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STRIVE study: Natalizumab in anti-JCV antibody seronegative patients with early MS

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INTRODUCTION

- Results from the TYSABRI® Observational Program (TOP) showed that natalizumab treatment was most effective in treatment-naïve patients[1] and in patients with lower Expanded Disability Status Scale (EDSS) scores[2]; however, the use of natalizumab in early multiple sclerosis (MS) has not been systematically studied.
- Natalizumab treatment is associated with a risk of progressive multifocal leukoencephalopathy (PML), a central nervous system infection caused by the JC virus (JCV).[3]
- Since the presence of anti-JCV antibodies is a known risk factor for PML,[3] the benefit/risk profile of natalizumab is enhanced when natalizumab is used to treat patients who test negative for anti-JCV antibodies.
- This poster presents the baseline characteristics of patients who were enrolled in the Study of TYSABRI in Early Relapsing-Remitting MS in Anti-JCV Antibody Negative Patients (STRIVE) as of March 8, 2013.

OBJECTIVES

- The primary objective of STRIVE is to assess characteristics associated with freedom from overall disease activity (no 24-week confirmed EDSS progression, no relapses, no gadolinium-enhancing [Gd+] lesions, and no new or enlarging T2-hyperintense lesions) at years 1 and 2 and freedom from clinical disease activity (no 24-week confirmed EDSS progression and no relapses) at years 3 and 4 in natalizumab-treated patients with relapsing-remitting MS (RRMS).

METHODS

Study design

- STRIVE is a phase 4, prospective, multicenter, single-arm, single-country, 4-year observational study of patients who are initiating natalizumab. Enrollment started in December 2011. Approximately 300 patients at 60 US centers are planned to be enrolled.
- Patients receive natalizumab 300 mg intravenously every 4 weeks.
  - The initial TYSABRI infusion could be given anytime after the baseline assessments were completed. It was preferred that the first natalizumab infusion be administered on the same day as the baseline visit or within 2 weeks after the baseline visit date.
- Key inclusion criteria include:
  - Patients 18–65 years of age with an RRMS diagnosis of ≤3 years' duration;
  - EDSS score ≤4.0;
  - Negative test result for anti-JCV antibodies within 6 months of screening visit or at baseline visit, with patients who converted to anti-JCV antibody positive status during the course of the study allowed to continue on natalizumab at the discretion of the treating neurologist;
  - Treatment naïve to disease-modifying therapy (DMT) or treated with DMT (including but not limited to intramuscular interferon beta-1a [IM IFNβ-1a], subcutaneous [SC] IFNβ-1b, SC IFNβ-1a, glatiramer acetate [GA], or fingolimod) for ≤36 months total prior to date of informed consent;
  - The decision to treat with natalizumab having preceded enrollment;
  - Satisfying the approved therapeutic indications for natalizumab.
- Key exclusion criteria include:
  - Any prior treatment with natalizumab;
  - Anti-JCV antibody positive at any time point prior to screening;
  - Contraindications to treatment with natalizumab as described in the US prescribing information;
  - History of PML or other opportunistic infections, or an increased risk for such infections;
  - History of diagnoses of primary progressive MS and/or secondary progressive MS;
  - Receiving immunomodulatory or immunosuppressive therapy or had prior history of immunosuppressive use.

Assessments

- Additional endpoints included:
  - Identification of prognostic factors at baseline that predict overall disease-free status at month 12, and yearly factors that predict overall disease-free status at month 24;
  - Identification of prognostic factors at baseline that predict clinical disease-free status at month 12, and yearly clinical factors that predict clinical disease-free status (relapse, EDSS) in subsequent years at months 24, 36, and 48;
  - Determination of:
    - Clinical disease-free status, annualized relapse rate, confirmed EDSS progression and improvement, and magnetic resonance imaging measures (T2, T1, T1 with Gd enhancement, brain atrophy) annually at months 12, 24, 36, and 48;
    - Retinal nerve fiber layer thickness (measured by optical coherence tomography [OCT]) and low-contrast visual acuity performed in a subset of 100 patients at months 24 and 48 and change from baseline;
    - Patient-reported outcomes, including cognitive impairment (as measured by the Symbol Digit Modalities Test [SDMT]), capacity for work (as measured by Work Productivity and Activity Improvement questionnaire), and quality of life (as measured by the Multiple Sclerosis Impact Scale-29) annually at months 12, 24, 36, and 48 and change from baseline.

Analyses of baseline characteristics

- This interim analysis represents data collected as of March 8, 2013.
- The following baseline data were summarized by frequency and percentage:
  - Demographics and clinical characteristics;
  - MS disease history;
  - Past medical conditions;
  - Disease characteristics;
  - MS treatment history.

RESULTS

- As of March 8, 2013, 80 patients have been enrolled. One patient discontinued treatment due to an adverse event.
- Baseline data for the enrollment population are presented.
- Mean (standard deviation [SD]) age was 32.0 (7.29) years; the majority of patients (78.8%) were female (Table 1).

