**Supplementary Appendix**

**MRI acquisition protocol in the SET cohort:**

For this study, only MRI scans performed at baseline prior to the treatment initiation and at 12, 24 and 36 months with a standardized protocol performed on the single 1.5-Tesla imager scanner (Gyroscan; Philips Medical Systems, Best, The Netherlands) were used. MRI examinations were performed at least 30 days after steroid administration. Although this was a multicentre study, all MR examinations were performed centrally on a single MRI scanner in the Department of Radiology of the General University Hospital in Prague.

Axial brain images were obtained by using fluid-attenuated inversion recovery (FLAIR) with 1.5-mm thickness (repetition time msec/echo time msec/inversion time msec, 11000/140/2600; flip angle, 90°; 256 × 181 matrix). Axial T1-weighted three-dimensional spoiled gradient-recalled images were acquired with 1-mm section thickness (25/5; flip angle, 30°; 256 × 204 matrix). Both FLAIR and spoiled-gradient recalled images had no gaps. In addition, patients underwent postcontrast T1 spin-echo 3-mm section thickness imaging 5 minutes after injection of a single dose of 0.1 mmol/kg of Gd-DTPA contrast agent (12/450).1

The T2 and number of CE lesions were obtained by using FLAIR, and lesion volumes were measured on T1 postcontrast images with a semiautomated edge detection contour and threshold technique previously described.2 By using software (FMRIB Linear Image Registration Tool; Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, University of Oxford, Oxford, England; http://www.fmrib.ox.ac.uk/fsl),3 all follow-up FLAIR and T1 spin-echo postcontrast images for a given subject were co-registered to the baseline FLAIR image by using a six-degrees-of-freedom rigid-body model. All subsequent lesion analysis was performed by using co-registered images. For each time point, T2 lesion activity analysis was performed with the aid of a subtraction image: the image from the previous time point was subtracted from the corresponding current image. The result was then smoothed with a Gaussian kernel of 0.5 mm. Cross-sectional regions of interest were overlaid on the subtraction image to facilitate the identification of new and enlarging T2 lesions.

Image analyses were performed at Buﬀalo Neuroimaging Analysis Center, Department of Neurology, Buﬀalo, NY, USA.4

**MRI acquisition protocol in the GeneMSA cohort:**

MRI analysis was performed centrally at the Medical Image Analysis Centre in Basel, blinded with respect to disease subtype, duration and treatment history. MRI examinations were performed at least 30 days after corticosteroid administration.

The measurement protocol included a three-dimensional T1-weighted scan (MPRAGE, TR/TI/TE/α = 2080 ms/1100 ms/3.93 ms/15°; spatial resolution 0.98×0.98×1 mm3), a double-echo proton density/T2-weighted sequence (TR/TE1/TE2 = 3980 ms/14 ms/108 ms; 0.98×0.98×3 mm3), and a T1-weighted spin echo sequence (TR/TE = 552 ms/ 17 ms; 0.98×0.98×3 mm3). The latter was acquired for 5 min following administration of a single dose (0.1 mM/kg) of contrast agent.

Qualitative analysis for the presence of gadolinium enhancement was performed on post-contrast T1-weighted images. Brain lesions were identified and marked by consensus reading on simultaneously viewed T2-weighted and proton density-weighted images.5 Additional evaluations were done for new T2 lesions, volume of T2 and T1 gadolinium enhanced lesions.

**References:**

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