P355

Stephen Hauser | stephen.hauser@ucsf.edu

Continuous Ofatumumab Treatment for Up to 7 Years Shows a Favourable Safety and Efficacy Profile in People With Relapsing Multiple Sclerosis

Stephen L. Hauser[1], Amit Bar-Or[2], Anne H. Cross[3], Xavier Montalban[4], Jérôme de Seze[5], Ralf Linker[6], Natalia Khachanova[7], Jun Li[8], Min Wu[9], Gregory Lewis Pearce[8], Maria Solonets[8], Anil Abeyewickreme[10], Gabriel Pardo[11]

[1]UCSF Weill Institute for Neurosciences, University of California, San Francisco, CA, USA; [2]Center for Neuroinflammation and Experimental Therapeutics and Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [3]Department of Neurology, Division of Neuroimmunology, Washington University School of Medicine, Saint Louis, MO, USA; [4]Department of Neurology/ Neuroimmunology, Centre d'Esclerosi Múltiple de Catalunya (Cemcat), Hospital Universitari Vall d'Hebron, Barcelona, Spain; [5]University Hospital of Strasbourg, Strasbourg, France; [6]Department of Neurology, University of Regensburg, Regensburg, Germany; [7]Pirogov Russian National Research Medical University, Moscow, Russia; [8]Novartis Pharma AG, Basel, Switzerland; [9]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [10]Novartis Pharmaceuticals UK Ltd, London, United Kingdom; [11]Oklahoma Medical Research Foundation, Oklahoma City, OK, USA

Non-author presenter: Damiano Boldrini – Medical department Novartis Italy

KEY FINDINGS & CONCLUSIONS

- Treatment of plwRMS with ofatumumab for up to 7 years demonstrated aconsistent safety profile, with no new safety concerns
  - The exposure adjusted incidence rate of adverse events, including topics of interest such as serious infections and malignancies remained consistent with no increased risks over 7 years
  - Mean IgG levels remained stable, whereas mean IgM levels initially decreased but then stabilised and remained above the LLN
- Ofatumumab treatment up to 7 years also showed sustained efficacy by maintaining low rates of relapse and MRI activity and high rates of participants free of disease activity (NEDA-3)
  - In line with previous analyses, 9 of 10 participants were free of disease activity in both the continuous and switch groups during Year 7
  - Participants who were initially treated with teriflunomide had significantly lower rates of NEDA-3, but these rates rapidly increased after switching to ofatumumab
- Limitations include a potential for attrition bias and the open-label nature of theextension study
- The 7-year results further confirm the long-term, favourable benefit-risk profile ofofatumumab and reinforce the benefit of early ofatumumab initiation in plwRMS

This study was sponsored by Novartis Pharma AG, Basel, Switzerland.
Poster P804 presented at the 41st congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), Barcelona, Spain, 24–26 September 2025.

INTRODUCTION

- Ofatumumab, a fully human anti-CD20 monoclonal antibody with a 20 mg subcutaneous monthly dosage regimen, is the only anti-CD20 approved for the treatment of relapsing multiple sclerosis (RMS) via self-administration[1,2]
- In the phase 3 ASCLEPIOS I/II trials, ofatumumab (up to 30 months) was superior to teriflunomide in reducing clinical and magnetic resonance imaging (MRI) disease activity, with a favourable safety profile in people living with RMS (plwRMS)[3]
- Up to 6 years of ofatumumab treatment in the ALITHIOS open-label extension study showed sustained efficacy and a favourable safety profile[4–6]
- Furthermore, previously reported data showed that with treatment up to 7 years, participants receiving continuous ofatumumab treatment maintained a favourable safety profile and experienced numerically fewer 6-month confirmed disability worsening (6mCDW) and progression independent of relapse activity events compared to those who switched from teriflunomide[7]

OBJECTIVE

- To describe the long-term safety and further efficacy (annualised relapse rate [ARR], no evidence of disease activity [NEDA-3] and MRI) outcomes of ofatumumab for up to 7 years in plwRMS (data cut-off: 25-Sep-2024)

METHODS

Safety population (N=1969)

- Safety analyses included participants receiving ≥1 dose of ofatumumab in ASCLEPIOS I/II, APOLITOS, APLIOS or the umbrella extension study ALITHIOS

Efficacy population (N=1882)

