



OFSEP

Observatoire Français
de la Sclérose en Plaques

OFSEP

The French MS registry

From life to science, MS data is our commitment

ECTRIMS 2022



www.ofsep.org

OFSEP scientific presentations at ECTRIMS 2022

OFSEP scientific presentations at a glance

Poster session 1 – Wednesday 26 October

P152 - NK-like CD8+ T cells with high cytotoxic properties are the reservoir of clonal cells and related to disease activity in multiple sclerosis

E. Dugast

P191 - Characterization of brain T2 lesions suggestive of demyelination in presymptomatic patients: the radiologically isolated syndrome cohort

C. Landes-Château

P306 - MS patients not treated in french expert centers: explanatory factors and evolution between 2016 and 2019

X. Moisset

P342 - Multiple sclerosis reactivation after fingolimod discontinuation for planning pregnancy: a monocentric experience

L. Jeantin

EP1069 - Natalizumab extended-interval dosing in a real-life context: efficacy study

L. Jeantin

Poster session 2 – Thursday 27 October

P421 - Pregnancy and post-partum in patients with myelin-oligodendrocyte glycoprotein antibody-associated disease

C. Carra-Dallière

e-Poster Tour 1 - Clinical

P456 - Deciphering multiple sclerosis disability progression in the elderly: a multicenter cohort study

J.-C. Ouallet

P466 - Influence of socio-economic status on excess mortality of multiple sclerosis

S. Wilson

P623 - Higher mean intensities in the lateral ventricular region of FLAIR MRI may indicate

higher disease activity in early RRMS

C. Chien

P769 - Predictors of treatment switching in the big multiple sclerosis data network – an update

T. Spelman

Oral communications – Thursday 27 October

Scientific Session 5: Progressive MS

🕒 12:05 - 12:12 - Room: Hall 12

O065 - Influence of disease modifying therapies on Expanded Disability Status Scale scores trajectories in treated and not-treated patients with secondary progressive multiple sclerosis - analysis from nine registries

Luigi Pontieri, Denmark

Scientific Session 8: Immune cell trafficking into the CNS

🕒 12:26 - 12:33 - Room: Forum

O082 - Mass cytometry blood immunophenotyping of RRMS patients at diagnosis helps in deciphering subtle changes in myeloid compartment associated to disease evolution

Stephane Rodriguez, France

OFSEP scientific presentations at a glance

Oral communications – Friday 28 October

Scientific Session RIMS 3: People with MS at work - the role of vocational rehabilitation

🕒 10:55 - 11:05 - Room: Forum

O154 - Impact of education level on multiple sclerosis disability progression in France

Mathilde LEFORT, France

The French MS registry

Collected data and nested cohorts

Clinical

FROM LIFE ...

