

DMT05

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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Disclosures and acknowledgements

Disclosures

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Background and objective

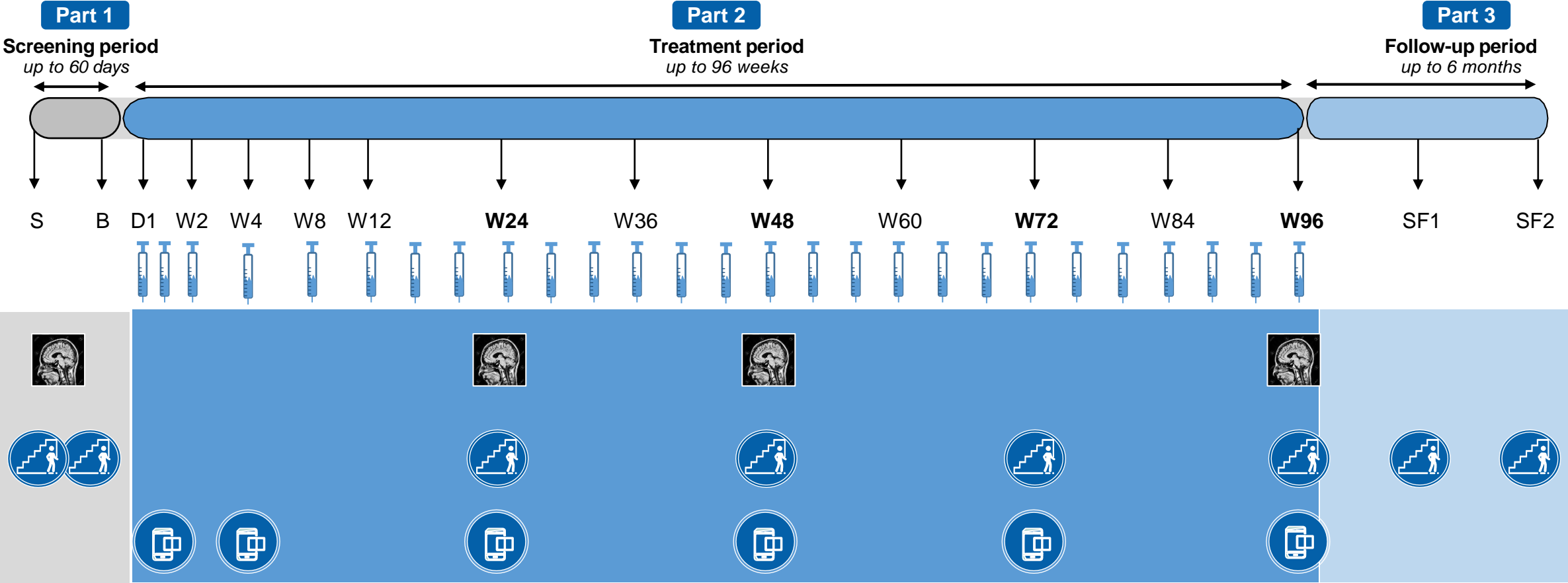
- Ofatumumab, a fully-human anti-CD20 monoclonal antibody with a 20-mg subcutaneous monthly dosing regimen, is approved by the US FDA for the treatment of relapsing forms of MS in adults, based on results from the ASCLEPIOS phase 3 studies¹
- MS patients switching from oral therapies such as DMF and 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

ARTIOS: Study design

A 3-part phase 3b study



 MRI  EDSS  PROs

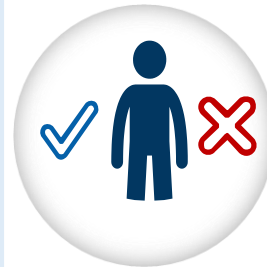
B, baseline; D, day; EDSS, Expanded Disability Status Scale; MRI, magnetic resonance imaging; PRO, patient-reported outcome; S, screening; SF, safety follow-up; W, week.

ARTIOS: Key inclusion and exclusion criteria



Key inclusion criteria

- Adults aged 18–60 years (inclusive) at screening
- Diagnosis of MS (revised McDonald 2017 criteria¹)
- Relapsing forms of MS, including RMS and SPMS²
- 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 (e.g., Gd+, new, or enlarging T2 lesions)
- Neurologically stable in the prior 1 month of first study drug administration





Key exclusion criteria





- Patients with PPMS³ or SPMS without disease activity (non-active SPMS)²
- Disease duration of >10 years since diagnosis
- Patients meeting criteria for neuromyelitis optica⁴
- 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	 PROs	 Biomarker evaluations
<ul style="list-style-type: none"> ▪ EDSS ▪ T25FW ▪ 9-HPT ▪ SDMT ▪ LCVA ▪ 3mCDW ▪ 6mCDW ▪ 6mCCD ▪ NEDA-3 	<ul style="list-style-type: none"> ▪ MSIS-29 ▪ Fatigue (FSMC) ▪ Treatment satisfaction (TSQM 1.4) ▪ Anxiety and mood (HADS) 	<ul style="list-style-type: none"> ▪ MRI <ul style="list-style-type: none"> ▪ Gd+ T1 lesions ▪ New or enlarging T2 lesions ▪ NfL ▪ GFAP
		 Digital evaluations
		<ul style="list-style-type: none"> ▪ 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