- **Continuous ofatumumab group (OMB-OMB):** Participants randomised to ofatumumab in ASCLEPIOS I/II and continuing ofatumumab in ALITHIOS
- **Switch group (TER-OMB):** Participants randomised to teriflunomide in ASCLEPIOS I/II and switched to ofatumumab in ALITHIOS

Key assessments

- **Safety:** Overall safety profile, serious infections, malignancies, IgG and IgM levels, and lymphocyte and neutrophil levels
- **Efficacy:** Cumulative data up to 7 years for ARR, NEDA-3 and brain MRI outcomes (mean number of gadolinium-enhancing [Gd+] T1 lesions per scan and number of new or enlarging T2 [neT2] lesions per year)

RESULTS

Participant population and baseline characteristics

- Of the 1882 participants in the efficacy population (OMB-OMB, n=946; TER-OMB, n=936), 1367 entered ALITHIOS (OMB-OMB, n=690; TER-OMB, n=677)
- At the time of data cut-off, 1043 of the 1367 participants (76.3%) entering ALITHIOS had completed the 5-year extension period, and of these, 944 had entered a subsequent 3-year extension period
  - Of the 1367 participants entering ALITHIOS, 300 (21.9%) had discontinued the study and 24 (1.75%) were still ongoing in the 5-year extension
  - The main reasons for discontinuing the study were participant/ guardian decision (131/1367 [9.6%]) and occurrence of adverse events (AEs; 70/1367 [5.1%])
- Baseline characteristics were typical of plwRMS and were well balanced across treatment groups

Overall safety profile

- The overall safety profile (based on the safety population: N=1969) remained consistent with the 6-year findings, with no new safety concerns[6] (**Table 1**)
- Exposure-adjusted incidence rates of serious AEs, including infections and malignancies, remained consistent up to 7 years

Table 1. Overall safety profile up to 7 years

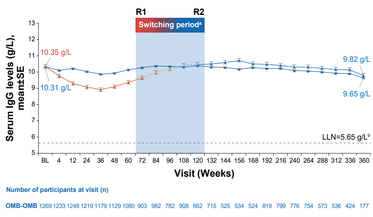
	Overall safety population (N=1969)	
	n (%)	EAIR (95% CI)
Participants with at least one AE	1826 (92.7)	112.95 (107.88–118.25)
Participants with at least one SAE	342 (17.4)	4.06 (3.65–4.51)
AEs leading to ofatumumab discontinuation	151 (7.7)	–
Infections and infestations	1423 (72.3)	37.12 (35.24–39.10)
Serious infections	123 (6.2)	1.37 (1.15–1.63)
Serious infections (excluding COVID-19)	78 (4.0)	0.86 (0.69–1.07)
Serious COVID-19 infections	51 (2.6)	0.55 (0.42–0.73)
Blood Ig levels		
IgG decrease	8 (0.5)	0.09 (0.04–0.17)
IgM decrease	284 (14.4)	3.30 (2.94–3.71)
Injection-related reactions	516 (26.1)	7.38 (6.77–8.04)
Injection-site reactions	261 (13.3)	3.16 (2.80–3.57)
Malignancies	29 (1.5)	0.31 (0.22–0.45)
Deaths	12[a]	–

EAIR per 100 PYs is defined as the expected number of participants with the given event over 100 years of exposure to a treatment, assuming the event rate is constant over time. This is estimated by Poisson regression where participants' time is taken until the first event occurrence or the last day the participant was at risk for those who did not have the event. [a]Including the following: Sudden death (n=1), oesophageal adenocarcinoma (n=1), completed suicide (n=1), COVID-19/COVID-19 pneumonia (n=1), COVID-19 (n=2), gastric ulcer perforation (n=1), COVID-19 pneumonia (n=1), intestinal metastasis (n=1), COVID-19 pneumonia/pneumothorax (n=1), pneumonia/septic shock (n=1) and injury (n=1).

