Effectiveness and Tolerability of Ofatumumab Versus First-line DMTs in Early RMS Patients: Phase 3b STHENOS Study Design

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Introduction

- Ofatumumab is a fully-human anti-CD20 monoclonal antibody approved for the treatment of relapsing MS in adults based on results from ASCLEPIOS phase 3 studies[1,2]
- STHENOS (NCT04788615) is a prospective, open-label, rater-blinded, multicentre, parallel-arm, active comparator study in early RMS patients

Objective

The STHENOS study will explore the efficacy, safety, tolerability and patient reported outcomes of ofatumumab versus platform first-line, self-administered DMTs of physician's choice (SoC). Here we present the design of the STHENOS study

Patients enrolled

RMS patients (Lublin et al 2014) defined as newly diagnosed or treatment-naive patients at study entry with ≤3 years from the first MS symptoms[3]

Study conduct

- Patients will be randomized (1:1) to ofatumumab or SoC platform DMT (glatiramer acetate, interferon, teriflunomide, or dimethyl fumarate)
- The study has a 15-month treatment period
- The study plans to enroll ~236 patients from ~50 sites across 5 countries (Figure 1)

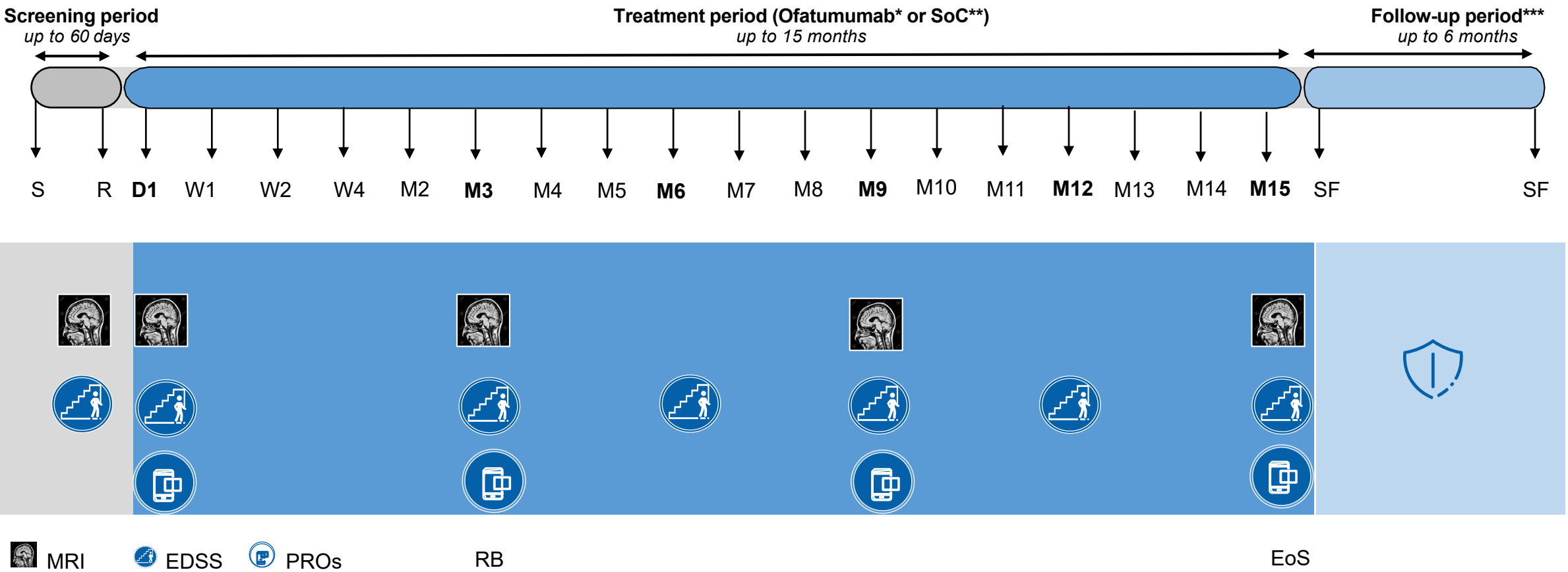
Figure 1: STHENOS study centres

DMT, disease-modifying treatments; RMS, relapsing multiple sclerosis; SoC, standard of care; 1. Kesimpta [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2020.; 2. Kesimpta. EMA: Kesimpta, INN-ofatumumab (europa.eu); 3. Lublin FD, et al. *Neurology*. 2014;83:278–86

STHENOS: Study design

A phase IIIb study

STHENOS



*The recommended dose is 20 mg administered subcutaneously with initial dosing at Baseline, Week 1, and Week 2, followed by subsequent monthly dosing. D1, M3, M6, M9, M12, and M15 study visits; **Glatiramer acetate, interferon, teriflunomide, dimethyl fumarate ***6-month observational safety period: patients who withdraw ofatumumab during the treatment period; D, day; EDSS, Expanded Disability Status Scale; EoS, End of study; MRI, magnetic resonance imaging; PRO, patient-reported outcome; R, Randomisation; RB, M, Month; MRI re-baseline; S, screening; SoC, standard of care; SF, safety observational follow-up; W, week.

