Introduction

- For neurologists and patients with MS, one major unmet need is to better appreciate the causal factors of disease progression and to obtain reliable predictive tools that could apply on the individual level and at different key moments in the disease course (landmarks).
- Taking advantage of the existing network of neurologists collecting data in daily practice, the French MS registry (OFSEP) initiated a "high-definition" (HD) cohort.
- Its overarching objective is to determine, at specific landmarks over the disease course, the prognostic factors of the evolution of disability in MS and the care practices that can modify this predicted evolution in real-life settings.
- The objective of this presentation is to describe the design of the OFSEP HD Cohort and his scientific program.

Study population

Inclusion criteria:
- Diagnosis of multiple sclerosis according to the most recent criteria at entry
- Age ≥ 15 years old at inclusion
- For patients with MS onset occurred before study start, regular follow-up has no programme end.

Non inclusion criteria:
- Inability to answer questionnaires
- Pregnant women at inclusion

Expected inclusion

5000 patients in two years from 1st July 2018; the patient follow-up has no programmed end.

Collection of data

- OFSEP core minimal clinical data (disability, neurological episode, treatment…), comorbidities
- MSFC; Timed 25-Foot Walk, Nine Holes Peg Test, Computerized Speed Cognition Test
- Quality of life: EQ5D-5L, SF12, MusiQoL
- Socioeconomic indicators, alcohol and tobacco consumption, vitamin D supplementation
- Brain MRI (OFSEP acquisition protocol)
- Serum lymphofatilament light chains and biocollection (serum, plasma, DNA) at T0.

Scientific program

The scientific program will start in 2020 and is constituted of four work packages (WP).

1/ Prognosis of disease evolution

This WP aims at identifying the determinants of the progression of disability in MS and of mortality without focus on disease-modifying treatments.

The study of the four landmarks retained will allow to predict the disease evolution:
- at diagnosis
- at diagnosis of progression
- after an activity
- after a "remission" state.

2/ Evaluating the marginal effectiveness and tolerability of DMTs in real life settings

This WP aims to compare therapeutic strategies, particularly:
- at diagnosis: early treatment vs. active surveillance without treatment; in secondary progressive MS: further continuation vs. stopping the ongoing treatment;
- after persistent disease activity: treatment continuation vs. switching from first- to second-line treatments.
- at a "remission": continue vs. stopping the treatment.

3/ Patient-centered stratified medicine

The objective of this WP is to propose stratified algorithms for medical decision for maximizing the number of years without disease progression and with good quality of life.

This requires having an accurate and updated knowledge from WP1 and WP2.

4/ Economic assessment

Economic analysis will be conducted under different approaches:
- a cost-of-illness and
- cost-effectiveness assessment approach.

In mid-term, a pharmaco-epidemiological approach should therefore be developed with the possibility to link our database with the French medico-administrative database "national health data system (SNDS)."

Conclusion

- For the first time in Europe a large cohort of MS patients with systematic extended collection of data will be open to researchers to improve knowledge on the disease.
- The main innovative feature of the OFSEP HD cohort is to propose to merge with high standard of quality data related to the clinical dimension, the quality of life, the socio-demographic context, imaging results from MRI, biological features and received treatments.
- The collection of the quality of life will constitute a major advantage to evaluate usefulness of prognostic tools in stratifying patients into two strata:
  - those who will susceptible to increase their wellbeing by being well treated (early, i.e. slowing the disease progression with the minimum impact on the quality of life).
  - those who will be more susceptible to increase their wellbeing by delaying the treatment (a low risk of disability progression with a maintain health-related quality of life).

The same approach will be developed regarding the three others landmark times.

Disclosure

Renske CASEY has no financial disclosure to declare. Francis GUETAMARK has grants to my institution from Merck, Biogen and Novartis. Giovanni Di Polo has received consulting and lecture fees from Biogen, Genzyme, Novartis, Sanofi-Aventis, Roche and Taal Pharma. Emmanuel DUFFAUD has received consulting and lecture fees from Biogen, Genzyme, Novartis, Merck Serono, Roche, Sanofi-Aventis and Taal Pharma.

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 "Investissements du Futur" program, under the reference ANR-10-CHHO-020 Observatoire Français de la Scénose en plaques (OFSEP). It also received support from the ARSEP Foundation and the Eugène Déve EDM/J's Foundation against MS.