



# The Effect of Ocrelizumab in the Treatment of Multiple Sclerosis

## *Multipl Skleroz Tedavisinde Okrelizumabın Etkinliği*

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### The Effect of Ocrelizumab in Multiple Sclerosis Treatment

Although multiple sclerosis (MS) is known as a T-cell-related disease, B cells are nowadays thought to be responsible for cortical demyelination and neurodegeneration via presenting antigens, producing antibodies and cytokines. Trials searching the efficacy of ocrelizumab, a humanized monoclonal antibody that targets CD20+ B cells, have been published recently.

Montalban et al. (1) performed a randomized, parallel-group, double-blind, placebo-controlled phase 3 trial (ORATORIO) in 732 patients with primary progressive MS (PPMS). Patients aged between 18-55 years who were diagnosed as having PPMS according to the 2005 McDonald criteria, patients with 'Expanded Disability Status Scale' (EDSS) scores 3.0-6.5, patients with Functional System Scale scores of at least 2, and patients with increased immunoglobulin IgG index or oligoclonal bands in cerebrospinal fluid were included in the study. The ocrelizumab group, which contained 488 patients who were given 600 mg intravenous ocrelizumab every 6 months for 120 months, was compared with a 244-patient placebo group. The primary endpoint was the disability progression at the end of 12 weeks. The secondary endpoints were the disability progression at 24 weeks, delay in the "25-foot walking test" at 120 weeks, change in total T2 lesion load at 120 weeks, and change in cerebral volume at 24-120 weeks. All these features evaluated in the study were found statistically significantly better in the ocrelizumab

group. The percentage of disability decreased by 24% ( $p=0.03$ ) at 12 weeks, and by 25% ( $p=0.04$ ) at 24 weeks in the ocrelizumab group. Total T2 lesion load decreased in the ocrelizumab group, whereas it increased in the placebo group (-3.4 vs. 7.4;  $p<0.001$ ). The decrease in cerebral volume was 0.9% in the ocrelizumab and 1.09% in the placebo group ( $p=0.02$ ).

Hauser et al. (2) compared ocrelizumab at the same dose with 44 µg subcutaneous interferon beta-1a (INF-β1a) 3 times a week in relapsing-remitting MS. Randomly assigned patients (ocrelizumab  $n=827$ ; INF-β1a  $n=829$ ) from OPERA I (ocrelizumab  $n=410$ ; INF-β1a  $n=411$ ) and OPERA II (ocrelizumab  $n=417$ ; INF-β1a  $n=418$ ) trials were evaluated in the study. Patients aged 18-55 years who were diagnosed as having MS according to the 2010 McDonald Criteria, who had lower than 5.5 EDSS scores, with at least 2 attacks in the last 2 years or 1 attack in the last 1 year, and who had lesions in brain magnetic resonance imaging compatible with MS were included in the study. The primary endpoint was the annualized relapse rate. The secondary endpoints were disability progression, contrast enhancing T1 lesion load, new or enlarging T2 lesion, new T1 lesion, MS functional composite evaluation, and change in cerebral volume. In both trials, the annualized relapse rate was 0.16% in the ocrelizumab group and 0.29% in the INF-β1a group ( $p<0.001$ ). The percentage of disability progression was statistically significantly lower in the ocrelizumab group (9.1% vs. 13.6% at 12 weeks,  $p<0.001$ ; and 6.9% vs. 10.5% at 24 weeks,

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$p=0.003$ ). The number of contrast-enhancing T1 lesions was 94% lower in OPERA I ( $p<0.001$ ) and 95% lower in OPERA II ( $p<0.001$ ) in the ocrelizumab group. The new or enlarging T2 lesion load was 77% lower in OPERA I ( $p<0.001$ ) and 83% lower in OPERA II ( $p<0.001$ ) in the ocrelizumab group.

Infusion-related reactions, which were often observed with the first dose, were the most common adverse events in patients receiving ocrelizumab (1,2). Other adverse events such as infection and malignancy were observed. The rate of formation of neutralizing antibodies was lower in the ocrelizumab group compared with the INF- $\beta$ 1a group (0.4-21.3%).

Ocrelizumab treatment seems promising in MS considering better efficacy compared with a first-line treatment, and favorable results in PPMS.

## References

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