Physician
visit or
hospitalization

Data collection
during patient visit

Collection

Clinical



Imaging



Biology



Standardized minimal data
+ additional data
for specific projects

Gathering

- Data reconciliation
- Control
- Queries

- Statistical analyses
- Reports

Data gathered in the
OFSEP
common database

Data
available for
researchers
Projects

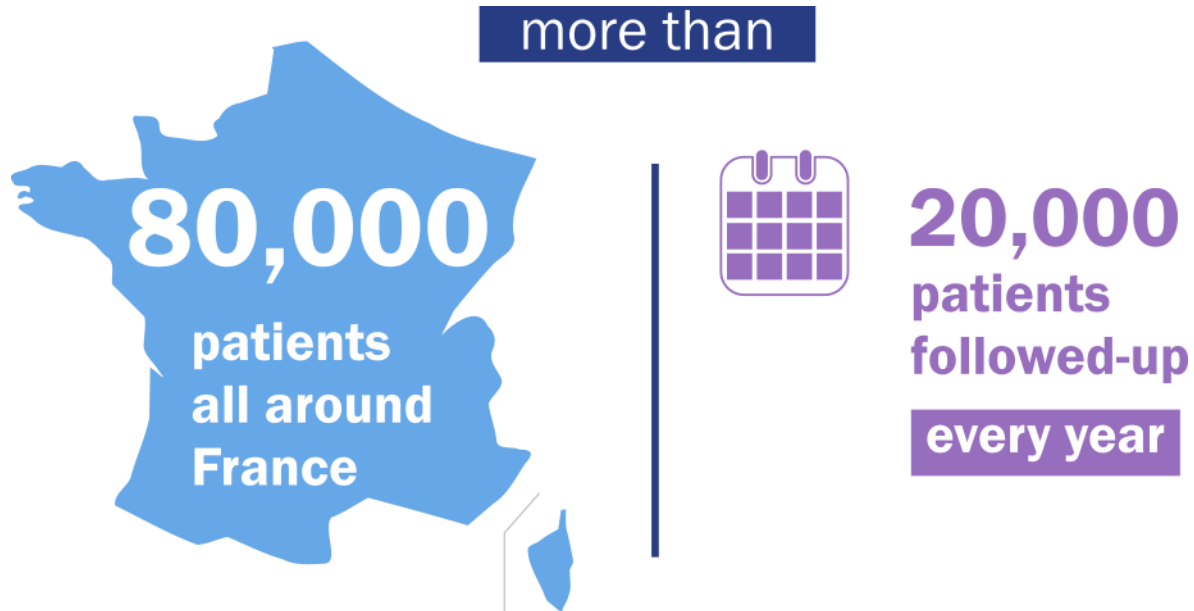
... TO SCIENCE

MS DATA IS OUR COMMITMENT

Clinical data collection

- Clinical data collected during routine follow-up visits, usually at least once a year, retrospectively at the first visit and prospectively thereafter
- Minimal mandatory data set:
 - demographic and socioeconomic characteristics
 - neurological episodes
 - disability
 - brain and spinal cord MRI reports
 - disease-modifying treatments
 - serious adverse events
- Patients with RIS, CIS, MS, NMOSD or MOGAD followed up in a participating centre are eligible
- All French MS expert centers and several peripheral centers participate in data collection

Clinical data collection



1,100,000 person-years of disease

> 500,000 person-years of prospective follow-up

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OFSEP cerebral and spinal cord MRI acquisition protocol*,

a consensus within the scientific community, feasible on all equipment and compatible with clinical acquisition times

Main sequences:

- **Brain:** 3D FLAIR, 3D T1, DWI, 3D T1 gado (*if necessary*)
- **Spine:** T2 SAG, T1 gado SAG (*if necessary*)

DICOM files stored on a centralized neuroimaging platform

** Brisset JC, Kremer S, Hannoun S, et al. New OFSEP recommendations for MRI assessment of multiple sclerosis patients: special consideration for gadolinium deposition and frequent acquisitions. J Neuroradiol. 2020;47(4):250-258.*

