The OFSEP high definition cohort: to prognosticate the evolution of multiple sclerosis at clinical key steps of the disease

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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 into the HD cohort
- Age ≥ 15 years old at inclusion
- Followed in one MS Clinical Reference Centre (CRC SEP)
- MS diagnosed after study start

or

- For patients with MS onset occurred before study start, regular follow-up in an OFSEP center with systematic OFSEP minimal data collection from 2011
- Irreversible disability ≤ 7.0 (permanent use of a wheelchair) on EDSS scale

Non inclusion criteria

- Inability to answer questionnaires
- Pregnant women at inclusion
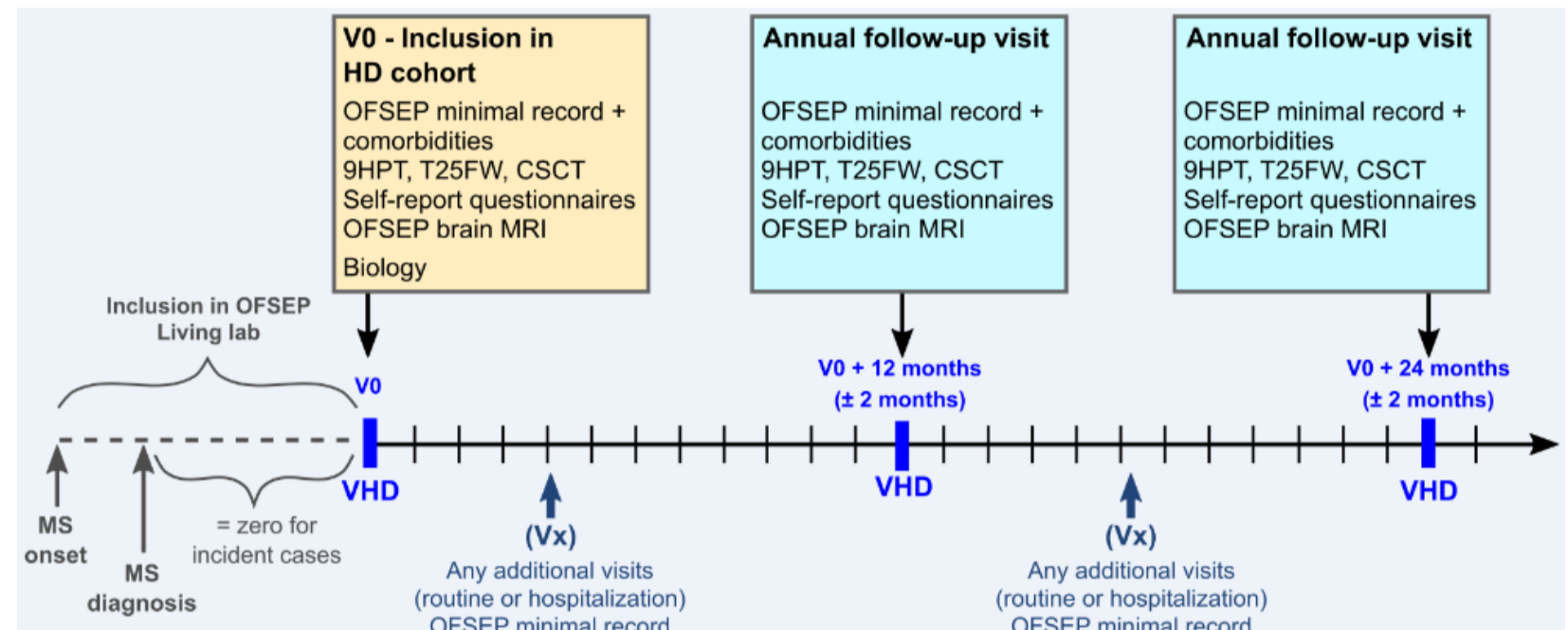
Expected inclusion

