Ocrelizumab and COVID-19

Overview

Data collection

- We are continuously collecting and assessing data from clinical trials, safety surveillance programs, and RWE[1,2]

COVID-19 in pwMS treated with OCR

- Vaccination against COVID-19 substantially decreased serious and fatal COVID-19 rates among OCR-treated patients in clinical trials[2]
- Serious and fatal cases have declined in the clinical trials population, compared to previous reports[2-4]
- Risk factors for severe COVID-19 have remained the same in vaccinated and unvaccinated ocrelizumab-treated patients[2]

Latest assessment of COVID-19 data

- As of November 2021:
  - 642 symptomatic cases of COVID-19 were identified from 5269 patients in the clinical trials; 463/642 (72.1%) cases were classed as non-serious, with most patients having recovered at the time of the report[1,2]
  - 2400 cases were identified in the global safety database with most cases being non-serious 1541/2400 (64.2%)[1,2]

OCR-Treated Clinical Trial Patients*

COVID-19 Outcomes

Table 1: Patient demographics and disease characteristics of OCR-treated clinical trial patients according to vaccination status

Parameter	Reference population			Unvaccinated/unknown vaccination status population			Vaccinated population		
	Reference population (n=5269)	Symptomatic COVID-19 (n=642)[a]	Serious COVID-19 (n=179)[a] (%)[b]	Unvaccinated/unknown vaccination status population (n=3459)	Symptomatic COVID-19 (n=559)[a]	Serious COVID-19 (n=162)[a] (%)[b]	Vaccinated population (n=1810)[c]	Symptomatic COVID-19 (n=83)[a]	Serious COVID-19 (n=17)[a] (%)[b]
EDSS, n (%)									
0–<3	2457	336	77 (22.9)	1586	292	70 (24.0)	871	44	7 (15.9)
3–<6	1876	211	73 (34.6)	1281	182	65 (35.7)	595	29	8 (27.6)
≥6	914	83	29 (34.9)	578	73	27 (37.0)	336	10	2 (20.0)
Missing	22	12	0 (0.0)	14	12	0 (0.0)	8	0	0 (0.0)
Sex, n (%)									
Female	3185	400	101 (25.3)	2124	352	94 (26.7)	1061	48	7 (14.6)
Male	2084	242	78 (32.2)	1335	207	68 (32.9)	749	35	10 (28.6)
Age, n (%)									
≤50 years	3762	467	110 (23.6)	2545	411	102 (24.8)	1217	56	8 (14.3)
>50 years	1507	175	69 (39.4)	914	148	60 (40.5)	593	27	9 (33.3)
BMI, n (%)									
<25	2609	278	63 (22.7)	1769	251	61 (24.3)	840	27	2 (7.4)
25–30	1492	195	57 (29.2)	939	170	52 (30.6)	553	25	5 (20.0)
>30	994	150	52 (34.7)	635	122	44 (36.1)	359	28	8 (28.6)
Missing	174	19	7 (36.8)	116	16	5 (31.3)	58	3	2 (66.7)
MS type, n (%)									
RMS/RRMS	3779	506	134 (26.5)	2576	445	120 (27.0)	1,203	61	14 (23.0)
PPMS/SPMS	1490	136	45 (33.1)	883	114	42 (36.8)	607	22	3 (13.6)
No comorbidity, n (%)	4233	475	118 (24.8)	2818	412	108 (26.2)	1,415	63	10 (15.9)
≥1 comorbidity, n (%)	1036	167	61 (36.5)	641	147	54 (36.7)	395	20	7 (35.0)
Time since first OCR dose, median years (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)

Reported cases were defined as symptomatic, as the vast majority of cases in our database are reported as such and no systematic collection of positive tests in asymptomatic patients has been implemented.
[a]Multiple COVID-19 infections in one patient were counted once at the highest severity. [b]Percentage of serious cases based on symptomatic cases. [c]271/1810 vaccinated patients had also received a booster vaccination.

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

[a]Descriptive analysis of the baseline characteristics does not allow for any conclusions regarding the cause–effect relationship.

Table 2: Overview of COVID-19 outcomes in OCR-treated clinical trial patients. Reference population N=5269

Parameter	Reference population		Unvaccinated/unknown vaccination status population		Vaccinated population	
	Symptomatic COVID-19 (N=642, 12.2%) n (%)	Serious COVID-19 (N=179, 3.4%) n (%)	Symptomatic COVID-19 (N=559, 10.6%) n (%)	Serious COVID-19 (N=162, 3.1%) n (%)	Symptomatic COVID-19 (N=83, 1.6%) n (%)	Serious COVID-19 (N=17, 0.3%) n (%)
Confirmed, n (%)						
PCR/antibody	583 (90.8)	169 (94.4)	502 (89.8)	152 (93.8)	81 (97.6)	17 (100.0)
Serious,[a] n (%)	179 (27.9)	–	162 (29.0)	–	17 (20.5)	–
Severity, n (%)						
Mild/moderate	445 (69.3)	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)	18 (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 resolved	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)

[a]Based on serious event definition of European Medicines Agency, 1995.

