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# Amiselimod: A New Oral Agent in the Treatment of Multiple Sclerosis

## *Multipl Skleroz Tedavisinde Yeni Oral Ajan Amiselimod*

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### Amiselimod: A New Oral Agent in the Treatment of Multiple Sclerosis

The first approved oral agent for multiple sclerosis, which is a chronic, inflammatory, demyelinating, and autoimmune disease of the central nervous system, was fingolimod. Fingolimod decreases circulating lymphocyte numbers by preventing their departure from lymphoid tissues due to its sphingosine-1-phosphate (S1P) receptor blocking effect. Fingolimod may cause temporary bradycardia within 6 hours of the first dose. This effect is due to "G protein coupled inwardly rectifying potassium channel" (GIRK) activation via S1P1 and S1P3 receptors in atrial myocytes. Amiselimod binds to S1P1 receptors with a higher affinity than S1P2-5 receptors and causes GIRK activation 5 times less compared with fingolimod.

MOMENTUM was a randomized, double-blind, phase 2 trial that compared the effectiveness and safety of Amiselimod with placebo. This study included patients with relapsing-remitting multiple sclerosis (RRMS) aged between 18-60 years who had an attack within the last 12 months, patients who had at least 2 attacks within the last 24 months and had an enhancing lesion within last 12 months, and patients who had an enhancing lesion within the last 3 months. Patients who were using an S1P modulator or previously used a lymphocyte-depleting agent were excluded. The patients were randomized equally to placebo, or 0.1 mg, 0.2 mg or 0.4 mg Amiselimod. After a 24-week treatment period, the patients were followed up for 12 weeks due to safety concerns, and magnetic resonance imaging, blood, and safety evaluations were performed every 4 weeks (1).

The primary endpoint of the study was the total number of enhancing lesions during the 8-24-week period. Two higher doses of Amiselimod caused a significant dose-related decrease in the number of enhancing lesions during the 8-24-week period [for 0.2 mg, 72% ($p=0.0005$) and for 0.4 mg 80% ($p<0.0001$)]. Also, during the 4-24-week period, the total number of new or growing T2 lesions was decreased (for 0.2 mg $p=0.0018$, and for 0.4 mg $p<0.0001$). The drug had no significant effect on brain atrophy. The authors explained this noting that no significant effect was seen in previous S1P modulator clinical trials during the first 6 months and the effect was detected later; MOMENTUM was a short-term study, as such, the detection of an effect was not expected (1).

Amiselimod was well tolerated in all treatment groups and treatment-related adverse effects were similar in all groups, including the placebo group. The most frequent adverse effects were headache and nasopharyngitis, and mild elevations in hepatic enzymes occurred. Macular edema was not seen in any patient and no effect was detected on cardiac rhythm (1).

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In conclusion, the effectiveness of Amiselimod was like fingolimod in RRMS and it had no significant effect on cardiac rhythm. Although studies with longer durations and more powerful are still needed, it is seen as a potential treatment choice in both RRMS and other autoimmune disorders.

## Reference

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