

Is NEDA a clinically relevant endpoint for therapeutic decisions? : Yes

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The gratifying development of new drugs for the treatment of MS has greatly broadened our therapeutic armamentarium over the past 10 years. Availability of more efficacious agents has also raised the bar and prompted definition of more ambitious treatment goals. Following an approach adopted by rheumatologists some time ago, the concept of treating to target has also been introduced in the management of MS. In the absence of curative therapies, earlier goals to reduce relapse rate and slow progression have been abandoned and redefined with the aim of silencing disease activity and halting disease progression. Proof of this comes from clinical assessment and MRI evaluation of disease activity and burden. The Disease activity freedom status (DAF) was first analyzed posthoc in the AFFIRM trial of natalizumab. Freedom from disease was operationally defined as absence of relapses, disease progression, gadolinium enhancing T1 lesions and new or enlarging T2 lesions. Havrdova et al could show superiority of natalizumab to placebo in attaining disease free status. Subsequently, completed phase 3 trials of new drugs were also analysed to determine what now is termed NEDA, no evidence of disease activity. Clearly, this aggregate outcome provides a more comprehensive view of the efficacy of a drug and is more sensitive to register impact of an agent than clinical or MR outcomes looked in isolation. More recently, in recognition of the importance of brain volume loss as a surrogate marker of the overall pathologic process and a predictor of disability, the composite NEDA 4 has been introduced integrating brain atrophy into the equation. There is discussion whether it might be possible to further enlarge the concept by adding measures of cognition, a very significant domain of neurological functioning impacted by the disease process. Looking at NEDA also aids in assessing relative efficacies of drugs in the absence of head-to-head trials.

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