Ocrelizumab and COVID-19

Overview

Data collection

- We are continuously collecting and assessingdata 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 report[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 5,269 patients in the clinical trials; 463/642 cases were classed as non-serious, with most patients having recovered at the time of the report[1,2]
  - 2,400 cases were identified in the global safety database with most cases being non-serious 1,541/2,400 (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=5,269)	Symptomatic COVID-19 (n=642)[a]	Serious COVID-19 (n=179)[a] (%)[b]	Unvaccinated/ unknown vaccination status population (n=3,459)	Symptomatic COVID-19 (n=559)[a]	Serious COVID-19 (n=162)[a] (%)[b]	Vaccinated population (n=1,810)[c]	Symptomatic COVID-19 (n=83)[a]	Serious COVID-19 (n=17)[a] (%)[b]
EDSS, n (%)									
0–<3	2,457	336	77 (22.9)	1,586	292	70 (24.0)	871	44	7 (15.9)
3–<6	1,876	211	73 (34.6)	1,281	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	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 (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	3,779	506	134 (26.5)	2,576	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 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)

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

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Table 2: Overview of COVID-19 Outcomes in OCR-Treated Clinical Trial Patients. Reference population N=5,269

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]	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)

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

OCR-treated post-marketing patients

COVID-19 outcomes

Table 3: Patient Demographics and COVID-19 Outcomes in Post-Marketing Cases

Parameter	Cumulative cases to 30 November 2021		
	All cases (n=2,400)	Serious cases (n=859, 35.8%)	Hospitalised 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	1,459 (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	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)

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

Figure 1a: Cumulative case seriousness over time for all cases

(Event onset unknown in 190/859 serious cases and 487/1,541 non-serious cases)

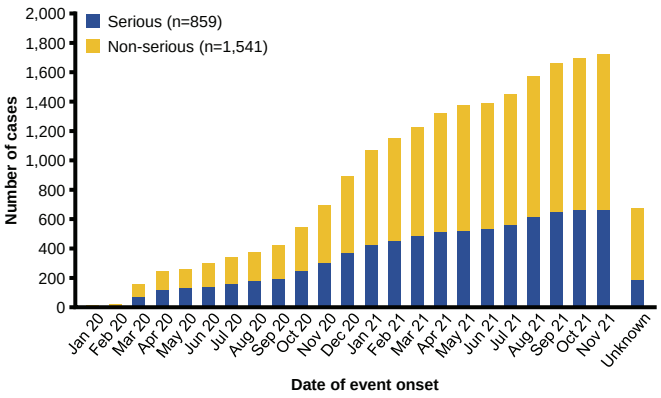
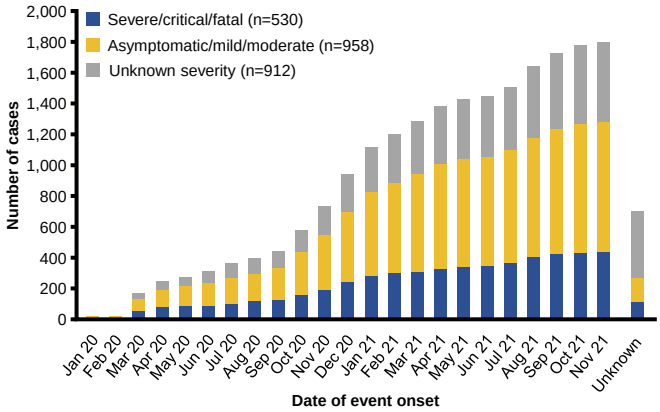


