Adherence and Compliance with Subcutaneous Administration of Ofatumumab in Relapsing Multiple Sclerosis

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Background

- Compliance to treatment is key to the optimum management of multiple sclerosis (MS)¹
- Ofatumumab, the first fully human anti-CD20 monoclonal antibody, administered with a monthly 20 mg subcutaneous (s.c.) dosing regimen, demonstrated superior efficacy versus teriflunomide, and a favorable safety profile in the two Phase 3 ASCLEPIOS I and II studies in relapsing MS (RMS)²
- ALITHIOS is an ongoing Phase 3b open-label, single-arm, multicenter extension study evaluating the long-term safety, tolerability and effectiveness of ofatumumab in RMS patients

Objectives

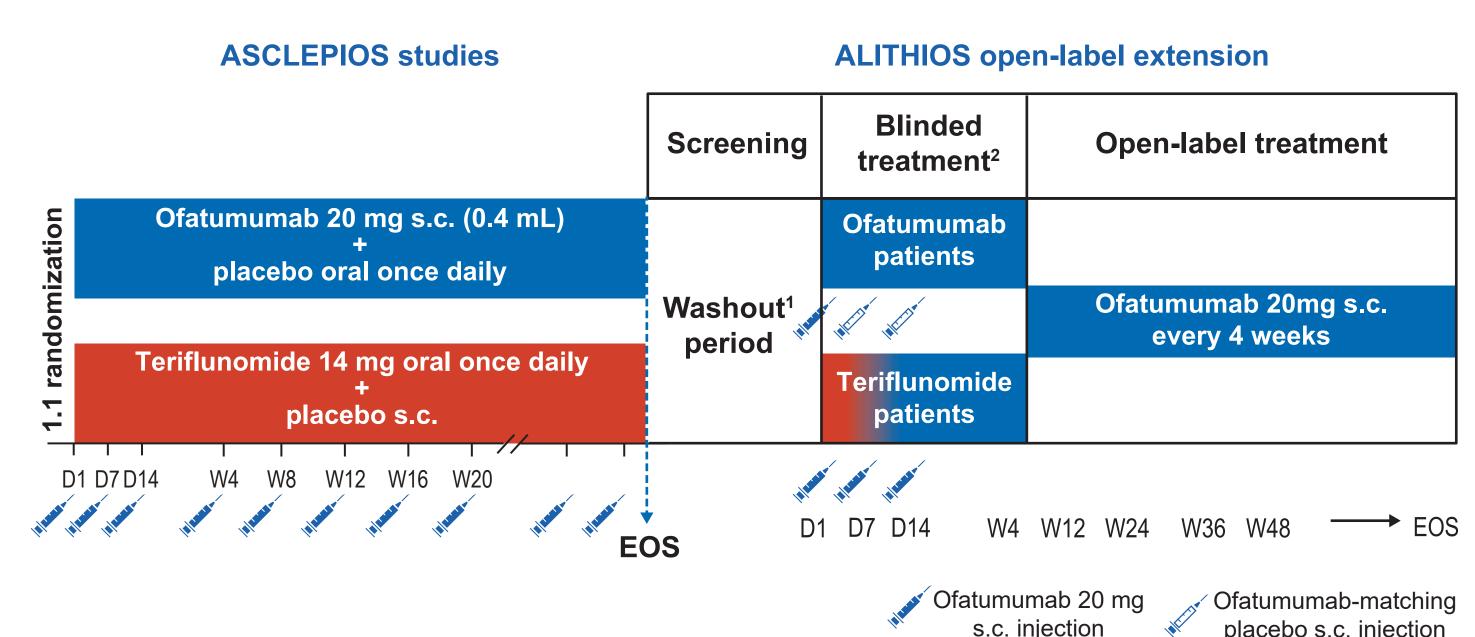
- To evaluate compliance with ofatumumab 20 mg s.c. versus oral teriflunomide in the Phase 3 ASCLEPIOS I/II studies, including treatment discontinuations
- To assess patients' acceptance of transitioning to the ALITHIOS extension study and compliance with ofatumumab 20 mg s.c. treatment, including discontinuations

