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DX03 No Evident Disease Activity (NEDA): Associations with Brain Atrophy and Functional Outcomes in Patients from the AFFIRM Study

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Disclosures

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- EF has received compensation from Biogen Idec, Genzyme/Sanofi, and Novartis for consulting services and research funding from the National Institutes of Health, Biogen Idec, and Genzyme/Sanofi
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Background

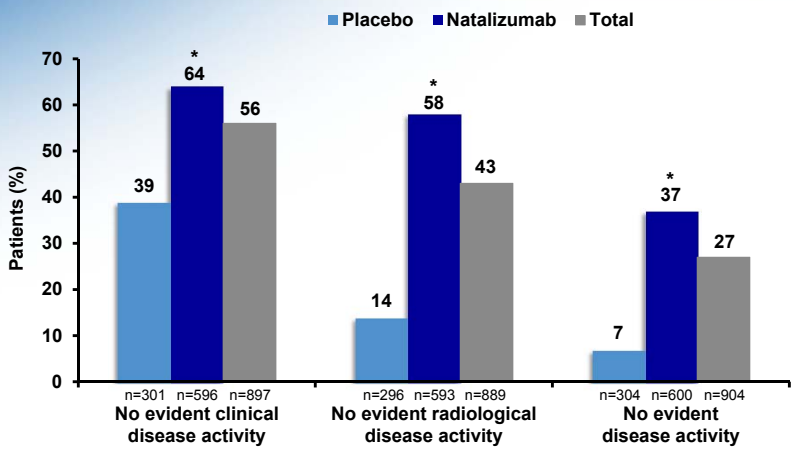
- The phase 3 AFFIRM study was the first study to report the proportion of patients with no evident disease activity (NEDA)[1]
  - NEDA has since become a treatment target for other therapies[2–7]
  - NEDA status has been associated with better scores on measures of physical aspects of quality of life[8]
- In AFFIRM, NEDA was defined as

- No relapses	*Clinical NEDA*
- No Expanded Disability Status Scale (EDSS) progression (12-week confirmed)	
- No gadolinium-enhancing (Gd+) lesions	
- No new/enlarged T2 lesions	*Radiological NEDA*

- 27% of patients in the natalizumab and placebo groups combined had NEDA over 2 years[1]

1. Havrdova et al. *Lancet Neurol*. 2009;8:254-260; 2. Kappos et al. Presented at AAN; April 9–16, 2011; Honolulu, HI; 3. Giovannoni et al. *Lancet Neurol*. 2011;10:329-337. 4. Giovanni et al. Presented at AAN; April 21–28, 2012; New Orleans, LA; 5. Freedman et al. Presented at AAN; April 21–28, 2012; New Orleans, LA. PD05.007; 6. Havrdova. *Mult Scler*. 2013 [Epub ahead of print]; 7. Kieseier et al. Presented at ECTRIMS; October 2–5, 2013; Copenhagen, Denmark; 8. Bates D et al. Presented at CMSC; May 27–30, 2009; Atlanta, GA. PS34.

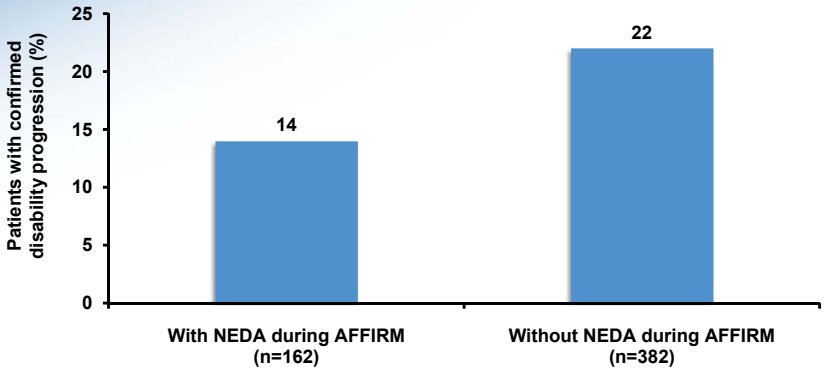
NEDA Status over 2 Years in AFFIRM



**P*<0.0001 for comparison between natalizumab and placebo.
No evident clinical disease activity was defined as no relapse and no 12-week confirmed EDSS progression; no evident radiological disease activity was defined as no Gd+ lesions and no new/enlarged T2 lesions.
Havrdova et al. *Lancet Neurol*. 2009;8:254-260.

