The inclusion of cognitive evaluation into NEDA3 (NEDA3/Co) further confirms the high efficacy of natalizumab in MS

Puthenparampil M, Federle L, Riccardi A, Cazzola C, Rinaldi F, Perini P, Pallo G

Introduction. Neuropsychological effects of NTZ are controversial. An improvement on Brief Repeatable Battery of Neuropsychological Tests and on self-reporting questionnaires has been described, but was not confirmed on Wisconsin Cart Sorting Test. However, the major limitation of these studies is the small number of RRMS patients included.

Aims. To evaluate clinical, neuropsychological and radiological data on a large cohort of MS patients treated with NTZ.

Materials and Methods. NTZ-treated patients were enrolled in a two-year longitudinal study. At therapy initiation, brain MRI, neurological examination by means of the expanded disability status scale (EDSS) and neuropsychological assessment by means of the Brief Repeatable Battery of Neuropsychological Tests (BRB-NT) were performed. Thereafter, EDSS evaluation was performed every 6 months, brain MRI every year and neuropsychological assessment at the end of the follow-up. NEDA-3 was evaluated at the end of follow up and was defined as no evidence of clinical activity (i.e., no relapse and no increase in EDSS= *clinically silent patient*, CS) and no evidence of MRI activity (i.e., no evidence of new/enlarging T2 lesions, no evidence of gadolinium enhancing lesions= *radiologically silent patient*, RS). MS patients with no evidence of cognitive decline (no evidence of cognitive impairment in at least one further item) at year 2 were defined as neuropsychological silent (NS) patients.

Results. On May 2017, 123 patients concluded the two-year follow-up: 80.9% were CS (Figure 1A) and 67.0% were RS (Figure 1B).
Seventy-three MS patients (59.2%) were NEDA-3 (Figure 1C), and 23.4% were also NEDA-3/NS (Figure 1D).
CS, RS, NS and NEDA-3 percentages did not differ between treatment-naïve and previously-treated patients. NS rates did not matched to CS or RS rates.
No clinical parameter at baseline was found to predicted NEDA-3/NS.
However, normal Word List Generation test at therapy initiation was associated to a higher probability of NEDA-3/NS (OR 4.95, $IC_{95\%}$ 1.3-18.8, $p<0.05$).

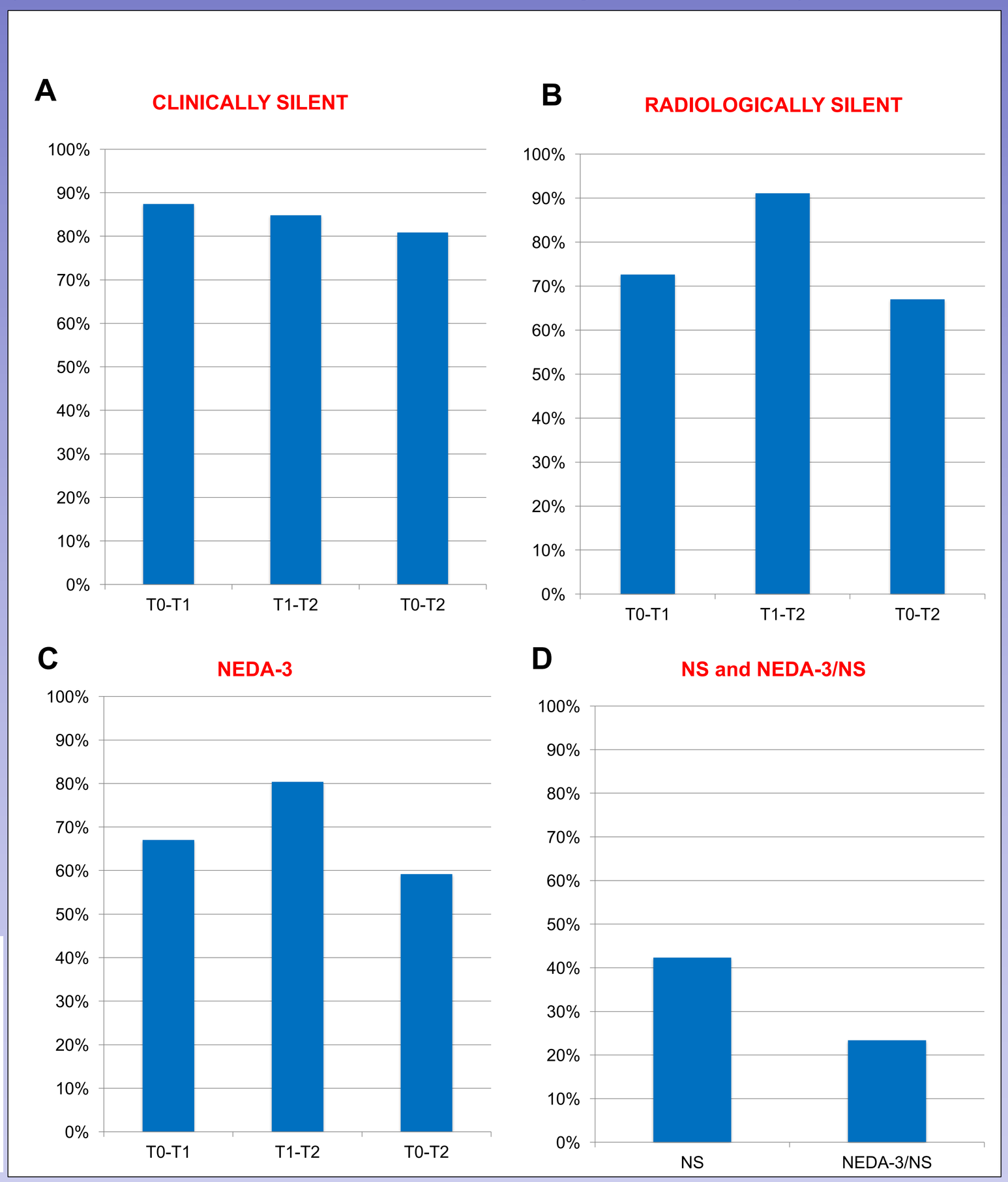

Figure 1. In clinical outcomes (A), natalizumab loss of effectiveness during two years of follow-up. The RS (B) and NEDA-3 (C) patients rates increased in the second year of treatment. At T2, 42.3% of all patients was NS (D), and this rate represented the 80.5% of NEDA-3 patients. At the end of the study, 23.4% of all patients were CS, RS and NS.

Conclusions. The inclusion of cognitive evaluation into NEDA-3 further proved the high efficacy of NTZ in MS patients. Since cognitive decline in MS is mainly related to cortical grey matter damage, the incorporation of cognitive impairment into NEDA-3 may help to monitor the effect of therapies on the neurodegenerative component of MS.

Puthenparampil Marco received travel grant from Novartis, Genzyme, Biogen Idec, Teva and Sanofi Aventis; he has been consultant for Genzyme. Rinaldi Francesca serves as an advisory board member of Biogen-Idec and has received funding for travel and speaker honoraria from Merck Serono, Biogen Idec, Sanofi-Aventis, Teva, Novartis and Genzyme Sanofi and Bayer Schering Pharma. Federle Lisa has received funding for travel from Novartis, Merck Serono, Biogen Idec, Sanofi-Aventis, Bayer Schering Pharma, Almirall, Genzyme, Teva and honoraria from MerkSerono, Teva and Almirall. Perini Paola has received funding for travel and speaker honoraria from Merck Serono, Biogen Idec, Sanofi-Aventis, and Bayer Schering Pharma and has been consultant for Merck Serono, Biogen Idec and Teva. Gallo Paolo has been a consultant for Bayer Schering, Biogen Idec, Genzyme, Merck Serono and Novartis; has received funding for travel and speaker honoraria from Merck-Serono, Biogen Idec, Sanofi-Aventis, Novartis Pharma and Bayer-Schering Pharma, Teva; has received research support from Bayer, Biogen Idec/Elan, MerkSerono, Genzyme and Teva; and has received research grant from the University of Padova, Veneto Region of Italy, the Italian Association for Multiple Sclerosis, the Italian Ministry of Public Health.