

Outcomes of COVID-19 in Patients With Relapsing Multiple Sclerosis Receiving Ofatumumab: Data From the ALITHIOS Study and Post-marketing Surveillance

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Introduction

- As of 31-January-2021, the WHO reported that >102 million people worldwide had been affected by COVID-19, with fatal outcome in >2.2 million people¹
- Baseline factors such as age and co-morbidities, and in people with multiple sclerosis (MS), MS phenotype, higher disability rate and treatment with disease-modifying therapies (DMTs) may affect COVID-19 severity and outcomes²⁻⁴
- In people with MS (treated or untreated with DMTs) variable rates of hospitalizations (9.7% to 36.5%) and deaths (1.6% to 10.3%) due to COVID-19 have been reported in the existing literature³⁻⁶
- Evidence from clinical studies and real world is required to better understand the impact of COVID-19 on patients with MS treated with DMTs

Objective

- To report the characteristics and outcomes of COVID-19 in patients with relapsing MS (RMS) receiving ofatumumab from the ongoing, open-label, long-term extension ALITHIOS trial and post-marketing reports

Methods

ALITHIOS open-label extension trial

- Cases of COVID-19 infection in patients receiving ofatumumab (data cut-off: 29 January 2021) were reviewed
- Cases were defined as confirmed (laboratory confirmation) or suspected COVID-19 (signs and symptoms but no laboratory confirmation)
- Seriousness category (including hospitalisation), severity and outcomes were presented as reported by the site investigators

Post-marketing reports

- Cases of COVID-19 infection in patients receiving ofatumumab (data cut-off: 31 January 2021) were reviewed
- COVID-19 cases were assessed as confirmed (laboratory confirmation or diagnosis) or suspected (lack of laboratory confirmation or diagnosis)
- Seriousness category (including hospitalisation), severity, and outcomes were presented as reported by the healthcare providers (HCPs) or non-HCPs

Results

ALITHIOS open-label extension trial

Baseline characteristics

- As of data cut-off, 139 of 1703 patients (8.2%) in ALITHIOS reported COVID-19 (confirmed: 115 [82.7%]; suspected: 24 [17.3%])
- Mean ± SD age at baseline: 37.7 ± 8.7 years and majority were female: 64%; mean ± SD BMI: 25.71 ± 5.886 kg/m²

Overall summary

- 10 patients (7.2%) experienced serious COVID-19; 94% cases were mild/moderate (**Table 1**)
- Treatment interruption was reported in 22 patients (15.8%), and none discontinued treatment except for 1 patient with a fatal outcome

Disclosures

Anne H. Cross has received consulting fees, support and honoraria from Biogen, Celgene, Bristol Myers Squibb, EMD fees from Biogen Idec, Celgene/Receptos, Janssen/Actelion, Merck/EMD Serono, Novartis, Roche and Sanofi Genzyme. Silvia Delgado has received fees as consultant on scientific advisory boards for Novartis. Brian J. Ward serves on a scientific advisory board for Novartis and reports personal fees from Novartis for this activity. He is also medical officer for Medicago Inc and holds parts of patents for vaccines targeting influenza, *Clostridioides difficile* and *Schistosoma mansoni*. In the last 5 years, he has held academic industry awards with Medicago, MIT Canada and Avitek Technologies. Bruce A. C. Cree has received personal compensation for consulting from Akili, Alexion, Atara, Autobahn, Biogen, EMD Serono, Novartis, Sanofi, Therion and TG Therapeutics and received research support from Genentech; institution has received compensation from Atara, Akili, Alexion, Biogen, EMD Serono, Novartis, Sanofi and TG Therapeutics. He has received publishing royalties from a publication relating to health care. Natalia Totolyan has received payment for conducting clinical trials. Ratnakar Pingili, Linda Mancione, Roseanne Sullivan, Wendy Su, Ronald Zielman and Ayan Das Gupta are employees of Novartis. Xavier Montalban has received speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years with Actelion, Alexion, Bayer, Biogen, Celgene, EMD Serono, Genzyme, Immucis, Medday, Merck, Mylan, Nervgen, Novartis, Roche, Sanofi-enzyme, Teva Pharmaceutical, TG Therapeutics, Excemed, MSIF and NMSS. Kevin Winthrop has received consulting fees from Novartis, Roche and Genentech.