Mean IgG/IgM levels

- Mean IgG levels remained stable up to 7 years of treatment; mean IgM levels initially decreased but then stabilised and remained above the lower limit of normal (LLN; **Figure 1A and 1B**)
- 96.8% and 64.5% of participants had IgG and IgM levels above LLN at all assessments, respectively
- Treatment interruption/discontinuation was reported in 3 (0.2%)/4 (0.2%) participants due to low IgG, and in 204 (10.4%)/71 (3.6%) participants due to low IgM

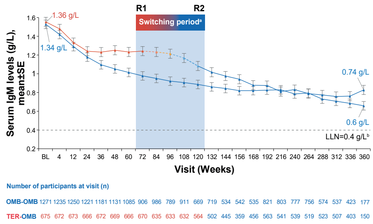
Figure 1A. Mean IgG levels over 7 years



Number of participants at visit (n)

OMB-OMB	1269	1233	1248	1219	1179	1129	1080	903	982	782	908	662	715	525	534	524	819	799	776	754	573	536	424	177
TER-OMB	675	672	673	666	672	669	666	670	635	633	631	564	495	442	350	454	582	542	539	518	523	507	404	151
Pre-switch	675	672	673	666	672	669	666	664	477	313	167	72												
Post-switch								06	158	320	464	492	495	442	350	454	582	542	539	518	523	507	404	151

Figure 1B. Mean IgM levels over 7 years



Number of participants at visit (n)

OMB-OMB	1271	1235	1250	1221	1181	1131	1085	906	986	789	911	669	719	534	542	535	821	803	777	756	574	537	423	177
TER-OMB	675	672	673	666	672	669	666	670	635	633	632	564	502	445	359	456	563	541	539	519	523	507	403	150
Pre-switch	675	672	673	666	672	669	666	664	477	313	167	72												
Post-switch								06	158	320	465	492	502	445	359	456	563	541	539	519	523	507	403	150

[a]Switching period refers to the participants started on teriflunomide and not applicable to the participants on ofatumumab in the core period. For the teriflunomide/ofatumumab group, data from the first dose of teriflunomide until the last dose of ofatumumab plus 100 days or analysis cut-off date has been used. R1: The first participant with first treatment-emergent assessment in ofatumumab period after switching to ofatumumab (72 weeks); R2: The last participant with last treatment-emergent assessment in teriflunomide period before switching to ofatumumab (120 weeks). [b]For all pooled analyses, a fixed value of LLN (using ALITHIOS study reference) was used: IgG: 5.65 g/L and IgM: 0.4 g/L.

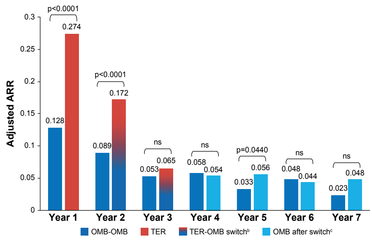
Lymphocyte and neutrophil levels

- A transient decline in the mean lymphocyte levels was observed up to Week 4 (% change: continuous, −11.9%; switch, −8.2%), followed by an increase back close to baseline levels in OMB-OMB and TER-OMB groups which was sustained through Week 360
- In the OMB-OMB group, the mean neutrophil level remained stable and above baseline for all visits up to Week 360, whereas in the TER-OMB group, the mean neutrophil level decreased up to Week 4 (−14.5%) and remained low during the pre-switch period followed by a reversal and stabilisation (reaching baseline levels) post-switch

Annualised relapse rate

- The ARR in the OMB-OMB group remained low over Years 1 to 7 (0.128–0.023) (**Figure 2**)
- Marked reductions in ARR were observed in the switch group during Years 2 to 3 (0.172–0.065) and were sustained through Years 3 to 7 (0.065–0.048) (**Figure 2**)

Figure 2. ARR[a] over 7 years



[a]Based on confirmed relapses (those accompanied by a clinically relevant change in the EDSS). ARR are obtained from a negative binomial model on treatment, period, region, number of relapses in previous year, baseline EDSS, baseline number of Gd+ lesions, age at baseline and a treatment by period interaction. Log-transformed exposure time (in years) per period is included as an offset variable to annualise the relapse rate in each period.[b]TER-OMB switch: participants transitioning from teriflunomide to ofatumumab; due to event-driven core study design (flexible duration), participants transitioned at various exposure time points, i.e. the switch from teriflunomide to ofatumumab started from Year 2 and was completed by Year 3. [c]OMB after switch: teriflunomide participants now on ofatumumab.

