Long-term safety, compliance, and effectiveness of ofatumumab in patients with relapsing multiple sclerosis: The ALITHIOS Phase 3b study

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Disclosures

Edward J. Fox has received fees for consulting, contracted research, and speaker's bureaus from Alexion, Biogen, Bristol-Myers Squibb, Chugai, EMD Serono, Genentech Roche, MedDay, Novartis, Sanofi Genzyme, and TG Therapeutics.

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Background and objective

- Ofatumumab, a FDA-approved, fully human anti-CD20 monoclonal antibody, with a 20 mg s.c. monthly dosing regimen, is indicated for the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults[1]
- Ofatumumab 20 mg s.c. demonstrated superior efficacy versus teriflunomide and a favorable safety profile in the Phase 3 ASCLEPIOS trials in RMS patients[2]
- Assessment of the long-term use of s.c. ofatumumab 20 mg is important to further understand its benefit-risk profile
- ALITHIOS, an open-label umbrella extension Phase 3b study, has been designed to assess the long-term benefit-risk profile of monthly ofatumumab 20 mg s.c. in RMS

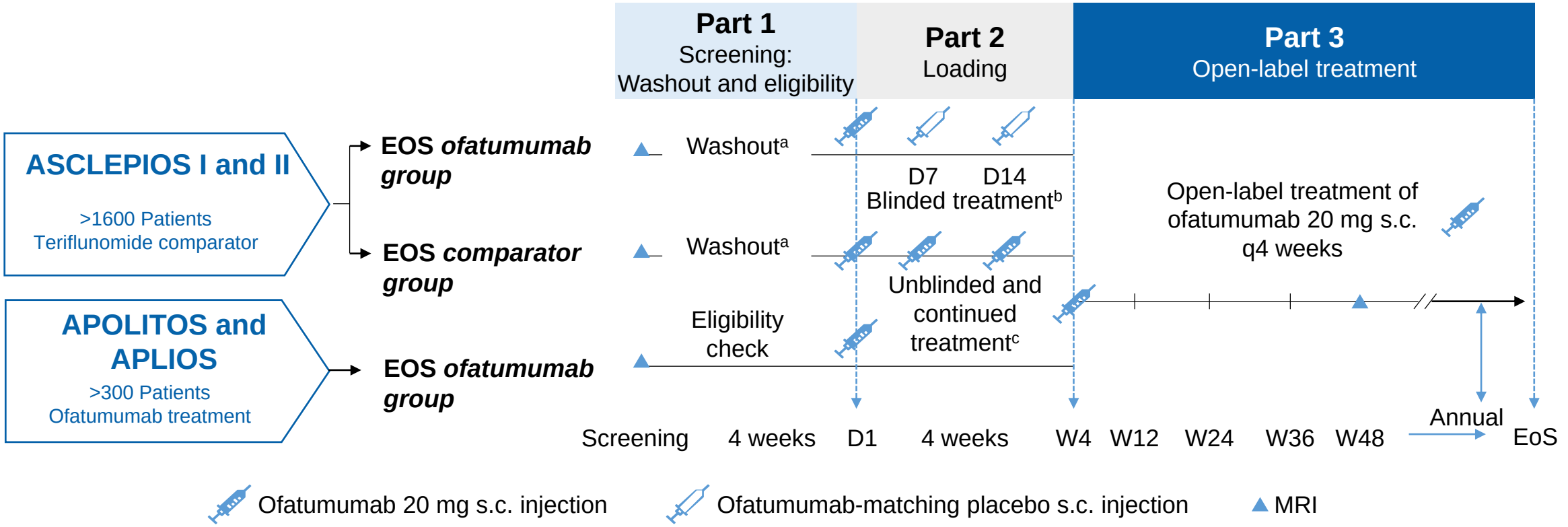
Objective	**To present the design of the ALITHIOS extension study and evaluate treatment compliance, including treatment discontinuations, in patients transitioning to the ALITHIOS study from other ofatumumab MS studies**

FDA, Food and Drug Administration; RMS, relapsing multiple sclerosis; s.c, subcutaneous

1. KESIMPTA® (ofatumumab) Prescribing Information. https://www.novartis.us/sites/www.novartis.us/files/kesimpta.pdf (accessed Aug 24, 2020).
2. Hauser SL, et al. N Engl J Med 2020;383:546−57.

