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DX01 Disability Progression in Multiple Sclerosis Patients in the TYSABRI® (Natalizumab) Observational Program (TOP)

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Disclosures

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2

Background and Objective

- TOP is an ongoing, open-label, 10-year prospective study of patients with relapsing-remitting multiple sclerosis (RRMS) in clinical settings in Europe, Australia, Argentina, and Canada[1]
- The majority of patients in TOP (89.2%) transitioned to natalizumab from glatiramer acetate or an interferon beta therapy, and 99% had ≥1 relapse in the year prior to transitioning[2]
- The objective of this analysis was to assess rates of disability progression (assessed by the Expanded Disability Status Scale [EDSS]), in particular overall 24-week and 48-week confirmed ≥1-point and ≥2-point EDSS progressions, as well as transitions to EDSS scores of 3.0, 4.0, and 6.0 in patients with RRMS treated with natalizumab for at least 24 months in TOP
- In natural history cohorts, the median time for progression from an EDSS score of 4.0 to an EDSS score of 6.0 was 5.7 years for MS patients with a relapsing-remitting onset[3]

1. Butzkueven H et al. *J Neurol Neurosurg Psychiatry*. 2014 Feb [Epub ahead of print];
2. Biogen Idec, data on file;
3. Confavreux C et al. *N Engl J Med*. 2000;343:1430-1438.

Methods

- Patients were evaluated at regular clinic visits every 24 weeks
- Rates of confirmed EDSS progressions were evaluated over 24 and 48 weeks and were defined in 2 ways:
  - An increase of ≥1.0 point sustained for 24 or 48 weeks
  - An increase of ≥2.0 points sustained for 24 or 48 weeks
- Rates of 24- and 48-week confirmed progressions to the following EDSS milestones were also evaluated for the specified subgroups:
  - ≥3.0 for patients with baseline EDSS scores 0.0–2.0
  - ≥4.0 for patients with baseline EDSS scores 0.0–3.0 and 2.0–3.0
  - ≥6.0 for patients with baseline EDSS scores 0.0–5.0, 3.0–5.0, and 4.0–5.0
- Rates of 24- and 48-week confirmed EDSS progressions were evaluated in patients with and without on-treatment relapses during the study

Study Population

- As of May 1, 2013, 5122 patients were enrolled in TOP
  - Of the 5122 patients, 1506 (29.4%) had discontinued treatment, and 2599 had been treated for ≥24 months
- The analysis population comprised the 2588 patients with available baseline EDSS scores who had completed ≥24 months ("24-month completers")
  - 24-month completers received a median of 36 doses of natalizumab

5

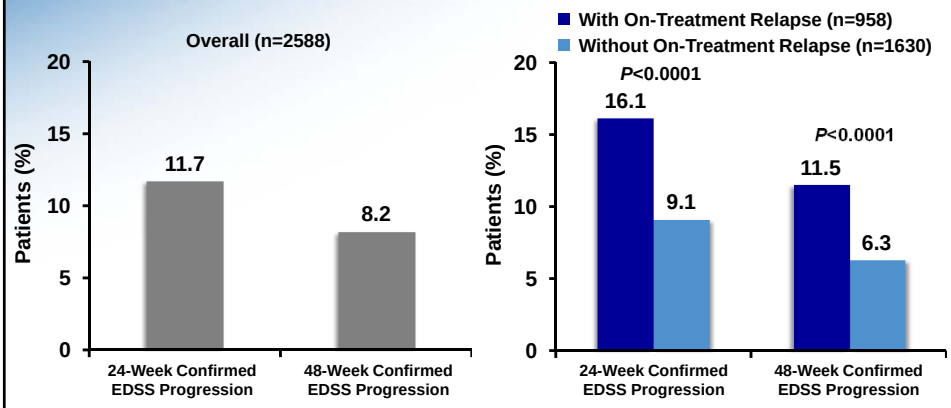
Baseline Characteristics of 24-Month Completers

Characteristic	N=2588
Age, mean (SD), years	37.2 (9.8)
Female, %	71
Relapses in prior year, mean (SD)	1.99 (1.03)
Number of relapses in prior year, n (%)	
≤1	910 (35)
>1	1678 (65)
≥1	2554 (99)
EDSS score, mean (SD)	3.4 (1.6)
Disease duration, median (range), years	7.2 (0–42.7)
Number of prior DMTs, n (%)	
0	213 (8.2)
1	1249 (48.3)
≥2	1126 (43.5)
Treatment duration prior to natalizumab, years	
Mean (SD)	4.0 (3.6)
Median (range)	3.1 (0–21.1)

SD=standard deviation; DMT=disease-modifying therapy.

