The Safety of Natalizumab Administration in the Home During the COVID-19 Pandemic for Patients with Multiple Sclerosis

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ABSTRACT

Background

Multiple sclerosis (MS) is a progressive autoimmune inflammatory disorder causing demyelination and degeneration of the central nervous system. Natalizumab is a highly effective monoclonal antibody for the treatment of relapsing-remitting multiple sclerosis (RRMS).[1] It is usually delivered as 300 mg 1-hour intravenous infusion every 4 weeks.[1] Natalizumab is generally well tolerated, however, there are infusion-related reactions associated with the drug, and a risk of progressive multifocal leukoencephalopathy (PML.) Patients were previously required to receive the infusions in an authorized infusion center under a restricted distribution program.[1] Due to the COVID-19 pandemic, there was concern for additional exposure of immunocompromised patients during health care facility visits. The manufacturer had obtained Food and Drug Administration (FDA) approval that temporarily permitted the infusion of natalizumab in the home under the TOUCH® Risk Evaluation and Mitigation Strategy (REMS) program.

Purpose

The study assessed the safety of natalizumab administration by comparing outcomes after receiving natalizumab infusions at home vs. infusion suites.

Methods

The study was a retrospective, non-inferiority multi-center chart review of patients receiving natalizumab in the home and outpatient infusion center. The primary outcome included safety (adverse events and infections), as assessed by pharmacist documentation. Non-inferiority was declared if the proportion of adverse events and infections for home infusion was no worse than the proportion for infusions performed in infusion suites, within statistical variability, by a margin of -3.0 percentage points. The study included MS patients over 18 years old prescribed natalizumab who have been treated for 6 consecutive uninterrupted natalizumab infusions prior to starting home infusion natalizumab. Exclusion criteria included natalizumab naive patients and patients receiving an MS concurrent therapy.

Results

Between May 4, 2020, and August 21, 2021, 7,699 natalizumab patients were screened based on referral information. Ninety-eight RRMS patients were randomly selected (natalizumab home infusion n=49 vs. natalizumab outpatient infusion n=49). Overall, there were no demographic differences between the 2 groups, other than female sex. Adverse events were reported in 6.1% (n=3) of the patients treated in an infusion suite and 8.2% (n=4) of patients treated in the home setting. There were no episodes of anaphylaxis, infections, unexpected toxicities, and no additional safety concerns identified.

Conclusion

The incidence of infusion-related events and adverse events was similar in both natalizumab groups. This retrospective study demonstrated a low incidence of adverse events in patients receiving natalizumab at home. These findings demonstrated that delivering natalizumab to patients who have received 6 consecutive uninterrupted infusions prior to starting home infusion natalizumab, is as safe as those who receive it in outpatient clinic. The convenience of the home setting should be considered in future care for immunocompromised patients. The results may be utilized in future studies to evaluate the safety of natalizumab infusions in the home setting. Furthermore, the framework of this study supports future studies to evaluate the safety of other monoclonal antibodies in the home setting.

Background

Multiple sclerosis (MS) is a progressive autoimmune inflammatory disorder causing demyelination and degeneration of the central nervous system, affecting 1 million people in the United States and about 2 million people worldwide.[1] Natalizumab is a highly effective monoclonal antibody therapy for the treatment of relapsing-remitting multiple sclerosis (RRMS).[1] It is usually delivered as 300 mg 1-hour intravenous infusion every 4 weeks.[1] Natalizumab is generally well tolerated by patients, however, the safety profile of natalizumab in long term can be associated with a rare brain infection called progressive multifocal leukoencephalopathy (PML). Because of the potential for infusion-related reactions of natalizumab and the risk of PML, it poses a great inconvenience to patients requiring them to receive the infusions in an authorized infusion center as part of a restricted distribution program called the TOUCH® Prescribing Program.[1] As part of the Coronavirus Disease 2019 (COVID-19) pandemic, patients and providers alike shared concerns about appointments in health care facilities that may increase immunocompromised patients' exposure risk to COVID-19. As such, the manufacturer had requested, and received U.S. Food and Drug Administration (FDA) advice that enabled the manufacture to temporarily offer in-home infusion of natalizumab for patients with RRMS under the TOUCH® REMS program during the COVID-19 Public Health Emergency. Previous studies in countries outside of the U.S., and therefore regulated under different drug safety authorities, have described natalizumab home infusion models with positive results in safety, outcomes, and patient satisfaction.[2,3]

To support the provision of patient-centered care and provide home care as a safe option to patients with multiple sclerosis, it is necessary to develop a new model of care in the U.S. to deliver safe and effective therapy going forward.

Purpose

The study purpose was to assess the safety of natalizumab administration by comparing rate of infusion reactions and infections after receiving natalizumab infusions at home vs. outpatient clinics.

Methods

This study was a retrospective, multi-center chart review analysis of patients receiving natalizumab in the home and alternate infusion site. The primary outcome included patient safety outcomes (adverse events and infections), as assessed by the information collected by pharmacists overseeing the care and dispensing for these patients. Study inclusion criteria included male and female patients over 18 years old diagnosed with MS who were prescribed natalizumab home infusions and have been treated for 6 consecutive uninterrupted infusions with natalizumab prior to starting home infusion natalizumab. The manufacturer has a shortened post-infusion observation period for those patients who have had ≥6 consecutive, uninterrupted natalizumab infusions (30 minutes vs. the current 60 minutes). Study exclusion criteria included naive patients who have never received natalizumab and were receiving a concurrent therapy. This study was deemed to be IRB exempt.

Statistical Analysis

Descriptive analyses of mean and standard deviation were reported for continuous variables and counts and frequency for dichotomous variables. Differences between continuous variables were calculated using Student's T test. Chi-square tests were performed when comparing dichotomous variables with cell sizes greater than n=5, and Fisher's Exact tests were performed when cell sizes were less than n=5.

Non-inferiority on the primary endpoint was determined using the confidence interval method, where the lower limit of the one-sided 97.5% confidence interval for the event rate in the investigational group versus the control group was greater than m = -0.3. Results of a power analysis showed that a sample size of 48 patients per study arm for a total of 96 was required to show non-inferiority at an alpha level of 0.025 with 80% power assuming that there is less than a 5% change in odds of adverse event between the control and treatment groups. All analysis was conducted using RStudio 2022.02.03 Build 492.

Results

Between May 4, 2020, and August 21, 2021, 7,699 patients were screened based on referral information received to the organization related to natalizumab at home and outpatient clinic infusions at 53 sites around the U.S. Ninety-eight patients were identified as meeting inclusion criteria (natalizumab home infusion n=49 vs. natalizumab outpatient infusion n=49). Overall, there were no statistically significant differences in demographics observed between the 2 treatment groups

as seen in Table 1. Most participants were female and had been receiving natalizumab over a mean of 3.7 years (home infusion) vs. 3.1 years (outpatient infusion). The mean age of participants was 43.3 years and 44.7 years in-home vs. clinic infusions, respectively. All were diagnosed as RRMS.

TABLE 1 | Summary of Baseline Patient Demographics for 98 Participants Receiving Natalizumab in Home vs. Outpatient Clinic

Variable	Home Infusion (n=49)	Outpatient Infusion (n=49)	Significance (*p*-value)
Age, mean (SD)	43.3 (10.4)	44.7 (11.1)	0.606
Gender			
Male, n (%)	14 (28.6%)	17 (34.7%)	0.664
Female, n (%)	35 (71.4%)	32 (65.31%)	
Years receiving natalizumab, mean (SD)	3.1 (1.8)	3.7 (2.8)	0.210

As shown in Figure 1, infusing natalizumab in the home setting was found to be non-inferior to infusions performed in an outpatient infusion center (OR=1.34, 95% CI: 0.217-9.780, m= -0.30). Events reported, as percentage, in patients receiving natalizumab at home included nausea/vomiting 2% (1), fatigue 2% (1), fever 2% (1), and arthralgia 2% (1). In outpatient clinic infusions, patients reported fatigue 2% (1), fever 2% (1), and arthralgia 2% (1). There were no episodes of anaphylaxis, infections, unexpected toxicities, and no additional safety concerns identified. There were no episodes or symptoms of PML observed in any of the patients.

Discussion

This retrospective study has demonstrated a low incidence of adverse events in patients receiving natalizumab at home. The study findings demonstrated that delivering natalizumab to "expert patients" who have received 6 consecutive uninterrupted infusions with natalizumab prior to starting home infusion natalizumab, is as safe as those who receive it in outpatient clinic. The convenience of the location of delivery of safe treatments should be considered into future design of services for those immunocompromised such as multiple sclerosis patients. The data results, although specific to one organization, may be utilized in future studies to evaluate the safety of natalizumab infusions in the home setting. Furthermore, the framework of this study supports future potential studies to evaluate the safety of other outpatient monoclonal antibodies in the home setting.

Limitations of this study include potential for confounders that were not measured as well as possible selection bias. Another limitation is reliance on manual documentation for adverse event data.

Conclusions

The incidence of infusion-related reactions was similar in both natalizumab infusions received at home and outpatient clinic. There was no difference in incidence of adverse events across both groups.

References

1. Tysabri (natalizumab) [prescribing information]. Cambridge, MA: Biogen Inc; June 2020.
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FIGURE 1 | Non-Inferiority and Adverse Events for Infusion in an Outpatient Infusion Center versus a Home Setting