Methods

ALITHIOS: An ongoing open-label, umbrella extension Phase 3b study for up to 5 years



- Patients were enrolled from >300 sites worldwide if they had completed the Phase 3 ASCLEPIOS I/II or Phase 2 APOLITOS and APLIOS trials
- Ofatumumab 20 mg is administered at the site on Day 1 followed by open-label treatment every 4 weeks

[a]Washout according to comparator product information; [b]Blinded treatment at D7/D14 – patients from ASCLEPIOS have a blinded loading part with two additional ofatumumab/matching placebo s.c. injections on D[illegible] D14; no blinding is required for those from the APOLITOS and APLIOS studies; [c]Continued ofatumumab treatment once every 4 weeks, no blinding or loading required

D, day; EoS, end of study; MRI, magnetic resonance imaging; s.c, subcutaneous; q, every ; W, week

Methods

ALITHIOS: Study population

Key inclusion criteria

- Must have participated in a Novartis sponsored ofatumumab MS study which dosed ofatumumab 20 mg s.c. every 4 weeks in patients with RMS aged ≥18 years and have completed the study on study treatment

Key exclusion criteria

- Premature discontinuation from previous ofatumumab studies
- EOS of the previous ofatumumab study >6 months prior to screening and/or treated with another DMT between EOS and screening
- Less than 3.5 months of washout of teriflunomide for subjects that will not complete the AEP prior to Day 1 (for ASCLEPIOS I/II)
- Subjects with neurological findings consistent with PML or confirmed PML
- Emergence of active chronic disease (or stable but treated with immune therapy) of the immune system other than MS during the previous ofatumumab study or prior to Day 1
- Life-threatening CTCAE (Grade 4) injection systemic reactions event that occurred during previous ofatumumab treatment

AEP, Accelerated Elimination Procedure; CTCAE, Common Terminology Criteria for Adverse Event; DMT, disease modifying therapy; EOS, end of study; MS, multiple sclerosis RMS, relapsing multiple sclerosis; s.c, subcutaneous; PML, Progressive Multifocal Leukoencephalopathy

Methods

ALITHIOS: Study objectives

Primary objectives

- Proportion of subjects with an adverse events
- Proportion of subjects with laboratory, vital signs, or ECG results meeting abnormal criteria
- Proportion of subjects meeting predefined criteria in the C-SSRS

Secondary objectives

Relapse rates

- Annualized relapse rate

Disability outcomes

- 3-month and 6-month CDW
- 6-month, 12-month, 24-month CDI

MRI outcomes

- Annualized T2 lesion rate
- Number of T1 Gd+ lesions per MRI scan
- Annual rate of change in brain volume

Serum neurofilament

- Change in serum NfL concentration

Patient-reported outcomes

CDI, confirmed disability improvement; CDW, confirmed disability worsening; C-SSRS, Columbia Suicide Severity Rating Scale; ECG, electrocardiogram; Gd+, gadolinium-enhancing; MRI magnetic resonance imaging; NfL, neurofilament light chain

Methods

Treatment compliance

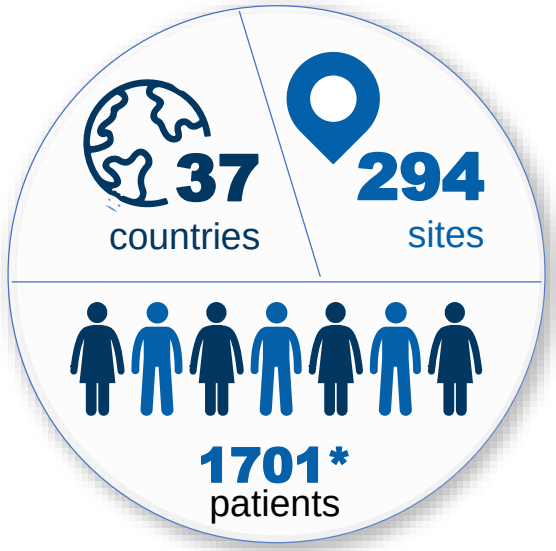
- The proportions of eligible patients who accepted transitioning to the ALITHIOS study from the Phase 3 ASCLEPIOS I/II trials and the Phase 2 APOLITOS and APLIOS trials were evaluated
- Treatment compliance and discontinuations in the Phase 3 ASCLEPIOS I/II trials and the Phase 2 APOLITOS and APLIOS trials were analyzed