6

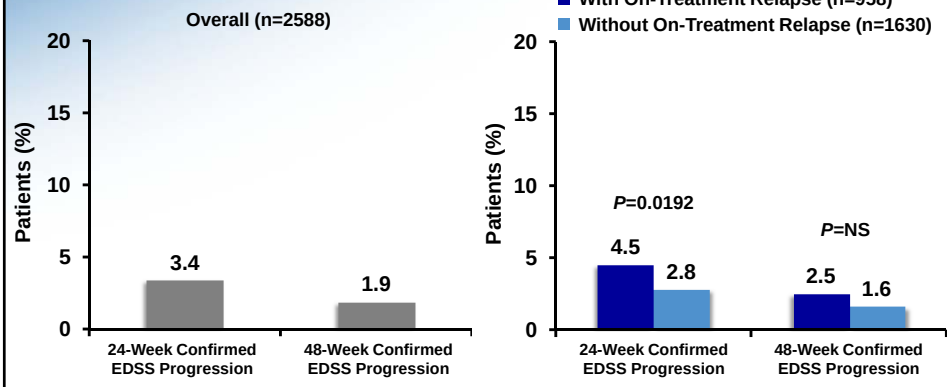
Overall Confirmed ≥1.0-Point EDSS Progression



The analysis population represents 2588 patients who completed ≥24 months of treatment out of 3336 patients who were expected to have completed ≥24 months as of May 1, 2013. 179/3336 (5.3%) patients had discontinued natalizumab treatment due to reported "lack of efficacy" and 569/3336 (17.1%) patients had discontinued treatment due to "reasons other than efficacy". Among patients who discontinued treatment because of reported "lack of efficacy," 11/179 (6.1%) had a 24-week confirmed EDSS progression when EDSS assessment records were included for up to 6 months since the last infusion of natalizumab to allow 6-month confirmation of the EDSS progression if there was any. A Kaplan-Meier analysis showed no difference in the probability of 24-week confirmed EDSS progression between the 2588 patients of the analysis population who completed ≥24 months of treatment and those who discontinued treatment due to "reasons other than efficacy."

7

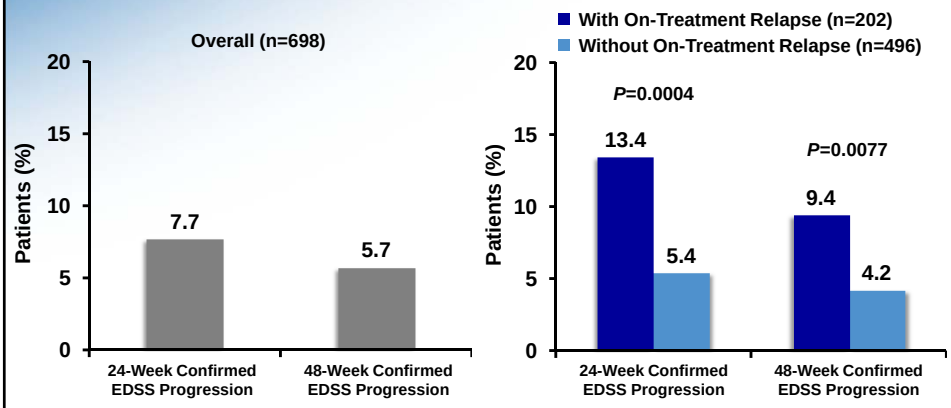
Overall Confirmed ≥2.0-Point EDSS Progression



NS=not significant.

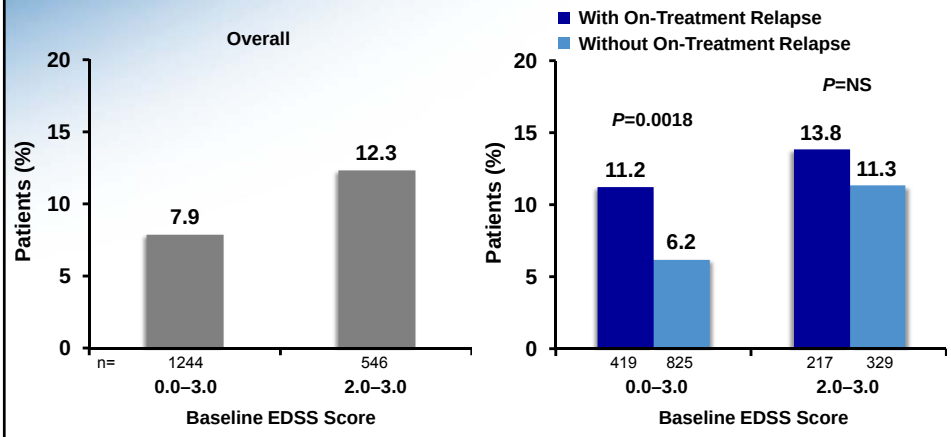
8

Confirmed Progression to an EDSS Score ≥3.0 in Patients with Baseline EDSS Scores 0.0–2.0



