INTRODUCTION

- Natalizumab and ocrelizumab are high-efficiency disease-modifying therapies (DMTs) approved in the United States to treat relapsing forms of MS.1,2
- Natalizumab has been shown to improve clinical outcomes, including relapse rates, relapse severity, and relapse recovery rates, in clinical trial and real-world settings.3
- Additional real-world head-to-head comparative data on relapse-related outcomes for high-efficiency DMTs are needed.
- In the current study, we performed a retrospective analysis using real-world administrative claims data to compare MS relapse-related outcomes for natalizumab and ocrelizumab.

AIM

- To compare claims-based relapses and relapse-related hospitalisation rates and associated costs for multiple sclerosis (MS) patients treated with natalizumab or ocrelizumab using data from a large insurance claims database.

METHODS

Study design

- This retrospective analysis utilised data from the Optum Clincformatics Data Mart US claims database from 1 April 2017 to 30 September 2020.
- Included patients had a diagnosis of MS (2119 patient or 42 outpatient claims of International Classification of Diseases (ICD)-9 code 340 or ICD-10 code G06), were naïve to study treatments in the year prior to the initial prescription (the index date), had at least 12 months of baseline insurance eligibility, and were treated with natalizumab or ocrelizumab during the study period.
- Patients were followed from the index date (defined as the date of first dispensing of natalizumab or ocrelizumab) to the end of the data window (30 September 2020) or until the first occurrence of any of the following:
  - Treatment discontinuation (defined as a gap in active prescription of ≥45 days, with assigned supply period of 30 days for natalizumab or 185 days for ocrelizumab).
  - End of loss of insurance coverage or disenrolment.
  - Switch to another study drug or a different DMT.

Outcomes

- Time until first relapse was defined as the number of days from the index date to the first claims-based relapse date.
- Claims-based relapses included the following:
  - Outpatient relapses with an MS diagnosis code followed by steroid use within 7 days, excluding steroid use occurring on treatment administration days.
  - Hospitalised relapses associated with inpatient hospitalisation with MS as the primary diagnosis code.
- Differences in mean annualised rates and in relapse-related mean annualised health care costs were also evaluated.

Statistical analyses

- Survival analysis of time to first relapse event was performed with weighted Kaplan-Meier analysis and a weighted Cox proportional-hazard model.
- Relapse outcomes were evaluated using weighted Cox proportional hazards, logistic regression, and generalised linear models.
- The average treatment effect of natalizumab was assessed by inverse probability weighting (IPW) to adjust for between-groups differences in baseline covariates. Propensity scores were calculated by logistic regression modelling of the probability of treatment with natalizumab conditional on 17 baseline covariates, including age, sex, number of MS symptoms, prior DMT use, comorbidities, and baseline (index) costs.

RESULTS

Patients

- The analysis included 835 natalizumab and 3467 ocrelizumab patients.
- After IPW, natalizumab and ocrelizumab patients were well balanced, including the proportion of patients with and without relapses at baseline, with all absolute standardised mean differences (SMDs) ≤0.1 (Table 1).
- Mean (standard deviation; 95% confidence interval) follow-up time was 0.9 (0.8) and 1.0 (0.8) years for natalizumab and ocrelizumab patients, respectively.
- The proportion of patients with baseline relapses were virtually identical in both groups, with 48% of natalizumab-initiating and 47% of ocrelizumab-initiating patients experiencing ≥1 relapse in the year prior to start of therapy (IPW adjusted, Table 1).

Time to first event of interest

- The cumulative probability of remaining free of any relapse was significantly higher with natalizumab than with ocrelizumab at 12 months (0.83 vs 0.76) and 24 months (0.70 vs 0.64, both P<0.001; Figure 1).
- Hazard ratios (HRs) for time to first relapse significantly favoured natalizumab over ocrelizumab for any relapse (HR=0.70; P<0.01) and outpatient relapse (HR=0.71; P<0.01; Figure 2).
- The HR for hospitalised relapse numerically favoured natalizumab over ocrelizumab but did not differ significantly between treatment groups (HR=0.81; P=0.11).
- The HRs for time to first MS-related ER visit did not differ significantly between groups (HR=1.05; P=0.81).

Annualised rates and costs

- Mean annualised relapse rates were significantly lower with natalizumab (0.35 vs 0.43; mean difference: −0.08; P<0.001) and for outpatient relapse (0.22 vs 0.36; mean difference: −0.14; P<0.001; Figure 3A).
- There was little or no difference in the annualised rates of MS-related ER visits or relapse-related hospitalisations between natalizumab and ocrelizumab (Figure 3A).
- Mean annualised costs associated with any relapse, outpatient relapse, hospitalised relapse, or total steroid use did not differ significantly between natalizumab and ocrelizumab (Figure 3B).

CONCLUSIONS

- This analysis of claims-based data provides a direct comparison of relapse-related outcomes and health care utilisation in MS patients treated with natalizumab or ocrelizumab in real-world settings.
- Patients treated with natalizumab had a significantly lower risk of any relapse or outpatient relapse than those treated with ocrelizumab.
- Mean on-treatment time was for approximately 1 year for the natalizumab and ocrelizumab patients.
- Mean annualised rates of any relapse and outpatient relapse also significantly favoured natalizumab over ocrelizumab.
- No significant differences in annualised costs for relapse-related hospital encounters or total steroid use were observed between natalizumab and ocrelizumab.
- The cost estimates are limited by relatively few relapse events with a wide range of costs associated with each event.
- Though relapses were insurance claims based and not physician reported, these results may provide useful information for health care providers considering high-efficiency treatment options for their patients with relapsing forms of MS.

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