclerosis.