Updated incidence of natalizumab-associated progressive multifocal leucoencephalopathy and its relationship with the pattern of natalizumab exposure over time

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Introduction: Since the 2012 identification of 3 risk factors for natalizumab-associated progressive multifocal leukoencephalopathy (PML)—presence of anti-JC virus (JCV) antibodies, prior immunosuppressant (IS) use, and longer treatment duration—changes in the PML incidence rate have been of interest. In a previous analysis using data as of December 2017, the overall incidence of natalizumab-associated PML was shown to be stable since mid-2016.

Objective: To update the natalizumab-associated PML incidence over time in the global postmarketing setting since introduction of the anti-JCV antibody assay and evaluate the relationship of PML incidence with natalizumab exposure over time.

Methods: The incidence of confirmed PML cases in Biogen's global safety database from November 2009 to July 2019 was evaluated retrospectively. Overall incidence in all exposed patients was determined by the estimated total number of patients ever exposed to natalizumab and the number of confirmed PML cases. Changes in natalizumab exposure patterns over time were evaluated by 12-infusion epochs.

Results: As of 31 July 2019, 201,384 patients worldwide had received ≥1 natalizumab dose (total exposure: 759,181 patient-years); overall natalizumab-associated PML incidence was 4.08/1000 patients. The increase in global incidence levelled off in mid-2016, remaining between 4.08-4.24/1000 patients over the last 41 months. PML incidence was greatest in the higher risk infusion epochs (37–48, 49–60, and 61–72). Since 2014 through 2018, PML incidence in these epochs decreased; however, the number of patients in the higher risk epochs increased over time.

Conclusions: These data confirm and extend previous findings (with 20 additional months of data) that overall global PML incidence in natalizumab-treated patients remained stable since

mid-2016. This stabilisation coincides with the introduction and publication of a new risk algorithm, suggesting that risk stratification factors are being incorporated into clinical practice and may continue to impact future PML incidence.