Table 1: Baseline demographics and characteristics for enrolled patients

Demographic and clinical characteristics	Patients (N=80)
Age, mean (SD)	32.0 (7.29)
Gender, n (%)	
Female	63 (78.8)
Male	17 (21.3)
Race, n (%)	
Asian	1 (1.3)
Black or African American	12 (15.0)
White	64 (80.0)
Other	3 (3.8)

- Among past medical conditions reported by patients, the most common were neurological (35.0%, n=28), psychosocial (32.5%, n=26), genitourinary (28.8%, n=23), allergic (26.3%, n=21), and HEENT (head, ears, eyes, nose, throat) (26.3%, n=21) in nature.
- Mean time from first symptoms of MS was 2.0 years; mean time from MS diagnosis was 0.7 years (Table 2).
  - In the previous 12 months, the mean number of relapses was 1.5.
- The mean (SD) baseline EDSS score was 1.9 (0.99); mean (SD) Multiple Sclerosis Severity Score (MSSS) was 4.5 (2.47) (Table 3).
- The majority of patients (53.8%, n=43) had no Gd+ lesions at baseline (Figure 1).

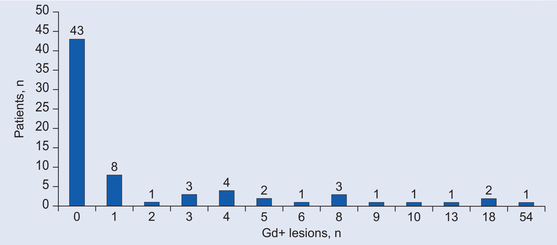
Table 2: MS disease history for patients enrolled

Disease history	Patients (N=80)
Time from first MS symptom (years)	
n	73
Mean (SD)	2.0 (2.39)
Median (min, max)	1 (0, 11)
Time from diagnosis of MS (years)	
n	73
Mean (SD)	0.7 (0.81)
Median (min, max)	1 (0, 3)
Relapses experienced within the past 12 months	
n	80
Mean (SD)	1.5 (0.97)
Median (min, max)	1 (0, 5)
Relapses experienced within the past 2 years	
n	80
Mean (SD)	1.7 (1.23)
Median (min, max)	2 (0, 7)

Table 3: Baseline disease characteristics for patients enrolled

Baseline disease characteristics	Patients (N=80)
EDSS score	
n	80
Mean (SD)	1.9 (0.99)
Median (min, max)	2 (0, 4)
MSSS score	
n	72
Mean (SD)	4.5 (2.47)
Median (min, max)	5 (0, 9.1)
SDMT score	
n	74
Mean (SD)	53.3 (13.77)
Median (min, max)	54.5 (13, 97)
T1 lesion volume (mL)	
n	70
Mean (SD)	1.5 (2.89)
Median (min, max)	1 (0, 16)
T2 lesion volume (mL)	
n	70
Mean (SD)	6.3 (7.77)
Median (min, max)	4 (0, 38)
Cortical grey matter atrophy (mL)	
n	70
Mean (SD)	38.1 (2.31)
Median (min, max)	38 (33, 43)
Normalized brain volume (mL)	
n	70
Mean (SD)	1,562,406.1 (69,620.36)
Median (min, max)	1,560,510 (1,362,948, 1,733,284)

Figure 1: Number of Gd+ lesions at baseline



- A total of 48.8% (n=39) of patients in the study had received prior MS treatment, with a mean (SD) treatment duration of 203 (152.7) days (Table 4).
  - Of the patients who received prior treatment, 71.8% had received GA (48.7%, n=19) and/or IM IFNβ-1a (23.1%, n=9).

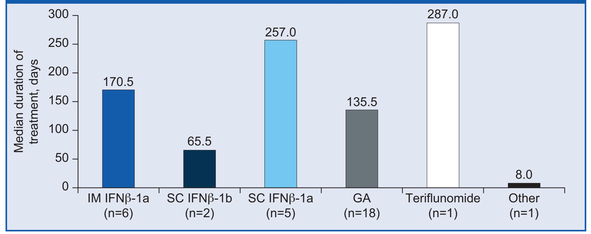
Table 4: MS treatment history for patients enrolled

Prior treatment	Patients (N=80)
Received any prior MS treatment, n (%)	39 (48.8)
Duration of all prior MS treatment, days[a]	N=31
Mean (SD)	203 (152.7)
Median (min, max)	190 (4, 732)
Number with prior MS treatment, n (%)	N=39
IM IFNβ-1a	9 (23.1)
SC IFNβ-1b	4 (10.3)
SC IFNβ-1a	7 (17.9)
GA	19 (48.7)
Teriflunomide	1 (2.6)
Other	1 (2.6)

[a]Total duration is calculated by summing the durations of all treatments but excluding any gaps and overlaps between treatments.

- The median duration of treatment varied among prior MS treatments, ranging between 8 days and 287 days (Figure 2).

Figure 2: Median duration of prior MS treatment by therapy



CONCLUSIONS

- The anti-JCV antibody negative patients enrolled in STRIVE have relatively low levels of disability, similar to patients who participated in the phase 3 natalizumab monotherapy trial (AFFIRM),[4] and a relatively short disease duration, allowing for further systematic examination of natalizumab use in early MS.
- This study will provide data on patient characteristics that most reliably predict freedom from disease activity in anti-JCV antibody negative patients over 2–4 years.
- This information may assist in benefit/risk–based treatment decisions for anti-JCV antibody negative patients with early RRMS.

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