

Supplementary Online Content

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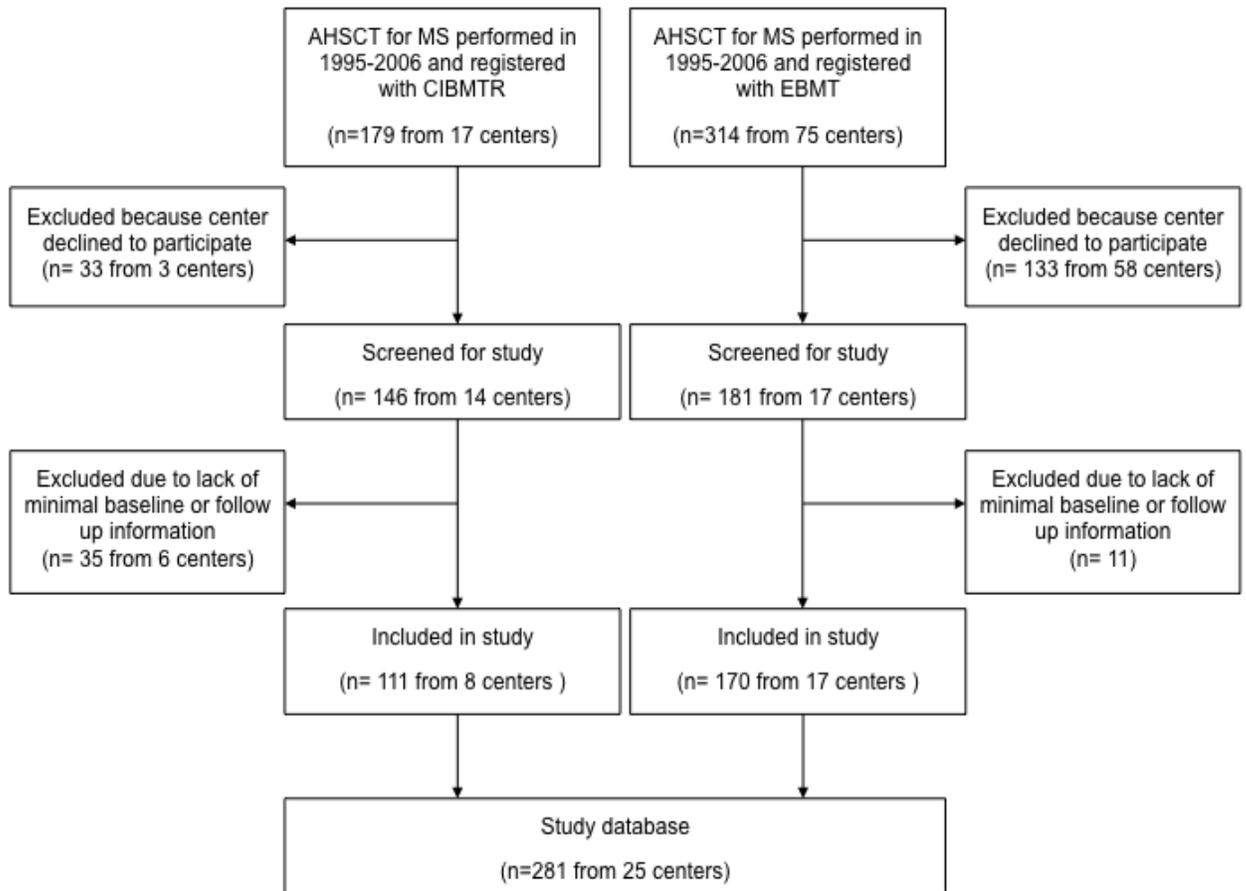
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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Supplemental Appendix

eFigure. CONSORT Type Diagram of Enrollment in the Study Database



eTable 1. Kurtzke Expanded Disability Status Scale (EDSS)

