Ocrelizumab and COVID-19 Pharmacovigilance Data

Main takeaways
- While it is too early to draw definitive conclusions, based on the limited information that is available from pharmacovigilance data, the risk factors for severe COVID-19 outcomes do not indicate a difference between ocrelizumab-treated patients and the general population, and may suggest that COVID-19 follows a similar course in ocrelizumab-treated patients with MS as in the general population.
- These risk factors for severe COVID-19 include old age and presence of comorbidities, such as hypertension, diabetes, obesity, smoking, and cardiovascular and lung disease.
- The known benefit-risk profile of ocrelizumab remains unchanged.

Incidence of COVID-19 cases in ocrelizumab-treated patients
- As of May 31, 2020, 201 cases of COVID-19 in ocrelizumab-treated patients were identified in pharmacovigilance reports; all cases were conservatively considered as having confirmed COVID-19 (including the cases with missing information on diagnosis confirmation, eg, by PCR).
- More than 160,000 people with MS have been treated with ocrelizumab globally, in clinical trial and real-world settings; data continue to show a consistent and favorable benefit/risk profile.
- Patients receiving ocrelizumab that are either exposed to SARS-CoV-2 or confirmed to have COVID-19 should contact their neurologist or other medical professional right away, and patients should consult their neurologist or other medical professional before discontinuing their medication.

Seriousness and outcomes of COVID-19 in ocrelizumab-treated patients
- Of the 201 cases, 61% (n=122/201) were reported as not serious, and 39% (n=79/201) were reported as serious.
  - Included in the serious cases were:
    - 2.0% (n=4/201) reported as life-threatening and 5.5% (n=11/201) reported as fatal outcome.
    - 65% (n=51/79) of cases classified as serious were done so on the basis of hospitalization.
    - Reasons for hospitalization were variable and included (but were not limited to) the following: treatment of pneumonia and treatment in ICU.
    - At the time of reporting, 32% (n=25/79) of the serious cases were reported as recovered/recovering, and 33% (n=26/79) of the serious cases had an unknown outcome.

Table 1: Reported outcomes by most serious seriousness criterion for all serious cases (n=79)

<table>
<thead>
<tr>
<th>Most serious seriousness criterion</th>
<th>Fatal</th>
<th>Recovered</th>
<th>Recovering</th>
<th>Not recovered</th>
<th>Missing information</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All serious cases</td>
<td>11</td>
<td>15</td>
<td>10</td>
<td>17</td>
<td>26</td>
<td>79</td>
</tr>
<tr>
<td>Medically significant</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>0</td>
<td>11</td>
<td>8</td>
<td>14</td>
<td>18</td>
<td>51</td>
</tr>
<tr>
<td>Disability</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Life-threatening</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Death</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11</td>
</tr>
</tbody>
</table>

Details of 11 cases with a fatal outcome
- For the 11 cases with fatal outcomes, the reported causes of death were: COVID-19 (n=8); COVID-19 pneumonia (n=1); coronavirus infection (n=1); and respiratory failure (n=1).
  - None of the 11 cases had an available autopsy report.
- Patient demographics for these cases were as follows: Sex: male (n=7), female (n=3), unspecified (n=1); Age range 43–66 years (n=10), unspecified (n=1).
- The majority (n=7) of the 11 cases with fatal outcomes had risk factors known to be associated with severe COVID-19 outcomes in the general population.
  - Reported previous DMTs (n=2); of note, as indicative of more advanced MS.
  - Reported EDSS 6.0–9.0 (n=5), indicating a more severe course; MS registries identified MS severity as risk factor for severe COVID-19 outcomes.
  - Risk factors were identified for all patients with COVID-19 confirmed by RT-PCR (n=4) and all patients who received mechanical ventilation (n=5).
  - Two patients were not assessable; follow-up for missing information is ongoing.
- Time from starting ocrelizumab to outcome ranged from 1.5 to 3 years, but was unknown in 2 cases.
Interpreting COVID-19 real-world data