Long-Term Disability Progression by NEDA Status During AFFIRM

- Confirmed disability progression 4 years after AFFIRM was less prevalent in patients with NEDA during AFFIRM than in patients without NEDA



Observed proportion was irrespective of length of follow-up up to 4 years. Confirmed disability progression was defined as an increase in EDSS score of ≥0.5 point from a baseline EDSS score ≥6.0 or ≥1.0 point from a baseline EDSS score ≥1.0 and <6.0 or ≥1.5 points from a baseline EDSS score of 0.0, lasting for at least 12 weeks.
Rudick RA et al. Presented at ECTRIMS; October 19–22, 2011; Copenhagen, Denmark: P513.

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Objectives and Methods

- To investigate the relationship between NEDA and measures of brain atrophy and functional outcomes in patients with RRMS from the AFFIRM study[1]
- Natalizumab and placebo groups were combined
- Outcomes were compared for patients with NEDA (n=242) and patients without NEDA (n=662) throughout the 2-year AFFIRM study using a rank-based analysis of covariance (ANCOVA) adjusting for the relevant baseline score

1. Polman CH et al. *N Engl J Med*. 2006;354:899-910.

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Outcome Measures

- Brain atrophy was measured by percent change in brain parenchymal fraction (BPF)
- Functional outcomes were measured by changes in actual scores for:
  - Paced Auditory Serial Addition Test-3 (PASAT)
  - Timed 25-Foot Walk (T25FW)
  - 9-Hole Peg Test (9HPT)

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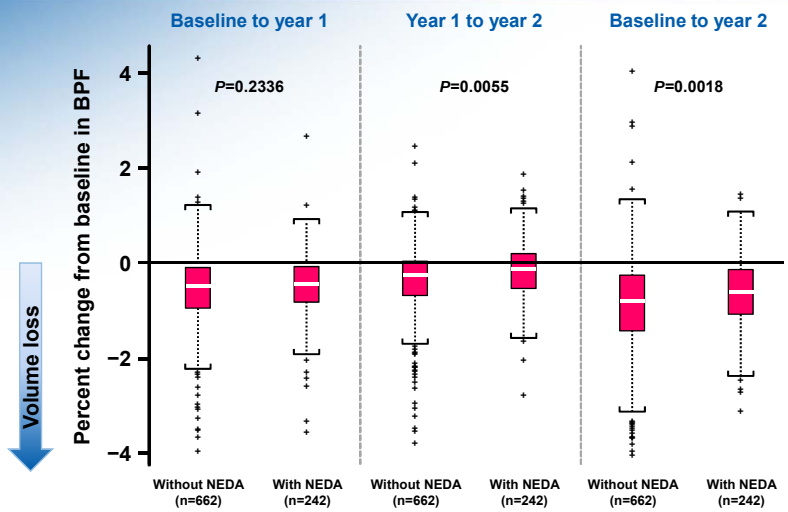
Percent Change in BPF by NEDA Status



Outliers with values less than −4 or greater than 4 were excluded from the plots. For the percent change from baseline to year 1, in the group without NEDA, 1 observation was greater than 4 (4.5). For the percent change from baseline to year 2, in the group without NEDA, 4 observations were less than −4, ranging from −7.3 to −4.3.

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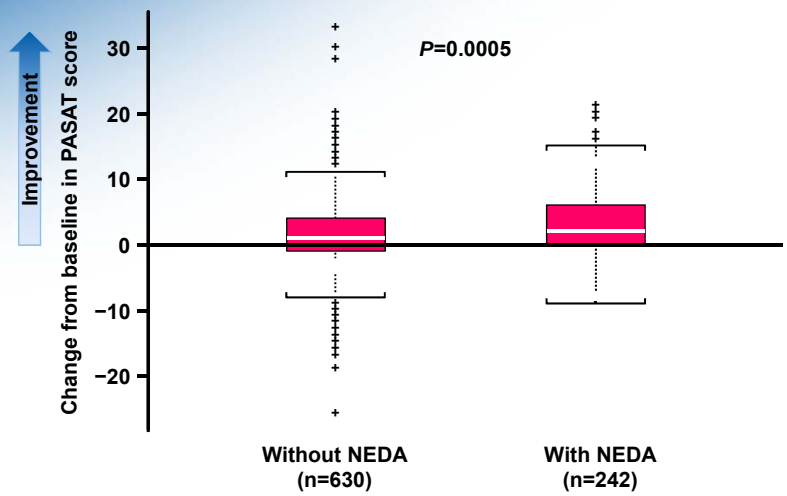
Change in PASAT Scores over 2 Years by NEDA Status



