

COVID-19 in People with Multiple Sclerosis Treated with Ocrelizumab: Clinical Outcomes in Vaccinated Patients

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BACKGROUND



The COVID-19 pandemic has led to more than 620 million confirmed cases worldwide to date¹



As of March 2022, >250,000 people with multiple sclerosis (pwMS) have been treated with ocrelizumab (OCR)²



Studies conducted prior to the availability of the COVID-19 vaccine have shown most COVID-19 cases in OCR-treated pwMS to be mild/moderate.^{3,4} This study will assess the effects of COVID-19 vaccination in pwMS who are receiving disease-modifying therapies such as OCR



To evaluate COVID-19 vaccination effect on development of symptomatic/serious COVID-19 and on risk factors for serious COVID-19 in OCR-treated pwMS

METHODS: PATIENT POPULATION AND COVID-19 STATUS

Data sources

- Suspected and confirmed COVID-19 cases were captured during the pre-Omicron era up to November 2021
- Clinical trial data:
 - The reference population refers to the clinical trial population and includes pwMS from 12 ongoing Roche/Genentech clinical trials³ who were receiving ongoing OCR treatment since January 2020, with confirmed/unknown/unvaccinated status. Symptomatic cases were captured from this population
- Post-marketing cases:
 - OCR-treated pwMS in the Roche/Genentech global safety database



Confirmed

- Laboratory confirmation using either a positive SARS-CoV-2 RT-PCR test or a serological test
- Radiological evidence consistent with COVID-19 pneumonia (post-marketing cases only)
- Described by the reporter as confirmed COVID-19 (post-marketing cases only)



Suspected

- Signs or symptoms consistent with COVID-19 where SARS-CoV-2 infection was suspected by the reporter

COVID-19 seriousness:

- Seriousness of cases was assessed according to the ICH guidelines⁵

COVID-19 case severity:

- Clinical trials reported using the CTCAE v5.0 grading system:
 - Mild: Asymptomatic or mild symptoms
 - Moderate: Minimal, local or non-invasive intervention
 - Severe: Medically significant but not life-threatening
 - Life-threatening: Urgent intervention indicated
 - Fatal⁶
- For post-marketing reports, assigned as per Hughes *et al.* (2020)⁴

¹OPERA1 (NCT01247324), OPERA II (NCT01412333), ORATORIO (NCT01194570), Phase II (NCT0076715), LIBERTO (NCT03099245), CONSONANCE (NCT03523858), ENSEMBLE (NCT03088810), VELOCE (NCT02545868), OCARINA (NCT03972306), OBOE (NCT03085910), MUSETTE (NCT04544438), GAVOTTE (NCT04548999); clinical cut-off date 30 November 2021; ²No fatalities were reported at the time of the publication on a case series of OCR-treated pwMS and COVID-19; the 'fatal' category was introduced for the July 2022 cut-off reported in Hughes R, *et al. Mult Scler Relat Disord* 2020;42:102192. ³CTCAE, Common Terminology Criteria for Adverse Events; ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; OCR, ocrelizumab; pwMS, people with multiple sclerosis; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

RESULTS

Patient Demographics and Disease Characteristics of OCR-Treated Clinical Trial Patients According to Vaccination Status