each year > **1,500** patients | > **8,000** exams | > **80,000** sequences

6,985
patients with at least
one MRI scan

23,147
brain exams

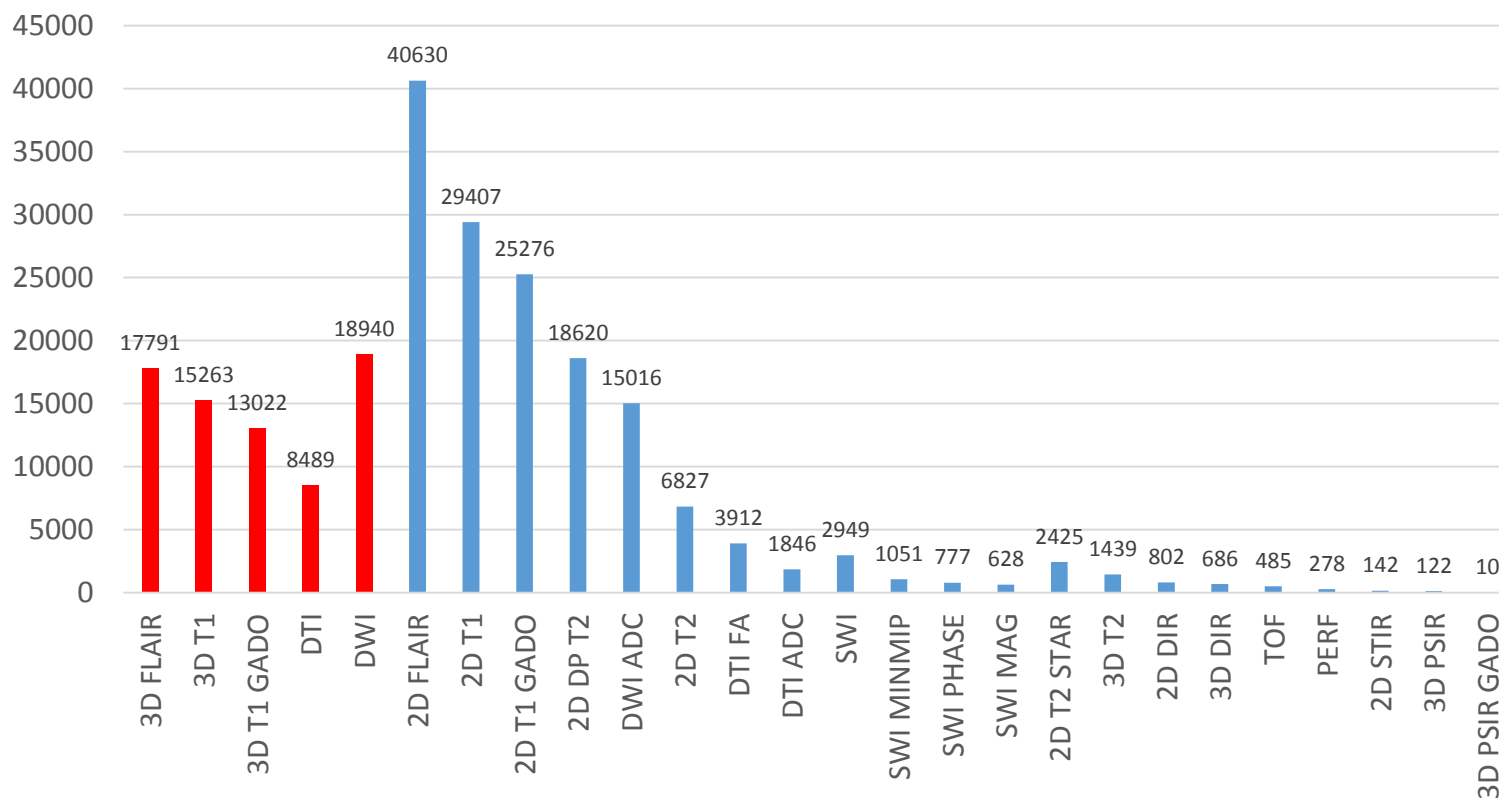
226,833
brain sequences

10,265
spinal cord exams

57,561
spinal cord sequences

23,147
brain exams

226,833
brain sequences



Siemens 54%, Philips 28%, GE 18%

1.5T 51%, 3T 49%

23,147

brain exams

226,833

brain sequences

Number of patients						
	1 TP*	2 TP	3 TP	4 TP	5-10 TP	> 10 TP
Brain IRM	2215	1584	999	621	1296	154

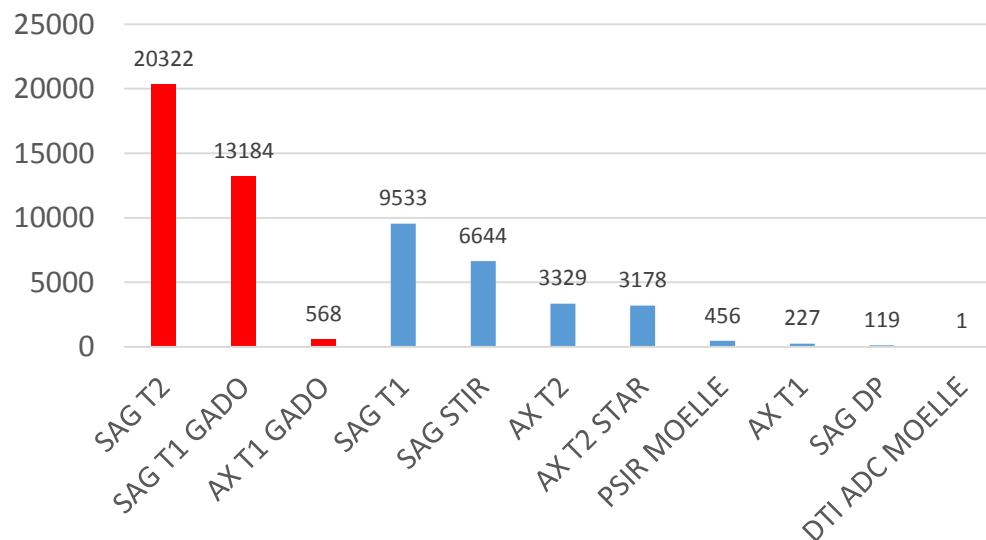
* Time point

Disease form at the first MRI	N
RIS	103
First attack	1770
RRMS	3574
SPMS	681
PPMS	472
NMOSD/MOGAD	162
Not currently identified	107

Spinal cord MRI

10,265
spinal cord exams

57,561
spinal cord sequences



Siemens 62%, Philips 25%, GE 13%

1.5T 67%, 3T 33%

Spinal cord MRI

10,265
spinal cord exams

57,561
spinal cord sequences

Number of patients						
	1 TP*	2 TP	3 TP	4 TP	5-10 TP	> 10 TP
Spinal cord MRI	2292	1097	541	301	362	15

* Time point

Disease form at the first MRI	N
RIS	63
First attack	1242
RRMS	2331
SPMS	421
PPMS	338
NMOSD/MOGAD	139
Not currently identified	74

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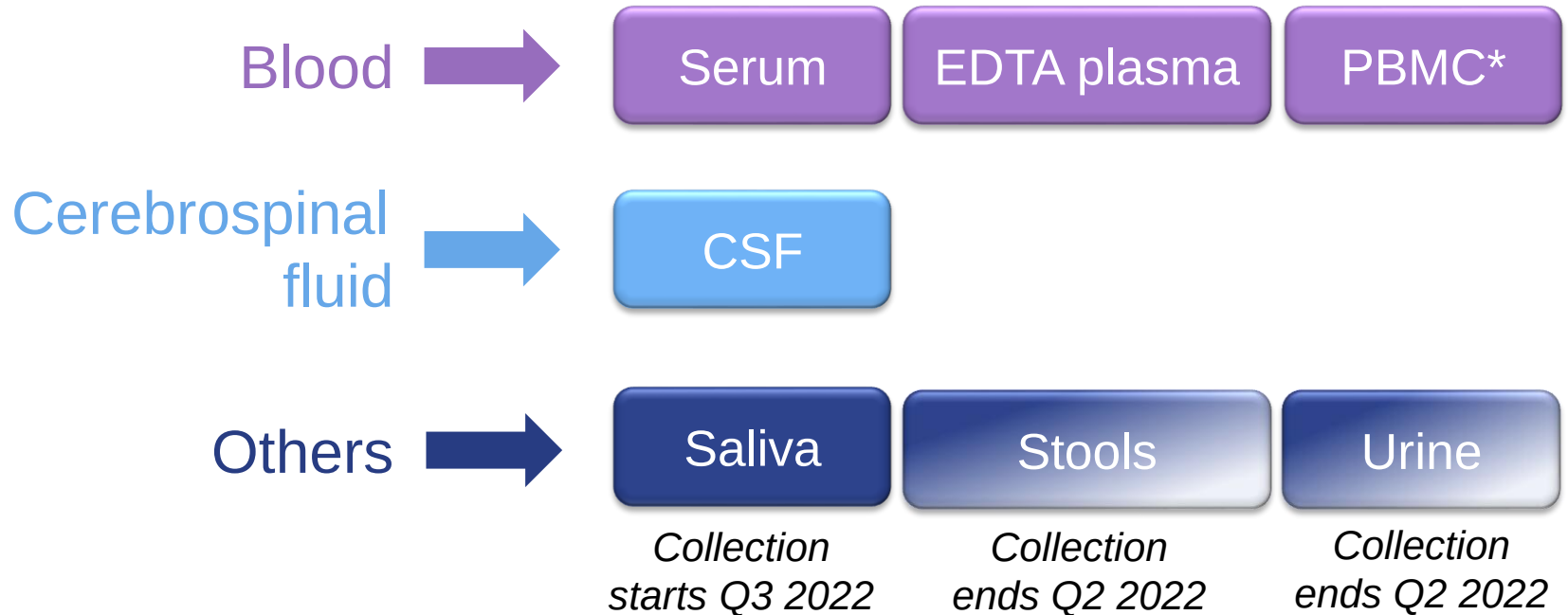
... TO SCIENCE

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Integrated cohorts with biological samples

