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

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Disclosures and Acknowledgments

Disclosures
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- AP and SB are employees of Biogen Idec

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

- 27% of patients in the natalizumab and placebo groups combined had NEDA over 2 years\(^1\)

![NEDA Status over 2 Years in AFFIRM](image)

2. Kappos et al. Presented at AAN; April 9–16, 2011; Honolulu, HI.
5. Freedman et al. Presented at AAN; April 21–28, 2012; New Orleans, LA; PD05.007.
7. Kieseier et al. Presented at ECTRIMS; October 2–5, 2013; Copenhagen, Denmark.

\(^*\)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.
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.

James et al. Presented at ECTRIMS; October 19–22, 2011; Copenhagen, Denmark: P513.

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.

- 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.

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)

Percent Change in BPF by NEDA Status

<table>
<thead>
<tr>
<th>Baseline to year 1</th>
<th>Year 1 to year 2</th>
<th>Baseline to year 2</th>
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<tbody>
<tr>
<td>Without NEDA (n=662)</td>
<td>With NEDA (n=242)</td>
<td>Without NEDA (n=662)</td>
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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.
Change in PASAT Scores over 2 Years by NEDA Status

Change from baseline in PASAT score

-20 -10 0 10 20 30

Without NEDA (n=630) With NEDA (n=242)

P=0.0005

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Change in T25FW Time over 2 Years by NEDA Status

Change from baseline in T25FW time (sec)

-6 -4 -2 0 2 4 6

Without NEDA (n=618) With NEDA (n=233)

P<0.0001

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.
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).

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
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.