Parameter	Reference population (n=2,400)			Unvaccinated/unknown vaccination status population (n=3,459)			Vaccinated population (n=1,216)		
	Reference population (n=2,400)	Symptomatic COVID-19 (n=427)	Serious COVID-19 (n=173)	Unvaccinated/unknown vaccination status population (n=3,459)	Symptomatic COVID-19 (n=557)	Serious COVID-19 (n=152)	Vaccinated population (n=1,216)	Symptomatic COVID-19 (n=63)	Serious COVID-19 (n=17)
EDSS, n (%)									
0-3	2,457	336	77 (22.9)	1,586	292	70 (24.0)	871	44	7 (15.9)
3-5	1,876	211	73 (34.6)	1,281	182	65 (35.7)	595	29	8 (27.8)
≥6	914	83	29 (34.9)	578	73	27 (37.0)	338	10	2 (20.0)
Missing	22	12	0 (0.0)	14	12	0 (0.0)	8	0	0 (0.0)
Sex, n (%)									
Female	3,185	400	101 (25.3)	2,124	352	94 (26.7)	1,061	48	7 (14.6)
Male	2,084	242	78 (32.2)	1,335	207	68 (32.9)	749	35	10 (28.6)
Age, n (%)									
≤50 years	3,762	467	110 (23.6)	2,545	411	102 (24.8)	1,217	56	8 (14.3)
>50 years	1,507	175	69 (39.4)	914	148	60 (40.5)	593	27	9 (33.3)
BMI, n (%)									
<25	2,609	278	63 (22.7)	1,769	251	61 (24.3)	840	27	2 (7.4)
25-30	1,492	195	57 (29.2)	939	170	52 (30.6)	553	25	5 (20.0)
>30	994	150	52 (34.7)	635	122	44 (26.1)	359	28	8 (28.6)
Missing	174	19	7 (38.8)	116	16	5 (13.3)	58	3	2 (66.7)
MS type, n (%)									
RMS/RRMS	3,779	506	134 (26.5)	2,578	445	120 (27.0)	1,203	61	14 (23.0)
PPMS/SPMS	1,490	136	45 (33.1)	883	114	42 (36.8)	607	22	3 (13.6)
No comorbidity, n (%)	4,233	475	118 (24.8)	2,818	412	108 (26.2)	1,415	63	10 (15.9)
≥1 comorbidity, n (%)	1,036	167	61 (36.5)	641	147	54 (36.7)	395	20	7 (35.0)
Time since first OCR dose, median (range)	3.76 (0.0-13.4)	3.50 (0.0-12.7)	6.48 (0.0-12.2)	-	-	-	3.00 (0.0-13.0)	2.81 (0.1-12.7)	3.80 (2.2-9.7)

Risk factors for serious COVID-19 in all populations were age >50 years, male sex, BMI >30, ≥1 comorbidity and EDSS score ≥3[†] (red boxes). There was a general decrease in incidence of serious COVID-19 in the vaccinated population compared with the unvaccinated/unknown vaccination status population

[†]Multiple COVID-19 infections in one patient were counted once at the highest severity. [‡]Percentage of serious cases based on symptomatic cases. [§]711/810 vaccinated patients had also received a booster vaccination. [¶]Descriptive analysis of the baseline characteristics does not allow for any conclusions regarding the cause-effect relationship. BMI, body mass index; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; OCR, ocrelizumab; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

Overview of COVID-19 Outcomes in OCR-Treated Clinical Trial Patients

Parameter	Reference population (n=2,400)		Unvaccinated/unknown vaccination status population (n=3,459)		Vaccinated population (n=1,216)	
	Symptomatic COVID-19 (n=427, 17.8%)	Serious COVID-19 (n=173, 7.2%)	Symptomatic COVID-19 (n=557, 16.1%)	Serious COVID-19 (n=152, 4.4%)	Symptomatic COVID-19 (n=63, 5.2%)	Serious COVID-19 (n=17, 1.4%)
Confirmed, n (%)						
PCR/antibody	583 (90.8)	169 (94.4)	502 (89.8)	152 (93.8)	81 (97.6)	17 (100.0)
Serious*	179 (27.9)	-	162 (29.0)	-	17 (20.5)	-
Severity, n (%)						
Mild/moderate	445 (89.3)	14 (7.8)	382 (68.3)	13 (8.0)	63 (75.9)	1 (5.9)
Severe	129 (20.1)	112 (62.6)	114 (20.4)	99 (61.1)	15 (18.1)	13 (76.5)
Life-threatening	18 (2.8)	17 (10.1)	17 (3.0)	17 (10.5)	1 (1.2)	1 (5.9)
Fatal	35 (5.5)	35 (19.6)	33 (5.9)	33 (20.4)	2 (2.4)	2 (11.8)
Missing	15 (2.3)	0 (0.0)	13 (2.3)	0 (0.0)	2 (2.4)	1 (5.9)
Outcome, n (%)						
Recovered and recovering	572 (89.1)	138 (77.1)	500 (89.4)	125 (77.2)	72 (86.7)	13 (76.5)
Not recovered	22 (3.4)	6 (3.4)	13 (2.3)	4 (2.5)	9 (10.8)	2 (11.8)
Fatal	35 (5.5)	35 (19.6)	33 (5.9)	33 (20.4)	2 (2.4)	2 (11.8)
Missing	13 (2.0)	0 (0.0)	13 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)