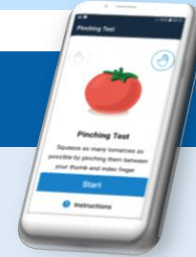
ARTIOS: Digital tools

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

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



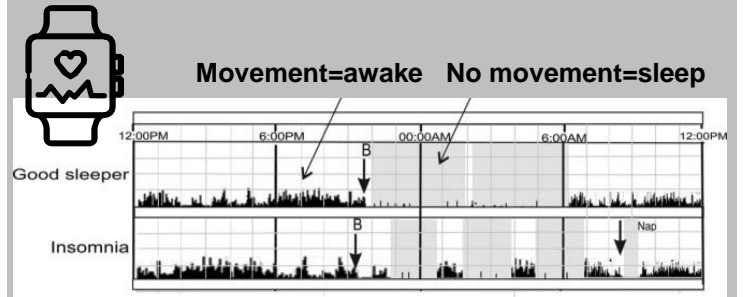
- Actigraph “watch”, useful for analyzing mobility/sleep patterns
- Provides high-resolution multi-axis data that can accurately characterize movement and mobility
- Data will be downloaded at each visit



PROs:

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




Test type	Active tests							Passive monitoring			
	Experience sampling	Cognition	Hand & arm	Gait & posture			Gait & posture				
Test name	Daily Mood	Symptom Tracker	MSIS-29	SDMT	Pinching Test	Draw a Shape Test	Static Balance Test	5 U-Turn Test	Two-Minute Walk Test	Gait Behavior	Mobility Pattern
Frequency	Daily	Fortnightly & ad-hoc	Fortnightly	Weekly	Daily	Daily	Daily	Daily	Daily	Continuous	Continuous

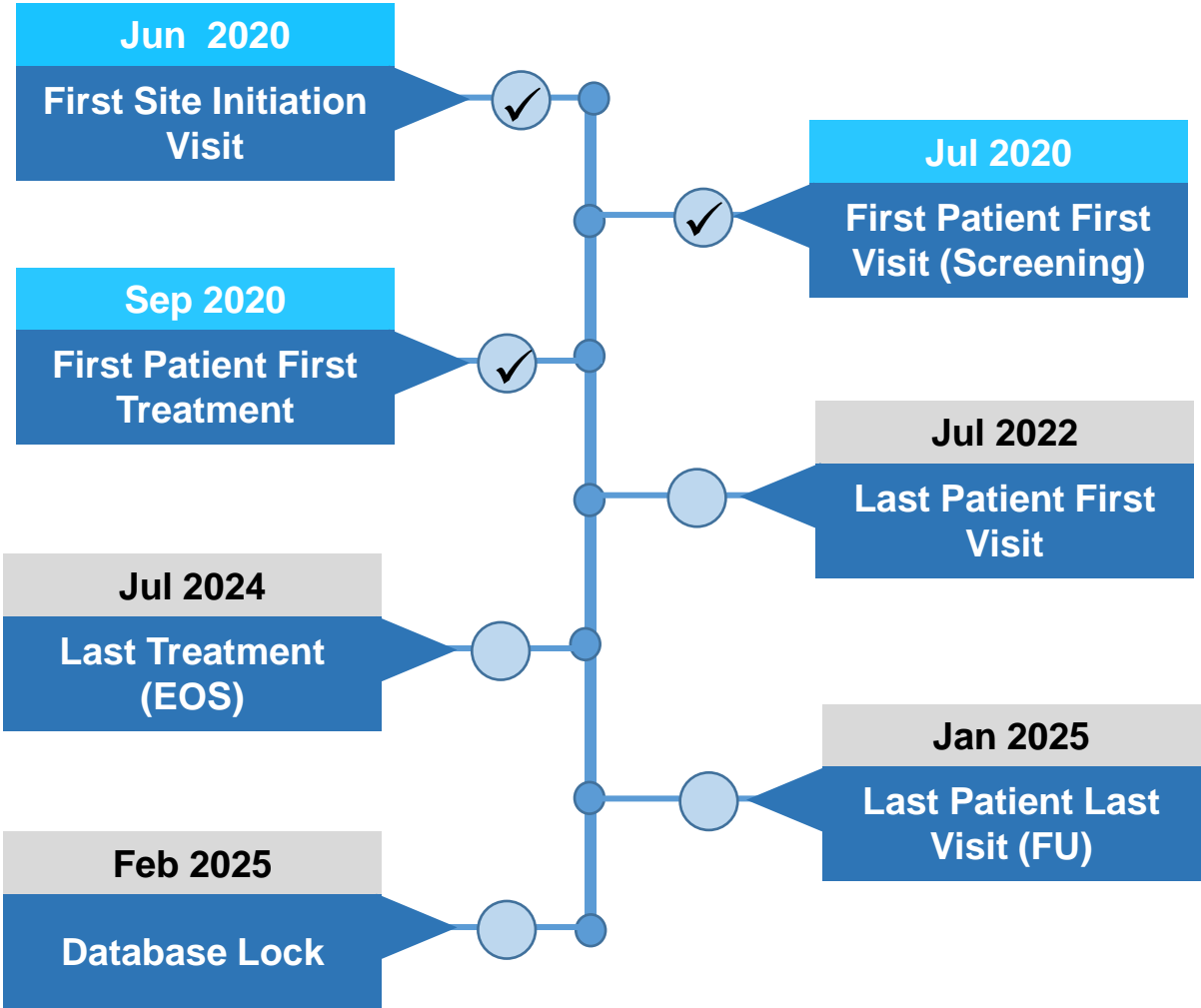


*In collaboration with Roche, Floodlight, one of the most advanced digital platforms containing exploratory tests and questionnaires measuring multi-dimensional functioning in MS patients, has been incorporated into the Novartis ARTIOS study

ARTIOS: Study timelines

Planned enrollment

-  **27 countries**
-  **175 sites**
-  **550 patients***



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

*Target enrollment planned to increase from 550 to 555 patients in Protocol Amendment 2, which will be released in Q4-2021

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