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Abstract 1669

Baseline serum neurofilament light levels have prognostic value for on-study MRI activity: Results from ASCLEPIOS trials

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Background

In the ASCLEPIOS I/II trials, ofatumumab significantly lowered serum neurofilament light (sNfL) levels, a marker of disease activity and treatment response, in the first assessment at month 3 and at all subsequent visits versus teriflunomide.

Objectives

To investigate the prognostic value of baseline sNfL for on-study disease activity and worsening in patients with relapsing MS, particularly in newly diagnosed, treatment-naïve patients.

Methods

Patients (pooled N=1882) were randomized to ofatumumab or teriflunomide, receiving treatment for up to 30 months. Patients were stratified by median baseline sNfL levels. We assessed annual on-study T2 lesion formation and brain volume loss (BVL, Jacobian integration) by sNfL category in all patients and in the subgroup of newly diagnosed within 3 year of screening without prior disease-modifying treatment (representing natural course of sNfL and disease at baseline) at month 24 or end of study. The annualized rate of new or enlarging T2 (neT2) lesions in year-2 versus year-1 was assessed in all patients by sNfL category (negative binomial model with time [in year] as offset).

Results

Patients with high sNfL (>median) levels at baseline developed more neT2 lesions per year on study than patients with low (≤median) sNfL levels (adjusted mean rate: ofatumumab: 0.95 vs 0.39, relative increase 143%, $p<0.001$; teriflunomide 5.28 vs 3.02, relative increase 74.5%, $p<0.001$). The prognostic value of baseline sNfL persists for year-2 (high vs low, ofatumumab: 0.09 vs 0.06, 64.5%, $p=0.124$; teriflunomide 4.53 vs 3.12, 45.6%, $p=0.003$. A single sNfL assessment at baseline had no prognostic value for on-study relapses and disability worsening. Patients with high baseline sNfL had higher annualized rate of BVL than patients with low sNfL (ofatumumab: 0.32% vs 0.23%, relative difference 37.3%, $p=0.045$; teriflunomide: 0.43% vs 0.29%, relative difference 49.4%, $p<0.001$). The results were consistent in the subgroup of newly diagnosed, treatment-naïve patients. The relative treatment effect of ofatumumab versus teriflunomide was similar across all measures in both the high and low sNfL groups.

Conclusions

Baseline sNfL levels were prognostic for on-study lesion formation and BVL for at least 2 years, in all patients and in the subgroup of newly diagnosed, treatment-naïve patients. sNfL levels can supplement clinical assessments and help identify patients at high risk for future disease activity.

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