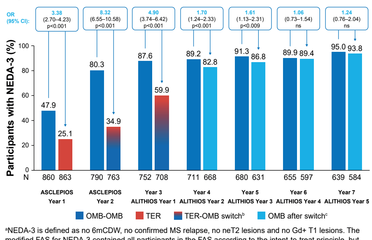
MRI lesion activity

- An almost complete suppression of Gd+T1 lesion activity (95.6% reduction for ofatumumab vs. teriflunomide in ASCLEPIOS I/II) was maintained from Years 1 to 7 in the OMB-OMB group and from Years 3 to 7 in the TER-OMB group
- An almost-complete suppression of neT2 lesions by Year 2 in the OMB-OMB group was also seen in the TER-OMB group by Year 4 and was maintained in both groups through Year 7

No evidence of disease activity

- High rates of NEDA-3 at Year 7, observed in more than 9 of 10 participants in both treatment groups, were in line with previous results (**Figure 3**)

Figure 3. NEDA-3[a] status over 7 years



[a]NEDA-3 is defined as no 6mCDW, no confirmed MS relapse, no neT2 lesions and no Gd+ T1 lesions. The modified FAS for NEDA-3 contained all participants in the FAS according to the intent-to-treat principle, but participants who discontinued from study drug prematurely for reasons other than 'lack of efficacy' or 'death' and had NEDA-3 before early discontinuations were excluded. Statistical model used logistic regression adjusting for treatment and region as factors, and age, baseline EDSS and number of Gd-lesions at baseline as covariates. Both scheduled and unscheduled MRI assessments are considered in the analysis. As some participants may have completed the 5-year extension prior to data cut-off and had less than 1 year exposure in the 7th year, there is a possibility that the NEDA-3 rates during Year 7 are overestimated. [b]TER-OMB switch: Participants transitioning from teriflunomide to ofatumumab; due to event-driven core study design (flexible duration), participants transitioned at various exposure time points, i.e. the switch from teriflunomide to ofatumumab started from Year 2 and was completed by Year 3. [c]OMB after switch: teriflunomide participants now on ofatumumab. OMB-OMB, continuous ofatumumab. N is the total number of participants in the treatment group.

Please also refer to the related posters being presented at the congress:

P805: Continuous Ofatumumab Treatment Up to 7 Years Shows a Consistent Safety and Efficacy Profile in Recently Diagnosed Treatment-Naive People Living With Relapsing Multiple Sclerosis

P812: Over 7 Years, the Risk of Serious Infections Remained Low With Long-Term Ofatumumab Treatment in People With Relapsing Multiple Sclerosis

P932: Immunoglobulin G Levels in Ofatumumab-Treated Participants With Episodes of Low Immunoglobulin M: An Analysis of 7-Year Data From the ALITHIOS Extension Study

References

1. Kesimpta (ofatumumab). Prescribing Information. Novartis; April 2024. Accessed 24 July 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/125326s079lbl.pdf.
2. Kesimpta (ofatumumab). Summary of product characteristics. Novartis, February 2025. Accessed 25 June 2025. https://www.ema.europa.eu/en/documents/product-information/kesimpta-epar-product-information_en.pdf.
3. Hauser SL, et al. *N Engl J Med*. 2020;383:546–557.
4. Cohen JA, et al. P8.004. Presented at: American Academy of Neurology (AAN) Annual Meeting, Boston, MA, USA; April 22–27, 2023.
5. Kappos L, et al. EPR-097. Presented at: European Academy of Neurology (EAN), Budapest, Hungary; July 1–4, 2023.
6. Weindl H, et al. P9.010. Presented at: American Academy of Neurology (AAN) Annual Meeting, Denver, CO, USA; April 13–18, 2024.
7. Pardo G, et al. P7.016. Presented at: American Academy of Neurology (AAN) Meeting, San Diego, CA, USA, April 5–9, 2025.

Abbreviations

6mCDW, 6-month confirmed disability worsening; **AE**, adverse event; **ARR**, annualised relapse rate; **BL**, baseline; **CI**, confidence interval; **EAIR**, exposure-adjusted incidence rate; **EDSS**, Expanded Disability Status Scale; **Gd+**, gadolinium enhancing; **Ig**, immunoglobulin; **LLN**, lower limit of normal; **MS**, multiple sclerosis; **NEDA**, no evidence of disease activity; **plwRMS**, people living with relapsing multiple sclerosis; **neT2**, new or enlarging T2; **ns**; non-significant; **OMB**, ofatumumab; **OMB-OMB**, continuous ofatumumab; **OR**, odds ratio; **PY**, patient-year; **SAE**, serious adverse event; **SE**, standard error; **TER**, teriflunomide; **TER-OMB**, switch from teriflunomide to ofatumumab.

