# COVID-19 in People with Multiple Sclerosis Treated with Ocrelizumab

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## KEY FINDINGS

### THE MAJORITY OF COVID-19 CASES IN OCRELIZUMAB-TREATED CLINICAL TRIAL PARTICIPANTS WERE MILD/MODERATE IN SEVERITY AND RESOLVED; MOST OF THE CASES REPORTED IN THE POST-MARKETING SETTING WERE NON-SERIOUS AND ALSO RESOLVED

**In the ongoing trials in patients with RMS and PPMS, the majority (85.5%) with symptomatic COVID-19 recovered or were recovering**

**Cox regression analysis in ocrelizumab-treated clinical trial patients with MS:**
**Indicated that comorbidities may increase the likelihood of symptomatic COVID-19**
**Identified high BMI as the most important factor for serious COVID-19**

**In the post-marketing cohort, risk factors associated with severe COVID-19 in the general and MS populations (e.g. increasing age, male gender and comorbidities such as hypertension, obesity and diabetes) were more common among ocrelizumab-treated pwMS with severe COVID-19**

## BACKGROUND

- The ongoing COVID-19 pandemic has led to more than 230 million[1] confirmed cases worldwide to date and questions remain about the effects of DMTs on the immune response to the SARS-CoV-2 virus
- It is imperative for MS treatment to be maintained during the pandemic and in order to inform treatment decisions, continued and rapid dissemination of data on COVID-19 in pwMS who are receiving DMTs is crucial
- As of December 2020, >200,000 pwMS (RMS and PPMS) have been treated with OCR

**AIMS: To understand the factors that affect the development of symptomatic COVID-19 and its outcome in pwMS treated with OCR**

## METHODS

### Data sources

**Clinical trial data:**
OCR-treated pwMS in 10 ongoing Roche/Genentech clinical and post-marketing trials[a]

**Post-marketing case reports:**
OCR-treated pwMS in the Roche/Genentech global safety database[b]

### Reference population for clinical trial data

Includes pwMS who were receiving ongoing OCR treatment at the beginning of January 2020 and newly enrolled patients thereafter; patients withdrawing from treatment between January 2020 and May 2021 were also included

**Confirmed COVID-19** | **Suspected COVID-19**

**COVID-19 cases include all confirmed and suspected reports**

### COVID-19 case severity:

- Clinical trials reported using the CTCAE v5.0 grading system[1] (mild, moderate, severe, life-threatening, fatal)[c]
- For post-marketing reports, assigned as per Hughes *et al*. (2020)[2]

**Multi-variable Cox regression models were used to evaluate risk factors associated with symptomatic COVID-19 and serious vs non-serious disease[d]**

## RESULTS

### OCR-Treated Clinical Trial Patients

#### COVID-19 Outcomes

**406 cases of COVID-19 were identified from 4,089 patients in the clinical trials; 132/406 cases were classed as serious. Of fatal cases, 6/32 occurred in each of Mexico and Poland, with 3/32 in Ukraine**

| Parameter | Symptomatic[a] COVID-19 (N=406, 9.9%) n (% of symptomatic cases) | Serious COVID-19 (N=132, 3.2%) n (% of serious cases) |
|---|---|---|
| **Confirmed, n (%)** | | |
| PCR/antibody | 357 (87.9) | 121 (91.7) |
| **Serious[b]** | 132 (32.5) | - |
| **Severity[c], n (%)** | | |
| Mild/moderate | 265 (65.3) | 10 (7.6) |
| Severe | 86 (21.2) | 76 (57.6) |
| Life-threatening | 13 (3.2) | 13 (9.8) |
| Fatal | 32 (7.9) | 32 (24.2) |
| Missing | 10 (2.5) | 1 (0.8) |
| **Outcome[d], n (%)** | | |
| Recovered/recovering | 347 (85.5) | 89 (67.4) |
| Not resolved | 18 (4.4) | 11 (8.3) |
| Fatal | 32 (7.9) | 32 (24.2) |
| Missing | 9 (2.2) | 0 |

#### Comorbidities[a] in Symptomatic/Serious Cases

**Most comorbidities known to be associated with severe COVID-19 were more prevalent in those patients who suffered from serious COVID-19**

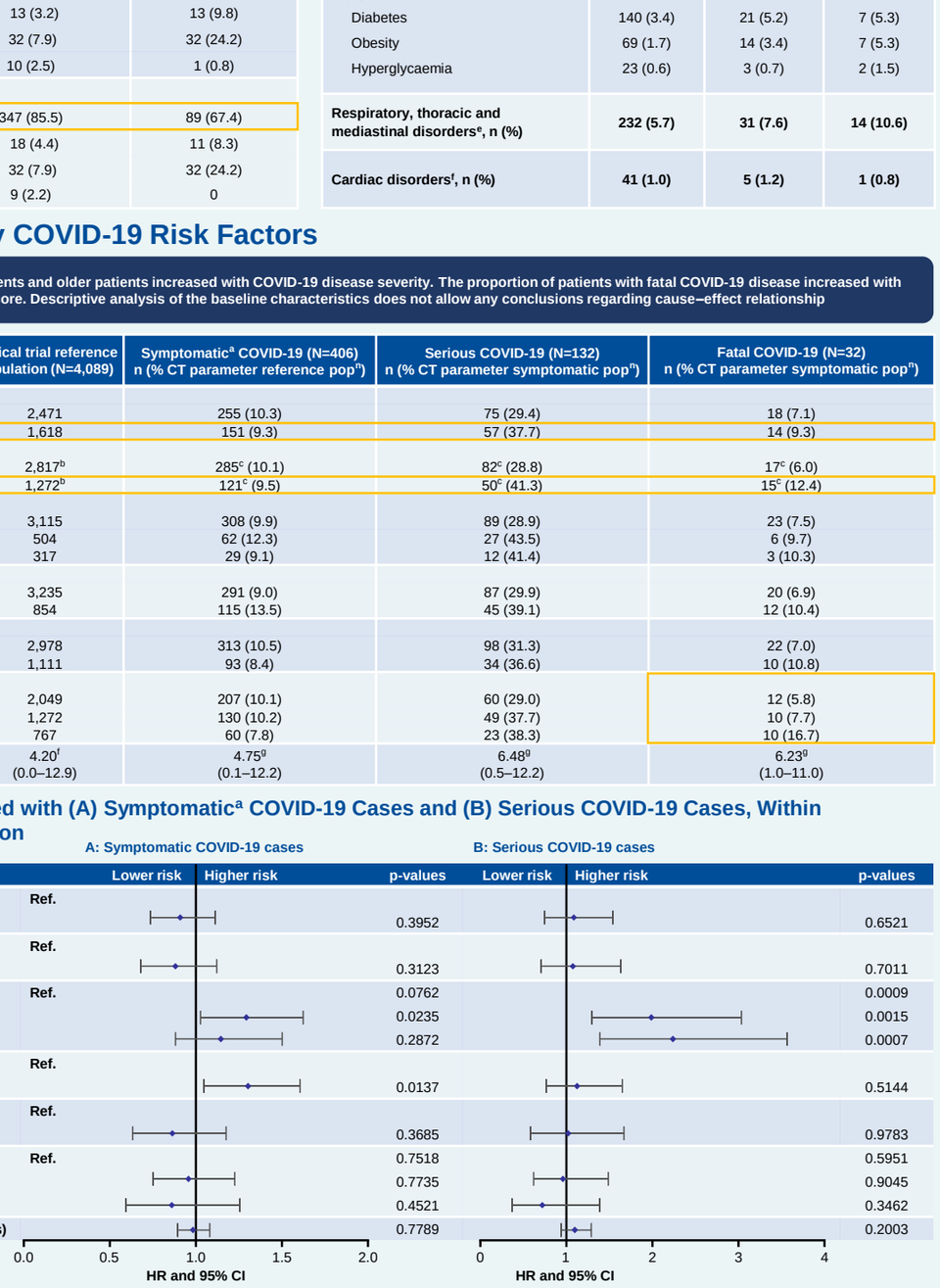
| | Reference population[b] (N=4,089) | Symptomatic[c] COVID-19 (n=406) | Serious COVID-19 (n=132) |
|---|---|---|---|
| **Total number of patients with ≥1 comorbidity, n (%)** | **854 (20.9)** | **115 (28.3)** | **45 (34.1)** |
| **Vascular disorders, n (%)** | **529 (12.9)** | **69 (17.0)** | **26 (19.7)** |
| Hypertension | 499 (12.2) | 64 (15.8) | 22 (16.7) |
| **Metabolism and nutrition disorders[d], n (%)** | **214 (5.2)** | **31 (7.6)** | **11 (8.3)** |
| Diabetes | 140 (3.4) | 21 (5.2) | 7 (5.3) |
| Obesity | 69 (1.7) | 14 (3.4) | 7 (5.3) |
| Hyperglycaemia | 23 (0.6) | 3 (0.7) | 2 (1.5) |
| **Respiratory, thoracic and mediastinal disorders[e], n (%)** | **232 (5.7)** | **31 (7.6)** | **14 (10.6)** |
| **Cardiac disorders[f], n (%)** | **41 (1.0)** | **5 (1.2)** | **1 (0.8)** |

#### Demographics by COVID-19 Risk Factors

**The proportion of male patients and older patients increased with COVID-19 disease severity. The proportion of patients with fatal COVID-19 disease increased with greater EDSS score. Descriptive analysis of the baseline characteristics does not allow any conclusions regarding cause–effect relationship**

| Parameter | Clinical trial reference population (N=4,089) | Symptomatic[a] COVID-19 (N=406) n (% CT parameter reference pop[n]) | Serious COVID-19 (N=132) n (% CT parameter symptomatic pop[n]) | Fatal COVID-19 (N=32) n (% CT parameter symptomatic pop[n]) |
|---|---|---|---|---|
| **Sex, n (%)** | | | | |
| Female | 2,471 | 255 (10.3) | 75 (29.4) | 18 (7.1) |
| Male | 1,618 | 151 (9.3) | 57 (37.7) | 14 (9.3) |
| **Age, n (%)** | | | | |
| ≤50 years | 2,817[b] | 285[c] (10.1) | 82[c] (28.8) | 17[c] (6.0) |
| >50 years | 1,272[b] | 121[c] (9.5) | 50[c] (41.3) | 15[c] (12.4) |
| **BMI, n (%)** | | | | |
| <30 | 3,115 | 308 (9.9) | 89 (28.9) | 23 (7.5) |
| 30–<35 | 504 | 62 (12.3) | 27 (43.5) | 6 (9.7) |
| ≥35 | 317 | 29 (9.1) | 12 (41.4) | 3 (10.3) |
| **Comorbidity[d], n (%)** | | | | |
| 0 | 3,235 | 291 (9.0) | 87 (29.9) | 20 (6.9) |
| ≥1 | 854 | 115 (13.5) | 45 (39.1) | 12 (10.4) |
| **Type of MS, n (%)** | | | | |
| RMS | 2,978 | 313 (10.5) | 98 (31.3) | 22 (7.0) |
| SPMS/PPMS | 1,111 | 93 (8.4) | 34 (36.6) | 10 (10.8) |
| **EDSS[e], n (%)** | | | | |
| 0–<3 | 2,049 | 207 (10.1) | 60 (29.0) | 12 (5.8) |
| 3–<6 | 1,272 | 130 (10.2) | 49 (37.7) | 10 (7.7) |
| ≥6 | 767 | 60 (7.8) | 23 (38.3) | 10 (16.7) |
| **Time since first OCR dose, median years (range)** | 4.20[f] (0.0–12.9) | 4.75[g] (0.1–12.2) | 6.48[g] (0.5–12.2) | 6.23[g] (1.0–11.0) |

#### Risk Factors Associated with (A) Symptomatic[a] COVID-19 Cases and (B) Serious COVID-19 Cases, Within the Reference Population

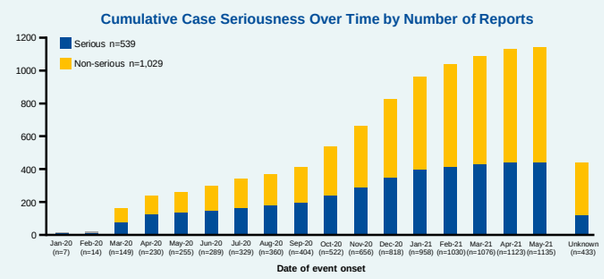


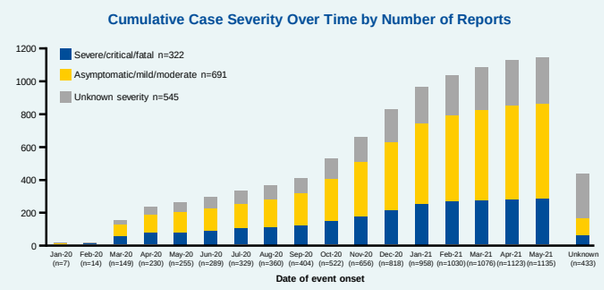

### OCR-Treated Post-Marketing Patients

#### Overview of Patient Demographics and COVID-19 Outcomes

**1,568 cases were identified in the global safety database as of 30 May 2021 using the company-wide standard search criteria. Most cases were non-serious 1,029/1,568 (65.6%), not hospitalised (1,074, 68.5%) and recovered/recovering (906, 57.8% NB: outcome was unknown/not reported in 406, 25.9% of cases)**
**For cases with sufficient information to assess clinical severity (n=1,023), most cases were asymptomatic, mild or moderate (691/1,023, 67.5%)**
**Clinical severity could not be assessed in 545/1,568 (34.8%) cases, but 75.4% (411/545) of these cases were non-serious**
**Proportion of serious/severe cases has decreased over time likely reflecting improved patient management and introduction of COVID-19 vaccines**