Methods

Study design and patient population

- The Phase 3 ASCLEPIOS I and ASCLEPIOS II, were double-blind, double-dummy active comparator-controlled, parallel-group, multi-center adaptive and flexible duration studies. Adults patients with RMS were randomized (1:1) to ofatumumab 20 mg s.c. using a prefilled syringe (at the clinic on Days 1, 7, 14 and Week 4 and administered monthly at home from Month 2 onwards) or teriflunomide 14 mg (orally once daily), for up to 30 study months
- Patients who completed the double-blinded phase of these studies on the study drug were offered to continue with open-label ofatumumab in the ALITHIOS study (Figure 1)
- Patients can also transition to the ALITHIOS study from previous ofatumumab Phase 2 studies
- Here, we report data from the double-blind treatment epoch of the ASCLEPIOS studies and patients who transitioned to the ALITHIOS study

Figure 1. ALITHIOS study design: Patients transitioning from the ASCLEPIOS I and II studies



Washout as described in the teriflunomide (Aubagio®) product information
 Blinded treatment D7/D14 – patients from the ASCLEPIOS studies receive two additional doses of ofatumumab 20 mg s.c. (in teriflunomide-switch patients) or ofatumumab-matching placebo for loading (ofatumumab patients)
 D, day; EOS, end of study; s.c., subcutaneous; W, week

Study assessments and statistical analysis

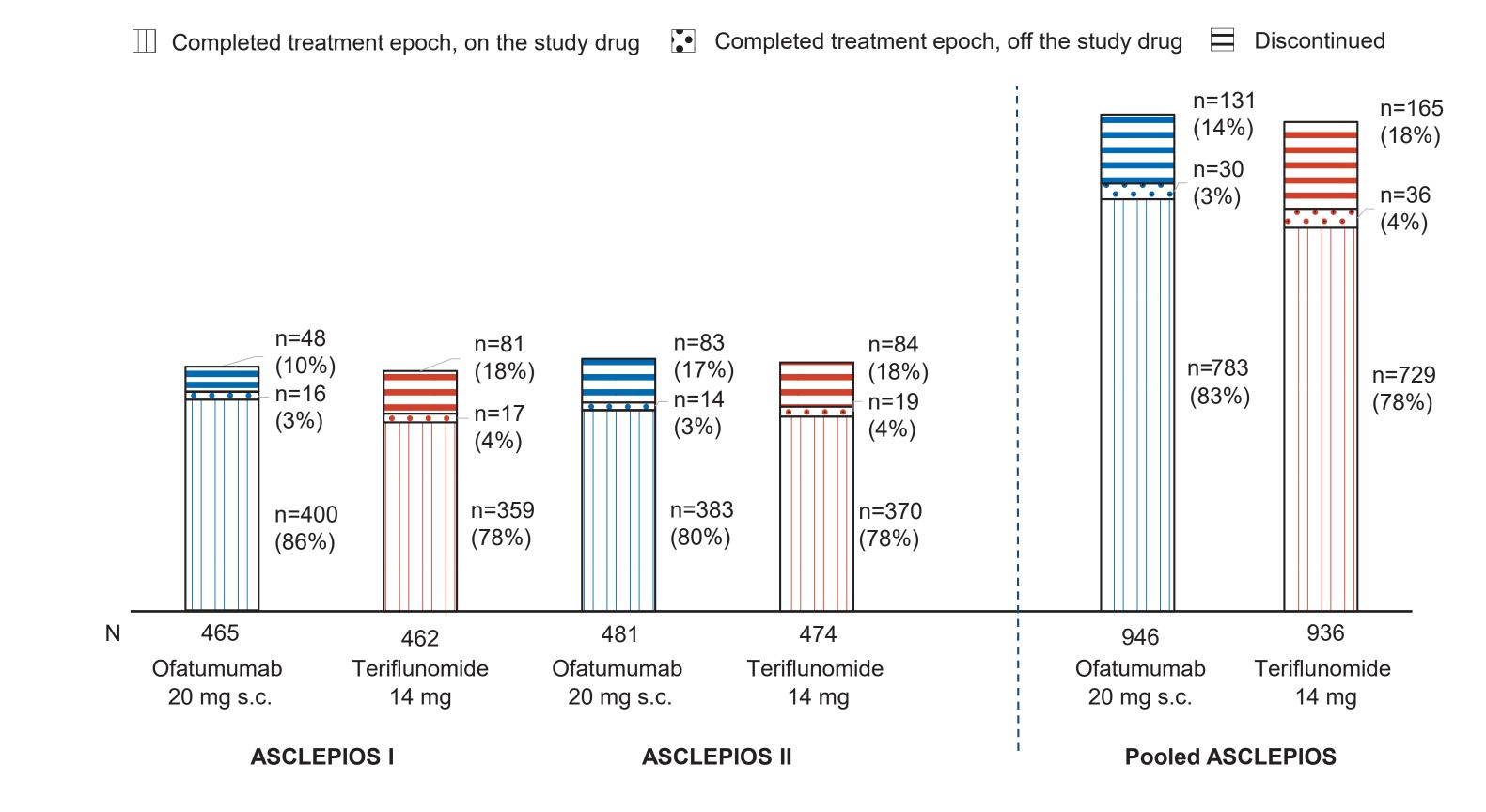
- Treatment compliance and discontinuations in the ASCLEPIOS I and II trials were analyzed:
- Compliance is calculated as the duration of exposure to the study drug, defined as (days)/duration of on-treatment period in (days)×100%. This means that compliance is measured during the time interval the patient took study medication; premature discontinuation from study drug was not considered as noncompliance
- The percentage of eligible ASCLEPIOS patients who accepted transitioning to the ALITHIOS study and compliance in this study were evaluated
- Data are presented using descriptive statistics