There were fewer serious and fatal cases in vaccinated patients compared with patients with unknown/unvaccinated status.

***Data sources:**

OCR-treated clinical trial patients

Clinical trial data: The reference population refers to the clinical trial population and includes pwMS from 12 ongoing Roche/Genentech clinical trials (OPERA I, OPERA II, ORATORIO, Phase 2, LIBERTO, CONSONANCE, ENSEMBLE, VELOCE, OCARINA, OBOE, MUSETTE, GAVOTTE; clinical cut-off date November 30, 2021) who were receiving ongoing OCR treatment since January 2020, with confirmed/unknown/unvaccinated status. Symptomatic cases were captured from this population.

OCR-treated post-marketing patients

OCR-treated pwMS in the Roche/Genentech global safety database.

COVID-19 seriousness

Seriousness of cases was assessed according to the ICH guidelines.[5]

COVID-19 case severity

Clinical trials reported using the CTCAE v5.0 grading system[6]: Mild: asymptomatic or mild symptoms; Moderate: minimal, local, or non-invasive intervention; Severe: medically significant but not life-threatening; Life-threatening: urgent intervention indicated; Fatal.

OCR-Treated Post-Marketing Patients

COVID-19 Outcomes

Table 3: Patient demographics and COVID-19 outcomes in post-marketing cases

Parameter	Cumulative cases to November 30, 2021		
	All cases (n=2400)	Serious cases (n=859, 35.8%)	Hospitalized cases[a] (n=725, 30.2%)
Median age (range)	47.0 (16–89)	50.0 (18–89)	51.0 (18–89)
Sex, n (%)			
Male	726 (30.3)	304 (35.4)	264 (36.4)
Female	1459 (60.8)	497 (57.9)	411 (56.7)
Not reported	215 (9.0)	58 (6.8)	50 (6.9)
Type of MS, n (%)			
Relapsing forms	1123 (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	1381 (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)

[a]Hospitalized cases are a subset of serious cases.

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

Figure 1a: Cumulative case seriousness over time for all cases (Event onset unknown in 190/859 serious cases and 487/1541 non-serious cases)

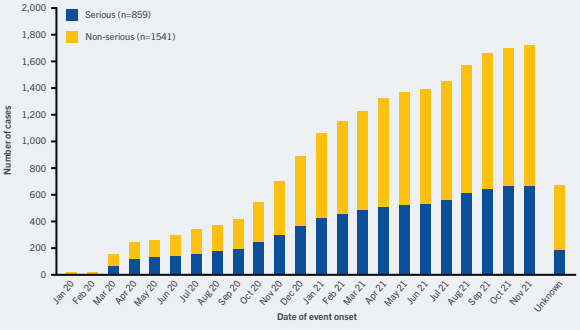
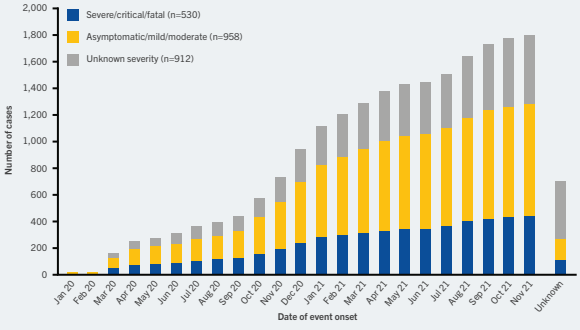


Figure 1b: Cumulative case severity over time for all cases (Event onset unknown in 152/958 asymptomatic/mild/moderate cases, 107/530 severe/critical/fatal cases, and 418/912 cases of unknown severity)

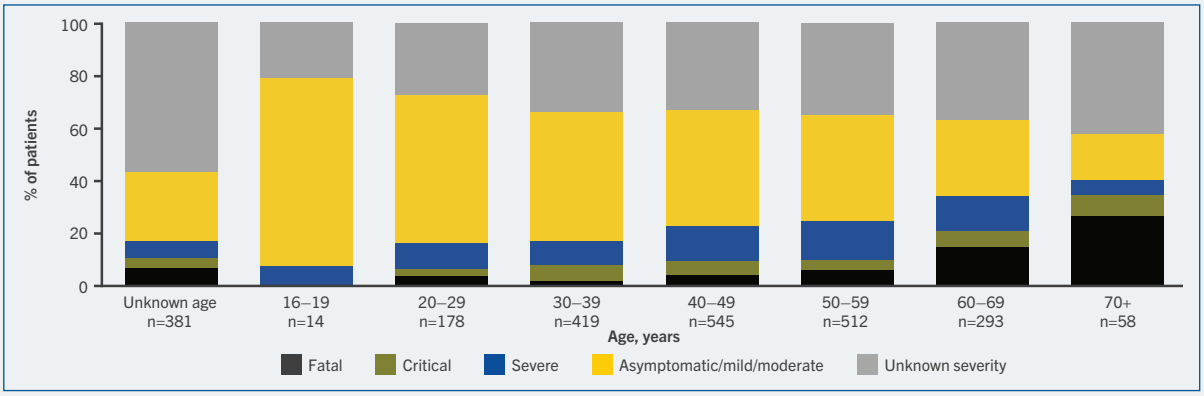


The proportion of serious/severe cases has decreased over time.