0	Normal neurological exam (all grade 0 in Functional Systems (FS); cerebral grade 1 acceptable).
1	No disability, minimal signs in one FS (i.e. one grade 1 excluding cerebral grade 1).
1.5	No disability, minimal signs in more than one FS (more than one grade 1 excluding cerebral grade 1).
2.0	Minimal disability in one FS (one FS grade 2, others 0 or 1).
2.5	Minimal disability in two FS (two FS grade 2, others 0 or 1).
3.0	Moderate disability in one FS (one FS grade 3, others 0 or 1), or mild disability in three or four FS (three-four FS grade 2, others 0 or 1).
3.5	Fully ambulatory but with moderate disability in one FS (one grade 3 and one or two FS grade 2) or two FS grade 3, others 0 or 1, or five FS grade 2, others 0 or 1.
4.0	Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability consisting of one FS grade 4 (others 0 or 1), or combinations of lesser grades exceeding limits of previous steps. Able to walk without aid or rest some 500 meters or 0.3 miles.
4.5	Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability. (Usually consisting of one FS grade 4 (others 0 or 1) or combinations of lesser grades exceeding limits of previous steps. Able to walk without aid or rest for some 300 meters or 975 ft).
5.0	Ambulatory without aid or rest for about 200 meters or 650 ft; disability severe enough to impair full daily activities (e.g., to work full day without special provisions). (Usual FS equivalents are one grade 5 alone (others 0 or 1); or combinations of lesser grades usually exceeding specifications for step 4.0.)
5.5	Ambulatory without aid or rest for about 100 meters or 325 ft; disability severe enough to impair full daily activities. (Usual FS equivalents are one grade 5 alone (others 0 or 1); or combinations of lesser grades usually exceeding specifications for step 4.0.)

6.0	Intermittent or constant unilateral assistance (cane, crutch, or brace) required to walk about 100 meters or 325 ft. with or without resting. (Usual FS equivalents are combinations with more than two FS grade 3+.)
6.5	Constant bilateral assistance (canes, crutches, or braces) required to walk about 20 meters or 65 ft. (Usual FS equivalents are combinations with more than two FS grade 3+.)
7.0	Unable to walk beyond about 5 meters or 16 ft. even with aid, essentially restricted to wheelchair, wheels self in standard wheelchair a full day and transfers alone; up and about in wheelchair some 12 hours a day. (Usual FS equivalents are combinations with more than one FS grade 4+; very rarely pyramidal grade 5 alone.)
7.5	Unable to take more than a few steps; restricted to wheelchair; may need aid in transfers, wheels self but cannot carry on in standard wheelchair a full day; may require motorised wheelchair. (Usual FS equivalents are combinations with more than one FS grade 4+.)
8.0	Essentially restricted to bed or chair or perambulated in wheelchair; but may be out of bed much of the day; retains may self-care functions; generally has effective use of arms. (Usual FS equivalents are combinations, generally grade 4+ in several systems.)
8.5	Essentially restricted to bed for much of the day; has some effective use of arm(s); retains some self-care functions. (Usual FS equivalents are combinations, generally grade 4+ in several systems.)
9.0	Helpless bed patient; can communicate and eat. (Usual FS equivalents are combinations, mostly grade 4.)
9.5	Totally helpless bed patient; unable to communicate or effectively eat/swallow. (Usual FS equivalents are combinations, almost all grade 4+.)
10	Death due to MS.

Reference: Kurtzke J.F. (1983) Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology. 33, 1444-1452

The EDSS provides a total score on a scale from 0 to 10. Scores of 1.0 to 4.5 refer to people with a high degree of ambulatory ability and subsequent levels 5.0 to 9.5 refer to loss of ambulatory ability. In addition, it quantifies disability in eight functional systems (FS) and allows neurologists to assign a Functional System Score (FSS) in each of these.

The functional systems are: (1) Pyramidal (2) Cerebellar (3) Brainstem (4) Sensory (5) Bowel and Bladder (6) Visual and (7) Cerebral or Mental.

The Functional systems are scored on a scale of 0-5 to best reflect the level of disability observed clinically. The 'other' category is not rated numerically.

