Interesting randomized clinical trial reviewing the efficacy and safety of two different Fingolimod doses against Glatiramer Acetate an established treatment for multiple sclerosis (MS). Both treatments are licenced to treat relapsing-remitting MS, with Fingolimod being the first oral treatment for MS.

Fingolimod 0.5mg or 0.25mg once a day were compared against Glatiramer 20mg subcutaneously once a day. The randomized clinical trial was not blinded the authors cited because you cannot administer the two Fingolimod doses with daily placebo injections for ethical reasons. This could indicate investigator bias in the study. The US FDA recommended doses lower than 0.5mg Fingolimod be compared in a head-to-head trial with established treatments to assess the efficacy and safety at the lower dose. The interest in the lower dose was to reduce the level of side effects that are experienced with Fingolimod. Some of those side effects are quite serious, but rare e.g. first-degree atrioventricular block, basal cell carcinoma.

The results of the study can only be generalized to treating relapsing-remitting MS, (the largest group) not relapsing progressive or primary progressive, there may also be a problem with the 74.4% of the study population being women, 74.2% were white, extrapolating the results to men or non-white groups may not produce the same results.

Of the 1461 adult patients screened to the study only 1064 participants started the study, and 859 patients completed the study, a 19.2% drop-out rate. The study had trouble recruiting a sufficient number of participants 2550 to show a 35% reduction in ARR (primary endpoint) for Fingolimod 0.5mg vs Glatiramer (95% power) and to show a 25% reduction in ARR for Fingolimod 0.25mg vs Glatiramer (80% power). The final sample, 1064 participants showed a significant reduction in the ARR of 41% for Fingolimod 0.5mg (power 71%) and a non-significant reduction of 15% in ARR for Fingolimod 0.25mg, (power 44%). The Study was under powered and failed to show a significant reduction in relapse rates (measured by ARR) in the lower Fingolimod 0.25mg dose. Generally anything below 80% power is unlikely to show a significant difference between groups, although it did in the 0.5mg group.

The authors cited the reason for the difficulty in recruiting was due to the availability of thrice-weekly Glatiramer Acetate and two other oral therapies. Many sites recruited small numbers of participants introducing potential selection bias, producing a non-random sample.

Overall I believe that the study missed its original aim of finding a significant difference with the lower 0.25mg dose of Fingolimod vs Glatiramer which had the potential of treating relapsing-remitting MS with lower side effect profile than higher doses of Fingolimod. Although the author cited that even if sufficient numbers of participants had been recruited Fingolimod 0.25mg would have still not shown any difference in effect compared to Glatiramer.