Results

Patient disposition: ASCLEPIOS I and II

- In both the ASCLEPIOS I and II trials, a higher proportion of patients receiving of atumumab completed the treatment-epoch on the study drug versus teriflunomide (**Figure 2**)
- ASCLEPIOS I: 86% (400/465) of patients versus 78% (359/462)
- ASCLEPIOS II: 80% (383/481) of patients versus 78% (370/474)
- Fewer patients discontinued the study drug with ofatumumab compared to teriflunomide

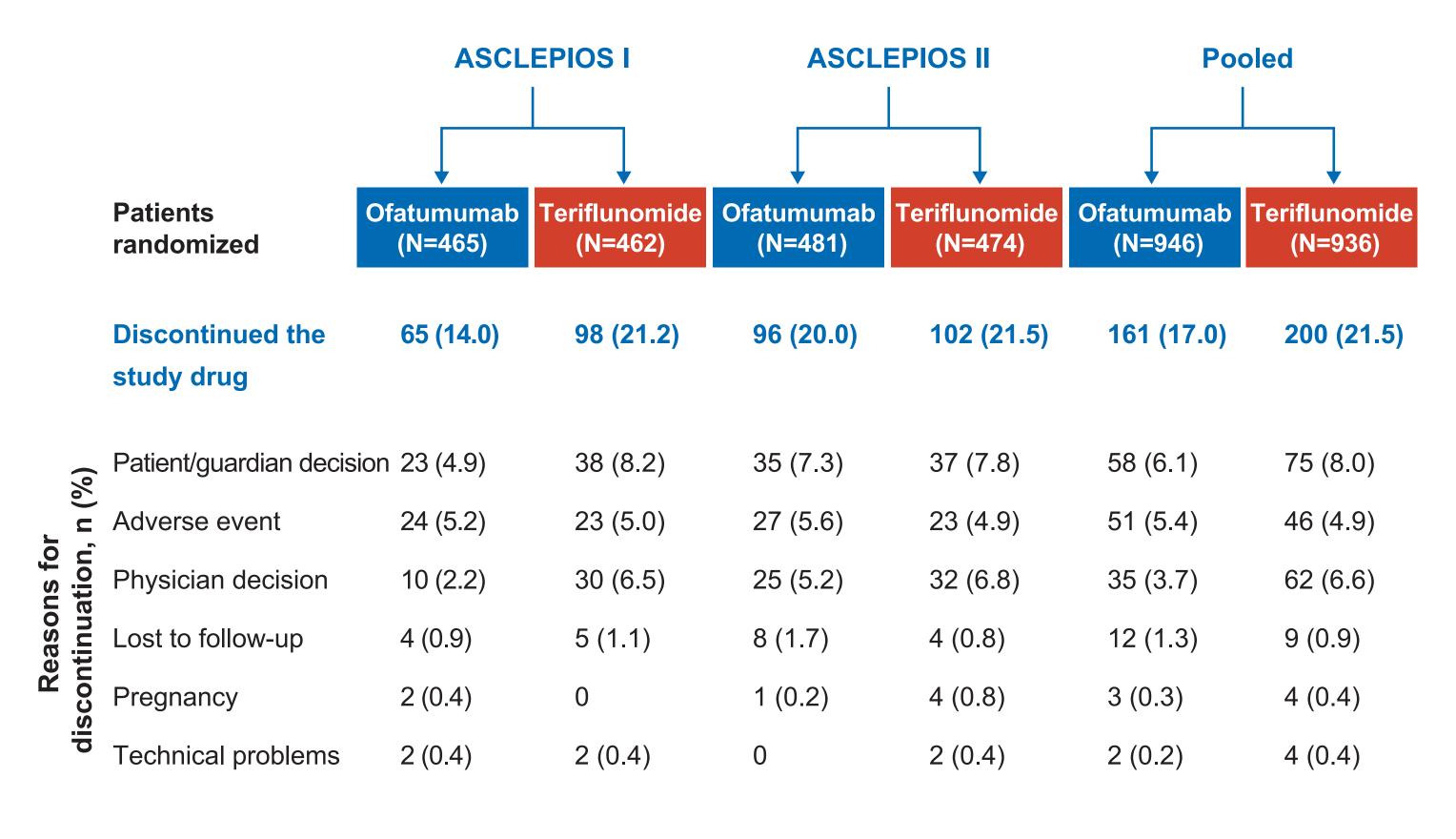
Figure 2. Patient disposition: ASCLEPIOS I and II



