Compliance and Persistence with Ofatumumab Treatment in Patients with Relapsing Multiple Sclerosis in Clinical Trials for up to 4 Years

P734

Enrique Alvarez[1], Carrie M. Hersh[2], Derrick Robertson[3], Ayan Das Gupta[4], Xixi Hu[5], Ronald Zielman[6], Ibolya Boer[7], Andy Cheadle[5], Jeffrey A. Cohen[8]

[1]University of Colorado School of Medicine, Aurora, CO, USA; [2]Cleveland Clinic Mellen Program for MS, Lou Ruvo Center for Brain Health, Las Vegas, NV, USA; [3]Multiple Sclerosis Division, Department of Neurology, University of South Florida, Tampa, FL, USA; [4]Novartis Healthcare Pvt. Ltd., Hyderabad, India; [5]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [6]Novartis Pharma B.V., Amsterdam, the Netherlands; [7]Novartis Pharma AG, Basel, Switzerland; [8]Department of Neurology, Mellen MS Center, Neurological Institute, Cleveland Clinic, Cleveland, OH, USA

Introduction

- Ofatumumab (OMB) demonstrated superior efficacy and a similar safety profile to teriflunomide in the ASCLEPIOS I/II studies in relapsing multiple sclerosis (RMS)[1]
- Sustained efficacy of OMB and a consistent safety profile have also been observed in the long-term ALITHIOS open-label extension study for up to 4 years[2,3]

Objective

- To evaluate the long-term compliance and persistence with OMB treatment in patients with RMS for up to 4 years

Methods

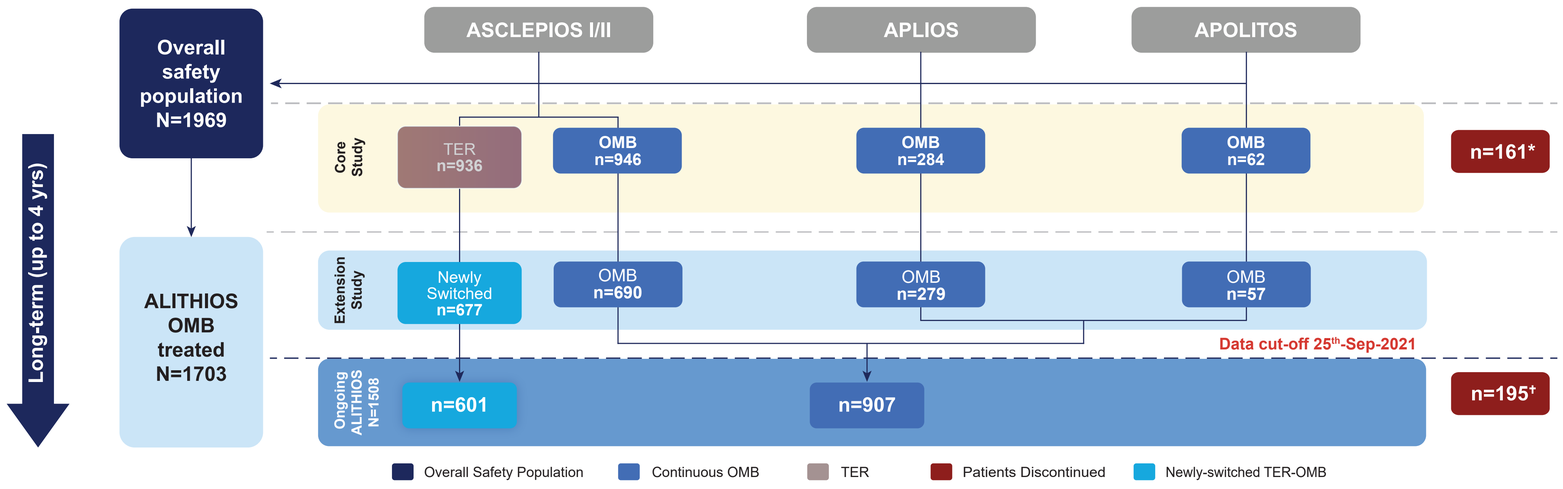
Patient population

- Patients who completed the core ASCLEPIOS I/II, APOLITOS and APLIOS trials could enter ALITHIOS, an ongoing, open-label, umbrella extension trial (**Figure 1**)

Compliance assessment

- Measurement of compliance was based on dosing information recorded by the patient in a study treatment diary
- Details captured included the time and date of each subcutaneous injection, any administration-related symptoms and records of missed doses

Figure 1. Patient disposition



Continuous group OMB-OMB, patients randomised to OMB in the core (ASCLEPIOS I/II); newly switched (TER-OMB), patients randomised to teriflunomide in the core study and were switched to OMB in ALTHIOS

*Primary reasons for discontinuation from OMB in ASCLEPIOS I/II – physician/subject decision: n=94 (9.9%); AE: n=51 (5.4%); other: n=6 (5.3%)

†Primary reasons for discontinuation from ALITHIOS – physician/subject/guardian decision: n=87 (5.1%); AE: n=66 (3.8%); SAE: n=6 (0.3%); death: n=6 (sudden death [n=1], completed suicide [n=1], COVID-19 pneumonia: [n=1], COVID-19: [n=1], intestinal metastasis [n=1], pneumonia and septic shock [n=1]); other: n=36 (2.1%)

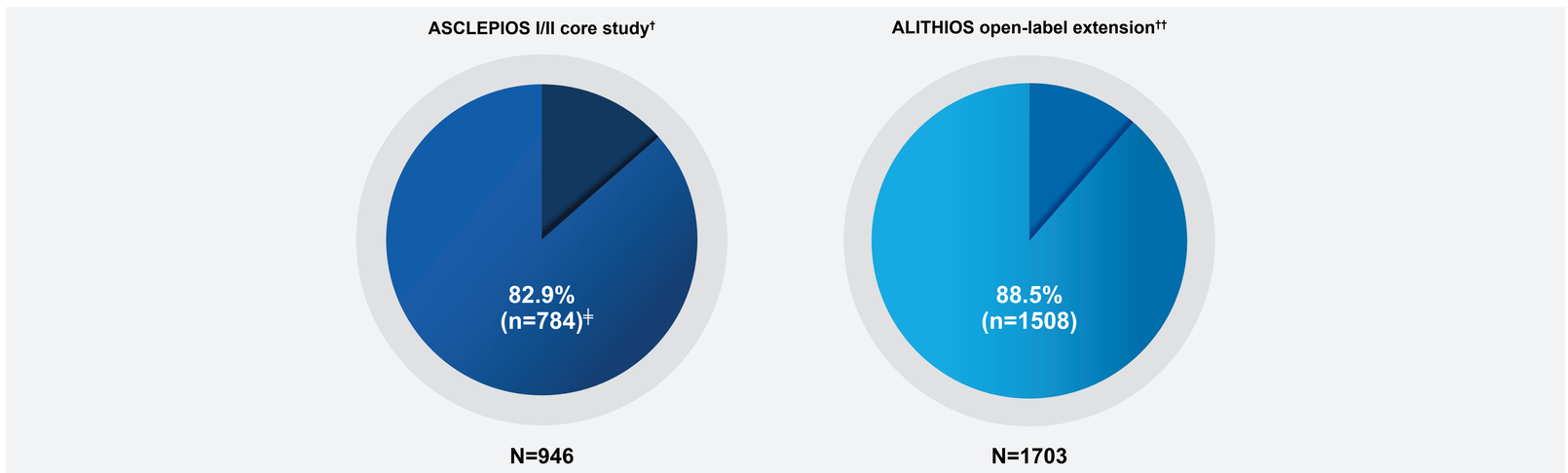
AE, adverse event; n, number of patients; N, the number of patients entering the core ASCLEPIOS I/II trial and open-label ALITHIOS extension trial respectively; OMB, ofatumumab; SAE, serious adverse event; TER, teriflunomide; yrs, years

- Compliance with OMB for up to 4 years (cut-off: 25th-September-2021) was analysed in the pooled ASCLEPIOS I/II core studies, in the overall ALITHIOS safety population and in the continuous OMB (treated with OMB in the core studies, regardless of whether they entered ALITHIOS) and newly switched (randomised to teriflunomide in the core studies and switched to OMB in ALITHIOS) subgroups
- Compliance was calculated as the duration of exposure to the study drug/duration of the on-treatment period×100%, with ≥80% defined as the threshold to indicate patients were compliant

Persistence assessment

- Persistence was measured as 1) the percentage of patients who completed the study on OMB in the pooled ASCLEPIOS I/II core studies, and 2) the percentage of patients remaining on OMB from entry into ALITHIOS up to the study cut-off date

Figure 3. Persistence in ASCLEPIOS I/II and in the ALITHIOS extension study*



*Due to study duration differences between the ASCLEPIOS I/II (up to 30 months), APLIOS (12 weeks) and APOLITOS (24 weeks) core studies, persistence was calculated for the pooled ASCLEPIOS I/II core studies only. In addition, patients who successfully completed the core studies could opt not to continue onto the extension study. Therefore, persistence calculations were restricted to each study epoch to ensure patients who were persistent in the core studies but did not enter the extension did not confound persistence in the overall population analysis; ‡One patient who completed OMB but had an end-of-study status as discontinued was not counted

†Persistence in patients randomised to OMB in the core study; ††Persistence in patients entering ALITHIOS up to the cut-off date of 25th-September-2021

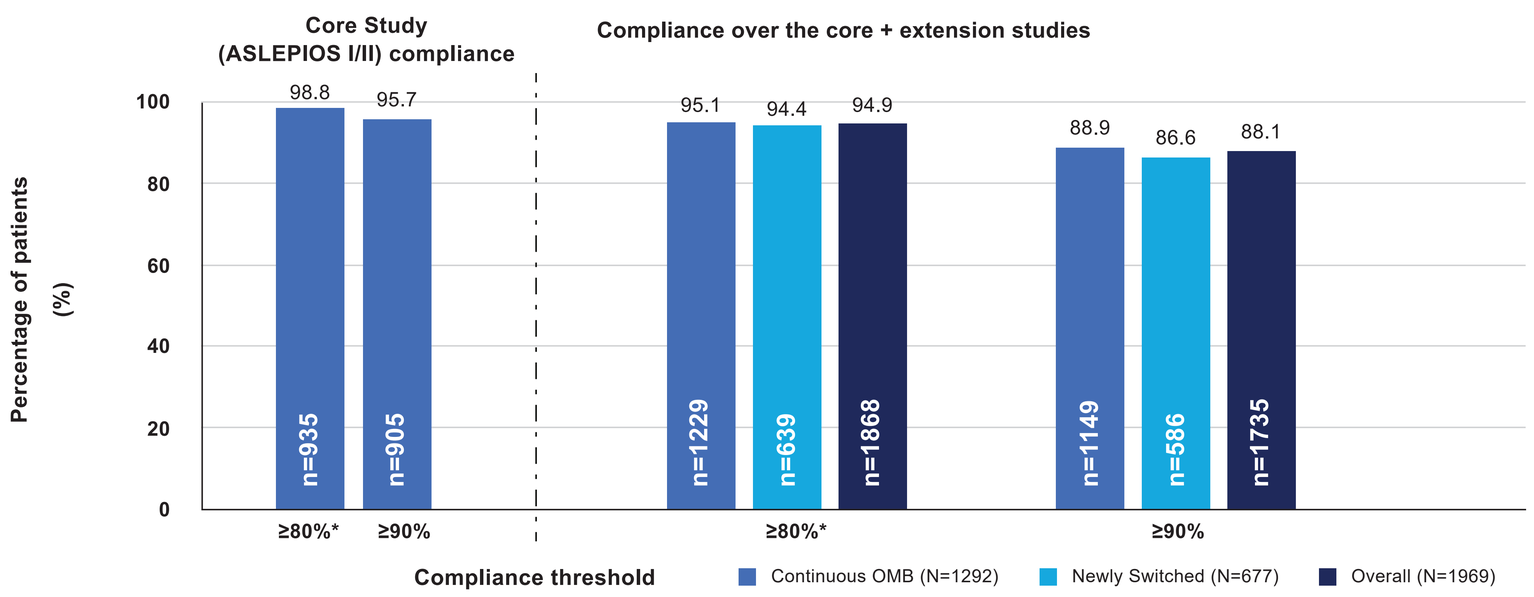
OMB, ofatumumab

- Persistence with OMB therapy remained high over the long term (**Figure 3**)
  - In the core ASCLEPIOS I/II studies, 82.9% of patients (784/946) randomised to OMB completed the study on treatment for up to 30 months
  - In the ongoing ALITHIOS studies, 88.5% of patients (1508/1703) remained on treatment at the time of the data cutoff (25th-September-2021)

Results

- In the overall safety population, 86.5% of patients (1703/1969) randomised in ASCLEPIOS I/II, APLIOS or APOLITOS completed the core studies and entered ALITHIOS (for patient disposition, see **Figure 1**)
- Compliance was high in ASCLEPIOS I/II and remained high over the long term for the overall, continuous OMB and newly switched subgroups (**Figure 2**)
  - As of 25th-September-2021, the proportion of patients compliant with OMB therapy was 94.9% (1868/1969) in the overall group, 95.1% (1229/1292) in the continuous OMB group, and 94.4% (639/677) in the newly switched group and was comparable to the core ASCLEPIOS I/II studies (98.8%)[4]

Figure 2. Patient compliance of the core ASCLEPIOS I/II and ALITHIOS studies



On-treatment period includes days from the first injection date until 30 days after the last injection date

*≥80% was defined as the threshold indicating a patient was compliant

n, number of patients; N, the number of patients entering the core ASCLEPIOS I/II trial and open-label ALITHIOS extension trial respectively; OMB, ofatumumab

Conclusions

- Approximately 95% of patients were ≥80% compliant with ofatumumab treatment over the long term (up to 4 years), indicating high compliance with monthly 20 mg subcutaneous therapy
- Persistence with ofatumumab remains high over the long term with nearly 9/10 patients remaining on treatment in the ongoing ALITHIOS open-label extension study

References

1. Hauser SL, et al. *N Engl J Med*. 2020;383:546–57
2. Hauser SL, et al. Poster Presentation at the American Academy of Neurology (AAN) 2022, #P5.004, April 02–07, 2022
3. Hauser SL, et al. Oral poster presentation at the American Academy of Neurology (ANN) 2022, #S14.004, April 04, 2022
4. Fox EJ, et al. Poster presented at The Consortium of Multiple Sclerosis Centers virtual meeting, #DXT18, June 01–04, 2020

Acknowledgements

The authors acknowledge the following Novartis employees: **Erik O'Hanlon** and **Paul Coyle** for medical writing assistance and coordinating author reviews, and **Dondapati China Srinivasa Rao** for creative design assistance. The final responsibility for the content lies with the authors.

Disclosures

The study was funded by Novartis Pharma AG, Basel, Switzerland.

Enrique Alvarez received compensation for consulting from Actelion/Janssen, Alexion, Bayer, Biogen, Celgene/BMS, EMD Serono/Merck, Genentech/Roche, Genzyme, Novartis, Sanofi, and TG Therapeutics and for research from Biogen, Genentech/Roche, Novartis, TG Therapeutics, Patient-Centered Outcomes Research Initiative, National Multiple Sclerosis Society, National Institutes of Health, and Rocky Mountain MS Center.

Jeffrey A. Cohen received personal compensation for consulting for Biogen, Bristol-Myers Squibb, Convelo, Genentech, Janssen, NervGen, Novartis, and PSI; speaking for H3 Communications; and serving as an Editor of Multiple Sclerosis Journal.

Carrie M. Hersh has received compensation for consulting and research from Novartis, Biogen and Genentech and for consulting from EMD Serono and consulting and speaker bureau from Genzyme.

Derrick Robertson has received fees for consulting, contracted research and speaker's bureau from Biogen, Celgene, EMD Serono, Genentech, Sanofi Genzyme, Janssen, TG therapeutics; consulting fees and speakers bureau for Bristol Myers Squibb, Horizon, and Alexion; consulting fees and contracted research for Novartis; consulting fees for Greenwich biosciences; contracted research for GW Pharmaceuticals, PCORI, Atara Biotherapeutics and CorEvitas.

Ayan Das Gupta, Xixi Hu, Ronald Zielman, Ibolya Boer, Andy Cheadle are employees of Novartis.

Poster presented at the 38th congress of the European Committee for Treatment and Research in Multiple Sclerosis, RAI Amsterdam, Amsterdam, Netherlands, 26th - 28th October, 2022.

Visit the web at:
https://bit.ly/ectrims2022

Presenter email address:
ENRIQUE.ALVAREZ@CUANSCHUTZ.EDU

Scan this QR code to download a copy Poster