

Treat to target disability reduction in multiple sclerosis: experience with monoclonal antibody therapy

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INTRODUCTION

Disability reduction can be observed in 20-30% of patients with relapsing-remitting multiple sclerosis (RRMS) treated with monoclonal antibodies (MABs), namely natalizumab and alemtuzumab. This suggests that the robust anti-inflammatory effects driven by MABs may promote endogenous remyelination mechanisms, leading to partial functional recovery in some patients. Therefore, the identification of baseline predictors for disability reduction deserves further investigation.

OBJECTIVE

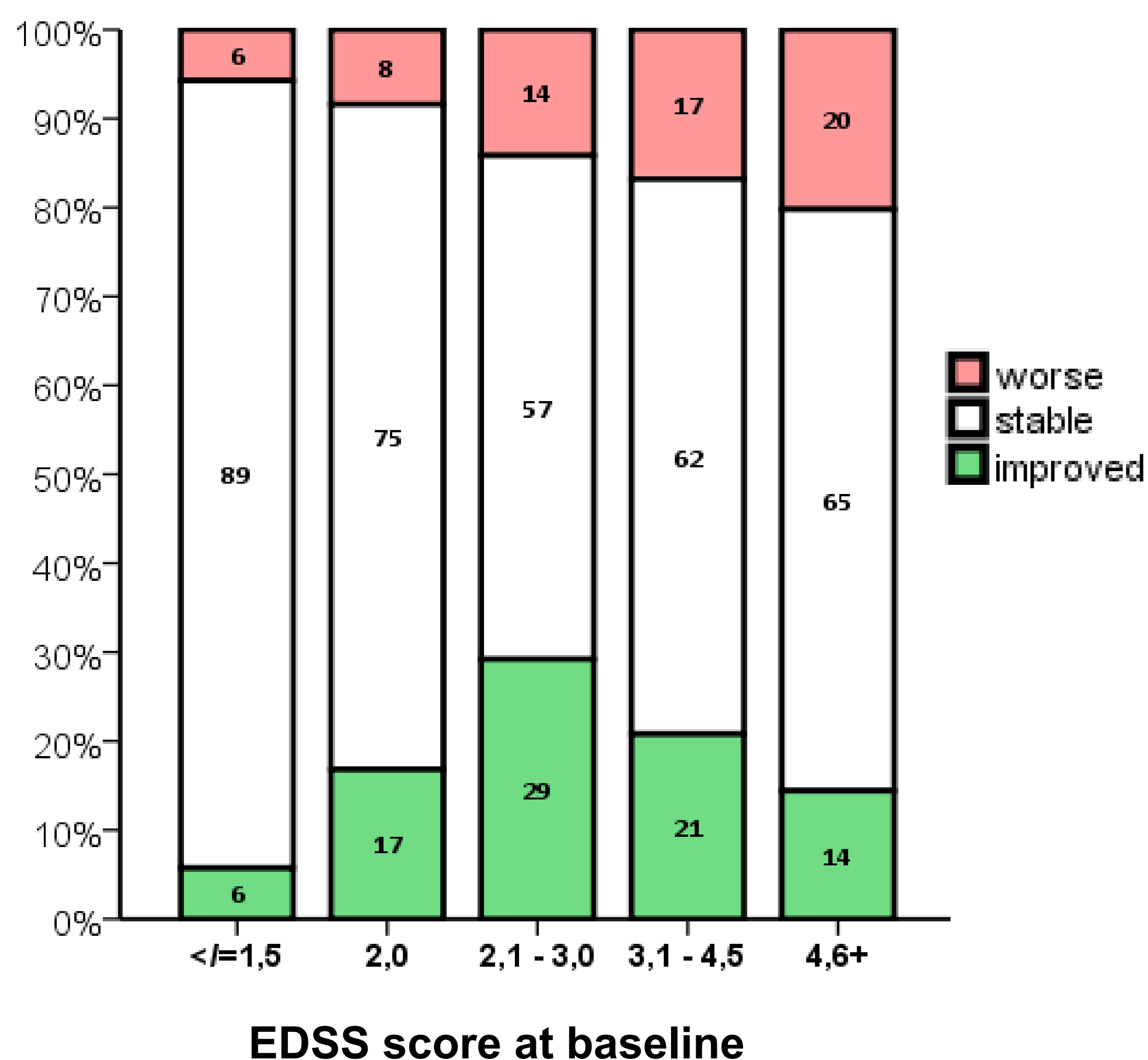
To explore which baseline variables are associated with disability reduction after natalizumab start.

METHODS

We prospectively collected data of RRMS patients starting natalizumab and followed up to 24 months according to an intention-to-treat approach. Changes in Expanded Disability Status Scale (EDSS) score were calculated at the end of the follow-up versus baseline and categorized as follows: disability reduction (≥ 1 -step EDSS decrease), stable disability (no change or ± 0.5 -point EDSS change); disability worsening (≥ 1 -step EDSS increase). The probability of disability reduction was plotted across each pre-treatment EDSS step. A classification and regression tree analysis (CART) was carried out to best discriminate patients with disability reduction over all potential baseline predictors.