N, total number of patients randomized; n, number of patients who completed or discontinued treatment epoch; On study drug: Patients who took the study drug until the treatment epoch completion. Off study drug: Patients who completed the treatment epoch but discontinued the study drug prematurely. In ASCLEPIOS I, six patients were considered ongoing; five completed the study medication prior to the cutoff date and one discontinued study drug and study prematurely. In ASCLEPIOS II, two patients were considered ongoing; all completed the study medication prior to the cutoff date.

- The reasons for discontinuation from the study drug are illustrated in Figure 3
- The most common reasons for discontinuation (>2% in any group) were patient/guardian decision, adverse event, and physician decision

Figure 3. Reasons for discontinuation from the study drug

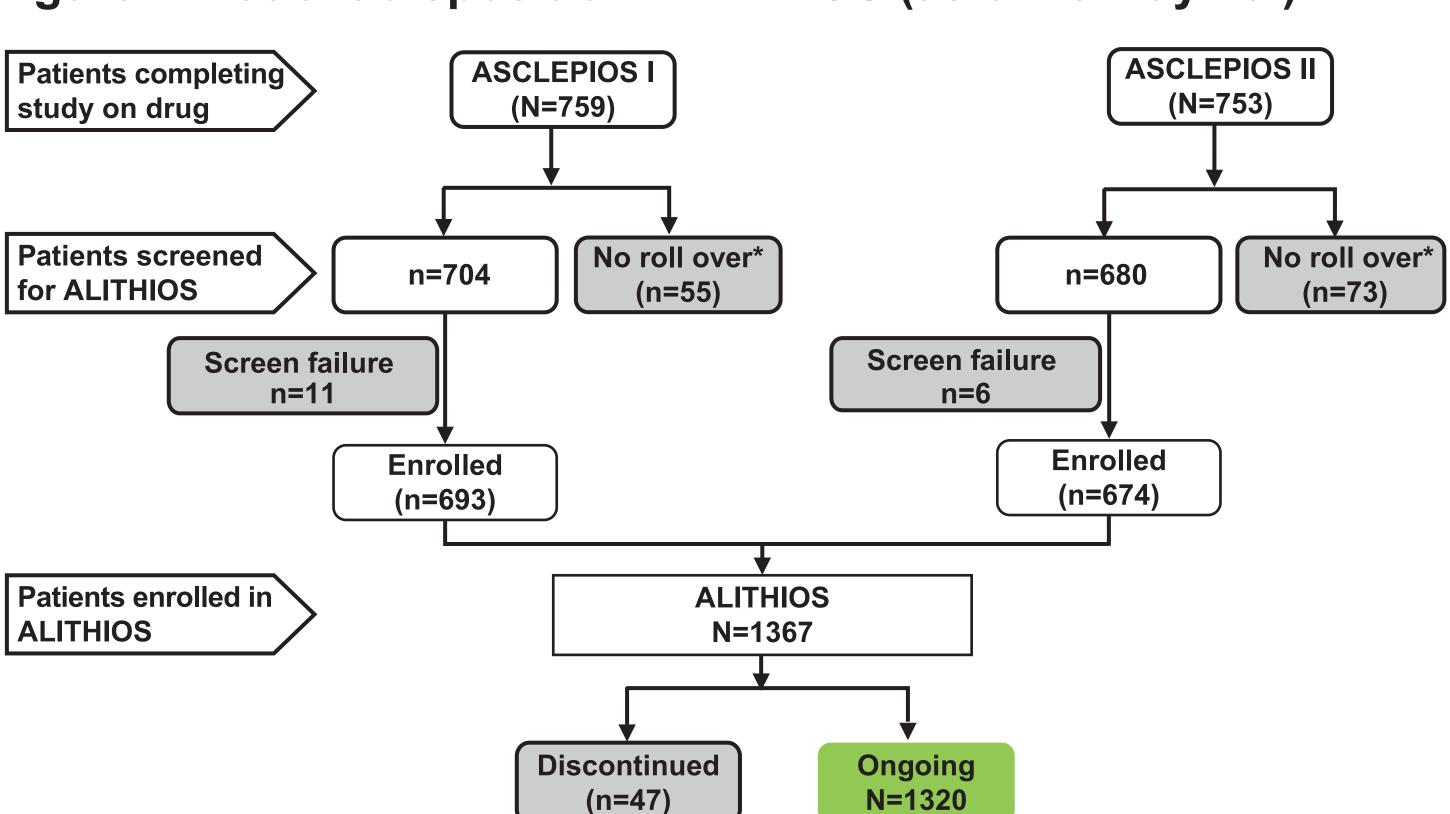


N, total number of patients; n, patients who discontinued

ALITHIOS: Patient transition and disposition

- In the ASCLEPIOS I and II, 759 and 753 patients completed respective trials on the study drug and were eligible for the transition to ALITHIOS
- Over 90% of eligible patients were willing to continue with the open-label of atumumab 20 mg s.c. in ALITHIOS (**Figure 4**)
- ASCLEPIOS I: 704/759 (92.7%) patients consented to participate
- ASCLEPIOS II: 680/753 (90.3%) patients consented to participate

