**Background:** BG-12 is a novel oral therapy being developed for the treatment of multiple sclerosis (MS). In addition to anti-inflammatory properties, BG-12 may exhibit potential neuroprotective properties through activation of Nrf2 and associated antioxidant and metabolic defense mechanisms. Magnetization transfer ratio (MTR) imaging is a variation on conventional magnetic resonance imaging (MRI). MTR has been proposed for use as a biomarker of changes in myelin content of brain white matter. **Objectives:** To determine the feasibility of using MTR imaging in large multicenter trials with MS patients. **Methods:** DEFINE and CONFIRM are two ongoing phase 3, randomized, multicenter, double-blind, placebo-controlled studies assessing efficacy and safety of BG-12 in subjects with relapsing-remitting MS, and will use MTR to further analyze the efficacy of BG-12. MTR scans are being obtained in a subset of patients at baseline and 6, 12, and 24 months, using manufacturer-supplied MT pulse sequences. MTR pulse parameters were provided by central imaging centers (NeuroRx Research for DEFINE and the NMR Research Unit for CONFIRM). Outcome measures include MTR in whole brain at baseline, the percent change in brain MTR over time, MTR in gadolinium (Gd)—enhancing lesions, and the subsequent change of MTR in these lesions. **Results:** MTR of whole brain was measured in a subgroup of baseline scans and normalized across this group. In DEFINE: 65 of 76 (86%) MRI facilities around the world were capable of performing adequate MTR imaging. Mean (SD) MTR was 40.2 (1.9) on GE scanners (n = 61), 44.6 (3.5) on Philips scanners (n = 31), and 31.7 (1.4) on Siemens scanners (n = 43). In CONFIRM: 107 of 110 (97%) MRI facilities around the world were capable of performing MTR. Mean (SD) MTR was 32.8 (5.8) on GE scanners (n = 78), 42.9 (5.6) on Philips scanners (n = 24), and 30.4 (1.4) on Siemens scanners (n = 58). **Conclusions:** The collection and analysis of MTR data in the context of large, multicenter clinical trials is feasible and promises to provide valuable data regarding demyelination and remyelination of axons in MS. The use of manufacturer-supplied MT pulses allows MTR data to be obtained on most modern scanners. Differences in MTR between scanners can be handled by using measures of MTR change over time and normalizing the MTR data.

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