Abstracts

Articles appearing in the September 2017 issue

α 4-Integrin receptor desaturation and disease activity return after natalizumab cessation

Objective To describe the time course of α 4-integrin receptor desaturation and disease activity return in patients with relapsing-remitting multiple sclerosis who discontinued natalizumab and to investigate baseline and on-study predictors for the recurrence of disease activity.

Methods In the course of TOFINO, a 32-week, patient- and rater-blinded multicenter, parallel-group study, we performed MRI, counted relapses, and measured α 4-integrin receptor occupancy (RO) at baseline and 8, 12, 16, 20, and 24 weeks. The relationship between RO and total number of new T1 gadolinium-enhancing (Gd+) lesions was modeled using Poisson linear regression.

Results Patients ($n = 142$) were randomized (1:1:1) to 8-, 12-, or 16-week washout (WO) groups. At randomization, the median RO in the 8-, 12-, and 16-week WO groups was 94.5%, 92.4%, and 90.9%, which declined to 79.8%, 30.7%, and 8.7% after 8, 12, and 16 weeks of WO, respectively. The percentage of patients with new T1 Gd+ lesions increased with longer WO period before commencing fingolimod: 2.1% (8 weeks), 9.1% (12 weeks), and 50.0% (16 weeks). Overall, 71% of patients with first relapse between weeks 6 and 18 had RO values below the time-matched population median. Higher T2 lesion volume (LV) at baseline predicted a higher number of new T1 Gd+ lesions.

Conclusions A faster decline in natalizumab RO, longer WO period, and higher T2 LV at baseline were associated with an increased risk for return of inflammatory disease activity. These results provide a mechanistic rationale and, together with the main outcomes of the TOFINO study, support initiation of fingolimod within 8 weeks of natalizumab discontinuation.

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Teriflunomide slows BVL in relapsing MS: A reanalysis of the TEMSO MRI dataset using SIENA

Objective To assess, using structural image evaluation using normalization of atrophy (SIENA), the effect of teriflunomide, a once-daily oral immunomodulator, on brain volume loss (BVL) in patients with relapsing forms of multiple sclerosis (MS) enrolled in the phase 3 TEMSO study.

Methods TEMSO MRI scans were analyzed (study personnel masked to treatment allocation) using SIENA to assess brain volume changes between baseline and years 1 and 2 in patients treated with placebo or teriflunomide. Treatment group comparisons were made via rank analysis of covariance.

Results Data from 969 patient MRI visits were included in this analysis: 808 patients had baseline and year 1 MRI; 709 patients had baseline and year 2 MRI. Median percentage BVL from baseline to year 1 and year 2 for placebo was 0.61% and 1.29%, respectively, and for teriflunomide 14 mg, 0.39% and 0.90%, respectively. BVL was lower for teriflunomide 14 mg vs placebo at year 1 (36.9% relative reduction, $p = 0.0001$) and year 2 (30.6% relative reduction, $p = 0.0001$). Teriflunomide 7 mg was also associated with significant reduction in BVL vs placebo over the 2-year study. The significant effects of teriflunomide 14 mg on BVL were observed in patients with and without on-study disability worsening.

Conclusions The significant reduction of BVL vs placebo over 2 years achieved with teriflunomide is consistent with its effects on delaying disability worsening and suggests a neuroprotective potential.

Classification of evidence Class II evidence shows that teriflunomide treatment significantly reduces BVL over 2 years vs placebo.

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