Figure 1b: Cumulative case severity over time for all cases

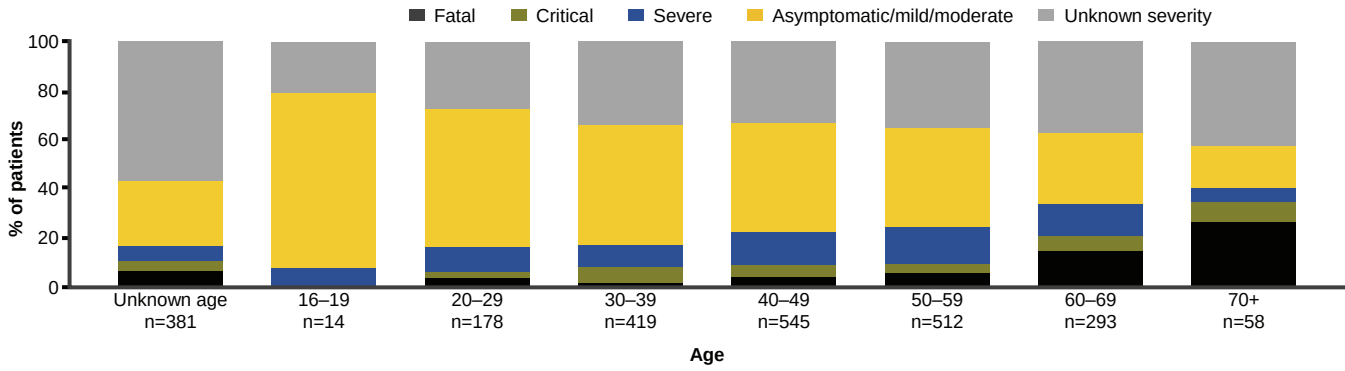
(Event onset unknown in 152/958 asymptomatic/mild/moderate cases, 107/530 severe/critical/fatal cases and 418/912 cases of unknown severity)



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

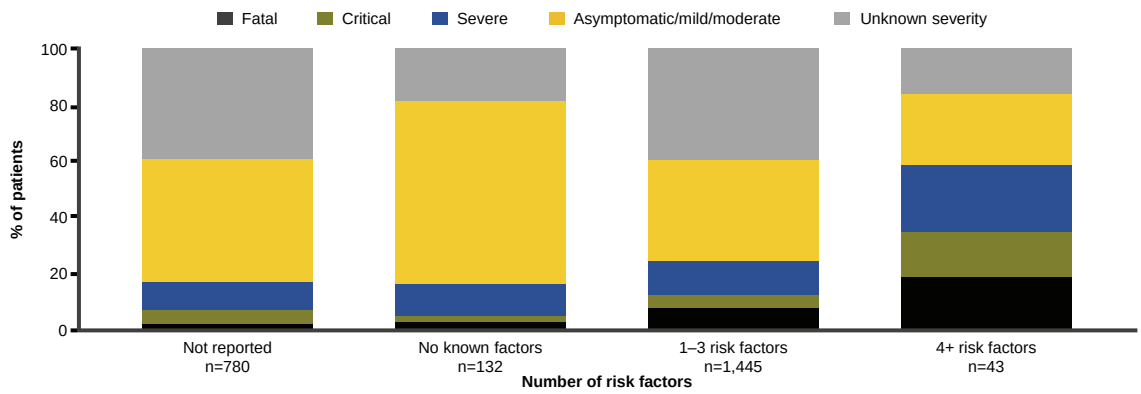
Factors affecting severity of COVID-19

Figure 2: COVID 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

Figure 3: COVID 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

Footnotes

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/Genetech clinical trials (OPERA I, OPERA II, ORATORIO, Phase II, LIBERTO, CONSONANCE, ENSEMBLE, VELOCE, OCARINA, OBOE, MUSETTE, GAVOTTE; clinical cut-off date 30 November 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/Genetech 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.

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

Table 1

[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]271/1,810 vaccinated patients had also received a booster vaccination;.[d]Descriptive analysis of the baseline characteristics does not allow for any conclusions regarding the cause–effect relationship *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;

Table 2

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

Table 3

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

Figure 1a

2,400 cases were identified in a global safety database as of 30 November 2021; 64.2% (1,541/2,400) were non-serious.

Figure 1b

For cases with sufficient information to assess clinical severity (n=1,488), 64.4% (958/1,488) cases were asymptomatic, mild or moderate.

Figure 2

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

Figure 3

[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.

Abbreviations

BMI, body mass index; COVID-19, coronavirus disease 2019; COVID, coronavirus disease; 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; 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

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