EDSS scores below 4.0 are determined by the FSS alone. Scores between 4.0 and 9.5 are determined by both gait abilities and the FSS.

eTable 2. Data on Factors Associated With Lower Overall Survival in the Patients Who Died During Follow-up

	Death within day 100	Death after day 100	Whole Cohort
Number of patients	8	29	281
Age, median (range), years	40 (38 - 57)	42 (20-60)	37 (15-65)
N aged 10-19	0	0	6 (2%)
N aged 20-29	0	3 (10%)	58 (21%)
N aged 30-39	4 (50%)	10 (35%)	107 (38%)
N aged 40-49	3 (38%)	13 (45%)	85 (30%)
N aged 50+	1 (12%)	3 (10%)	25 (9%)
EDSS prior to mobilization			
N evaluated	5 (63%)	21 (72%)	281(100%)
Median EDSS (range)	6.5 (6.0-7.5)	7.0 (5.0-9.0)	6.5 (1.5-9.0)

MS disease type at baseline			
Relapsing	1 (12%)	2 (7%)	63 (22%)
Progressive	7 (88%)	27 (93%)	218 (78%)
Conditioning regimen			
High Intensity	2 (25%)	11 (38%)	53 (19%)
CY+TBI+ATG	1 (12%)	8 (28%)	28 (10%)
BU+CY+ATG	1 (12%)	3 (10%)	15 (6%)
BU+ATG	0	0	10 (3%)
Intermediate Intensity	6 (75%)	15 (52%)	179 (64%)
BEAM+ATG	6 (75%)	9 (31%)	109 (39%)
BEAM	0	6 (21%)	40 (14%)
CY+THIO	0	0	7 (3%)
TLI+Melphalan	0	0	5 (2%)

BCNU+CY+ATG	0	0	18 (6%)
Low Intensity	0	3 (10%)	49 (17%)
CY+ATG	0	2 (7%)	46 (16%)
CY+FLUD	0	1 (3%)	3 (1%)

eTable 3. Causes of Death and Prior MS Treatments**A. Causes of death within 100 days from transplant**

	n	Prior MS treatments*
<i>Patients at risk</i>	281	
Infection	2	IFNb (n=2), AZA (n=1)
Accident	1	IFNb1a, mitox
Veno-occlusive disease	1	IFNb1a
Hemorrhage	1	IFNb
EBV lympho- proliferative disorder	1	IFNb1a, IFNb1b, GA, mitox
Not reported	2	IFNb (n=2), mitox (n=1)
Total	8 (2.8%)	

B. Causes of death after post-transplant day 100

	n	Prior MS treatments
<i>Patients at risk</i>	273	
MS progression	9	IFNb (n=7)
Infection	5	IFNb (n=3), CY, mitox
Malignancies	3	IFNb (n=2), CY (n=1), AZA (n=1)
Accident	1	IFNb1a
Diverticulitis	1	Methotrexate
Organ failure	1	Corticosteroids only
Rejection/poor graft function	1	AZA, IvIG, IFNb1a, IFNb1b, mitox
Arterial thromboembolism lower limbs	1	None reported
Interstitial pneumonia	1	IFNb, AZA

Sepsis	1	IFNb
Gastrointestinal bleeding	1	IFNb
Not reported	4	IFNb (n=3)
Total	29 (10%)	

* Immune-modifying treatments given for MS are listed for each cause of death. Numbers indicate how many patients within each subgroup received the stated treatment. Individual patients may, and in most cases will, have received >1 treatment. Abbreviations: AZA, azathioprine; CY, cyclophosphamide; GA, glatiramer acetate; IFNb, interferon beta; mitox, mitoxantrone.

eTable 4. Late Adverse Events

A. Malignancies

Myelodysplastic syndrome		3
Breast cancer		2
Squamous cell carcinoma		1
Prostate cancer		1
Cervical Carcinoma		1
Glioblastoma Multiforme		1

Total 9

B. New Autoimmune Disease

Autoimmune thyroid disease		3
Autoimmune thrombocytopenia		3
Acquired haemophilia		2
Crohn's disease		1

Total 14