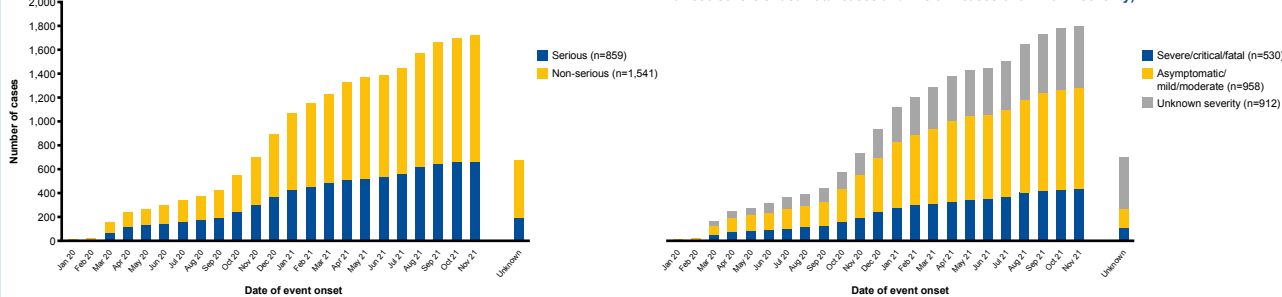
Reference population n=2,400. Based on serious event definition of European Medicines Agency, 1995. PCR, polymerase chain reaction.

Serious and fatal cases decreased in vaccinated patients, compared with patients with unknown/unvaccinated status

Overview of COVID-19 in Post-Marketing Cases as of 30 November 2021

- 2,400 cases were identified in a global safety database as of 30 November 2021; 64.2% (1,541/2,400) were non-serious
- For cases with sufficient information to assess clinical severity (n=1,488), 64.4% (958/1,488) cases were asymptomatic, mild or moderate

Cumulative case seriousness over time for all cases (Event onset unknown in 190/859 serious cases and 487/1,541 non-serious cases)



The proportion of serious/severe cases were less frequent over time, likely reflecting improved patient management and introduction of COVID-19 vaccines

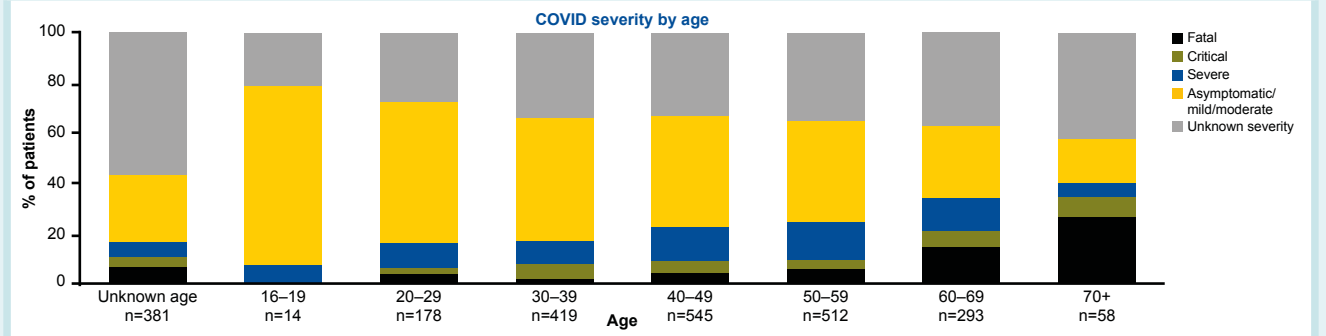
Patient Demographics and COVID-19 Outcomes in Post-Marketing Cases