- COVID-19 is caused by a new strain of coronavirus called SARS-CoV-2, so knowledge about how it may affect people with MS remains limited.11,12
  - The limited data that are emerging on COVID-19 in people with MS are mainly derived from real-world data sources and it is important to recognize the limitations (and biases) inherent in these sources.13,14
- From the limited real-world evidence available globally, the MS population in general does not seem to be at higher risk from COVID-19 and no association between any DMTs and fatal COVID-19 outcomes has been reported
  - Major risk factors identified for severe/fatal COVID-19 in the MS population are advanced age (>50 years old), high levels of disability, progressive form of MS, and presence of comorbidities, such as hypertension, diabetes, obesity, smoking, and cardiovascular and lung disease.8,9,15
  - Treatment decisions should therefore be made between a patient and their treating neurologist or other medical professional based on a benefit/risk assessment specific to the individual patient

- We are aware of many efforts to collect real-world evidence to inform communities’ understanding of COVID-19 and the impact on patients with MS, including the COVISEP (French) and MuSC-19 (Italian) registries.
- Real-world evidence is complex and challenging to interpret as there are many limitations and biases in the datasets, including significant unknown and/or unreported data, differences in data collection and reporting (patient-reported vs healthcare professional-reported), suspected vs confirmed COVID-19 cases, identification of other comorbidities, and generally a reporting bias towards more severe cases

Table 2: Number of cases and deaths in the general population, as of July 14, 2020

<table>
<thead>
<tr>
<th>Country</th>
<th>Confirmed COVID-19 cases, n(^{a})</th>
<th>COVID-19 deaths, n(^{b})</th>
<th>Case–fatality rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>209,640</td>
<td>30,032</td>
<td>14.3</td>
</tr>
<tr>
<td>Italy</td>
<td>243,230</td>
<td>34,967</td>
<td>14.4</td>
</tr>
<tr>
<td>USA</td>
<td>3,363,056</td>
<td>135,605</td>
<td>4.0</td>
</tr>
<tr>
<td>Global</td>
<td>13,127,030</td>
<td>573,663</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Table 3: Number of cases and deaths in MS datasets, including reported ocrelizumab cases

<table>
<thead>
<tr>
<th>MS datasets</th>
<th>COVISEP France(^{a}) (as of May 21, 2020)</th>
<th>MuSC-19 Italy(^{17}) (as of May 31, 2020)</th>
<th>COVIMS North America(^{18}) (as of July 16, 2020)</th>
<th>MSDA/MSIF Global(^{16,19}) (as of June 10, 2020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 cases (OCR cases), n(^{c})</td>
<td>347 (38)</td>
<td>789 (83)</td>
<td>362 (110)</td>
<td>457 (85)</td>
</tr>
<tr>
<td>COVID-19 deaths (OCR cases), n</td>
<td>12 (0)</td>
<td>13 (1)</td>
<td>24 (4)</td>
<td>18 (3)</td>
</tr>
<tr>
<td>Case–fatality rate (OCR cases), %</td>
<td>3.5 (0.0)</td>
<td>1.6 (1.2)</td>
<td>6.6 (3.6)</td>
<td>3.9 (3.5)</td>
</tr>
</tbody>
</table>

NB: numbers and percentages in parentheses indicate ocrelizumab cases

- Due to limitations of real-world data and countries being affected differently by the pandemic, there may be differences in emerging data and interpretations
  - Publication in peer-reviewed journals of the real-world evidence will provide a robust assessment of the data quality and analytical methods, especially accounting for potential confounders and biases, which is essential to understand the impact of COVID-19 in MS

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

Footnotes:

- \(^a\)Serious event is defined as one that requires in-patient hospitalization, prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is life-threatening or fatal; includes both clinically suspected and cases, includes data from Germany, Sweden, Denmark, Brazil, and North America; overall dataset includes 527 cases, with alive/death status available for 457 laboratory-confirmed patients.
- \(^b\)Confirmed COVID-19 cases includes both clinically suspected and cases; includes data from Germany, Sweden, Denmark, Brazil, and North America; overall dataset includes 527 cases, with alive/death status available for 457 laboratory-confirmed patients.

Abbreviations:

- COVID-19=coronavirus disease 2019; COVMS=COVID-19 Infections in MS & Related Diseases; COVISEP=Epidemiological Characteristics of COVID-19 in Patients With MS or NMO; DMT=disease-modifying therapy; EDSS=Expanded Disability Status Scale; ICU=intensive care unit; MS=multiple sclerosis; MuSC-19=Multiple Sclerosis and COVID-19; OCR=ocrelizumab; PCR=reverse transcription PCR; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

References:


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www.ocrelizumabinfo.com