

Reduced risk of progressive multifocal leukoencephalopathy (PML) associated with natalizumab extended interval dosing (EID): updated analysis of the TOUCH® Prescribing Program database

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Objective: To update the assessment of PML risk with natalizumab EID compared with standard interval dosing (SID) using TOUCH data as of June 1, 2018.

Background: Natalizumab treatment is associated with an increased risk of PML. A June 2017 analysis of the TOUCH dataset demonstrated that natalizumab EID was associated with significantly lower PML risk than SID in anti-JC virus (JCV) antibody positive multiple sclerosis patients.

Design/Methods: TOUCH data as of June 1, 2018, were used to assess the effect of EID/SID on PML risk using the three pre-planned analyses specified for the 2017 study: primary analysis (EID/SID over the last 18 months of doing history); secondary analysis (prolonged period of EID/SID occurring at any time); tertiary analysis (dosing history consisting primarily of EID/SID). Anti-JCV seropositive patients with dosing intervals of ≥ 3 to ≤ 12 weeks were included. PML hazard ratios (HRs) for EID and SID were compared using adjusted Cox regression models and Kaplan-Meier estimates.

Results: Compared with 2017, this update increased the number of patients in all 3 analysis groups (primary: 14,305 SID [8.9% increase] and 2266 EID [14.0% increase] patients; secondary: 16,648 SID [7.9% increase] and 3726 EID [11.9% increase] patients; tertiary: 24,870 SID [7.3% increase] and 931 [14.2% increase] EID patients). For all analyses, EID patients had longer median natalizumab exposure durations (months) (primary, 60 vs 44; secondary, 57 vs 26; tertiary, 43 vs 26) than SID patients. The PML HR (95% confidence interval) was 0.10 (0.03–0.27; $P < 0.001$) for the primary analysis and 0.20 (0.10–0.41; $P < 0.001$) for the secondary analysis (both in favor of EID). As in the 2017 analysis, no EID PML cases were observed in the tertiary analysis (Kaplan-Meier log-rank test $P = 0.011$).

Conclusions: Updated analyses of TOUCH data demonstrate that natalizumab EID is associated with significantly lower PML risk compared with SID.