Parameter	All cases (n=2,400)	Cumulative cases to 30 November 2021	
		Serious cases (n=439, 18.3%)	Hospitalised cases* (n=725, 30.2%)
Median age (range)	47.0 (16-89)	50.0 (18-89)	51.0 (18-89)
Sex, n (%)			
Male	728 (30.3)	304 (35.4)	264 (36.4)
Female	1,459 (60.8)	487 (57.9)	411 (56.7)
Not reported	215 (9.0)	58 (6.8)	50 (6.9)
Type of MS, n (%)			
Relapsing forms	1,123 (46.8)	390 (45.4)	316 (43.6)
Progressive forms	355 (14.8)	154 (17.9)	144 (19.9)
Not reported	922 (38.4)	315 (36.7)	265 (36.6)
Severity			
Asymptomatic, mild or moderate	958 (39.9)	108 (12.6)	78 (10.8)
Severe	278 (11.6)	270 (31.4)	218 (30.1)
Critical	110 (4.6)	110 (12.8)	106 (14.6)
Fatal	142 (5.9)	142 (16.5)	122 (16.8)
Unknown	912 (38.0)	229 (26.7)	201 (27.7)
Outcomes, n (%)			
Recovered/recovering	1,381 (57.5)	521 (60.7)	440 (60.7)
Not recovered	282 (11.8)	80 (9.3)	71 (9.8)
Died	142 (5.9)	142 (16.5)	122 (16.8)
Unknown/not reported	595 (24.8)	116 (13.5)	92 (12.7)

*Hospitalised cases are a subset of serious cases. MS, multiple sclerosis.

The proportion of older patients, males and those with progressive MS was found to increase among serious and hospitalised cases, compared with total cases

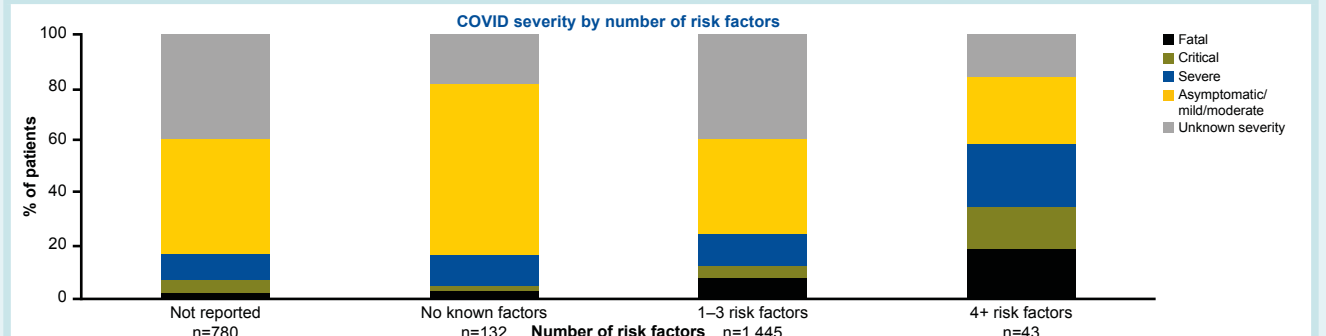
COVID-19 Severity by Age in Post-Marketing Cases



Although clinical severity could not be determined in 912/2,400 (38.0%) cases due to lack of information, 74.9% (683/912) of these cases were non-serious

COVID-19 severity increases with increasing age – reflecting the trends seen in the general population, the proportion of severe, critical or fatal cases increased with each decade

COVID-19 Severity by Number of Known Risk Factors in Post-Marketing Cases



COVID-19 severity increased according to the presence/number of risk factors* known to be associated with disease severity in the general population

*Real factors for serious COVID-19 include age >50, hypertension, diabetes mellitus, BMI ≥25, chronic kidney disease, dementia, coronary heart disease, malignancy, chronic pulmonary disease and pregnancy. BMI, body mass index.

Risk Factors for Severe COVID-19 in Post-Marketing Cases

- Risk factors for severe COVID-19 in OCR-treated pwMS are in line with those seen in the general population: older age, underlying comorbidities and male sex
- Information on vaccination status is limited, but all assessable fatal breakthrough infections (n=14) occurred in those with underlying risk factors

CONCLUSIONS

- COVID-19 vaccination substantially decreased serious and fatal COVID-19 rates among ocrelizumab-treated patients in clinical trials
- Compared with previous reports, serious and fatal cases have declined in the clinical trials population, even during the more virulent Delta wave
- Risk factors for severe COVID-19 have remained the same in vaccinated and unvaccinated ocrelizumab-treated patients

- The majority of COVID-19 cases reported in the post-marketing setting were non-serious and resolved
- Risk factors known to be associated with severe COVID-19 in the general and MS populations were also apparent in severe COVID-19 in ocrelizumab-treated pwMS

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DISCLOSURES

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