Effectiveness, Safety, and Patient-Reported Outcomes of Ofatumumab in Relapsing Multiple Sclerosis Patients Switching from Dimethyl Fumarate or Fingolimod: ARTIOS Phase 3b Study Design

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ePoster presentation: P042

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Poster Presentation at ACTRIMS Forum 2021, February 25–27, 2021

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Disclosures

Matthew Craner has received honoraria for educational events and/or consultancy from Biogen, Merck, Roche, AbbVie and Novartis (as of Nov 2020)

Riley Bove has received research support and/or served on Advisory Boards and/or steering committees of Alexion, Biogen, EMD Serono, Genzyme Sanofi, Novartis, Roche Genentech

Dawn Langdon has received consultancy from Celgene, Novartis, Biogen, Merck; research grants from Biogen, Novartis, Merck; speaker bureau fees from Sanofi, Merck, Novartis, Biogen, Bayer

Tobias Derfuss has received speaker fees, research support, travel support, and/or served on Advisory Boards and/or steering committees of Actelion, Alexion, Biogen, Celgene, GeNeuro, Merck Serono, MedDay, Mitsubishi Pharma, Novartis, Roche, Sanofi-Genzyme

Daniel Detka, Javier Ricart, Alomi Mistry, Patricia Maxwell, Chaitali Babanra Pisal, Pruthvi Desireddy, Dee Stoneman, Marina Ziehn are employees of Novartis

Background and objective

- Ofatumumab, a fully-human anti-CD20 monoclonal antibody with a 20-mg subcutaneous monthly dosing regimen, is approved by the US FDA for the treatment of relapsing forms of MS in adults, based on results from the ASCLEPIOS phase 3 studies[1]
- MS patients switching from oral therapies such as DMF and fingolimod because of breakthrough disease activity were under-represented within the ASCLEPIOS studies
- Exploring the efficacy and safety of ofatumumab in patients with RMS who are switching from oral therapies such as DMF and fingolimod is important to complement ASCLEPIOS I/II studies
- Here we present the innovative design of the ARTIOS study in patients with RMS

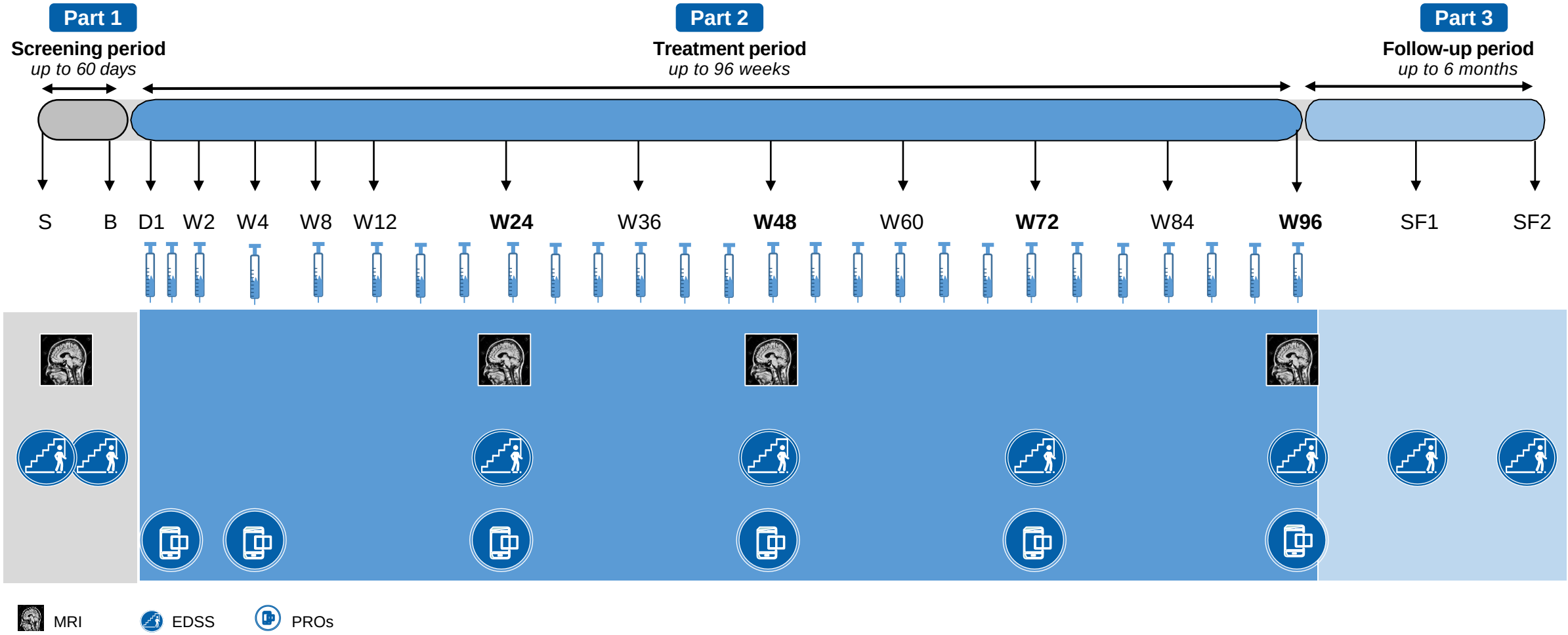
To demonstrate the effectiveness of ofatumumab 20 mg, administered subcutaneously every 4 weeks, in patients with RMS who had breakthrough disease on DMF or fingolimod, as measured by annual relapse rate at the 96-week endpoint