STHENOS: Key inclusion exclusion criteria and study endpoints

Key Inclusion criteria

- Adults aged 18-45 years with consent
- Diagnosed with MS as per the revised McDonald criteria[1]
- Relapsing MS as defined by Lublin et al (2014)[2]
- Treatment-naïve patients ≤ 3 years since first MS symptom
- EDSS score: 0–3
- Suitable to be treated with platform DMT physician's choice* or ofatumumab
- At least 1 relapse or 1 Gd+ enhanced lesion in the year before screening
- Able to obtain MRI assessment

Key Exclusion criteria

- Diseases other than MS/progressive MS phenotypes
- Use of other experimental or investigational drugs
- Relapse between screening and baseline visits
- Pregnancy or breastfeeding
- Other active immune chronic disease/ active infections
- Received any live or live-attenuated vaccines within 4 weeks prior to first study drug administration

Endpoints

Primary

- **NEDA-3 status** (yes/no) at month 15
  - ✓ absence of confirmed clinical relapse
  - ✓ absence of new MRI activity** with MRI re-baselined at Month 3
  - ✓ absence of 3mCDW

Key Secondary

- ARR
- Time to first relapse
- % of relapse-free patients: 3,9,15 months
- % of relapsed free patients with MRI activity free: 3,9,15 months
- 3mCDW/6mCDW
- Change in EDSS from baseline to EoS
- Number/volume of Gd+ T1 lesions
- Volume of new/enlarging T2 lesions
- Safety and tolerability; treatment compliance

Exploratory

- % of patients who discontinued treatment
- SDMT

PRO

- Change in MSIS-29, FSIQ-RMS, TSMQ-1.4, MSTCQ, MHI-5
- Work productivity/social life and activities impact

Biomarkers

- Serum biomarkers (neurofilament light chain and glial fibrillary acidic protein)

STHENOS will provide clinical data and patient reported outcomes for an early RMS population treated with ofatumumab in Europe

*glatiramer acetate, IFNs, teriflunomide or DMF, according to EMA SmPC; **Gd+ T1 lesion or new/enlarged T2 lesion; ARR, annualized relapse rate; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; EoS, end of study; FSIQ, Fatigue symptoms and impacts questionnaire; Gd+, gadolinium-enhancing; MHI, Mental Health Inventory; MRI, magnetic resonance imaging; MSIS, Multiple Sclerosis Impact Scale; MSTCQ, Multiple Sclerosis Treatment Concerns Questionnaire; NEDA, No evidence of disease activity; MS, multiple sclerosis; RMS, relapsing MS; SDMT, Symbol Digit Modalities Test; TSMQ, Treatment Satisfaction Questionnaire For Medication; 3mCDW, 3-month Confirmed Disability Worsening; 6mCDW, 6-month Confirmed Disability Worsening ;. 1. Thompson AJ, et al. *Lancet Neurol*. 2018;17:162–73; 2. Lublin FD, et al. *Neurology*. 2014;83:278–86.

Disclosures

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Xavier Montalban has received speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years with Actelion, Alexion, Bayer, Biogen, Celgene, EMD Serono, Genzyme, Immunic, Medday, Merck, Mylan, Nervgen,Novartis, Roche, Sanofi-enzyme, Teva Pharmaceutical, TG Therapeutics, Excemed, MSIF and NMSS

Ralf Linker has received speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years with Biogen, Celgene, Janssen, Merck, Novartis, Roche and Sanofi-Genzyme.

Diego Centonze acted as an Advisory Board member of Actelion, Almirall, Celgene, BMS, Bayer Schering, Biogen, GW Pharmaceuticals, Merck Serono, Novartis, Roche, Sanofi-Genzyme, and Teva.. He has received honoraria for speaking or consultation fees from Almirall, Bayer Schering, Biogen, BMS, GW Pharmaceuticals, Lundbeck, Merck Serono, Novartis, Roche, Sanofi-Genzyme, and Teva. He is also a principal investigator in clinical trials for Abbvie, Bayer Schering, Biogen, Merck Serono, Mitsubishi, Novartis, Roche, Sanofi-Genzyme and Zambon.

Ben Turner received travel grants and educational grants and honoraria for advisory boards from Novartis, Biogen, Roche, Merck-Serono

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