Cohort	Iterative sample
Radiologically isolated syndromes (RIS)	Every year until conversion
Clinical isolated syndromes and relapsing-remitting MS (CIS / RRMS) - Sample at less than 6 months of the first inflammatory event of the central nervous system - DMT naive at first sample	At year 1, 3 and 5 and during a relapse
Primary progressive multiple sclerosis (PPMS) - Less than 6 years disease duration - Untreated patient	No
Neuromyelitis optical spectrum disorders (NMOSD) and Myelin oligodendrocyte glycoprotein-IgG (MOG-IgG) associated disorder (MOGAD) – NOMADMUS cohort	At year 1, 3 and 5 and during a relapse for patients included at less than 1 year of the first relapse
Acute Disseminated EncephaloMyelitis (ADEM)	No
Progressive Multifocal Leukoencephalopathy (PML)	No
Covid-19 - Sampling within 3 months after biological confirmation of the diagnosis by PCR or onset of symptoms	No
MS patients included in High Definition (HD) cohort	Every 2 years

Biological samples



*Peripheral blood mononuclear cells

Biological samples

- 2 000 patients with OFSEP kit (blood including PBMC, urine, cerebrospinal fluid (CSF) and stools) and 2 700 HD patients with only blood sample.

Patients	Number of patients	Blood*	PBMC	Urine	CSF	Faeces
RIS	141	141	140	126	74	5
First attack	1046	1046	682	683	600	32
RRMS	1932	1932	219	221	138	28
SPMS	323	323	15	16	9	2
PPMS	379	379	244	226	165	13
NMOSD/MOGAD	480	480	474	404	39	8
ADEM	18	18	18	14	3	0
Covid-19	26	26	25	21	0	0

* serum, EDTA plasma, DNA

- Each year : > 350 patients with OFSEP kit

Merging with medico- administrative database

French National Insurance
database

Merging with medico-administrative database

- **French National Insurance database (SNDS)**
 - Reimbursements made by all health insurance plans (consulting, drug dispensing, medical procedures, biological exams, issuance of technical aids, long-term disease)
 - Hospital medical activity (hospitalizations, diagnoses, medical procedures, external consultations)
 - Death causes
- **Allows to access non-specific MS data** including comorbidities, co-prescriptions, recourse to care...

Merging with medico-administrative database



SNDS extraction
2009 ~ 2019

>40,000
patient files

85%
successfully
merged

**If possible, update
every year**

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OFSEP HD cohort

OFSEP HD cohort

Inclusion criteria

- **Diagnosis of multiple sclerosis** according to the most recent criteria
- Age ≥ 15 years
- **Irreversible disability ≤ 7.0 (permanent use of a wheelchair) on EDSS**
- Followed up in one **MS expert center**
- New cases diagnosed after the beginning of the study
or
- For patients diagnosed before the beginning of the study, **regular follow-up** (at least one visit every two years since the date of the first EDSS assessment) with **prospective collection of minimal dataset in EDMUS since 2011**

Follow-up

- Annual follow-up ($\pm$ 2 months) with rebaseline at the first disease activity
- Continuation of the study at least until the end of 2026

Specific data every year

- PRO : sociodemographic data, medical background, quality of life (EQ5D-5L, SF-12, MusiQoL), tobacco, cannabis and alcohol consumption
- Walk test (T25FW), test of upper extremity function (9HPT), test for the detection of information processing speed (CSCT)
- MRI (post-processing) : T2 and new T2 lesions, cerebral volume and atrophy

Population

- 2842 patients included between July 2018 and September 2020.
- At inclusion
 - 73% ♀
 - age = 43 years (± 12)
 - disease duration = 11 years (± 9)
 - prospective follow-up = 8 years (± 7)
 - 80% RRMS, 14% SPMS, 6% PPMS
 - untreated patients or all types of ongoing treatments

Biocollection

- Blood sample and dosages (at inclusion and every two years) :
NF-L, GFAP, vitamin D

NOMADMUS cohort

- **Inclusion criteria**

Patients meeting the international NMOSD criteria (Wingerchuk criteria 1999 and 2006, IPND 2015) including Aquaporin 4 – IgG positive patients (AQP4+)

- or Isolated, recurrent or not, acute extensive transverse myelitis
- or Isolated atypical optic neuritis
- or Myelin Oligodendrocyte Glycoprotein – IgG positive patients associated disease (MOGAD)
- or MOGAD-like patients (MOG-IgG negative patients presenting clinical and/or radiological MOGAD features)

- The **NOMADMUS expert group** validates inclusions with a focus on double seronegative (AQP4 and MOG) patients and MOGAD-like patients
- **Minimal mandatory data** set specific to NMOSD/MOGAD

