Ocrelizumab and COVID-19

Patient safety is Roche/Genentech’s highest priority and we are closely monitoring the evolving coronavirus disease (COVID-19) situation. We believe that treatment decisions should be made between a patient and their treating neurologist/healthcare professional based on a benefit/risk assessment specific to the individual patient.

COVID-19 is caused by a new strain of coronavirus called SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), so knowledge about how it may affect people with multiple sclerosis (MS) and those treated with ocrelizumab is currently unavailable.

Like many other disease-modifying therapies for MS, ocrelizumab works by making changes to the immune system.

Per the ocrelizumab US Prescribing Information (USPI; Section 5.2 Infections):

A higher proportion of ocrelizumab-treated patients experienced infections compared to patients taking REBIF or placebo. In RMS trials, 58% of ocrelizumab-treated patients experienced one or more infections compared to 52% of REBIF-treated patients. In the PPMS trial, 70% of ocrelizumab-treated patients experienced one or more infections compared to 68% of patients on placebo. Ocrelizumab increased the risk for upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes-related infections [see Adverse Reactions (6.1)]. Ocrelizumab was not associated with an increased risk of serious infections in MS patients

In patients with active infections, treatment with ocrelizumab should be delayed until the infection is resolved.

Frequently Asked Questions

1. Do you believe patients on ocrelizumab are at a higher risk of coronavirus?
   - COVID-19 is caused by a new strain of coronavirus called SARS-CoV-2, so knowledge about how it may affect people with multiple sclerosis (MS) and those treated with ocrelizumab is currently unavailable. Additionally, there are no data currently available to inform specific recommendations or changes to treatment protocols for people treated with ocrelizumab.
   - We are actively discussing with the neurology community insights and perspectives relating to MS and COVID-19; however, we believe that treatment decisions should be made between a patient and their treating neurologist or other medical professional based on a benefit/risk assessment specific to the individual patient.
   - Physicians and patients should consult the ocrelizumab USPI for relevant information regarding the safety of ocrelizumab. For additional information and context surrounding the risk of infections with ocrelizumab, please consult the website section on infections [link here]
2. Do you recommend any change to patients’ treatment with ocrelizumab because of COVID-19?
   - We are actively discussing with the neurology community insights and perspectives relating to MS and COVID-19 as we do not yet know how it will affect people with MS. Additionally, there are no data currently available to inform specific recommendations or changes to treatment protocols for people treated with ocrelizumab.
   - While we understand that some neurological and patient societies recommend the delay of treatment initiation or re-treatment, we believe patients should speak with their neurologist or other medical professional before discontinuing or delaying treatment, so that decisions can be made based on a benefit/risk assessment specific to the individual patient.

3. What guidance can you provide for the treatment with ocrelizumab following a delay of a scheduled dose?
   - The current clinical situation may necessitate to delay a scheduled dose of ocrelizumab due to logistical reasons or based on an individual benefit/risk decision.
   - Per the ocrelizumab US Prescribing Information (USPI; Section 2.3 Recommended Dosage and Dose Administration):
     Subsequent doses: single 600 mg intravenous infusion every 6 months.
   - Per the ocrelizumab USPI (Section 2.4 Delayed or Missed Doses):
     If a planned infusion of ocrelizumab is missed, administer ocrelizumab as soon as possible; do not wait until the next scheduled dose. Reset the dose schedule to administer the next sequential dose 6 months after the missed dose is administered. Doses of ocrelizumab must be separated by at least 5 months [see Dosage and Administration (2.3)].
   - Based on limited data available from the ORCHESTRA studies, there is no evidence that a delay in ocrelizumab dosing will increase the rate of infusion-related reactions (IRRs) with the next 600-mg dose administered as a single infusion.

4. Clinical trial data shows that patients on ocrelizumab have an increased risk of developing infections. How are you assessing the potential risk to ocrelizumab patients?
   - COVID-19 is caused by a new strain of coronavirus called SARS-CoV-2, so knowledge about how it may affect people with MS and those treated with ocrelizumab is currently unavailable.
   - Like many other disease-modifying therapies for MS, ocrelizumab works by making changes to the immune system.
   - Per the ocrelizumab USPI (Section 5.2 Infections):
     A higher proportion of ocrelizumab-treated patients experienced infections compared to patients taking REBIF or placebo. In RMS trials, 58% of ocrelizumab-treated patients experienced one or more infections compared to 52% of REBIF-treated patients. In the PPMS trial, 70% of ocrelizumab-treated patients experienced one or more infections compared to 68% of patients on placebo. Ocrelizumab increased the risk for upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes-
related infections [see Adverse Reactions (6.1)]. Ocrelizumab was not associated with an increased risk of serious infections in MS patients.