- All 139 COVID-19 cases (100%) had IgG levels above lower limit of normal (5.65 g/L) either before or during the period effected by COVID-19
- Immune response to SARS-CoV-2 was assessed independently of this study (funded by Novartis) in 3 cases with mild confirmed COVID-19. While no antibody response was observed, T-cell immunity against SARS-CoV-2 was observed in all 3 patients (using an interferon-γ ELISpot assay)

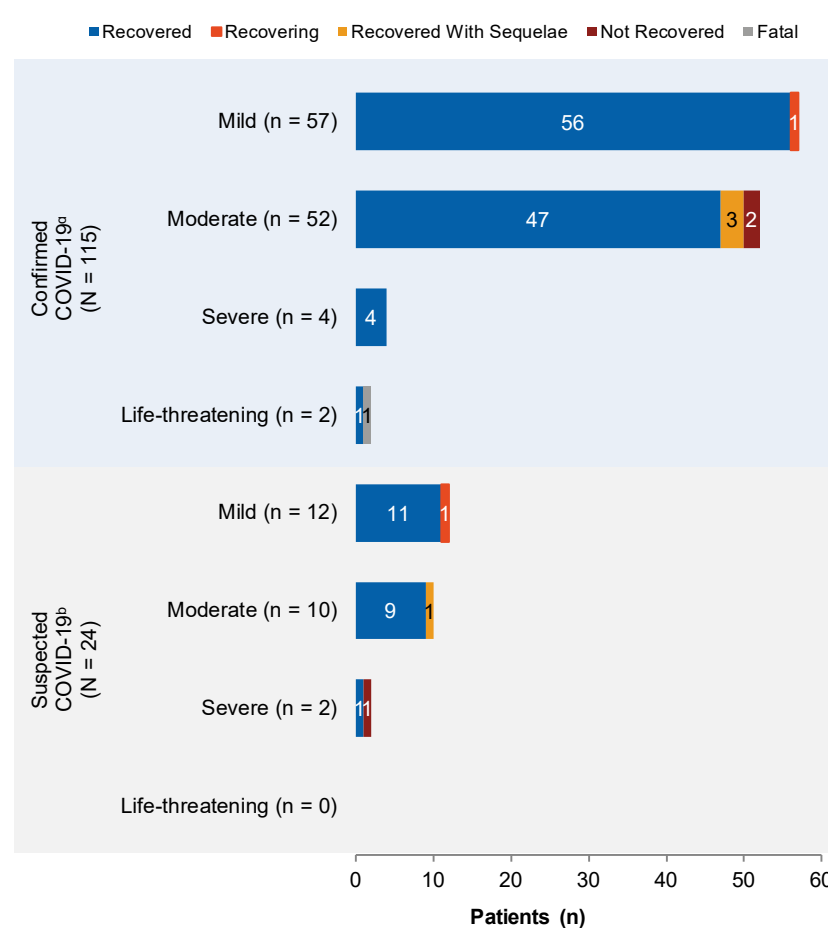
Table 1. Summary of COVID-19 Cases From ALITHIOS (N = 1703)

	Confirmed COVID-19 N=115 ^a	Suspected COVID-19 N=24	Total COVID-19 N=139
COVID-19 duration, days, mean (SD)	19.8 (12.35)	19.5 (12.74)	19.7 (12.36)
COVID-19 onset time since first dose of ofatumumab, years, mean (SD)	2.3 (1.00)	1.7 (0.90)	2.2 (1.00)
COVID-19 pneumonia, n (%)	12 (10.4)	1 ^b (4.2)	13 (9.4)
COVID-19 seriousness, n (%)			
Non-serious	107 (93.0)	22 (91.7)	129 (92.8)
Serious	8 (7.0)	2 (8.3)	10 (7.2)
Hospitalisation	8 (7.0)	2 (8.3)	10 (7.2)
Fatal outcome	1 (0.9)	0	1 (0.7)
COVID-19 maximum severity, n (%)			
Mild	57 (49.6)	12 (50.0)	69 (49.6)
Moderate	52 (45.2)	10 (41.7)	62 (44.6)
Severe	4 (3.5)	2 (8.3)	6 (4.3)
Life-threatening	2 (1.7)	0	2 (1.4)

Grading by CTCAE v5.0. Values expressed as mean (SD) unless specified.
^a Includes 1 asymptomatic patient.
^b Confirmation of positive SARS-CoV-2 laboratory test was not available by data cut-off date.

