Prescribing Information

Progressive Multifocal Leukoencephalopathy (PML) is an opportunistic viral infection of the brain caused by the John Cunningham (JC) virus that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability.

Although no cases of PML were identified in ocrelizumab clinical trials, JC virus infection resulting in PML has been observed in patients treated with other anti-CD20 antibodies and other MS therapies and has been associated with some risk factors (eg, immunocompromised patients, polytherapy with immunosuppressants).

At the first sign or symptom suggestive of PML, withhold ocrelizumab and perform an appropriate diagnostic evaluation. MRI findings may be apparent before clinical signs or symptoms. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

When switching from drugs with prolonged immune effects, such as daclizumab, fingolimod, natalizumab, teriflunomide, or mitoxantrone, consider the duration and mode of action of these drugs because of additive immunosuppressive effects when initiating ocrelizumab.[1]

Ocrelizumab & PML

As of June 2018, there have been 4 confirmed cases of carry-over PML* in MS patients treated with ocrelizumab:

Report Date	Case Description
May 2017	Case was from a compassionate-use program in a JCV+ patient who switched to ocrelizumab after 36 infusions of natalizumab. Assessment of the case resulted in it being reported to regulators as related to natalizumab and not ocrelizumab.[2]
April 2018	The patient had increasingly worsening neurological symptoms and MRI changes prior to discontinuing treatment with fingolimod in December 2017. The patient started treatment with ocrelizumab in March/April 2018. In April 2018, MRI changes, worsening clinical presentation, and JCV DNA in the CSF confirmed the diagnosis of PML. The case was reported to regulators as a carry-over PML from fingolimod as assessed by the physician.[3]
April 2018	A JCV+ patient was previously treated with natalizumab for 7 years. Due to MRI changes and worsening clinical symptoms, natalizumab was discontinued in February 2018. The patient received a single infusion of ocrelizumab in April 2018. The case was reported by the physician as a carry-over PML from natalizumab.[3]
June 2018	A JCV+ patient was previously treated with natalizumab for a total of over 6 years, with the last infusion in March 2018. The patient had new and progressive symptoms since February 2018 prior to commencing treatment with ocrelizumab (first 2 infusions) in April/May 2018. In late May, brain MRI was consistent with PML, supported by a subsequent brain biopsy. The physician assessed the PML as related to natalizumab.[3]

Note: All of the above PML cases were non-fatal as of the time of each respective report.

*Carry-over PML: PML that develops a few months after stopping one disease modifying therapy (DMT) and starting a different DMT. In these cases, PML could have developed without causing symptoms while the patient was still on the previous DMT, or shortly after stopping the previous DMT.[4]

CSF=cerebrospinal fluid; DNA=deoxyribonucleic acid; JCV=John Cunningham virus; MRI=magnetic resonance imaging; MS=multiple sclerosis.

References:
1. https://www.gene.com/download/pdf/ocrevus_prescribing.pdf; 2. Hauser SL, et al. Presented at: ECTRIMS-ACTRIMS 2017 (Poster P676); 3. Genentech data on file; 4. Giovannoni G, et al. Pract Neurol. 2016;16:389–393.

Information current as of June 2018.

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OCR/032218/0083a(4)

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