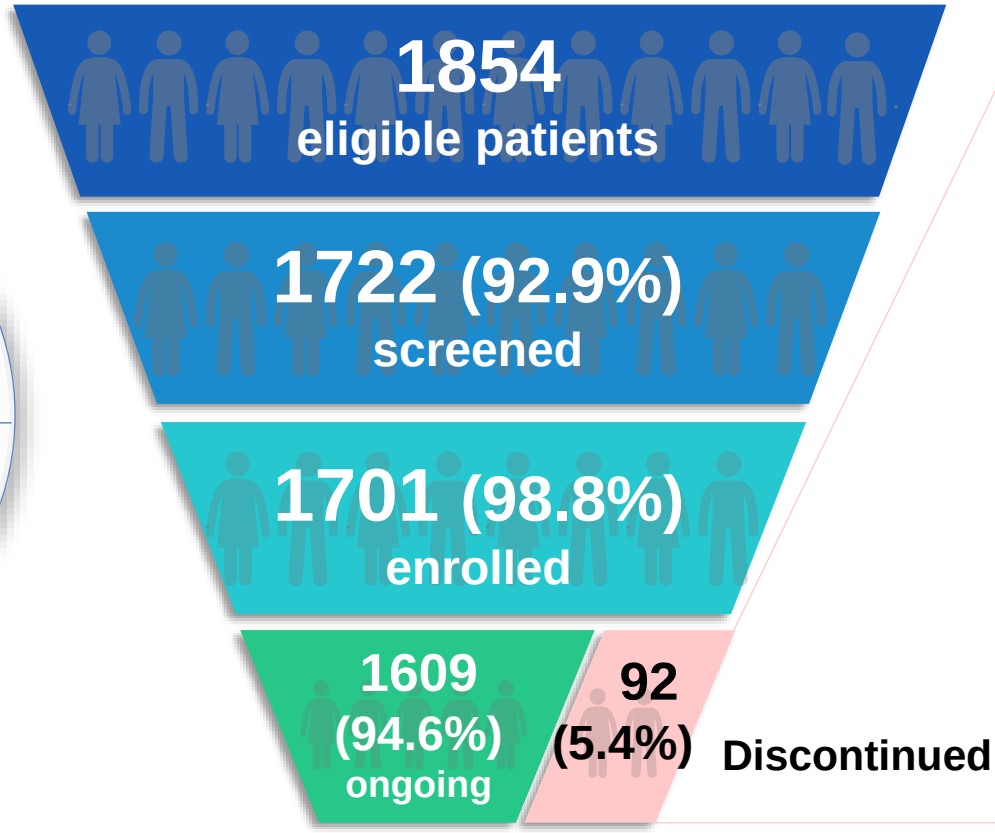
Compliance (%) = Duration of exposure to the study drug (days) / Duration of the on-treatment period (days) × 100

Results

Patient disposition

As of 6 August 2020





Reasons for discontinuation	Patients, n (%)
Patient/guardian decision	**36 (2.1)**
Adverse event	**24 (1.4)**
Physician decision	**10 (0.6)**
Unknown*	9 (0.5)
Lack of efficacy	5 (0.3)
Lost to follow-up	3 (0.2)
Pregnancy	2 (0.1)
Protocol Deviation	1 (0.1)
IMP non-compliance	1 (0.1)
Death	1 (0.1)

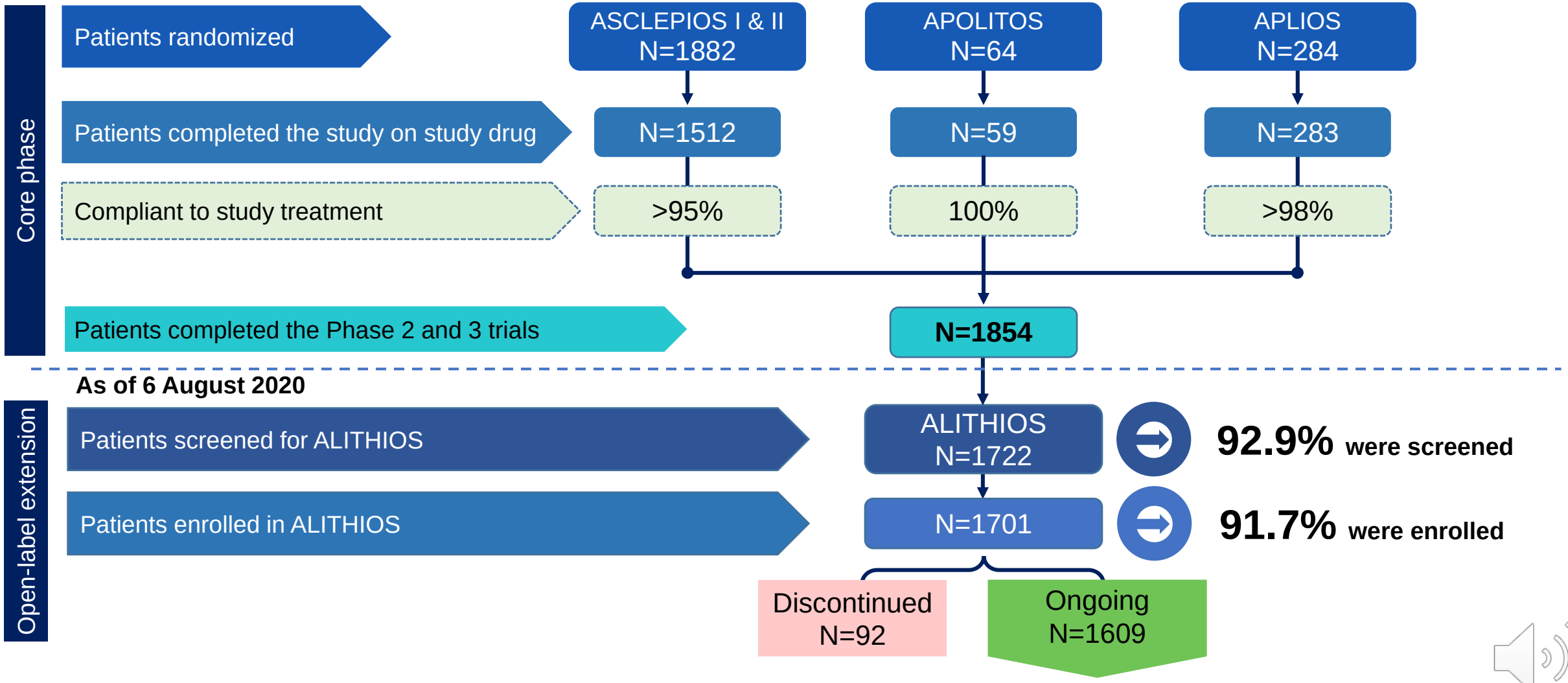
*Data not yet entered into the EDC Database

- **The study completion date is estimated in 2028**

*This is the current enrollment status as of 6 Aug 2020, but NOT FINAL enrollment.

Results

Compliance in Phase 2/3 studies and acceptance of transitioning to ALITHIOS



Conclusions

- Compliance with self-administered s.c. ofatumumab 20 mg was high in all studies (>95%), and fewer patients discontinued ofatumumab treatment versus the comparators in phase 2/3 studies
- The majority of eligible patients accepted transitioning to the open-label ALITHIOS umbrella extension study
- The ALITHIOS study is designed to allow patients who participated in prior ofatumumab studies to continue with the treatment or switch from placebo/teriflunomide to ofatumumab, and to further assess the benefit-risk profile of ofatumumab in RMS patients and its tolerability with long-term use

Thank you

RMS, relapsing multiple sclerosis; s.c., subcutaneous