Disclosures

Stephen L. Hauser currently serves on the scientific advisory boards of Accure, Alector, Annexon and Hinge. He has previously consulted for BD, Moderna, NGM Bio and Pheno Therapeutics and served on the Board of Directors of Neurona. Dr. Hauser also has received travel reimbursement and writing support from F. Hoffmann-La Roche and Novartis Pharma AG for anti-CD20 therapy–related meetings and presentations. **Amit Bar-Or** has received personal compensation for serving as a consultant for Roche Genentech, Novartis, Biogen, Merck/EMD Serono, Sanofi-Genzyme and Cabaletta and for serving on a scientific advisory or data safety monitoring board for Roche Genentech, Novartis, Merck/EMD Serono and Sanofi Genzyme. The institution of Dr. Bar-Or has received research support from Novartis, Biogen and Roche/ Genentech. **Anne H. Cross** has received fees or honoraria for consulting for Biogen, Bristol Myers Squibb, EMD Serono, F. Hoffmann-La Roche Ltd, Genentech, Horizon Pharmaceuticals, Janssen, Novartis, Octave, Sanofi and TG Therapeutics. Gabriel Pardo has received personal compensation for serving as a consultant for Biogen, Genentech, Genzyme, Greenwich Neuroscience, Celgene, EMD Serono, Horizon Therapeutics, TG Therapeutics and Novartis. He has also received personal compensation for serving on a speakers' bureau for Biogen, Bristol Myers Squibb, Celgene, Novartis, EMD Serono and Viela Bio. **Xavier Montalban** has received compensation for lecture honoraria and travel expenses, participation in scientific meetings, clinical trial steering committee membership, or clinical advisory board participation in recent years from AbbVie, Actelion, Alexion, AstraZeneca, Autolus, Bial PD, Biogen, Bristol-Myers Squibb/Celgene, EMD Serono, Genzyme, F. Hoffmann–La Roche, Immunic Therapeutics, Indivi, Janssen Pharmaceuticals, Juviné Pharmaceutical, Eli Lilly, MedDay, Medscape, Merck, Mylan-Viatris, NervGen, Neuraxpharm, Novartis, PeerVoice, Rewind Therapeutics, Samsung-Biosys, Sandoz, Sanofi-Genzyme, Teva Pharmaceuticals, TG Therapeutics, Zenas Biopharma, Excemed, ECTRIMS, MSIF and NMSS or any of their affiliates. **Jérôme de Seze** has received personal compensation for serving on a scientific advisory or data safety monitoring board for Pharma. **Ralf Linker** received compensation for activities with Biogen, Celgene, Genzyme, Merck, Novartis and Roche as well as research support from Biogen and Novartis. **Natalia Khachanova** has received honoraria for participation in clinical trials or as a speaker from Biocad, Generium, Jonhson & Jonhson, Merck, Novartis, Roche, Sanofi, TG Therapeutics and Valenta. **Gabriel Pardo** has received personal compensation for serving as a Consultant for Roche Genentech, Sanofi Genzyme, EMD Serono, Novartis, TG Therapeutics, Alexion Pharmaceuticals and Amgen and for serving on a speakers' bureau for Biogen, Bristol Myers Squibb, EMD Serono, Novartis, Roche Genentech, Janssen, Sanofi Genzyme, TG Therapeutics, Horizon Therapeutics and Alexion Pharmaceuticals. **Jun Li, Min Wu**, **Gregory Lewis Pearce**, **Maria Solonets** and **Anil Abeyewickreme** are employees of Novartis.

Acknowledgements

Medical writing support was provided by **Anupam Dwesar** (Novartis Healthcare Pvt. Ltd., Hyderabad, India) and **Paul Coyle** (Novartis Ireland Ltd., Dublin, Ireland) and design support by **Madhavi Kanithi** (Novartis Healthcare Pvt. Ltd., Hyderabad, India). The final responsibility for the content lies with the authors.

Scan to obtain poster:

To download a copy of this poster, visit the web at:
https://tinyurl.com/ectrims2025