The approved indication may vary from country to country. In the EU, fingolimod is approved for the treatment of patients with highly active RRMS. In the USA, it is approved for the treatment of relapsing MS.

CONCLUSIONS

- The unadjusted risk of 3-month and 6-month confirmed disability improvement was significantly higher in patients receiving fingolimod in PANGAEA than in those receiving BRACE therapies in PEARL (p<0.001 for both).
- The results of this analysis provide further evidence to show that in clinical practice fingolimod is significantly more effective than BRACE therapies in improving disability outcomes in patients with active multiple sclerosis (MS).

INTRODUCTION

- MS is a chronic, inflammatory disease of the central nervous system that affects an estimated 2.3 million people worldwide.1
- Disease-modifying therapies (DMTs) for patients with MS aim to reduce the frequency of episodes of neurological dysfunction (relapses), to slow disease progression and postpone the accrual of disability.2
- Once-daily fingolimod 0.5 mg (FTY720; Gilenya®, Novartis Pharma AG) is a sphingosine 1 phosphate receptor modulator approved for the treatment of relapsing MS.
- Approximately 125,000 patients have been treated with fingolimod in both the clinical trial and post-marketing settings; total patient exposure now exceeds 240,000 patient-years.3
- Results from phase 3, randomized, controlled trials have demonstrated that fingolimod reduced relapse rates, slowed disability progression, and improved magnetic resonance imaging and brain atrophy outcomes compared with injectable IFN beta 1a (Avonex®) or placebo.4,5
- Findings from phase 3 trials have been complemented by real-world evidence, which has shown that fingolimod was associated with significantly lower rates of relapses than those observed with BRACE (Betaseron®, Betaseron®, Rebif®, Avonex,Copaxone®, Extavia®) therapies in patients with MS who have a history of relapse.6
- PANGAEA, a large, 5-year, national, prospective, non-interventional German registry study, is investigating the safety and efficacy of fingolimod in daily practice.7
- The results of PANGAEA can be compared with those of PEARL, a similar 2-year, prospective, non-interventional German registry study, which collected analogous data for BRACE therapies.8
- An analysis of data from these two studies has shown that patients receiving fingolimod in PANGAEA had a lower risk of confirmed disability progression than patients receiving BRACE therapies in PEARL.9
- The approved indication may vary from country to country. In the EU, fingolimod is approved for the treatment of relapsing MS. In the USA, it is approved for the treatment of patients with relapsing forms of MS.10

OBJECTIVE

- To compare confirmed disability improvement in propensity score-matched cohorts of patients receiving fingolimod or BRACE therapies, using data from PANGAEA and PEARL, respectively.

METHODS

- Patients with RRMS who were currently participating in PANGAEA or who had participated in PEARL, who had at least one relapse in the year before the study (active disease) and who had received only BRACE therapies before participating in the study were included in the analysis cohorts of PANGAEA and PEARL.
- Patients were excluded from the analysis if they had not received DMTs, had received therapies other than BRACE therapies, had missing information on the number of relapses in the previous year or had not provided informed consent. Furthermore, patients in PANGAEA who had participated in PEARL were also excluded from the analysis.
- Patients in PANGAEA and PEARL who met the inclusion criterion were propensity score matched (3:1) using a nearest-neighbour method (with 0.5 caliper) according to the probability of being enrolled in PANGAEA (fingolimod) versus PEARL (BRACE therapies).
- Covariates considered in the propensity score regression model included the following baseline demographic and clinical characteristics: age, gender, number of relapses in the previous year, time since MS diagnosis, pre-study DMTs (BRACE therapies) and Expanded Disability Status Scale (EDSS) score.
- The EDSS score is based on neurological examination, the ability to walk specified distances with or without assistance and an assessment of self-care.11
- Confirmed disability improvement, defined as a decrease in EDSS score of at least 1 point for all patients, regardless of baseline EDSS score, with the decrease in disability confirmed at a visit after 3 months or 6 months in the absence of a relapse, was compared in the PANGAEA (fingolimod) and PEARL (BRACE therapies) cohorts.
- Time to 3-month and 6-month confirmed disability improvement was assessed using a Kaplan-Meier approach. Unadjusted hazard ratios (HRs) for the risk of confirmed disability improvement (fingolimod versus BRACE therapies) were estimated using a Cox proportional hazards model adjusted for treatment. Patients without confirmed disability change were censored at the last available visit.
- To allow for residual confounding, analyses were also conducted adjusting for baseline covariates (age and gender) and for pre-study clinical characteristics (DMTs, relapses, time since diagnosis and EDSS score).
- Similar analyses were performed for the subgroup of matched patients from the PANGAEA and PEARL cohorts with at least 1 year of follow-up data in order to investigate the possible impact of difference in follow-up time between the cohorts.

RESULTS

Study population

- A total of 2555 and 587 patients met the criteria for inclusion in the PANGAEA and PEARL cohorts, respectively. After propensity score matching, 1535 patients were retained for the final confirmed disability improvement analysis (163 in the PANGAEA cohort and 372 in the PEARL cohort).
- In the subgroup of matched patients with at least 1 year of follow-up data, 961 patients were eligible for the confirmed disability improvement analysis (684 in the PANGAEA cohort and 297 in the PEARL cohort).

Proportion of patients with confirmed disability improvement

- A significant 2-fold higher proportion of patients receiving fingolimod in the PANGAEA cohort had 3-month and 6-month confirmed disability improvement compared with those receiving injectable BRACE therapies (interferons [IFNs] or glatiramer acetate [GA]) in PEARL (p<0.001 for both).
- Furthermore, the unadjusted risk of 3-month and 6-month confirmed disability improvement was significantly higher in patients receiving fingolimod in PANGAEA than in those receiving BRACE therapies in PEARL (p<0.001 for both).
- The results of this analysis provide further evidence to show that in clinical practice fingolimod is significantly more effective than BRACE therapies in improving disability outcomes in patients with active multiple sclerosis (MS).