- Patient safety is Roche/Genentech’s highest priority. As a company we are closely following developments regarding COVID-19 and we are committed to keeping the MS community updated with any new information to help inform health decisions related to ocrelizumab.

5. Can you provide more detail about the upper and lower respiratory tract infections from Pivotal Clinical Trials?
- The upper and lower respiratory tract infections reported in patients treated with ocrelizumab were predominantly mild to moderate (80–90%).
- The proportion of respiratory tract infections was higher in ocrelizumab-treated patients compared with those taking interferon beta-1a or placebo.
  - In the RMS clinical trials, 40% of ocrelizumab-treated patients and 33% of interferon beta-1-a-treated patients experienced an upper respiratory tract infection, and 8% of ocrelizumab-treated patients and 5% of interferon beta-1-a-treated patients experienced a lower respiratory tract infection.
  - In the PPMS clinical trial, 49% of ocrelizumab-treated patients and 43% of patients who received placebo experienced an upper respiratory tract infection, and 10% of ocrelizumab-treated patients and 9% of patients who received placebo experienced a lower respiratory tract infection.

6. Which type of infections were generally observed during treatment with ocrelizumab?
- Rates of serious infection in all patients exposed to ocrelizumab in clinical trials remain consistent with rates of infection-related hospitalization in real-world MS cohorts.
  - Ocrelizumab was not associated with an increased risk of serious infections in patients with MS, as shown in our phase 3 clinical studies vs comparators (interferon beta-1a or placebo). Of those serious infections that occurred, the vast majority were bacterial, and the patients responded to standard of care treatment. Longer-term data through continued observation in our open-label extension studies have revealed no new or particular pattern of serious infections in patients with MS treated with ocrelizumab.
  - Ocrelizumab has been shown to have an increased risk of contracting certain infections, including upper respiratory tract infections that were predominantly mild to moderate (classified as non-serious).
  - A higher proportion of ocrelizumab-treated patients experienced non-serious infections compared with patients taking Rebif (interferon beta-1a) (58.5% vs 52.5%) or placebo (72.2% vs 69.9%). These infections were predominantly mild to moderate, were equally likely to be bacterial or viral, and resolved with standard of care treatment and in most cases patients remained on treatment with ocrelizumab.
7. Are there data that show how treatment with ocrelizumab affects the body’s ability to create an adaptive immune response?
   - Per the ocrelizumab USPI (Section 7.2 - Vaccinations):
     
     A phase 3b randomized, open-label study (VELOCE) examined the concomitant use of ocrelizumab and several non-live vaccines in adults 18-55 years of age with relapsing forms of MS (68 subjects undergoing treatment with ocrelizumab at the time of vaccination and 34 subjects not undergoing treatment with ocrelizumab at the time of vaccination). Concomitant exposure to ocrelizumab attenuated antibody responses to tetanus toxoid-containing vaccine, pneumococcal polysaccharide, pneumococcal conjugate vaccines, and seasonal inactivated influenza vaccines. The impact of the observed attenuation on vaccine effectiveness in this patient population is unknown.

     - In the VELOCE study, humoral responses were attenuated at all time points in patients who were B-cell depleted and received ocrelizumab compared with those who did not, but patients were nonetheless able to mount humoral responses to the vaccines and neoantigen studied. For more information, please go to the most recent ocrelizumab safety data (link here).

8. Have any ocrelizumab-treated patients been infected by coronavirus?
   - We are aware of reports of patients with MS on ocrelizumab treatment who have been diagnosed with COVID-19.
   - Patient safety is Roche/Genentech’s highest priority, and consistent with our safety reporting processes we report to health authorities in accordance with standard pharmacovigilance processes.
   - With the worldwide situation in relation to COVID-19 evolving, it is anticipated that the number of COVID-19 cases will increase. As a result, it is likely that the number of COVID-19 cases in people with MS that are being treated with disease modifying treatments will also rise.
   - We are aware that physicians in Italy are evaluating setting up a registry to record cases of COVID-19 in relation to patients with MS to gather any insights and data that could potentially inform future recommendations.

References: