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Oncology Pharmacy Newsletter

Ocrelizumab (Ocrevus®)

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Ocrelizumab (Ocrevus ®) is a monoclonal antibody recently approved for the treatment of relapsing and primary progressive forms of multiple sclerosis (MS).[1] The pivotal ORATORIO trial showed high quality evidence of efficacy in patients receiving ocrelizumab. In fact, ocrelizumab is the only disease-modifying therapy in primary progressive MS (PPMS) with this level of evidence.[2] Table 1 summarizes the results observed in the ORATORIO trial.

Table 1: Results of the ORATORIO Trial[3]

	Ocrelizumab N = 488 (%)	Placebo N = 244 (%)	P-Value
12-week confirmed disability progression	32.9	39.3	0.03
24-week confirmed disability progression	29.6	35.7	0.04
25-foot walk worsening at 120 weeks	38.9	55.1	0.04
Brain Volume Loss	0.90	1.09	0.02
Brain lesions	Decreased by 3.4	Increased by 7.4	<0.001

Based on these study results, ocrelizumab is the first drug approved by the FDA for the treatment of PPMS.[2] Ocrelizumab's place in therapy for the relapsing-remitting form of MS remains to be clarified pending additional safety data on rates of infection and neoplasm.[4]

Mechanism of Action:

The exact mechanism of ocrelizumab's therapeutic effect in MS has yet to be elucidated. It binds to CD20, a cell surface antigen present on pre-B and mature B lymphocytes. After binding, ocrelizumab causes antibody-dependent cellular cytolysis and complement-mediated lysis.[1]

Dosing:

Ocrelizumab is initially dosed at 300mg as an intravenous infusion followed by a second 300mg dose two weeks later. Subsequent doses are given as single 600mg intravenous infusions every 6 months.[1] If a planned infusion is missed, ocrelizumab should be given as soon as possible. Do not wait for the next administration date. Additionally, readjust the infusion schedule based on the new administration date. Infusions must have a minimum of 5 months in between administrations.[1]

Considerations Prior to Administration :

Prior to administration, patients should be screened for hepatitis B virus (HBV), as ocrelizumab is contraindicated in active HBV infections confirmed by positive results for hepatitis B surface antigen (HBsAg) and anti-HBV tests.[1] Consult a liver disease expert if a patient is positive for hepatitis B core antibody (HBcAB+) and negative for HBsAG, or if they are carriers of HBV (HBsAg+).[1]

Prior to every infusion of ocrelizumab, patients should also be assessed for active infections. If an active infection is present, ocrelizumab should be delayed until the infection resolves.[1] Vaccination with live-attenuated or live vaccines is not recommended during treatment with ocrelizumab and after treatment until B-cell repletion. Administer all necessary vaccines at least 6 weeks prior to the initiation of ocrelizumab. [1]

Pre-medication with an oral antihistamine, such as diphenhydramine, 30-60 minutes prior and 100mg IV methylprednisolone (or equivalent corticosteroid) 30 minutes prior to ocrelizumab infusion is recommended for all patients for each infusion session.[1] The addition of an antipyretic such as acetaminophen can be considered.[1]

Administration:

Ocrelizumab is diluted with normal saline (NS) and administered using a dedicated line with an inline 0.2 or 0.22 micron filter. Close medical supervision with adequate medical support to manage severe reactions is required. Patients should be monitored for at least one hour after infusion completion. [1]

The initial 300mg dose of ocrelizumab is diluted in 250mL NS and infused at an initial rate of 30mL/hr. The rate is increased by 30mL every 30 minutes to a maximum infusion rate of 180mL/hr. Infusion duration is 2.5 hours or longer.[1]

Subsequent 600mg doses are diluted in 500mL NS and infused at an initial rate of 40mL/hr. The rate is increased by 40mL every 30 minutes to a maximum infusion rate of 200mL/hr. Infusion duration is 3.5 hours or longer. [1]

Preparation & Storage:

The vials should not be shaken, and diluents other than NS should not be used. Ocrelizumab contains no preservatives, and is intended for single use only. Prior to infusion, the preparation should be brought to room temperature. The ocrelizumab preparation lasts for 8 hours at room temperature up to 77°F and 24 hours when refrigerated at 36 – 46°F. [1]

Infusion Reaction Management:

In clinical trials, 34 – 40% of pre-medicated patients experienced infusion reactions, with the highest incidence occurring during the first infusion. No fatal infusion reactions were reported, but 0.3% of patients experienced serious infusion reactions that required hospitalization. If a patient experiences a life-threatening infusion reaction, ocrelizumab should be permanently discontinued. For less severe reactions, ocrelizumab can be temporarily halted, infused at a lower rate, or treated symptomatically. [1]

Adverse Effects:

The most common adverse effects seen in clinical trials with ocrelizumab include: upper respiratory tract infections (40 – 49%), infusion reactions (34 – 40%), skin infections (14%), lower respiratory tract infections (8 – 10%), depression (8%), cough (7%), peripheral edema (6%), back pain (6%), herpes virus–associated infection (5 – 6%), and extremity pain (5 %) [1]

References:

1: Ocrevus ® [package insert]. South San Francisco, CA: Genentech, Inc; 2017.

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