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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Background

- 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 people[1]
- 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 outcomes[2-4]
- 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 literature[2-6]
- 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

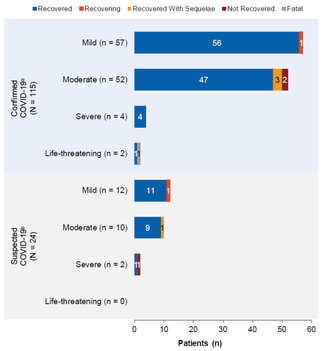
- 10 patients (7.2%) experienced serious COVID-19; 94% cases were mild/moderate (**Table 1**)
- Treatment interruption was reported in 22 patients (15.8%), and none discontinued treatment except for 1 patient with a fatal outcome
- All 139 COVID-19 cases (100%) had IgG levels above lower limit of normal (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.

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.

Outcomes

- 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)

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)**

Outcomes

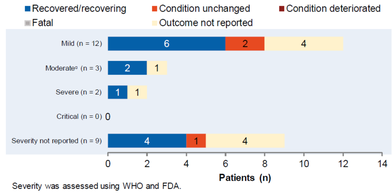
- Of data available for patients (N = 16), all patients (100%) had either recovered (n = 13) or the condition was unchanged at the time of reporting (n = 3))

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 received from non-HCPs.
[d] Percentages are calculated based on available information for severity (N= 17) and not reported for 9 patients.

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 DMTs[2-6]
- The majority of COVID-19 infections in ofatumumab-treated patients are self-limited

References

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Disclosures

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