Changes in Whole Brain Volume and Cortical Gray Matter over 3 Years of Natalizumab Treatment: Updated Results from the STRIVE Study

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Conclusions

- In this analysis of anti–JC virus (JCV) antibody negative patients diagnosed with relapsing-remitting multiple sclerosis (RRMS) <3 years prior to baseline, brain volume loss appeared to slow after the first year of treatment, with stabilization in the second and third years.
  - The greater reduction in whole brain volume observed in the first year may be due to pseudoatrophy, which has previously been observed during the first year of natalizumab treatment.[1,2]
- The cortical gray matter (CGM) fraction remained consistent over 3 years of natalizumab treatment.
- These analyses extend previous analyses of STRIVE[3,4] demonstrating the clinical effectiveness of natalizumab treatment early in the RRMS disease course and in a population with highly active disease.

Introduction

- Brain volume loss has emerged as a clinically relevant endpoint in multiple sclerosis (MS).
  - Brain volume loss occurs early in the MS disease course.[5] This early degeneration has been associated with long-term worsening in disability and cognition,[6-8] suggesting that early treatment with a therapy that can slow brain volume loss may be important for preserving physical and cognitive functioning.
- In the phase 3 AFFIRM trial, natalizumab significantly reduced disease activity as reflected by brain imaging measures, clinical relapse rate, and confirmed disability worsening in patients with RRMS compared with placebo.[9]
- In the second year of AFFIRM, natalizumab-treated patients exhibited significantly less brain volume loss than placebo-treated patients.[1]
- The STRIVE study in patients with early RRMS (<3 years since diagnosis) initiating natalizumab demonstrated the effectiveness of natalizumab in improving clinical outcomes,[3,4] but the effect of natalizumab on brain volume changes in these patients is unknown.

Objective

- To evaluate changes in whole brain volume and the CGM fraction over 3 years of natalizumab treatment in patients with early RRMS in an analysis of data from the STRIVE study.

Methods

- STRIVE (NCT01485003) is an ongoing, multicenter, observational open-label study in anti-JCV antibody negative patients with early RRMS initiating natalizumab.
- Magnetic resonance imaging scans were obtained at baseline and 1, 2, and 3 years; these scans were analyzed by NeuroRx Research (Montreal, Quebec, Canada).
  - Percentage brain volume change (PBVC) was assessed using the structural image evaluation, using normalization, of atrophy (SIENA) method; normalized brain volume and CGM volumes were calculated using the SIENA cross-sectional (SIENAX) method.
  - CGM atrophy was assessed as a percentage of total brain parenchyma volume.
- Analyses were conducted in the intent-to-treat (ITT) population (ie, all patients who had received ≥1 dose of natalizumab in the study) with data available at baseline and 1–3 years.
- Exploratory analyses also evaluated PBVC and CGM fraction by no evidence of disease activity (NEDA) status at 1 year.
  - NEDA was defined as no disability worsening (sustained for ≥24 weeks on the Expanded Disability Status Scale [EDSS]), no relapses, no gadolinium-enhancing (Gd+) lesions, and no new or enlarging T2-hyperintense lesions.

Results

Patient characteristics

- The ITT population consisted of 222 patients (Table 1) who had early RRMS at baseline, based on the short time since their MS diagnosis (mean, 1.6 years) and their relatively low EDSS score (mean, 2.0); 50% of these patients had not received prior disease-modifying therapies (DMTs).
  - At baseline, 42.1% of patients had Gd+ lesions, the mean normalized brain volume was 1550.2 mL, and the mean CGM (as a percentage of total brain parenchyma volume) was 37.75%.
- In the ITT population, yearly PBVC and CGM data were available from baseline through 3 years for 109 and 120 patients, respectively.
  - Of the 109 patients with PBVC data at all time points, 45 (41.2%) had NEDA during their first year on natalizumab.
  - Of the 120 patients with CGM data at all time points, 54 (45.0%) had NEDA during their first year on natalizumab.

