Evaluation of safety monitoring guidelines based on MRI lesion activity in multiple sclerosis.

OBJECTIVE: We evaluate variants of a commonly used data safety monitoring guideline in clinical trials in multiple sclerosis (MS) that flags patients who, at a follow-up visit, have 5 or more contrast-enhancing lesions (CELS) above their baseline count.

METHODS: We apply the guideline to a relapsing cohort and a secondary progressive cohort. We assess the number of patients that meet the guideline and describe the characteristics of these patients; we also examine the value of the guideline in predicting relapse occurrence in the 28 days following that MRI. These analyses were repeated for thresholds varying from 1 to 10 CELS above baseline.

RESULTS: Between 4% and 6% of patients met the threshold of 5 in both cohorts; patients with higher baseline counts and higher T2 lesion burden were more apt to meet the threshold. After adjustment for other covariates, the odds ratio (OR) of relapse associated with meeting the threshold is significant ($p < 0.05$) or near significant ($0.05 \leq p < 0.10$) for thresholds between 5 and 8 for the relapsing cohort, but not for the secondary progressive cohort. Across thresholds, the adjusted OR is consistently greater than 1, and there is an increasing trend as the threshold increases from 1 to 7.

CONCLUSIONS: A guideline based on crossing a threshold CEL count above baseline may be valuable in monitoring patient safety. Further study should be conducted using different datasets to assess the generalizability of these guidelines.
results.

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