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

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Disclosures

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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.

- Ofatumumab 20 mg s.c. demonstrated superior efficacy versus teriflunomide and a favorable safety profile in the Phase 3 ASCLEPIOS trials in RMS patients.

- 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.
Methods

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

Part 1
Screening: Washout and eligibility

Part 2
Loading

Part 3
Open-label treatment

ASCLEPIOS I and II
>1600 Patients
Teriflunomide comparator

APOLITOS and APLIOS
>300 Patients
Ofatumumab treatment

• 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

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

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

ALITHIOS: Study objectives

**Primary objectives**

- Proportion of subjects with an adverse event
- 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 (%) = \( \frac{\text{Duration of exposure to the study drug (days)}}{\text{Duration of the on-treatment period (days)}} \times 100 \)
Results

Patient disposition

As of 6 August 2020

1854 eligible patients
1722 (92.9%) screened
1701 (98.8%) enrolled
1609 (94.6%) ongoing
92 (5.4%) Discontinued

Reasons for discontinuation

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

*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

Patients randomized

- ASCLEPIOS I & II
  - N=1882
  - Patients completed the study on study drug
    - N=1512
    - >95% compliant to study treatment

- APOLITOS
  - N=64
  - Patients completed Phase 2 and 3 trials
    - N=59
    - 100% compliant to study treatment

- APLIOS
  - N=284
  - Patients enrolled in ALITHIOS
    - N=283
    - >98% compliant to study treatment

As of 6 August 2020

- Patients screened for ALITHIOS
  - 92.9% were screened
  - N=1722
- Patients enrolled in ALITHIOS
  - 91.7% were enrolled
  - N=1701

Discontinued
- N=92

Ongoing
- N=1609
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