A: 2400 cases were identified in a global safety database as of November 30, 2021; 64.2% (1541/2400) were non-serious. B: For cases with sufficient information to assess clinical severity (n=1488), 64.4% (958/1488) cases were asymptomatic, mild, or moderate.

Factors Affecting Severity of COVID-19

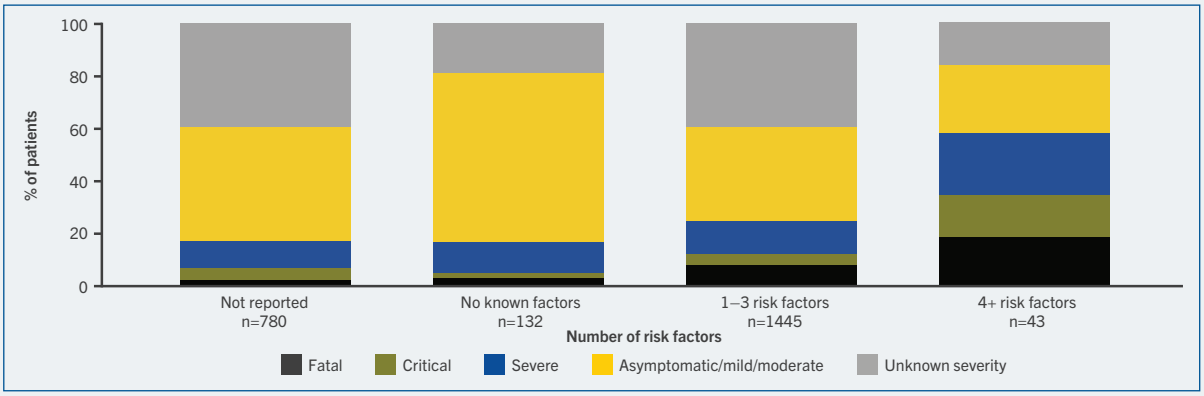
Figure 2: COVID-19 severity by age



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

Although clinical severity could not be determined in 912/2400 (38.0%) cases due to lack of information, 74.9% (683/912) of these cases were non-serious.

Figure 3: COVID-19 severity by number of risk factors



COVID-19 severity increased with the presence and number of risk factors[a] known to be associated with disease severity in the general population.

[a]Risk factors for severe COVID-19 include age >50, hypertension, diabetes mellitus, BMI >25, chronic kidney disease, dementia, coronary heart disease, malignancy, chronic pulmonary disease, and pregnancy.

COVID-19 case severity

For post-marketing reports, assigned as per Hughes et al. (2020).[7]

There are well-recognized limitations that should be considered when interpreting spontaneous post-marketing safety reports, including events that may not be causally related to drug exposure; in the real-world setting, events are frequently confounded by factors such as multiple drug use and the presence of pre-existing comorbidities; reporting bias may exist for more significant outcomes, which may result in an overrepresentation of the more serious outcomes; and reporting rates can be stimulated by external factors, such as press reports. The causes of infections are recorded as reported to the company; while the company follows up on all reports to identify the cause, an exact diagnosis is not always possible. Some of the investigations remain ongoing and, therefore, the information may be subject to change.

The Prescribing Information is the primary source of information on the known and potential risks associated with ocrelizumab.

Abbreviations:

BMI=body mass index; COVID-19=coronavirus disease 2019; CTCAE=Common Terminology Criteria for Adverse Events; EDSS=Expanded Disability Status Scale; ICH=The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; MS=multiple sclerosis; OCR=ocrelizumab; PCR=polymerase chain reaction; PPMS=primary progressive MS; pwMS=people with MS; PV=pharmacovigilance; RMS=relapsing MS; RRMS=relapsing remitting MS; RWE=real-world evidence; SPMS=secondary progressive MS.

References:

1. Genentech. Data on file. 2. Hauser SL, et al. Presented at: ECTRIMS 2022. October 26–28, 2022. Amsterdam, The Netherlands. Poster EP1238. 3. Hauser SL, et al. Presented at: ECTRIMS 2021. October 13-15, 2021. Virtual. Poster P933. 4. Richardson S, et al. *JAMA*. 2020;323:2052–2059. 5. European Medicines Agency. ICH Harmonised Tripartite Guideline E2A. June 1995. Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-15.pdf. Accessed September 14, 2022. Accessed October 21, 2022. 6. U.S. Department of Health and Human Services NIH, NCI. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0, 2017. Available at: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf. Accessed October 21, 2022. 7. Hughes R, et al. *Mult Scler Relat Disord*. 2020;42:102192.

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