Abstract 1829

Update on the risk estimates of progressive multifocal leukoencephalopathy related to fingolimod

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Background

Progressive multifocal leukoencephalopathy (PML) is a serious and potentially fatal complication of some multiple sclerosis (MS) disease-modifying therapies, including fingolimod. Precise estimates and risk stratification tools are not available for fingolimod-related PML.

Objectives

To estimate the global risk of PML in MS patients receiving fingolimod, and to investigate the effect of treatment duration and age on the risk of PML.

Methods

The number of PML cases identified from the manufacturer safety database, attributed to fingolimod by expert adjudication (based on criteria published by Berger et al. in 2014) as of 28 February 2020, was compared with the estimated global number of fingolimod-treated patients at risk (overall, by treatment duration, and by assumed age at fingolimod treatment initiation).

Results

It was estimated that approximately 299,600 patients were treated with fingolimod globally as of 28 February 2020, corresponding to >778,900 patient-years (PYs) of exposure. Of the 188 suspected PML cases reported during fingolimod treatment, 37 confirmed cases were clearly attributed to fingolimod through expert adjudication. In 17 cases, PML was attributed to previous natalizumab treatment. The remaining 134 cases either had inadequate information to confirm the diagnosis of PML or were classified as either possible or not PML. The estimated incidence rate was 4.75 (95% confidence interval [CI]: 3.34; 6.55) per 100,000 PYs. The estimated crude incidence was 0.12 (95% CI: 0.09–0.17) per 1,000 patients. The incidence of PML appears to increase with treatment duration and approach a plateau at approximately 0.13 per 1,000 patients during Year 5, after which data were scarce. Incidence of PML appears to increase between 30 and 50 years of age and then stabilize but the exact shape of the relationship with age is uncertain due to wide CIs, underlying assumptions, and other unknown confounding factors. For both treatment duration and age at treatment initiation, the precision of the incidence estimates was low due to the small number of cases.

Conclusions

PML risk associated with fingolimod is low. Although, the estimated risk of fingolimod-associated PML appears to

increase with cumulative exposure, the precise pattern of this relationship remains uncertain. There may be an increase in PML risk with increased age at treatment initiation, although the exact pattern of this possible relationship is also uncertain.

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