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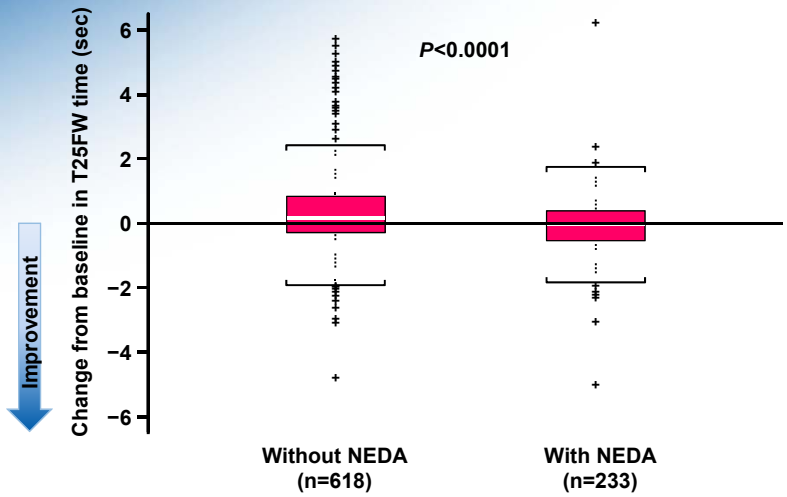
Change in T25FW Time over 2 Years by NEDA Status



Outliers with values less than −7 or greater than 7 were excluded from the plot. In the group without NEDA, 2 observations were less than −7 (−16.95 and −12.2), and 13 observations were greater than 7, ranging from 7.8 to 41.8. In the NEDA group, 3 observations were greater than 7, ranging from 14.1 to 15.95.

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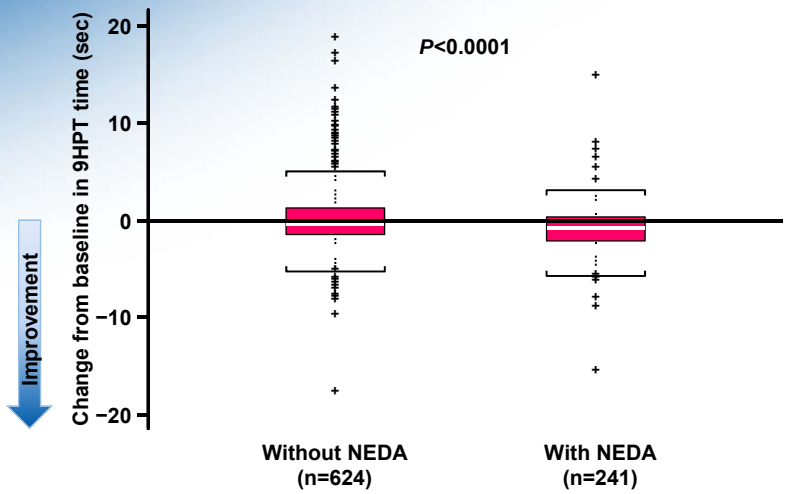
Change in 9HPT Time over 2 Years by NEDA Status



Outliers with values less than −20 or greater than 20 were excluded from the plot. In the group without NEDA, 1 observation was less than −20 (−52.375) and 2 observations were greater than 20 (24.175 and 52.025).

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Conclusions

- Patients with NEDA had less brain atrophy over 2 years than patients without NEDA
- Patients with NEDA had significantly better results on the functional outcomes of cognition, walking speed, and upper extremity function than patients without NEDA

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Implications and Future Directions

- This is the first report demonstrating favorable outcomes using brain atrophy and performance measures in patients with NEDA
- Long-term follow-up studies are needed to determine whether the benefits of NEDA observed during this 2-year trial increased or attenuated over time
- NEDA may be an excellent single-outcome measure for relapsing MS studies because it combines imaging, relapse, and EDSS outcomes, and it correlates with performance measures and brain atrophy

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