DMF, dimethyl fumarate; FDA, Food and Drug Administration; MS, multiple sclerosis; RMS, relapsing MS.

1. Kesimpta [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2020.

ARTIOS: Study design

A 3-part phase 3b study



B, baseline; D, day; EDSS, Expanded Disability Status Scale; MRI, magnetic resonance imaging; PRO, patient-reported outcome; S, screening; SF, safety follow-up; W, week.

ARTIOS: Key inclusion and exclusion criteria

Key inclusion criteria

- Adults aged 18–60 years (inclusive) at screening
- Diagnosis of MS (revised McDonald 2017 criteria[1])
- Relapsing forms of MS, including RMS and SPMS[2]
- EDSS score of 0–4 at screening
- MS treatment history with a maximum of 3 DMTs
  - Most recent DMT either DMF or fingolimod, administered for at least 6 months, prior to transition to study drug
- Breakthrough disease activity while the patient was adequately using DMF or fingolimod prior to transitioning, as evidenced by one or more clinically reported relapses or one or more signs of MRI activity (eg, Gd+, new, or enlarging T2 lesions)
- Neurologically stable in the prior 1 month of first study drug administration

Key exclusion criteria

- Patients with PPMS[3] or SPMS without disease activity (non-active SPMS)[2]
- Disease duration of >10 years since diagnosis
- Patients meeting criteria for neuromyelitis optica[4]
- Patients with active bacterial, viral (including COVID-19), or fungal infections
- Emergence of any clinically significant condition/disease during previous ofatumumab study
- Patients with neurological findings consistent or confirmed with PML
- Pregnant or nursing women; OR, women of childbearing potential not using highly effective methods of contraception
- Patients at risk of developing, or with a history of, hepatitis, syphilis, or tuberculosis
- History of malignancy within the past 5 years, significant cardiac disease, respiratory disease, severe hepatic and renal impairment, hyperproteinemia

COVID-19, coronavirus disease 2019; DMF, dimethyl fumarate; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; MRI, magnetic resonance imaging; MS, multiple sclerosis; PML, progressive multifocal leukoencephalopathy; PPMS, primary progressive MS; RMS, relapsing MS; SPMS, secondary progressive MS.

1. Thompson AJ, et al. *Lancet Neurol*. 2018;17:162–73; 2. Lublin FD, et al. *Neurology.* 2014;83:278–86; 3. Polman CH, et al. *Ann Neurol.* 2011;69:292–302; 4. Wingerchuk DM, et al. *Neurology.* 2006;66:1485–9.

ARTIOS: Study evaluations

Primary

Efficacy
- ARR

Secondary

Safety
- AEs
- Laboratory abnormalities
- Treatment discontinuations

Exploratory

- **EDSS**
- **T25FW**
- **9-HPT**
- **SDMT**
- **LCVA**
- **3mCDW**
- **6mCDW**
- **6mCCD**
- **NEDA-3**

PROs

- **MSIS-29**
- **Fatigue (FSMC)**
- **Treatment satisfaction (TSQM 1.4)**
- **Anxiety and mood (HADS)**

Biomarker evaluations

- **MRI**
  - Gd+ T1 lesions
  - New or enlarging T2 lesions
- **NfL**
- **GFAP**

Digital evaluations

- **Floodlight**
- **Actigraphy**

9-HPT, 9-Hole Peg Test; AE, adverse event; ARR, annualized relapse rate; CCD, confirmed cognitive decline; CDW, confirmed disability worsening; EDSS, Expanded Disability Status Scale; FSMC, Fatigue Scale for Motor and Cognitive Functions; Gd+, gadolinium-enhancing; GFAP, glial fibrillary acidic protein; HADS, Hospital Anxiety and Depression Scale; LCVA, low-contrast visual acuity; m, month; MRI, magnetic resonance imaging; MSIS-29, Multiple Sclerosis Impact Scale-29; NEDA, no evidence of disease activity; NfL, neurofilament light chain; PRO, patient-reported outcome; SDMT, Symbol Digit Modalities Test; T25FW, Timed 25-Foot Walk; TSQM, Treatment Satisfaction Questionnaire for Medication.

