Platform Therapy Compared with Natalizumab for Multiple Sclerosis: Relapse Rates and Time to Relapse Among Propensity Score-Matched US Patients

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Abstract

Background Multiple sclerosis (MS) registry data, primarily from Europe, suggest that treatment with natalizumab delays time to relapse compared with platform therapy (interferon beta/glatairam acetate).

Objective This study uses US administrative claims data and propensity score matching (PSM) to compare relapse rates and time to relapse among patients with MS using either platform therapy or natalizumab.

Methods Adults with MS receiving either platform therapy or natalizumab between January 1, 2009 and April 1, 2012 were identified in the Truven Health MarketScan Research Databases. Patients were included if they had 12 months of continuous enrollment both before and after the index date (the first claim for either drug cohort) and had 12 months of claims data suggesting consistent treatment adherence during the follow-up period. Characteristics used in PSM included demographics, selected comorbidities and concomitant medications, MS severity, baseline relapse rates, and expenditures. A relapse was defined as an MS-related hospitalization or corticosteroid use.

Results A total of 882 patients were matched. Relapse occurred among significantly fewer patients in the natalizumab group (26.5 %) than platform therapy (35.5 %, p < 0.001) (hazard ratio 0.69; 95% CI 0.59–0.82). Relapses were also significantly later for those on natalizumab (308 vs 283 days without relapse, p < 0.001).

Conclusion Treatment with natalizumab was associated with a significantly lower risk and rate of MS relapse and longer MS relapse-free time compared with platform therapies.

Key Points

To our knowledge, this is the first US administrative claims study of natalizumab compared with platform therapy for MS (interferon beta/glatairam acetate).

Patients on natalizumab experienced fewer relapses compared with patients on platform therapy (26.5 vs 35.5 %, p < 0.001).

Patients on natalizumab had longer relapse-free periods compared with patients on platform therapy (308 vs 283 days, p < 0.001).

1 Introduction

Multiple sclerosis (MS) is a leading cause of disability among young adults, affecting approximately 400,000 people in the US and 2.5 million worldwide [1, 2]. Research has shown that early treatment with an FDA-approved disease-modifying therapy (DMT) following an MS diagnosis reduces the severity and frequency of relapses and some therapies may slow worsening of disease [3]. Several factors that influence which DMT a patient...
initiates include the desired clinical outcome, the patient’s risk–benefit profile and the patient’s preference for route and frequency of administration. In the phase III AFFIRM (natalizumab safety and efficacy in relapse-remitting MS) trial, natalizumab, when compared to placebo, showed a 68 % reduction in annual relapse rate at 2 years and a 42 % reduction in the risk of disability progression confirmed at 12 weeks [4]. Platform therapies (interferon beta (IFN)-1a, IFN)-1b and glatiramer acetate) have also been shown to be efficacious by achieving an approximate 30 % reduction in the annual relapse rate versus placebo, but not all platform therapies have shown a significant reduction in disability progression [5–7].

Few studies have attempted to evaluate disability worsening outside of a clinical trial, and over a longer follow-up period. One retrospective analysis of the AFFIRM study by Havrdova et al. reported that over a 2-year study period, 64 % of natalizumab patients were free of clinical disease activity, 58 % were free of radiological disease activity and 37 % were free of combined activity (p < 0.0001) [8]. In a recent health resource utilization study, Bonafede et al. demonstrated that the results from clinical trials often translate well to real-world reductions in utilization [9]. In the 12 months following natalizumab initiation, 68.5 % fewer patients experienced an MS-related inpatient admission and half as many (50.6 %) required corticosteroids. In a prospective observational study of MS patients from two Italian MS centers, Prosperini et al. found that escalating to natalizumab resulted in a significant reduction in relapse compared with switching among platform therapies [10]. In a retrospective observational study analyzing data from three Italian MS center databases, Lanzillo et al. reported that patients who switched to natalizumab from platform therapy experienced a significant reduction in the annualized relapse rate over the 12-month follow-up period [11].

While observational studies present more realistic data than those obtained from randomized clinical trials (RCTs), they are subject to selection bias. For instance, in the Lanzillo study, patients with certain clinical or demographic characteristics were more likely to be switched to natalizumab. To counter these confounding effects, Spelman et al. used propensity scores to match the comparison groups on characteristics such as disability, disease duration, and relapse history to report the effectiveness of natalizumab compared with platform therapy in a real-world population using data from MS registries, largely in Europe. Consistent with previous literature, patients in this matched population who switched from platform therapy to natalizumab had significantly longer time to relapse than patients who switched to a different platform therapy [12].

To our knowledge, this study is the first to corroborate these European findings with US administrative claims data. We used propensity score matching (PSM) to compare relapse rates and time to relapse among commercially insured patients with MS who were administered platform therapy or natalizumab for 12 months.

2 Materials and Methods

The Truven Health MarketScan® Commercial and Medicare Supplemental Databases were used to identify adults initiating platform therapy (interferon beta/glatiramer acetate) or natalizumab between January 1, 2009 and April 1, 2012. The first claim with a National Drug Code (NDC) or Healthcare Common Procedure Coding System (HCPCS) code for these drugs was designated as the index date, and the study period spanned January 1, 2008 to March 31, 2013. The MarketScan® Commercial Claims and Encounters Database consists of employer- and health plan-sourced medical and drug data. Over 43 million individuals are included in the 2012 database, comprising employees, their spouses, and dependents covered by employer-sponsored private health insurance. Medical claims are linked to outpatient prescription drug claims and person-level enrollment information. The MarketScan® Medicare Supplemental Database profiles the healthcare experience of retirees with Medicare supplemental insurance paid for by employers. It includes the Medicare-covered portion of payment, the employer-paid portion, and any out-of-pocket patient expenses. Over 4 million individuals are included in the 2012 database.

Patients were included if they had a medical claim with an International Classification of Diseases, ninth revision, clinical modification (ICD-9-CM) diagnosis code for MS (ICD-9-CM code 340) during the 12 months prior to the index date (pre-period). Patients were also required to have medical and prescription claims history and continuous eligibility during the pre-period and for the 12 months following the index date (post-period). Patients were required to remain on their index drug for the entire 12-month post-period, which was verified by the presence of at least one claim for the index drug in each of the 12 follow-up months. Patients who had claims with a diagnosis of pregnancy or delivery during any point in the pre- or post-period and those with evidence of using a non-index MS therapy in the pre-period were excluded from the analysis. Platform therapies consisted of the following DMTs: IFNβ-1a (AVONEX®, REBIF®), IFNβ-1b (BETASERON®, EXTAVIA®), and glatiramer acetate (COPAXONE®). Natalizumab was listed as brand-name TYSABRI®.

Demographic and clinical characteristics were captured for the index date and during the pre-period, respectively. Demographic characteristics included age, gender,
Relapse with Platform Therapy vs Natalizumab in MS

505

geographic region, health insurance plan type and urbanicity. Comorbidities and concomitant medications during the pre-period were also described and included those common in patients with MS (e.g., bladder dysfunction, fatigue, headache, other chronic pain, depression, and use of corticosteroids, benzodiazepine, muscle relaxants, antispasmodics and antidepressants).

The patient’s MS severity was measured using a claims-based algorithm adapted from Kurtzke’s Functional System (KFS) [13]. The algorithm assigns a weight (1–6) to each of the measures in Kurtzke’s FS using ICD-9-CM codes on administrative claims (and for one measure, prescription claims) which correspond to each measure in seven out of the eight functional systems. For example, one measure of pyramidal functions is “abnormal signs without disability”; this was recorded if a patient had a claim coded to ICD-9-CM 781.2 (abnormality of gait), and assigned a weight of 1. A more severe measure, “the inability to swallow or speak” in brainstem functions, was recorded if a patient had a claim coded to ICD-9-CM 438.82 (other late effects of cerebrovascular disease, dysphagia), 787.2x (dysphagia) or v41.6 (problems with swallowing and mastication) and assigned a weight of 5. The sum of a patient’s weights across the 65 measures of function thus generated a severity score.

To adjust for differences in patient profiles which may confound findings, PSM using a logistic regression model was conducted on the probability of a patient receiving natalizumab. Patients in the natalizumab treatment arm were matched 1:1 to the pool of patients in the platform treatment arm with a similar predicted probability using the nearest neighbor matching technique with a caliper of 0.25 standard deviations (SD) of the propensity score. Matching factors included age, gender, region, health plan type, index year, selected comorbidities and concomitant medications, MS severity, pre-period relapse (binary variable indicating presence of an MS-related inpatient admission or use of corticosteroids), and pre-period expenditures. To examine the quality of the match, we calculated the standardized difference, which does not depend on sample size. The match was considered successful if the standardized difference was <10 for the majority of matching factors [14].

Post-period outcome measures consisted of relapse rate and time to relapse. Relapse was defined using an adaptation of a claims-based algorithm first described by Ollendorf et al. [15] and subsequently validated by Chastek and colleagues [16]. The presence of any of the following during the post-period indicated relapse: an MS-related inpatient stay (hospitalization with ICD-9-CM 340 as the primary diagnosis), or intravenous (IV) or oral corticosteroid use. Time to relapse was calculated as the number of days from the index date until the earliest occurrence of a relapse. This outcome was evaluated using a univariate Cox Proportional Hazard model to compare the time to relapse between the group who received platform therapy and those who received natalizumab. A sensitivity analysis was performed using a Cox Proportional Hazard model adjusting for the following confounders: age, gender, pre-period MS-related inpatient admissions, pre-period corticosteroid use (any, IV, oral), pre-period expenditures and MS severity. Multicollinearity of the independent variables was tested by calculating the variance inflation factor (VIF). The Schoenfeld test and a variety of graphical methods were used to verify that all variables met the proportionality assumption of the Cox modeling approach.

3 Results

The total sample comprised 897 natalizumab patients and 6605 platform therapy patients who met all study inclusion and exclusion criteria. After 1:1 matching, 882 natalizumab patients (mean age 45.4 [SD 10.0] years, 69 % female) were matched to 882 platform therapy patients (mean age 45.3 [SD 10.5] years, 70 % female). Over one-third of patients (35–37 %) had evidence of other chronic pain, more than one in four had a headache diagnosis and at least 16 % had been diagnosed with bladder dysfunction, depression or fatigue. Approximately half of the final study sample (49–52 %) had been prescribed antidepressants and up to 40 % had prescriptions for muscle relaxants (37–41 %), corticosteroids (37–39 %), benzodiazepines (32–33 %) and anti-spasmodic agents (30–35 %). Cohorts were well matched with standardized differences <10 for all matching factors (Table 1).

Individual measures within the seven functional systems differed between the two cohorts before matching, with a greater proportion of platform patients having a disturbance of skin sensation (21.4 vs 8.7 %) and a lower proportion having abnormality of gait (8.3 vs 10.5 %) and a prescription for dalfampridine (0.3 vs 2.2 %) compared with natalizumab. After matching, the proportions of patients with these characteristics were similar (9.6 vs 8.8 %, 9.8 vs 10.3 % and 0.9 vs 1.9 %, platform vs natalizumab, respectively) (Fig. 1).

After matching, significantly fewer natalizumab patients experienced post-period relapses compared with those on platform therapy (26.5 vs 35.5 %, p < 0.001). Natalizumab patients had a significantly lower risk of relapse (hazard ratio [HR] 0.695; 95 % confidence interval [CI] 0.59–0.82) during the 12-month post-period; the adjusted Cox model yielded the same result (HR 0.693; 95 % CI 0.59–0.82) (Table 2; Fig. 2). Duration of relapse-free time was also longer for the natalizumab patients; they experienced 25 more days without a relapse during the 12-month post-
### Table 1 Baseline demographic and clinical characteristics pre- and post-propensity score matching

| Variables                        | Pre-match |                  | Post-match |                  |
|----------------------------------|-----------|------------------|------------|------------------|
|                                  | Platform  | N = 6605         | N = 897    | N = 882          |
|                                  | therapy   |                  |            |                  |
| Platform                         | Natalizum |                  | N = 882    |                  |
|                                  | therapy   |                  |            |                  |
| Age (mean, SD)                   |           |                  |            |                  |
| Age range (N, %)                 | 18–34     | 11.6 % 135 15.1 % | –10.03     | 146 16.6 % 130 14.7 % | 4.99 |
|                                  | 35–44     | 25.2 % 286 31.9 % | –14.86     | 275 31.2 % 278 31.5 % | –0.73 |
|                                  | 45–54     | 35.1 % 300 33.4 % | 3.48       | 281 31.9 % 299 33.9 % | –4.35 |
|                                  | 55–64     | 24.5 % 162 18.1 % | 15.78      | 165 18.7 % 161 18.3 % | 1.17 |
|                                  | 65+       | 3.6 % 14 1.6 % | 12.75      | 15 1.7 % 14 1.6 % | 0.89 |
| Female (N, %)                    |           |                  |            |                  |
|                                  | 4911 74.4 % | 622 69.3 % | 11.16 | 618 70.1 % 611 69.3 % | 1.73 |
| Geographic region (N, %)         |           |                  |            |                  |
|                                  | northeast | 1112 16.8 % 147 16.4 % | 1.20 | 140 15.9 % 145 16.4 % | –1.54 |
|                                  | mid west  | 2077 31.4 % 259 28.9 % | 5.61 | 251 28.5 % 255 28.9 % | –1.00 |
|                                  | south     | 2018 30.6 % 336 37.5 % | –14.62 | 335 38.0 % 331 37.5 % | 0.94 |
|                                  | west      | 1359 20.6 % 148 16.5 % | 10.50 | 151 17.1 % 144 16.3 % | 2.13 |
|                                  | unknown   | 39 0.6 % 7 0.8 % | –2.30 5 0.6 % | 7 0.8 % | –2.76 |
| Rural residence (N, %)           |           |                  |            |                  |
|                                  | 976 14.8 % 108 12.0 % | 8.04 | 128 14.5 % 108 12.2 % | 6.66 |
| Insurance type (N, %)            |           |                  |            |                  |
|                                  | comprehensive | 229 3.5 % 30 3.3 % | 0.68 | 34 3.9 % 30 3.4 % | 2.43 |
|                                  | hmo       | 1419 21.5 % 114 12.7 % | 23.47 | 121 13.7 % 111 12.6 % | 3.36 |
|                                  | pos       | 403 6.1 % 85 9.5 % | –12.62 | 80 9.1 % 82 9.3 % | –0.79 |
|                                  | ppo or epo | 3959 59.9 % 594 66.2 % | –13.04 | 582 66.0 % 585 66.3 % | –0.72 |
|                                  | cdhp or hdhp | 262 4.0 % 41 4.6 % | –2.99 | 35 4.0 % 41 4.6 % | –3.35 |
|                                  | other/unknown | 333 5.0 % 33 3.7 % | 6.68 | 30 3.4 % 33 3.7 % | –1.83 |
| Common comorbid conditions (N, %)|           |                  |            |                  |
| Bladder dysfunction              | 724 11.0 % 145 16.2 % | –15.24 | 143 16.2 % 140 15.9 % | 0.93 |
| Depression                       | 734 11.1 % 135 15.1 % | –11.70 | 142 16.1 % 132 15.0 % | 3.13 |
| Fatigue                          | 899 13.6 % 127 14.2 % | –1.58 | 148 16.8 % 127 14.4 % | 6.57 |
| Gastrointestinal disease and     | 719 10.9 % 99 11.0 % | –0.48 | 103 11.7 % 98 11.1 % | 1.78 |
| symptoms                         | Headache   | 1880 28.5 % 238 26.5 % | 4.32 | 254 28.8 % 234 26.5 % | 5.07 |
| High blood pressure              | 1485 22.5 % 161 17.9 % | 11.31 | 154 17.5 % 161 18.3 % | –2.07 |
| Neuropathic pain                 | 870 13.2 % 73 8.1 % | 16.37 75 8.5 % | 72 8.2 % | 1.23 |
| Other chronic pain               | 2458 37.2 % 317 35.3 % | 3.90 | 325 36.8 % 312 35.4 % | 3.07 |
| Urinary tract infection          | 700 10.6 % 118 13.2 % | –7.91 | 115 13.0 % 114 12.9 % | 0.34 |
| Concomitant medications (N, %)   |           |                  |            |                  |
| Anti-depressants                 | 2427 36.7 % 445 49.6 % | –26.19 | 461 52.3 % 435 49.3 % | 5.90 |
| Anti-spasmodic agents            | 1011 15.3 % 278 31.0 % | –37.85 | 305 34.6 % 268 30.4 % | 8.97 |
| Benzodiazepines                  | 1852 28.0 % 289 32.2 % | –9.12 | 293 33.2 % 283 32.1 % | 2.42 |
| Corticosteroids                  | 2494 37.8 % 327 36.5 % | 2.70 | 346 39.2 % 322 36.5 % | 5.61 |
| Oral                             | 1930 29.2 % 207 23.1 % | 14.01 205 23.2 % 205 23.2 % | 0.00 |
| IV                               | 1196 18.1 % 209 23.3 % | –12.84 | 229 26.0 % 205 23.2 % | 6.32 |
| Immunosuppressive agents         | 115 1.7 % 17 1.9 % | –1.15 | 21 2.4 % 17 1.9 % | 3.12 |
| Muscle relaxants                 | 1595 24.1 % 334 37.2 % | –28.66 | 357 40.5 % 323 36.6 % | 7.93 |
period (308 vs 283 days, \( p < 0.001 \)). Additionally, natalizumab patients had lower rates of MS-related inpatient admissions (1.0 vs 2.6 %), IV corticosteroid use (15.6 vs 19.0 %) and oral corticosteroid use (15.4 vs 23.1 %) compared with platform therapy patients (all \( p < 0.001 \)).

Among propensity-matched patients, the presence of baseline corticosteroid use was associated with a significantly increased risk of relapse during the follow-up period (HR 2.0; 95 % CI 1.42–2.88; \( p < 0.001 \)); however, there was no increased risk associated with baseline MS-related inpatient admissions (HR 1.1; 95 % CI 0.73–1.56; \( p = 0.731 \)). Overall, patients with an MS severity score >0 had an increased risk of relapse. Compared with patients 18–34 years of age, those 45–54 years of age were more likely to experience a relapse (HR 1.44; 95 % CI 1.10–1.88; \( p = 0.007 \)). Higher pre-period expenditures were also associated with an increased risk of relapse (HR 1.16; 95 % CI 1.03–1.30; \( p = 0.014 \)). In contrast, significant interactions were not seen for sex or among any of the other age groups.

4 Discussion

Findings from the current study suggest that initial treatment with natalizumab compared with platform therapy significantly reduces the risk of relapse among commercially insured patients in the US. Patients who were being

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treated with platform therapy were 34% more likely to have a relapse compared with those treated with natalizumab. Patients on natalizumab went nearly a month longer without relapse compared with matched patients on platform therapy. During the 12-month post-period, patients on natalizumab had significantly fewer MS-related inpatient admissions and significantly less corticosteroid use than their matched platform therapy counterparts.

These findings are consistent with a similar comparison among propensity-score-matched patients across two separate MS registries in which patients who switched to natalizumab had an annualized relapse rate 83% lower than those who remained on platform therapy [12]. In an analysis of MS patients initiating or switching to natalizumab, Bonafede et al. reported similar findings to the current study [9]. Significant reductions in MS-related inpatient admissions and corticosteroid use were noted during a 12-month follow-up period for both initiators and switchers (77.1 and 44.7% reduction in admissions; 64.5 and 52.5% reduction in corticosteroid use, respectively) [9].

In this study, natalizumab and platform patients were substantively different in terms of disease severity and baseline demographics and clinical characteristics prior to matching. Differences in baseline characteristics suggest (but does not confirm) the presence of channeling bias whereby more complicated or severe patients may have been channeled to natalizumab instead of platform therapies. Similar differences in patient characteristics prior to matching were also described by Spelman et al. [12]. According to Spelman et al., baseline differences in the unmatched cohorts significantly impacted the study outcome of relapse rate as natalizumab patients had significantly greater disease severity.

Our findings are also supported by results of the phase III AFFIRM study in which the annualized relapse rate for

### Table 2 Time to relapse and relapse rates measured in the post period, pre- and post-propensity score matching

| Relapse                        | Pre-match |       |       | Post-match |       |       |
|-------------------------------|-----------|-------|-------|------------|-------|-------|
|                               | Platform therapy | N = 6605 | Natalizumab | N = 897 | Platform therapy | N = 882 | Natalizumab | N = 882 |
| Time without relapse (mean, SD) | 297.5 118.0 | 307.7 110.9 | 0.015 | 283.0 127.6 | 307.7 110.8 | <0.001 |
| Relapse (N, %)                 | 1997 30.2 % | 240 26.8 % | 0.033 | 313 35.5 % | 234 26.5 % | <0.001 |
| Time to relapse in days (mean, SD) | 141.7 106.2 | 146.2 107.7 | 0.241 | 134.0 107.0 | 145.4 106.9 | 0.221 |
| MS-related inpatient (IP) stay (N, %) | 89 1.3 % | 9 1.0 % | 0.394 | 23 2.6 % | 9 1.0 % | <0.001 |
| Time to MS-related IP stay (mean, SD) | 146.7 96.1 | 165.2 106.8 | <0.001 | 139.9 109.0 | 165.2 106.8 | 0.557 |
| Any corticosteroid use (N, %)  | 1,962 29.7 % | 236 26.3 % | 0.036 | 303 34.4 % | 231 26.2 % | <0.001 |
| Time to any corticosteroid use (mean, SD) | 142.2 106.5 | 147.0 108.1 | 0.203 | 134.4 107.4 | 146.2 107.3 | 0.210 |
| IV corticosteroid use (N, %)   | 953 14.4 % | 141 15.7 % | 0.304 | 168 19.0 % | 138 15.6 % | <0.001 |
| Time to IV corticosteroid use (mean, SD) | 149.8 109.0 | 150.5 103.7 | 0.860 | 134.9 109.8 | 151.4 103.2 | 0.180 |
| Oral corticosteroid use (N, %) | 1437 21.8 % | 138 15.4 % | <0.001 | 204 23.1 % | 136 15.4 % | <0.001 |
| Time to oral corticosteroid use (mean, SD) | 150.0 106.5 | 167.9 116.6 | <0.001 | 146.8 106.4 | 166.0 116.2 | 0.117 |

*IV* intravenous, *MS* multiple sclerosis, *N* number, *SD* standard deviation

![Fig. 2 Probability of no relapse among propensity score-matched patients: natalizumab versus platform therapy](image-url)
patients on natalizumab compared with those on placebo decreased by 68% at year 1 [4]. Furthermore, in their interim analysis of the ongoing TOP (Tysabri Observational Program) prospective observational study, Butt-kueven et al. reported that the mean annualized relapse rate decreased significantly in the first year after natalizumab treatment and was lower for those patients who used natalizumab as their first treatment [17]. In their prospective observational study, Prosperini et al. compared patients who switched from platform therapy to natalizumab with patients who switched from one platform therapy to another [10]. Prosperini reported that a lower proportion of patients who escalated to natalizumab experienced a relapse compared with those who switched to a different platform therapy. A similar result was present in this current analysis, suggesting better effectiveness with natalizumab versus platform therapy for treatment-naive or previously treated patients after controlling for differences in patient and disease severity characteristics among platform and natalizumab users.

5 Limitations

Several limitations are noteworthy. First, the study population in our analysis is limited to those individuals with commercial health coverage or private Medicare supplemental coverage. Consequently, results of this analysis may not be generalizable to MS patients with other insurance or without health insurance coverage. Secondly, as with any claims databases, the MarketScan Research Databases rely on administrative claims data for clinical detail, some of which is missing because it is not captured in claims and are subject to data coding limitations and data entry error. Although the Kurtzke's FS score was used as a proxy to determine severity, other key clinical measures are not available in claims data, so the cohorts could not be matched for all disease severity measures. Additionally, the KFS algorithm is currently experimental and future planned work includes validating the algorithm. Thirdly, the number of relapse events captured is likely to be an underestimate as the criteria (evidence of MS-related hospitalization or IV/oral corticosteroid use) did not capture less severe relapses that would not have resulted in a hospitalization or corticosteroid use. Fourthly, the patients in the current study were required to stay on therapy for the 12-month post-period, so patients who discontinued therapy or switched to another therapy within the 12-month post-period were not analyzed. Fifthly, pre-index exposure to other MS-specific disease-modifying treatments was not included in the match as the study design (and data source) is not adequate to define total time on DMT therapy or time since MS diagnosis as they contain only a relatively short portion of patient-time for the MS patient. Sixthly, because administrative claims data were used, we were unable to examine relapse or time to relapse for different types of MS (e.g., remitting-relapsing, secondary progressive), which are not distinguished in the ICD-9-CM coding. Lastly, the inferences drawn by this study are reliant upon the data available for inclusion in the PSM and multivariate analysis. We could not assess if differences in unobserved characteristics between the treatment cohorts might impact the study results or conclusions.

6 Conclusion

Use of natalizumab for MS was associated with significantly lower risk and rate of relapse compared with treatment with IFNβ/glatiramer acetate (platform therapy) among propensity score-matched patients. Natalizumab patients also had significantly more relapse-free time than platform patients during the 12-month follow-up period.

Acknowledgments The authors wish to acknowledge Bong Chul Chu for his statistical contributions to the study.

Compliance with Ethical Standards

Funding Truven Health Analytics was awarded a research contract by Biogen to conduct this study. Open Access was funded by Biogen.

Conflicts of interest Two authors (BHJ and MMB) are employees of Truven Health Analytics. The third author (CW) is an employee and shareholder of Biogen.

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