PBVC

- Mean (95% confidence interval [CI]) PBVC was −0.68% (−0.82, −0.53) in the first year after initiating natalizumab treatment (Figure 1).
- Mean (95% CI) PBVCs from baseline to 2 and 3 years were −1.04 (−1.23, −0.86) and −1.47 (−1.68, −1.25), respectively.
- No significant differences were observed in mean PBVC across the 3-year assessment period between patients who did and did not achieve NEDA at 1 year (Table 2).

CGM atrophy

- The mean (95% CI) CGM fraction was 37.75% (37.33%, 38.17%) at baseline and remained relatively constant over 3 years on natalizumab (Figure 2).
- No significant differences were observed in the CGM fraction across the 3-year assessment period between patients who did and did not achieve NEDA at 1 year (Table 2).

Table 1. Baseline characteristics (ITT population)

Baseline characteristic	Natalizumab-treated patients (N=222)
Age, mean (SD), years	34.0 (8.97)
Female, n (%)	161 (72.5)
Time from diagnosis of MS, mean (SD), years	1.6 (0.77)
Number of relapses in the past year, mean (SD)	1.4 (1.15)
EDSS score, mean (SD)	2.0 (1.13)
Prior DMT treatment, n (%)	111 (50.0)
Patients with Gd+ lesions, n (%)	83 (42.1)[a]
Normalized brain volume, mean (SD), mL	1550.2 (79.3)[b]

SD=standard deviation.
[a]N=197; [b]N=196.

Table 2. Mean (95% CI) PBVC and CGM fraction by NEDA status at 1 year in ITT patients with data at baseline and 1–3 years

	1 year	2 years	3 years
PBVC			
With NEDA (n=45)	−0.76 (−1.04, −0.48)	−1.17 (−1.55, −0.78)	−1.56 (−1.99, −1.13)
Without NEDA (n=64)	−0.62 (−0.77, −0.47)	−0.96 (−1.12, −0.79)	−1.40 (−1.62, −1.18)
CGM fraction			
With NEDA (n=54)	37.75 (37.03, 38.46)	37.40 (36.69, 38.11)	37.16 (36.43, 37.88)
Without NEDA (n=66)	37.56 (37.00, 38.11)	37.39 (36.80, 37.99)	37.08 (36.45, 37.72)

Figure 1. Mean PBVC at 1, 2, and 3 years in the ITT population with complete data (n=109)