ARTIOS: Study endpoints

Primary endpoint

- Annualized relapse rate over 96 weeks

Secondary endpoints

Proportion of patients with:

- Adverse events, including injection-related reactions
- Laboratory results or vital signs meeting abnormal criteria
- Discontinuing treatment due to lack of efficacy or tolerability/safety reasons

Exploratory endpoints

- Change from baseline in EDSS, T25FW, 9-HPT, SDMT, LCVA
- Time to 3mCDW, 6mCDW, 6mCCD (defined as a 4-point worsening on SDMT)
- MRI activity: number of Gd+ T1 lesions, new, or enlarging T2 lesions
- Patient-reported outcomes: MSIS-29, TSQM 1.4, FSMC, HADS
- Change from baseline in NfL and GFAP
- Proportion of patients with NEDA-3
- Correlation between Floodlight assessments and other clinical assessments performed in the study
- Daily activity and sleep patterns via actigraphy

9-HPT, 9-Hole Peg Test; CCD, confirmed cognitive decline; CDW, confirmed disability worsening; EDSS, Expanded Disability Status Scale; FSMC, Fatigue Scale for Motor and Cognitive Functions; Gd+, gadolinium-enhancing; GFAP, glial fibrillary acidic protein; HADS, Hospital Anxiety and Depression Scale; LCVA, low-contrast visual acuity; m, month; MRI, magnetic resonance imaging; MSIS-29, Multiple Sclerosis Impact Scale-29; NEDA, no evidence of disease activity; NfL, neurofilament light chain; SDMT, Symbol Digit Modalities Test; T25FW, Timed 25-Foot Walk; TSQM, Treatment Satisfaction Questionnaire for Medication.

ARTIOS: Digital tools

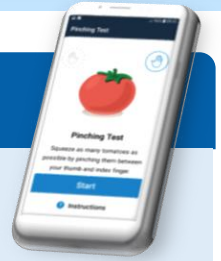
eDiary

- A smartphone with preinstalled electronic injection diary
- Collects ePROs at protocol-defined intervals (approx. every 3 months)
- Subjects will also record information about injections and pregnancy tests

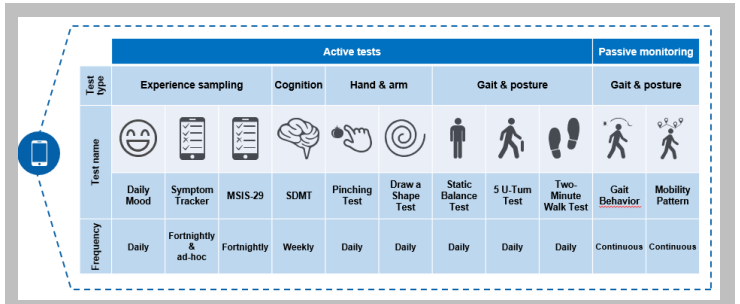
PROs:

- Psychological/physical impact
- Fatigue
- Treatment satisfaction
- Anxiety/depression

Floodlight*

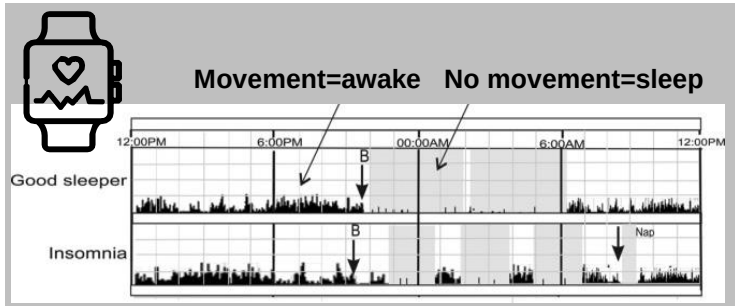


- Study-specific app pre-installed on a smartphone for ARTIOS subjects with daily, weekly or fortnightly exploratory tests
- Exploratory passive monitoring when phone is carried by the study subject



Actigraphy

- Actigraph “watch”, useful for analyzing mobility/sleep patterns
- Provides high-resolution multi-axis data that can accurately characterize movement and mobility
- Data will be downloaded at each visit