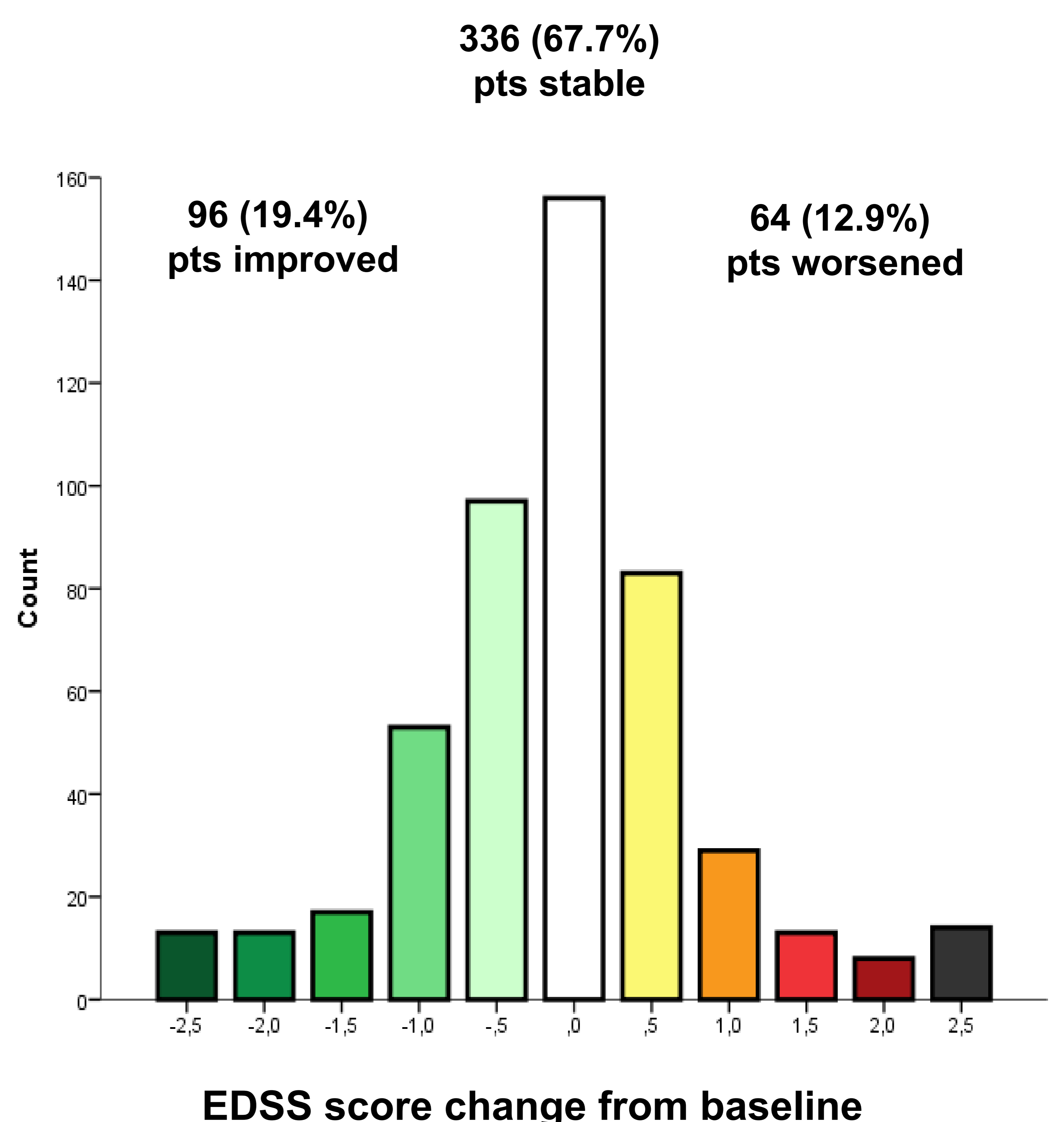
Baseline patients' characteristics (N= 496)

Male gender, n (%)	156 (31.5%)
Mean age (SD)	36.2 (9.5)
Time since first symptom, years	
Mean (SD)	8.6 (6.0)
Median EDSS score [range]	3.0 [1.0-8.5]



RESULTS

We collected data of 496 (340 women, 156 men) with a mean age of 36.2 \pm 9.5 years, mean time since first symptom of 8.6 \pm 6.0 years, and median EDSS score of 3.0 (range 1.0-8.5). At follow-up, disability reduction was observed in 96 (19.4%), stable disability in 336 (67.7%), and disability worsening in 64 (12.9%) patients. The probability of disability reduction showed an inverted U-shaped distribution, being higher at intermediate EDSS steps (EDSS 3.0-4.0). The CART analysis revealed distinct baseline predictors for disability reduction according to the pre-treatment EDSS score, i.e. a lower number of pre-treatment relapses in patients scoring less than 3.0 (adjusted-p=0.009) and a younger age in those ones scoring equal or above 3.0 (adjusted-p=0.017). Lastly, a shorter disease duration could be still associated with increased likelihood of disability reduction even in older patients with higher EDSS score (adjusted-p=0.008).



CONCLUSION

The detection of functional recovery may be challenging at low disability level, mainly due to the floor effect of the EDSS. Starting natalizumab after multiple relapses and age-related processes may independently preclude the potential of functional recovery.

References:

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