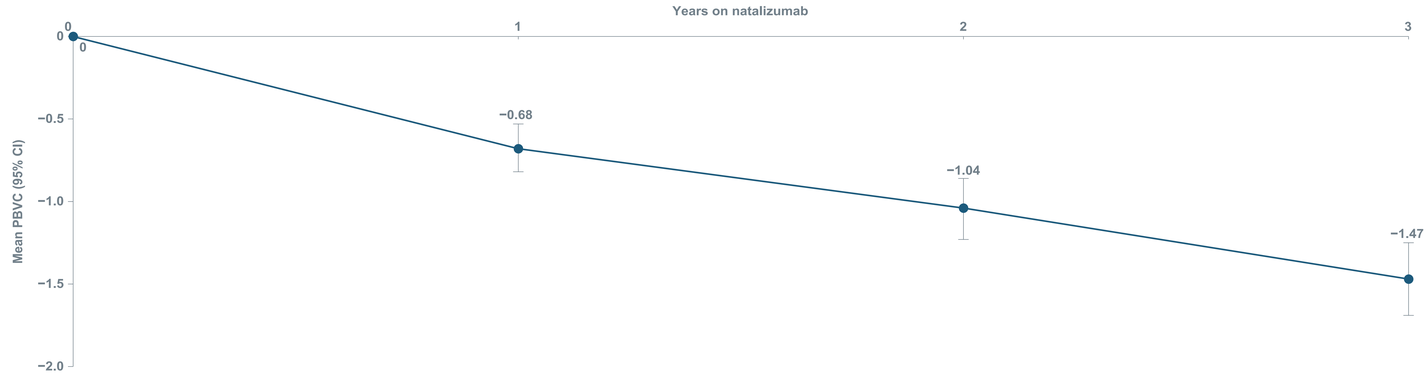
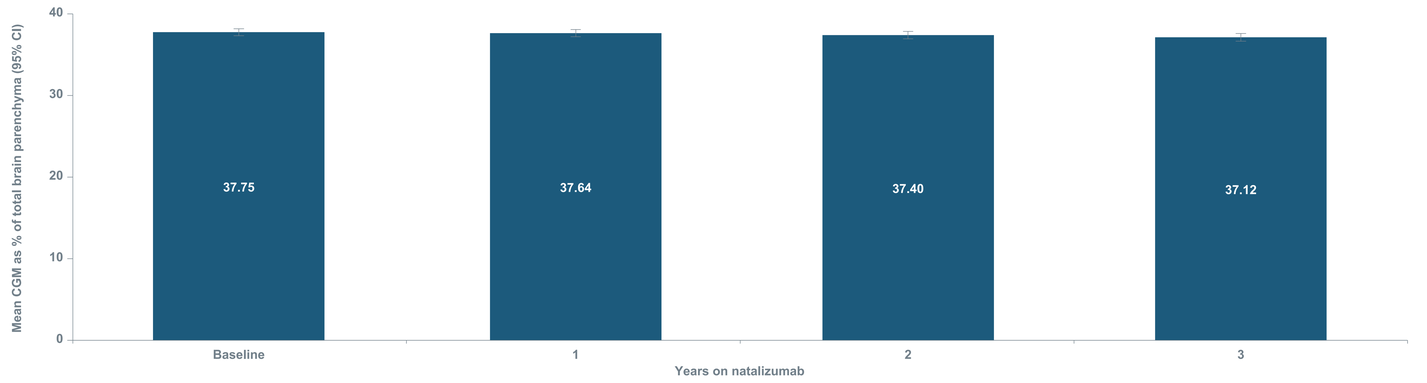


Figure 2. Mean CGM fraction at 1, 2, and 3 years in the ITT population with complete data (n=120)



References 1. Miller DH, *et al. Neurology*. 2007;68:1390-1401; 2. Vidal-Jordana A, *et al. Mult Scler*. 2013;19:1175-1181; 3. Perumal J, *et al.* Presented at ECTRIMS; October 25–28, 2017; Paris, France. EP1787; 4. Perumal J, *et al.* Presented at ECTRIMS; October 25–28, 2017; Paris, France. P1264; 5. Pérez-Miralles F, *et al. Mult Scler*. 2013;19:1878-1886; 6. Rudick RA, *et al. Mult Scler*. 2000;6:365-372; 7. Deloire MSA, *et al. Neurology*. 2011;76:1161-1167; 8. Maghzi AH, *et al. Mult Scler Relat Disord*. 2014;3:720-727; 9. Polman CH, *et al. N Engl J Med*. 2006;354:899-910. **Disclosures** This study was funded by Biogen. JP: consulting fees from Acorda, Biogen, Genzyme, Teva. RJF: consulting fees from Actelion, Biogen, Genentech, Mallinckrodt, MedDay, Novartis, Teva, XenoPort; advisory board fees from Biogen, Novartis; grant/research support from Novartis. RB: consulting fees from Biogen, Sanofi, Teva; grant/research support from Biogen. LB: consulting fees from Biogen, Genzyme. SG: consulting fees from Biogen. CS, SS, XJ, EF, CH, LL: employees of and hold stock and/or stock options in Biogen. **Acknowledgments** All named authors meet the International Committee of Medical Journal Editors criteria for authorship for this poster and take responsibility for the integrity of the work as a whole. Biogen provided funding for editorial support in the development of this poster; Alison Adams, PhD, and Sally K. Laden, MS, of Ashfield Healthcare Communications (Middletown, CT) wrote the first draft of the poster based on input from authors, and Joshua Safran of Ashfield Healthcare Communications copyedited and styled the poster per congress requirements. Biogen reviewed and provided feedback on the poster to the authors. The authors had full editorial control of the poster and provided their final approval of all content.