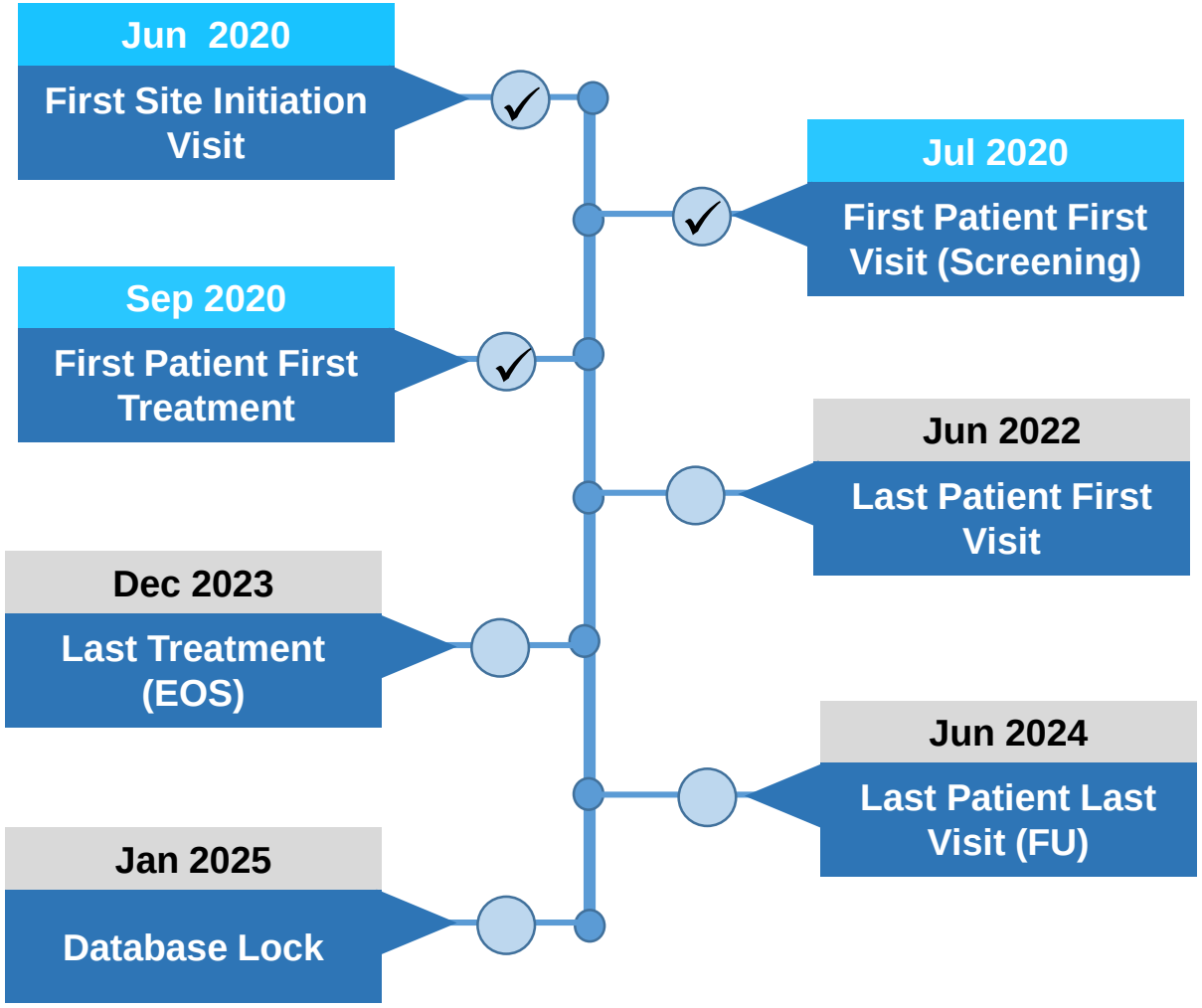
***In collaboration with Roche, Floodlight, one of the most advanced digital platforms containing exploratory tests and questionnaires measuring multi-dimensional functioning in MS patients, has been incorporated into the Novartis ARTIOS study**

(e)PRO, (electronic) patient-reported outcome; MS, multiple sclerosis; MSIS-29, Multiple Sclerosis Impact Scale-29; SDMT, Symbol Digit Modalities Test.

ARTIOS: Study timelines

Planned enrollment

- 27 countries
- 170 sites
- 550 patients



EOS, end of study; FU, follow-up.

Conclusions

- The ARTIOS phase 3b study will address relevant clinical practice questions on the effectiveness, safety, and PROs in patients with relapsing MS who are switching to ofatumumab from high-efficacy oral therapies such as DMF and fingolimod because of suboptimal response
- This evidence is highly relevant for neurologists and other clinicians and practitioners in the real-world setting
- ARTIOS will explore the utility of biomarkers (including serum NfL and GFAP) for treatment monitoring in patients with relapsing MS
- The study will also evaluate the added benefit of digital tools over clinical assessments alone in the assessment and treatment of patients living with MS

Thank you

DMF, dimethyl fumarate; GFAP, glial fibrillary acidic protein; MS, multiple sclerosis; NfL, neurofilament light chain; PRO, patient-reported outcome.