SUPPLEMENTARY APPENDIX

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: JA Cohen et al. Pilot trial of intravenous autologous culture-expanded mesenchymal stem cell transplantation in multiple sclerosis.

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1 STUDY OVERSIGHT

Steering Committee

Jeffrey A Cohen, MD (Chair), Mellen Center, Neurological institute, Cleveland Clinic
Elizabeth Fisher, PhD, Biomedical Engineering, Lerner Research Institute, Cleveland Clinic [a]
Stanton L Gerson, MD, Case Comprehensive Cancer Center, and National Center for Regenerative Medicine, Case Western Reserve University; Seidman Cancer Center, University Hospitals Cleveland Medical Center
Peter B Imrey, PhD, Quantitative Health Sciences, Lerner Research Institute, and Mellen Center, Neurological Institute, Cleveland Clinic
Hillard M Lazarus, MD, Case Comprehensive Cancer Center, and National Center for Regenerative Medicine, Case Western Reserve University; Seidman Cancer Center, University Hospitals Cleveland Medical Center
Jane Reese Koc, MBA, Case Comprehensive Cancer Center, and National Center for Regenerative Medicine, Case Western Reserve University; Seidman Cancer Center, University Hospitals Cleveland Medical Center

Medical Monitor

Robert J. Fox, MD, Mellen Center, Neurological institute, Cleveland Clinic

Data Safety Monitoring Committee

Stephen C. Reingold, PhD (Chair), Scientific and Clinical Review Associates
Jack P Antel, MD, Montreal Neurological Institute, McGill University
Gary R Cutter, PhD, Department of Biostatistics, School of Public Health, University of Alabama-Birmingham
Andrew D. Goodman, MD, Department of Neurology, University of Rochester Medical Center
Marcelo Pasquini, MD, Division of Neoplastic Diseases and Related Disorders, Medical College of Wisconsin

Advisory Committee

Arnold Caplan, PhD, Departments of Biology and General Medical Sciences, Case Western Reserve University
Robert Miller, PhD, Departments of Biology and General Medical Sciences, Case Western Reserve University School of Medicine [b]
Michael D Phillips, MD, Imaging Sciences, Imaging Institute, Cleveland Clinic
Richard A Rudick, MD, Mellen Center, Neurological institute, Cleveland Clinic [a]

[a] Current affiliation: Biogen
[b] Current affiliation: School of Medicine and Health Sciences, George Washington University

2 MRI PROTOCOL

Over the course of the study, up to 7 MRI studies were acquired for each participant.

All images were acquired on the same **3T scanner** for all patients at each time point. The sequences acquired for this study included a SPACE 3D FLAIR, a 3D Turboflash series with and without an MT saturation pulse, a 30-direction DTI series, T1-weighted MPRAGE, and T1-weighted FLASH images with and without contrast. Each study scan was reviewed for acceptable image quality by the analysis center prior to approval. If a scan was not approved, due to excessive patient motion, for example, it was repeated.

Prior to scanning the first participant for this study, a test image set (i.e., "dummy scan") was approved by the analysis center in order to verify that the protocol was set up correctly.

Images were acquired in an axial or oblique axial orientation with the slices parallel to the inferior aspect of the corpus callosum. The angle of the slice planes was determined using a standard scout scan. For each participant, a sufficient number of slices was planned to guarantee complete coverage of the brain, including the cerebellum. The most superior and inferior slices did not contain brain tissue.

MS-MSC MRI Protocol			
Image Type	**Sequence times (ms)**	**Sequence details**	**Voxel size (mm^3)**
SPACE 3D FLAIR	TR = 6500 TE = 404 TI = 2000	flip angle = variable	1.0 x 1.0 x 1.4
3D Turboflash without MT saturation pulse	TR = 24 TE = 3.81	flip angle = 10	1 x 0.8 x 1
3D Turboflash with MT saturation pulse	TR = 24 TE = 3.81	flip angle = 10; MT pulse: Gaussian, 2 kHz off resonance	1 x 0.8 x 1
30-direction DTI	TR = 7000 TE = 95	b=1000s/mm^2	2 x 2 x 2
T1-weighted MPRAGE	TR = 1860 TE = 2.8 TI = 1100	flip angle = 10	0.9 x 0.9 x 0.9
T1-weighted FLASH without contrast	TR = 300 TE = 2.45		0.7 x 0.8 x 3
T1-weighted FLASH with contrast	TR = 300 TE = 2.45	Acquired 5 minutes after injection of gadolinium-DTPA (0.1 mmol/kg body weight)	0.7 x 0.8 x 3

The images were evaluated at the Cleveland Clinic MS-MRI Analysis Center using automated image analysis software developed in-house. The quantitative MRI parameters measured included:

- Number and volume of gadolinium-enhancing lesions
- Number of new or enlarged T2-hyperintense lesions
- Volume of T2-hyperintense lesions

- Volume of non-enhancing T1-hypointense lesions
- Brain parenchymal fraction and gray matter fraction
- Diffusions tensor imaging: whole brain mean diffusivity and fractional anisotropy
- Whole brain magnetization transfer ratio