- 1852 patients included
- 3073 biological samples (serum, plasma, PBMC, CSF...) corresponding to 989 patients in a dedicated biobank (in addition to the 480 patients sampled in the OFSEP biobank)
- 862 patients with at least one MRI in the imaging bank (diagnostic MRI in general) in a dedicated database (in addition to the 162 patients with MRI in the OFSEP imaging bank)

Pre-RIS/RIS cohort

- **Inclusion criteria**
 - MRI lesions suggestive of multiple sclerosis according to 2005 DIS criteria
 - EDSS=0
 - Index MRI indication not consistent with demyelinating disease
- **Exclusion criteria**
 - Any focal neurological manifestation prior to the acquisition of the MRI
- The **RIS expert group** validates all inclusions
- The RIS expert group is member of the Radiologically Isolated Syndrome Consortium (RISC)
- **Mandatory data set** specific to RIS and RIS conversion
- 496 RIS patients including 137 MS conversion
- 251 Pre-RIS patients including 70 MS conversion

Recent publications

Recent publications

Signori A, Lorscheider J, Vukusic S, Trojano M, Iaffaldano P, Hillert J, et al.

Heterogeneity on long-term disability trajectories in patients with secondary progressive MS: a latent class analysis from Big MS Data network.

J Neurol Neurosurg Psychiatry. 2022 Sep 28;jnnp-2022-329987.

Simoneau G, Jiang X, Rollot F, Tian L, Copetti M, Guéry M, et al.

Overall and patient-level comparative effectiveness of dimethyl fumarate and fingolimod: A precision medicine application to the Observatoire Français de la Sclérose en Plaques registry.

Mult Scler J Exp Transl Clin. 2022 Sep;8(3):20552173221116590.

Roos I, Malpas C, Leray E, Casey R, Horakova D, Havrdova EK, et al.

Disease Reactivation After Cessation of Disease-Modifying Therapy in Patients With Relapsing-Remitting Multiple Sclerosis.

Neurology. 2022 Aug 17;10.1212/WNL.0000000000201029.

Lefort M, Sharmin S, Andersen JB, Vukusic S, Casey R, Debouverie M, et al.

Impact of methodological choices in comparative effectiveness studies: application in natalizumab versus fingolimod comparison among patients with multiple sclerosis.

BMC Med Res Methodol. 2022 May 30;22(1):155.

Lefort M, Vukusic S, Casey R, Edan G, Leray E, OFSEP investigators.

Disability Progression in Multiple Sclerosis Patients using Early First-line Treatments.

Eur J Neurol. 2022 May 26;

Recent publications

El Khoury Y, Gebelin M, de Sèze J, Patte-Mensah C, Marcou G, Varnek A, et al.

Rapid Discrimination of Neuromyelitis Optica Spectrum Disorder and Multiple Sclerosis Using Machine Learning on Infrared Spectra of Sera.

Int J Mol Sci. 2022 Mar 3;23(5):2791.

Demuth S, Guillaume M, Bourre B, Ciron J, Zephir H, Sirejacob Y, et al.

Treatment regimens for neuromyelitis optica spectrum disorder attacks: a retrospective cohort study.

J Neuroinflammation. 2022 Mar 2;19(1):62.

Lefort M, Le Corre G, Le Page E, Rizzato C, Le Port D, Michel L, et al.

Ten-year follow-up after mitoxantrone induction for early highly active relapsing-remitting multiple sclerosis: An observational study of 100 consecutive patients.

Rev Neurol (Paris). 2022 Feb 15;S0035-3787(22)00043-1.

Rollot F, Couturier J, Casey R, Wiertlewski S, Debouverie M, Pelletier J, et al.

Comparative Effectiveness of Natalizumab Versus Anti-CD20 in Highly Active Relapsing-Remitting Multiple Sclerosis After Fingolimod Withdrawal.

Neurotherapeutics. 2022 Feb 25;

Papeix C, Castelnovo G, Leray E, Coustans M, Levy P, Visy JM, et al.

Long-Term Effectiveness, Safety and Tolerability of Fingolimod in Patients with Multiple Sclerosis in Real-World Treatment Settings in France: The VIRGILE Study.

Neurol Ther. 2022 Feb 11;

Acknowledgement



This work was done within the framework of OFSEP, the French multiple sclerosis registry

OFSEP is 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" program, under the reference ANR-10-COHO-002.

It is also supported by Eugène Devic EDMUS Foundation against multiple sclerosis and ARSEP Foundation





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