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

Collection of data

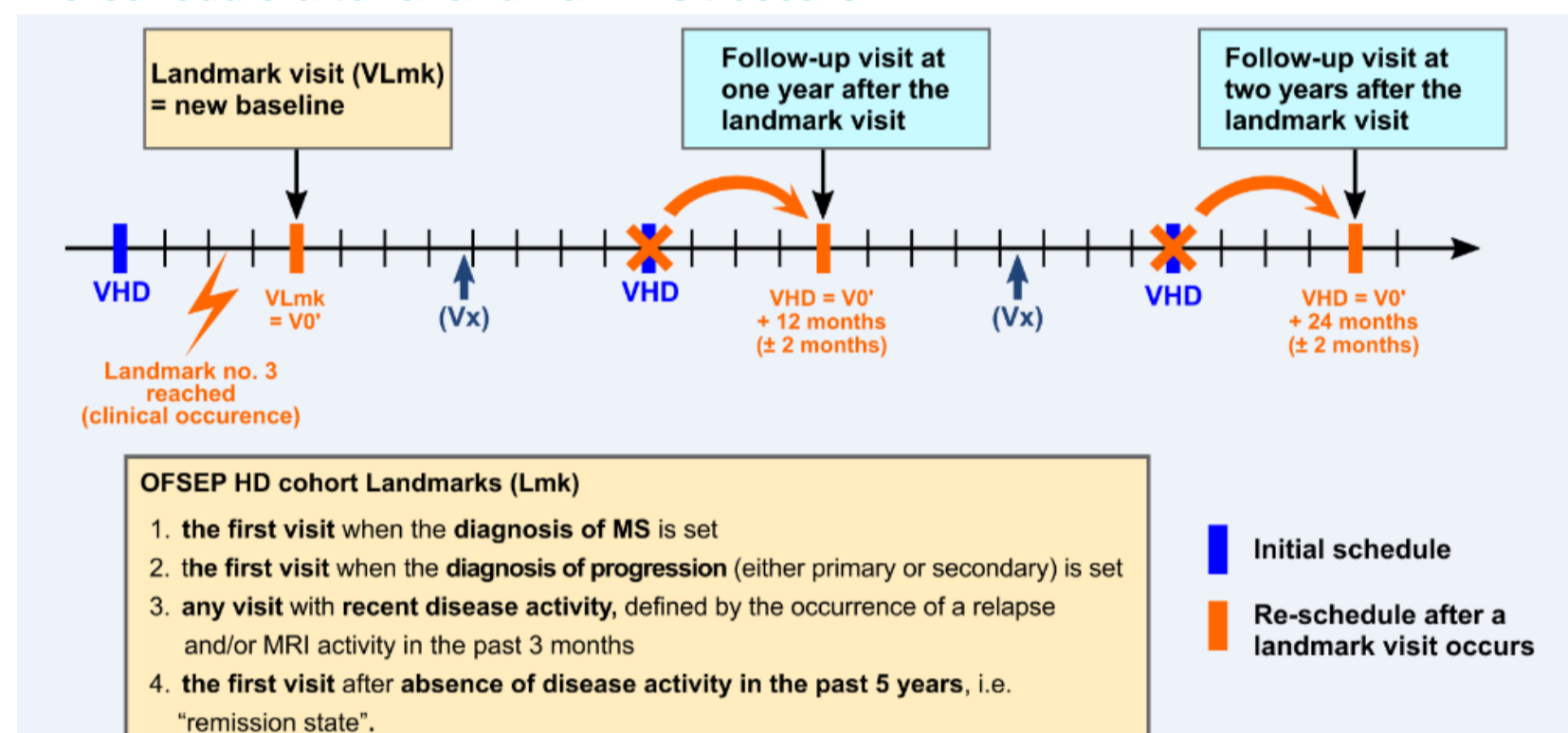- OFSEP core minimal clinical data (disability, neurological episode, treatment…), comorbidities
- MSFC: Timed 25-Foot Walk, Nine Holes Peg Test, Computerized Speed Cognition Test
- Quality of life: EQ5D-5L, SF12, MusiQoL
- Socioeconomic indicators, alcohol and tobacco consumption, vitamin D supplementation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

Study schedule

At inclusion

Re-schedule after a landmark visit occurs

OFSEP HD cohort Landmarks (Lmk)
1. the **first visit** when the **diagnosis of MS** is set
2. the **first visit** when the **diagnosis of progression** (either primary or secondary) is set
3. any **visit** with **recent disease activity**, defined by the occurrence of a relapse and/or MRI activity in the past 3 months
4. the **first visit** after **absence of disease activity in the past 5 years**, i.e. "remission state".

Outcomes

- Clinical: disability, MSFC, relapses, progression, death.
- Quality of life outcomes.
- MRI outcomes: lesion load, active lesion, cerebral atrophy, black hole…
- Combined outcomes: activity and progression (Lublin 2014), NEDA 3 and NEDA 4, Rio scores, OFSEP specific indicators.

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 and
- after a "remission" state.

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

This WP aims is 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" state: 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.

At diagnosis, our objective is to propose a classification of patients into two strata:

- those who will be susceptible to increase their wellbeing by being treated early (decreasing the risk of the disability progression with an acceptable impact of the treatment on the health-related 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.

4/ Economic assessment

Economic analysis will be conducted under two 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 stratified medicine, **our objective being to drive treatments for maximizing the patient well-being, *i.e.* slowing the disease progression with the minimum impact on the quality of life**.