Outcomes

Figure 1. COVID-19 outcomes by severity in patients from ALITHIOS



Grading by CTCAE v5.0.
^a Includes 1 asymptomatic patient.
^b Confirmation of positive SARS-CoV-2 laboratory test was not available by data cut-off date for one COVID-19 pneumonia suspected case

- Majority of patients recovered, recovered with sequelae or were recovering (96.4%) and 4 had not recovered as of data cut-off (**Figure 1**)
- One patient with confirmed COVID-19 and pneumonia had a fatal outcome (48 years old at COVID-19 onset; BMI 28.3 kg/m²; recent MS relapse)

References

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Post-marketing reports

Baseline characteristics

- As of data cut-off, 28 patients (confirmed: 26; suspected: 2) were reported to have COVID-19
- Among 26 confirmed cases
 - Mean age at baseline: 44 (20-65) years
 - Majority were female: 18 patients

Seriousness or severity category

- Most cases were non-serious, and none were fatal or life-threatening
- Majority of the cases were mild/moderate (**Table 2**)

Table 2. Summary of COVID-19 Cases From Post-marketing Reports

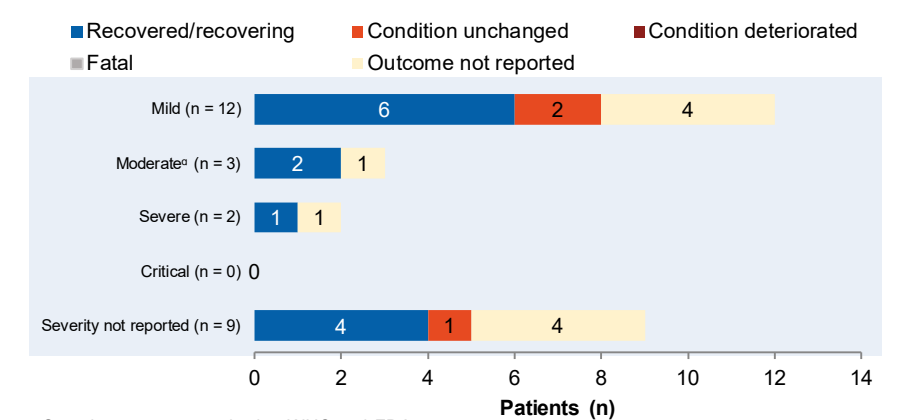
	Confirmed COVID-19 N = 26
COVID-19 seriousness^a, n (%)	
Non-serious	20 (76.9)
Serious ^b	6 (23.1)
Fatal	0
Hospitalisation	3 (11.5)
Life-threatening	0
Medically significant ^c	3 (11.5)
COVID-19 maximum severity^d, n (%)	
Mild	12 (70.6)
Moderate	3 (17.6)
Severe	2 (11.8)
Critical	0

Severity was assessed using WHO and FDA.
^a Percentages are calculated based on available information for seriousness (N=26).
^b No information regarding co-morbidities was provided; in the post-marketing setting serious cases are likely to be reported more frequently than non-serious cases.
^c All 3 cases were reported from non-HCPs.
^d Percentages are calculated based on available information for severity (N=17) and not reported for 9 patients.

Outcomes

- Of data available for patients (N = 16), all patients (100%) had either recovered (n = 13) or the condition was unchanged at the time of reporting (n = 3)

Figure 2. Confirmed COVID-19 outcomes from post-marketing reports



Severity was assessed using WHO and FDA.

Conclusions

- Of the 139 patients (8.2%) from the ALITHIOS open-label extension trial who reported COVID-19,
 - Most COVID-19 cases (>94%) were mild or moderate
 - A small number of hospitalisations (~7%) were noted, with one (<1%) fatal outcome
 - Most cases (>96%) recovered within 20 days
- Similar observations were seen in the post-marketing reports (26 confirmed cases) where all were assessed as recovered or condition unchanged and no fatal or life-threatening cases
- There was no evidence of increase in COVID-19 incidence or severe outcomes in ofatumumab-treated RMS patients when compared to the general population^{1,7} or MS patients treated with or without DMTs²⁻⁶
- The majority of COVID-19 infections in ofatumumab-treated patients are self-limited

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