Compliance to Subcutaneous Administration of Ofatumumab in Relapsing Multiple Sclerosis

DXT18

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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

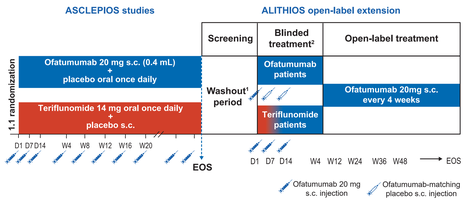
- To evaluate compliance with ofatumumab 20 mg s.c. versus oral teriflunomide in the Phase 3 ASCLEPIOS I and II studies, including treatment discontinuations
- To assess patients' acceptance of transitioning to the ALITHIOS extension study and compliance with ofatumumab 20 mg s.c. treatment, including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



1. Washout as described in the teriflunomide (Aubagio®) product information
2. 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

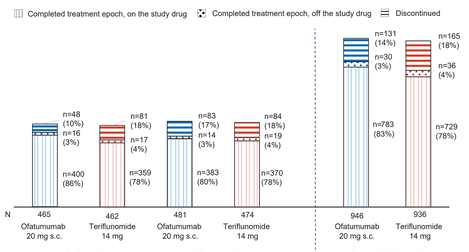
- Treatment compliance and discontinuations in the ASCLEPIOS I and II studies were analyzed:
  - Compliance is calculated as the duration of exposure to the study drug, defined as (days)/duration of on-treatment period in (days)×100%. This means that compliance is measured during the time interval the patient took study medication; premature discontinuation from study drug was not considered as non-compliance
- 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 studies, a higher proportion of patients receiving ofatumumab 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

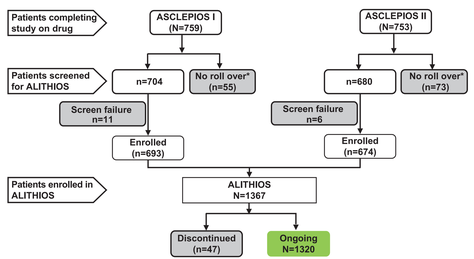
	ASCLEPIOS I		ASCLEPIOS II		Pooled	
Patients randomized	**Ofatumumab (N=465)**	**Teriflunomide (N=462)**	**Ofatumumab (N=481)**	**Teriflunomide (N=474)**	**Ofatumumab (N=946)**	**Teriflunomide (N=936)**
Discontinued the study drug	**65 (14.0)**	**98 (21.2)**	**96 (20.0)**	**102 (21.5)**	**161 (17.0)**	**200 (21.5)**
Reasons for discontinuation, n (%)						
Patient/guardian decision	23 (4.9)	38 (8.2)	35 (7.3)	37 (7.8)	58 (6.1)	75 (8.0)
Adverse event	24 (5.2)	23 (5.0)	27 (5.6)	23 (4.9)	51 (5.4)	46 (4.9)
Physician decision	10 (2.2)	30 (6.5)	25 (5.2)	32 (6.8)	35 (3.7)	62 (6.6)
Lost to follow-up	4 (0.9)	5 (1.1)	8 (1.7)	4 (0.8)	12 (1.3)	9 (0.9)
Pregnancy	2 (0.4)	0	1 (0.2)	4 (0.8)	3 (0.3)	4 (0.4)
Technical problems	2 (0.4)	2 (0.4)	0	2 (0.4)	2 (0.2)	4 (0.4)

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 ofatumumab 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 Oral once daily, n (%)
ASCLEPIOS I	≥90%	95%	97%
ASCLEPIOS II		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. *Presented at the ECTRIMS* 2019; S17.OP336

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