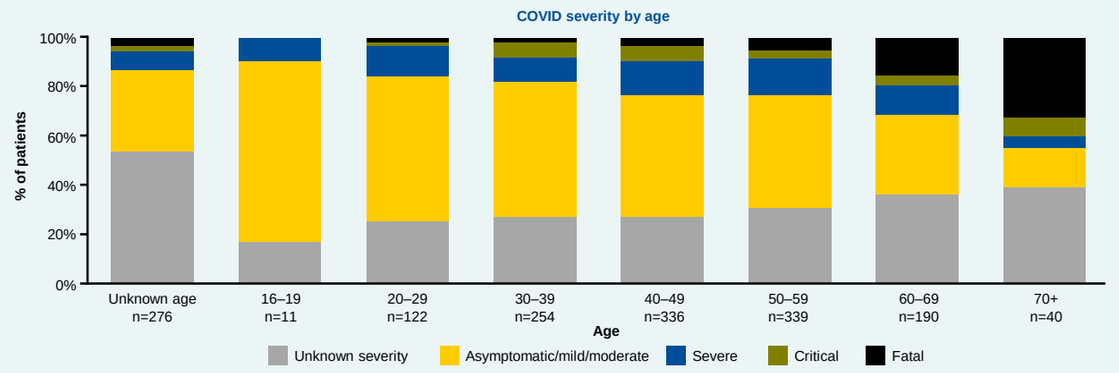
| | All cases (n=1,568) | Serious cases (n=539, 34.4%) | Demographic parameters as risk factors for serious COVID (% based on all cases) |
|---|---|---|---|
| **Age, median years (range)** | 48.0 (16–89)[a] | 50.0 (18–89)[b] | |
| **Sex, n (%)** | | | |
| Male | 470 (30.0) | 199 (36.9) | 199/470 (42.3) |
| Female | 938 (59.8) | 302 (56.0) | 302/938 (32.2) |
| Not reported | 160 (10.2) | 38 (7.1) | 38/160 (23.8) |
| **Type of MS, n (%)** | | | |
| Relapsing forms | 712 (45.4) | 233 (43.2) | 233/712 (32.7) |
| Progressive forms | 236 (15.1) | 106 (19.7) | 106/236 (44.9) |
| Not reported | 620 (39.5) | 200 (37.1) | 200/620 (32.3) |
| **Severity[c], n (%)** | | | |
| Asymptomatic, mild or moderate | 691 (44.1) | 80 (14.8) | |
| Severe | 187 (11.9) | 180 (33.4) | N/A |
| Critical | 64 (4.1) | 64 (11.9) | |
| Fatal | 81 (5.2) | 81 (15.0) | |
| Not reported | 545 (34.8) | 134 (24.9) | |
| **Outcomes, n (%)** | | | |
| Recovered or recovering | 906 (57.8) | 327 (60.7) | |
| Not recovered at time of report | 175 (11.2) | 49 (9.1) | N/A |
| Fatal | 81 (5.2) | 81 (15.0) | |
| Unknown/not reported | 406 (25.9) | 82 (15.2) | |



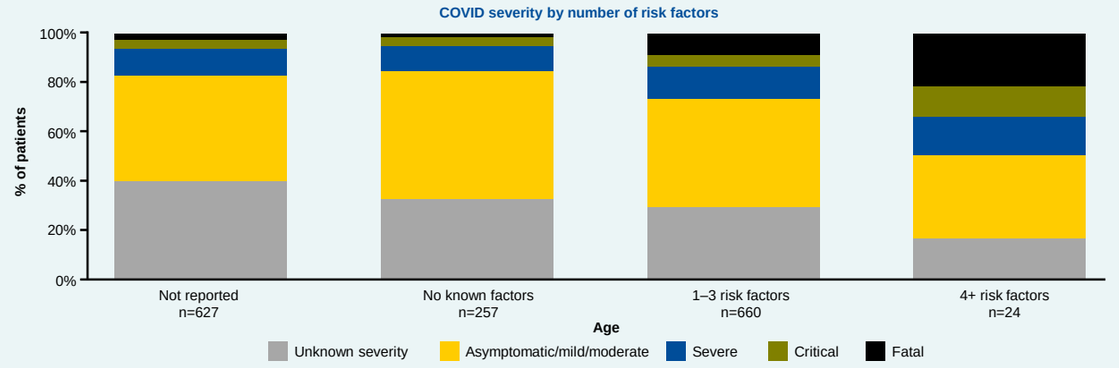




#### Factors Affecting Severity of COVID-19

**COVID 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 and median age also increased: 48 years (all cases) → 50 years (serious cases) → 61 years (fatal cases)**




**COVID-19 severity increases according to the presence/number of risk factors known to be associated with disease severity in the general population.***
**NB information on risk factors was missing in 627 cases**




*Risk factors for severe COVID-19 included: age >50, hypertension, diabetes mellitus, BMI>25, chronic kidney disease, coronary heart disease, chronic pulmonary disease, asthma, dementia and malignancy.

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