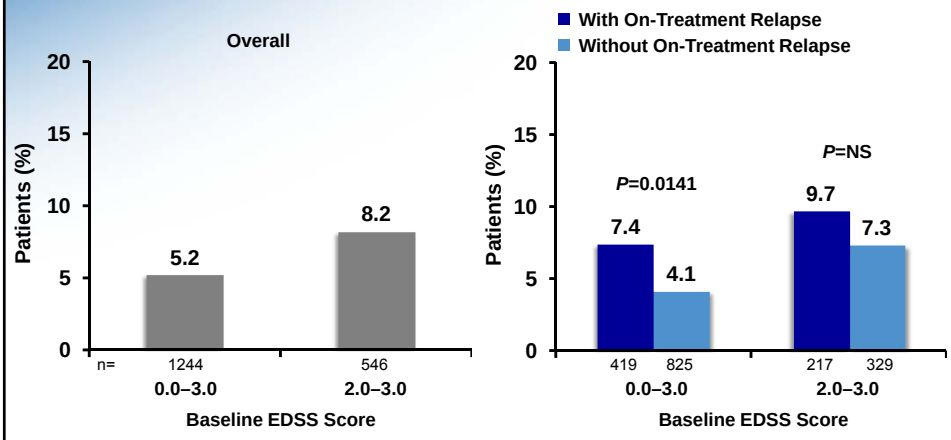
9

24-Week Confirmed Progression to an EDSS Score ≥4.0 Stratified by Baseline EDSS Score



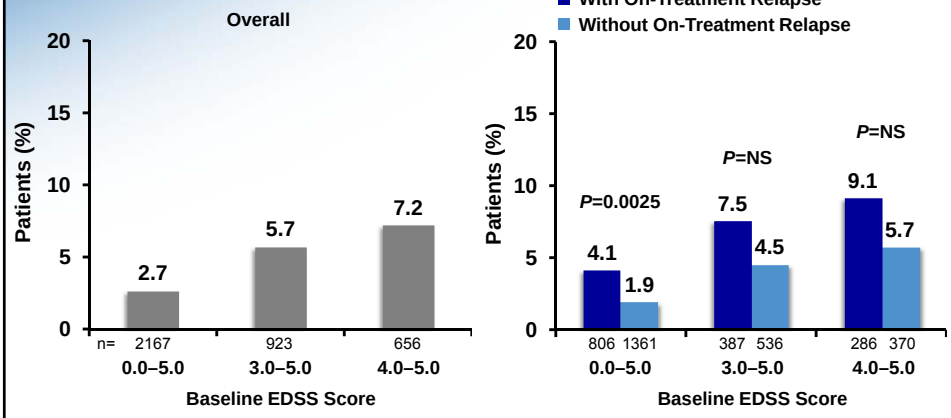
10

48-Week Confirmed Progression to an EDSS Score ≥4.0 Stratified by Baseline EDSS Score



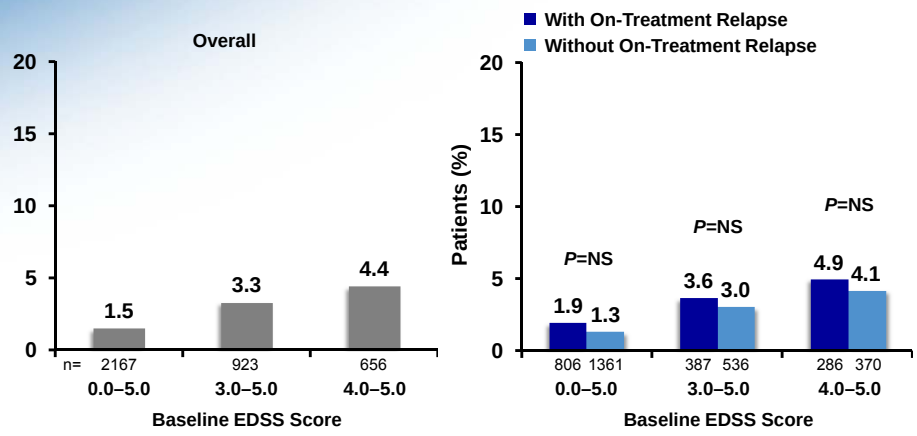
11

24-Week Confirmed Progression to an EDSS Score ≥6.0 Stratified by Baseline EDSS Score



12

48-Week Confirmed Progression to an EDSS Score ≥6.0 Stratified by Baseline EDSS Score



13

Summary and Conclusions

- With long-term natalizumab treatment in TOP and after a median exposure time of approximately 3 years (36 infusions):
  - Rates of 48-week confirmed EDSS progression were consistently lower than rates of 24-week confirmed EDSS progression
    - 92% of patients were free from 48-week confirmed ≥1-point EDSS progression, and 98% of patients were free from 48-week confirmed ≥2-point EDSS progression
  - Rates of disease progression to significant disability milestones were low
    - The rate of progression to an EDSS score ≥4.0 was lower for relapse-free patients than for patients with on-treatment relapses, whereas the rate of progression to an EDSS score ≥6.0 was low overall and was not significantly impacted by the persistence of relapses
  - The low rate of 48-week confirmed ≥1.0-point EDSS progression in the absence of relapse (6.3%) and the low rate of 48-week confirmed progression from EDSS 4.0–5.0 to EDSS ≥6.0 (4.4%) suggest a low level of secondary progression of the disease in patients treated with natalizumab

14