Figure 4. Patient disposition: ALITHIOS (as of 13 May 20#)



#Final data-validation ongoing. *Reasons may include patient's decision (wanted to get pregnant, moving to different location) and administrative problems (such as non-approval of site or ALITHIOS study protocol and patient not meeting study inclusion criteria of ASCLEPIOS end of study <6 months)

Treatment compliance

- Compliance to the treatment schedule was high across treatment groups (Table 1)
- More than 95% of patients were compliant to treatment over 90% of the study duration

Table 1. Compliance with study treatment schedule

Study	Compliance category	Ofatumumab 20 mg s.c. every 4 weeks, n (%)	Teriflunomide 14 mg
ASCLEPIOS I	≥90%	95%	97%
ASCLEPIOSII		96%	97%

Conclusions

- In the ASCLEPIOS studies, compliance with home-administered s.c. ofatumumab was high and fewer patients discontinued ofatumumab as compared to teriflunomide during the study
- The majority of eligible patients accepted transitioning to the open-label ALITHIOS extension study to continue treatment with ofatumumab

References

- 1. World Health Organization Report: Adherence to Long-Term Therapies. Geneva, WHO, 2003 https://www.who.int/chp/knowledge/publications/adherence_report/en/
- 2. Hauser SL, et al. *N Engl J Med.* 2020;383(6):546–557.

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