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Risk of cardiovascular disease in patients treated with fingolimod compared to natalizumab: A nationwide cohort study in Denmark

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Introduction:

Clinical trials and real-world studies have shown fingolimod to be efficacious and to have a manageable safety profile.

Objectives/Aims:

The aim was to examine long-term safety in terms of cardiovascular disease (CVD) in patients with multiple sclerosis (MS) treated with fingolimod using different data sources for MS treatment and adverse effects. We hypothesized that fingolimod, compared to natalizumab, treated patients would be at higher risk of developing CVD.

Methods:

We conducted a nationwide cohort study by linking individual-level data from The Danish Multiple Sclerosis Registry with Danish national health registries. We included 2095 patients with MS aged 18 years or older free of CVD. Exposure to fingolimod (N=1131) and natalizumab (N=964), respectively, was defined by the first treatment of at least three months with cohort entry from 2011 to 2018. We defined CVD using a combined measure of hypertension, ischemic heart disease, atrial fibrillation, heart failure, and stroke based on in- and outpatient hospital admissions, causes of death, and use of prescription drugs. We used Cox regression adjusted for sex, age, and cohort year entry. Follow-up was from three months of exposure until first CVD event, time of exposure treatment stop plus one year, emigration, death due to non-CVD causes, or end of study (March 1, 2023), whichever came first.

Results:

In total, 66% (N=745, fingolimod) and 69% (N=666, natalizumab) were female. At follow-up start, mean age was 38.7 years (SD=9.3), and disease duration was 8.5 years (SD=6.6) in fingolimod treated patients. These numbers were 36.8 (SD=9.5) and 7.2 (SD=6.6) in the natalizumab group. The average annualized relapse rates at follow-up start were 0.8 (SD=0.8) and 0.9 (SD=0.9) in the fingolimod and natalizumab groups, respectively. Median expanded disability status scores were 2.0 (IQR: 1.5;3.0, fingolimod) and 2.5 (IQR: 1.5;3.5, natalizumab). During 10,174 person-years, we identified 244 CVD events, 28.8 and 17.4 per 1000 person-years in fingolimod and natalizumab groups, respectively. Compared to natalizumab treated patients, patients treated with fingolimod had a higher risk of developing CVD (HR=1.57; 95%CI 1.19-2.07). Number of patients needed to be treated with fingolimod for one patient to be harmed was 101.

Conclusion:

We found an increased risk of developing CVD in patients with MS with no pre-existing CVD treated with

fingolimod. Neurologists should consider patients' risk profile and possible adverse effects when prescribing fingolimod.

Disclosures:

Elisabeth Framke has nothing to disclose. Lau Caspar Thygesen has nothing to disclose. Morten Malmborg has nothing to disclose. Morten Schou reports lecture fees from Novartis, Astra Zeneca, Bohringer and Novo outside the current work. Finn Sellebjerg has served on scientific advisory boards for, served as consultant for, received support for congress participation or received speaker honoraria from Alexion, Biogen, Bristol Myers Squibb, Merck, Novartis, Roche and Sanofi Genzyme. His laboratory has received research support from Biogen, Merck, Novartis, Roche and Sanofi Genzyme. Melinda Magyari has served on scientific advisory board, as consultant for, received support for congress participation or speaker honoraria from Biogen, Sanofi, Roche, Novartis, Merck, Alexion, Bristol Myers Squibb. The Danish MS Registry received research support from Biogen, Genzyme, Roche, Merck, Novartis.