

Subject	Sex/Age at Mobilization	Disease Duration, years	Prior MS Medications (Total/List)	No. Relapses in 18 Months Prior to Screening	Baseline EDSS	Baseline MSIS-29	Baseline MSFC	Baseline MRI		
								Number Gd+ Lesions	T1 Lesion Volume	T2 Lesion Volume
1	F/28	7	6/GA, IFNA, IFNB, MET, MPE, MTX	2	5.0	119.0	-0.09	5	0.21	52.12
2	F/26	2	1/GA	3	4.5	66.0	-0.31	3	1.56	24.73
3	F/46	4	2/GA, MTX	3	4.5	137.0	-0.21	0	0.00	0.37
4	M/27	2	1/IFNA	5	4.5		-0.23	1	0.05	6.36
5	F/38	11	4/GA, IFNA, MPE, OTH	2	3.0	74.0	-0.42	0	0.85	8.89
6	F/31	3	2/GA, IFNA	3	5.0	90.0	0.19	0	0.07	2.35
7	M/28	5	4/GA, IFNA, MTX, NAT	2	4.5	70.0	-0.70	28	1.43	8.23
8	F/27	1	2/GA, IFNA	3	4.5	41.4	-0.11	1	0.28	11.06
9	M/34	6	4/GA, IFNA, MTX, NAT	3	5.0	88.0	0.39	0	1.24	10.51
10	M/34	3	3/IFNA, IFNB, MTX	2	4.5	82.9	-0.89	0	0.42	4.58
11	M/40	5	2/GA, IFNA	3	4.0	46.0	-1.44	1	12.85	41.69
12	F/33	6	3/GA, IFNA, MTX	2	4.0	99.0	0.11	0	0.00	0.11
13	M/42	2	1/IFNA	5	4.0	51.0	0.99	0	0.03	1.25
14	F/52	9	4/GA, IFNA, MTX, NAT	2	4.0	94.0	-0.30	0	0.21	4.27
15	F/37	2	3/GA, IFNA, MPE	4	4.0	77.0	0.24	1	0.31	5.35
16	F/49	11	1/GA	2	5.5			2		
17	F/41	2	1/IFNB	4	4.0	80.0	0.56	0	0.00	0.77
18	F/43	7	3/GA, IFNA, IFNB	4	3.5	53.0	0.66	0	0.42	3.14
19	F/26	2	4/IFNA, MPE, NAT, OTH	6	5.5	76.0	0.57	6	0.00	1.51
20	F/39	5	2/IFNA, NAT	3	4.0	40.0	0.67	0	0.04	0.41
21	F/47	12	3/GA, IFNA, MPE	2	4.0	110.0	-0.47	7	0.87	9.43
22	M/41	4	3/GA, IFNA, MPE	2	5.5	79.0	-0.29	0	0.68	8.37
23	F/37	3	3/CY, GA, IFNA	3	4.0	120.0	-0.59	0	3.63	22.26
24	M/31	10	4/IFNA, MTX, NAT, PRE	2	5.0	58.0	-0.44	0	1.46	26.47
*	F/44	11	3/GA, IFNA, IFNB	5	4.0	81.2	-0.20	0	3.95	12.11
Median	-/37	5	3	3	4.5	79.0	-0.20	0	0.36	7.30

**Table e-1: Patient Level Baseline Characteristics**

\*= Subject not transplanted on study due to heparin induced thrombocytopenia following mobilization.

ALE = Alemtuzumab; AZA = Azathioprine; CY = Cyclophosphamide; GA = Glatiramer Acetate; INFA = Interferon Beta-1a; IFNB = Interferon Beta-1b; IGG = Immunoglobulin Prep.; NAT = Natalizumab; MET = Methotrexate; MPE = Methylprednisone; MTX = Mitoxantrone; PRE = Prednisone; RIT = Rituximab; OTH = Other.

	Primary Analysis [a]	Primary Event Component Analysis [b,e]	Total Events [c]	Individual Component Analysis [d,e]
<b>Year 1</b>				
Number (%) at Risk	23 (95.8%)			
Post-transplant event-free survival probability	95.8%			
90% Confidence Intervals [5]	(80.2%, 99.2%)			
Number of Treatment Failure Events:	1		2	
EDSS increase > 0.5	0	100.0% (100.0%, 100.0%)	0	100.0% (100.0%, 100.0%)
Clinical Relapse	1	95.8% (80.2%, 99.2%)	1	95.8% (80.2%, 99.2%)
Two or more MS lesions on MRI	0	100.0% (100.0%, 100.0%)	1	95.8% (80.2%, 99.2%)
Death	0	100.0% (100.0%, 100.0%)	0	100.0% (100.0%, 100.0%)
<b>Year 2</b>				
Number (%) at Risk	19 (79.2%)			
Post-transplant event-free survival probability	82.8%			
90% Confidence Intervals [5]	(65.0%, 92.0%)			
Number of Treatment Failure Events:	4		5	
EDSS increase > 0.5	2	90.9% (73.7%, 97.1%)	2	91.3% (74.7%, 97.2%)
Clinical Relapse	2	91.0% (73.9%, 97.1%)	2	91.5% (75.2%, 97.3%)
Two or more MS lesions on MRI	0	100.0% (100.0%, 100.0%)	1	95.8% (80.2%, 99.2%)
Death	0	100.0% (100.0%, 100.0%)	0	100.0% (100.0%, 100.0%)
<b>Year 3</b>				
Number (%) at Risk	18 (75.0%)			
Post-transplant event-free survival probability	78.4%			
90% Confidence Intervals [5]	(60.1%, 89.0%)			
Number of Treatment Failure Events:	5		7	
EDSS increase > 0.5	2	90.9% (73.7%, 97.1%)	2	91.3% (74.7%, 97.2%)
Clinical Relapse	3	86.3% (68.1%, 94.5%)	3	86.9% (69.5%, 94.7%)
Two or more MS lesions on MRI	0	100.0% (100.0%, 100.0%)	1	95.8% (80.2%, 99.2%)
Death	0	100.0% (100.0%, 100.0%)	1	95.7% (79.4%, 99.1%)
<b>Year 4</b>				
Number (%) at Risk	16 (66.7%)			
Post-transplant event-free survival probability	73.8%			
90% Confidence Intervals [5]	(55.0%, 85.7%)			
Number of Treatment Failure Events:	6		9	
EDSS increase > 0.5	2	90.9% (73.7%, 97.1%)	2	91.3% (74.7%, 97.2%)
Clinical Relapse	3	86.3% (68.1%, 94.5%)	3	86.9% (69.5%, 94.7%)
Two or more MS lesions on MRI	1	94.1% (73.0%, 98.8%)	2	91.0% (73.9%, 97.1%)
Death	0	100.0% (100.0%, 100.0%)	2	91.1% (74.2%, 97.1%)
<b>Year 5</b>				
Number (%) at Risk	14 (58.3%)			
Post-transplant event-free survival probability	69.2%			
90% Confidence Intervals [5]	(50.2%, 82.1%)			
Number of Treatment Failure Events:	7		11	
EDSS increase > 0.5	2	90.9% (73.7%, 97.1%)	2	91.3% (74.7%, 97.2%)
Clinical Relapse	3	86.3% (68.1%, 94.5%)	3	86.9% (69.5%, 94.7%)
Two or more MS lesions on MRI	2	88.2% (67.0%, 96.2%)	3	86.3% (68.1%, 94.5%)
Death	0	100.0% (100.0%, 100.0%)	3	86.3% (68.3%, 94.5%)

**Table e-2. Primary Event-free Survival and Component Analyses**

**[a]** Events are defined as clinical relapse, death, disease progression (defined as increased EDSS > 0.5 from baseline) or presence of two or more independent MS lesions (found on MRI) indicative of MS disease activity.

**[b]** The primary endpoint component analysis considers an event to be within a component only if it was a primary endpoint (first) event. Events for this analysis correspond to the events in the primary analysis column.

**[c]** Includes events that occurred after a subject has met primary endpoint.

**[d]** The individual endpoint component analysis considers all events within a component, including events that occurred after a subject met primary endpoint. Events for this analysis correspond to the total events column. The survival estimate provided for death in the individual component analysis corresponds to overall survival.

**[e]** Kaplan-Meier estimates of survival probability, with Wald-type CI based on Greenwood's formula for standard error. Subjects who withdrew early are censored at the date of last follow-up.

	Baseline	Month 6	Year 1	Year 2	Year 3	Year 4	Year 5
<b>EDSS</b>							
n	24	24	23	21	20	18	17
Median (Range)	4.50 (3.0, 5.5)	4.00 (2.0, 6.5)	4.00 (2.0, 6.0)	3.50 (1.5, 7.0)	3.75 (1.5, 6.5)	3.75 (1.5, 7.0)	3.00 (1.5, 5.5)
Mean (SD)	4.42 (0.637)	4.15 (1.108)	3.78 (0.951)	3.71 (1.241)	3.68 (1.217)	3.78 (1.263)	3.47 (1.082)
P value <sup>a</sup>		0.133	0.003	0.004	0.007	0.046	0.001
<b>MSFC Score<sup>b</sup></b>							
n	23	24	20	21	18	14	15
Median (Range)	-0.21 (-1.4, 1.0)	0.06 (-1.9, 1.1)	0.18 (-2.6, 1.0)	0.22 (-0.7, 0.9)	0.20 (-5.3, 1.1)	0.44 (-0.4, 1.2)	0.34 (-0.7, 1.0)
Mean (SD)	-0.09 (0.574)	-0.02 (0.664)	0.03 (0.809)	0.20 (0.497)	-0.07 (1.367)	0.39 (0.439)	0.26 (0.524)
P value <sup>a</sup>		0.116	0.032	0.013	0.011	0.068	0.303
<b>Timed 25-Foot Walk (sec)</b>							
n	23	24	21	21	19	17	16
Median (Range)	6.25 (3.2, 18.5)	5.48 (3.7, 28.4)	5.20 (3.5, 65.0)	4.80 (3.6, 11.2)	5.25 (3.6, 13.3)	5.45 (3.3, 10.1)	5.60 (3.7, 12.6)
Mean (SD)	6.77 (3.115)	6.82 (5.105)	9.33 (13.685)	5.43 (1.806)	6.20 (2.545)	5.74 (1.756)	5.95 (2.009)
z Score, Median (Range)	0.29 (-0.8, 0.6)	0.36 (-1.6, 0.5)	0.38 (-4.9, 0.5)	0.42 (-0.1, 0.5)	0.37 (-13.7, 0.5)	0.36 (-0.0, 0.5)	0.35 (-0.3, 0.5)
P value <sup>a</sup>		0.015	0.062	0.004	0.379	0.229	0.811
<b>9-Hole Peg Test (sec)<sup>c</sup></b>							
n	23	24	21	22	20	18	16
Median (Range)	22.88 (16.0, 59.7)	21.78 (16.4, 53.0)	22.48 (16.8, 53.9)	21.30 (16.2, 46.2)	21.94 (17.0, 53.1)	21.35 (16.3, 68.1)	21.44 (16.3, 51.3)
Mean (SD)	26.55 (10.157)	25.18 (8.599)	25.13 (9.337)	24.05 (7.662)	25.53 (9.689)	25.56 (13.289)	23.99 (9.277)
z Score, Median (Range)	0.00 (-2.6, 1.9)	0.20 (-2.5, 1.7)	0.18 (-2.1, 1.5)	0.32 (-2.6, 1.8)	0.17 (-3.0, 1.5)	0.29 (-2.4, 1.7)	0.29 (-2.3, 1.7)
P value <sup>a</sup>		0.101	0.231	0.100	0.087	0.067	0.298
<b>PASAT-3 (Percent Correct)</b>							
n	23	24	20	22	18	15	15
Median (Range)	66.67 (23.3, 100.0)	75.00 (0.0, 100.0)	81.67 (31.7, 100.0)	89.17 (30.0, 100.0)	90.00 (53.3, 100.0)	95.00 (43.3, 100.0)	90.00 (13.3, 100.0)
Mean (SD)	68.62 (26.774)	70.76 (26.676)	73.92 (24.491)	77.35 (23.149)	84.07 (16.747)	84.11 (20.382)	81.89 (23.349)
z Score, Median (Range)	-0.42 (-2.6, 1.2)	0.00 (-3.7, 1.2)	0.33 (-2.2, 1.2)	0.70 (-2.2, 1.2)	0.74 (-1.1, 1.2)	0.99 (-1.6, 1.2)	0.74 (-3.1, 1.2)
P value <sup>a</sup>		0.540	0.475	0.340	0.049	0.423	0.336
<b>MSIS-29 Score<sup>d</sup></b>							
n	22	23	21	20	20	18	16
Median (Range)	78.00 (40.0, 137.0)	66.00 (33.0, 104.0)	49.00 (32.0, 111.0)	59.50 (36.0, 115.0)	58.50 (34.0, 114.0)	66.50 (34.0, 102.0)	63.00 (32.0, 102.0)
Mean (SD)	79.60 (26.414)	65.14 (19.750)	56.71 (21.868)	62.97 (21.420)	61.40 (23.592)	68.96 (25.508)	64.69 (20.326)
P value <sup>a</sup>		0.016	<0.001	0.016	0.016	0.248	0.091

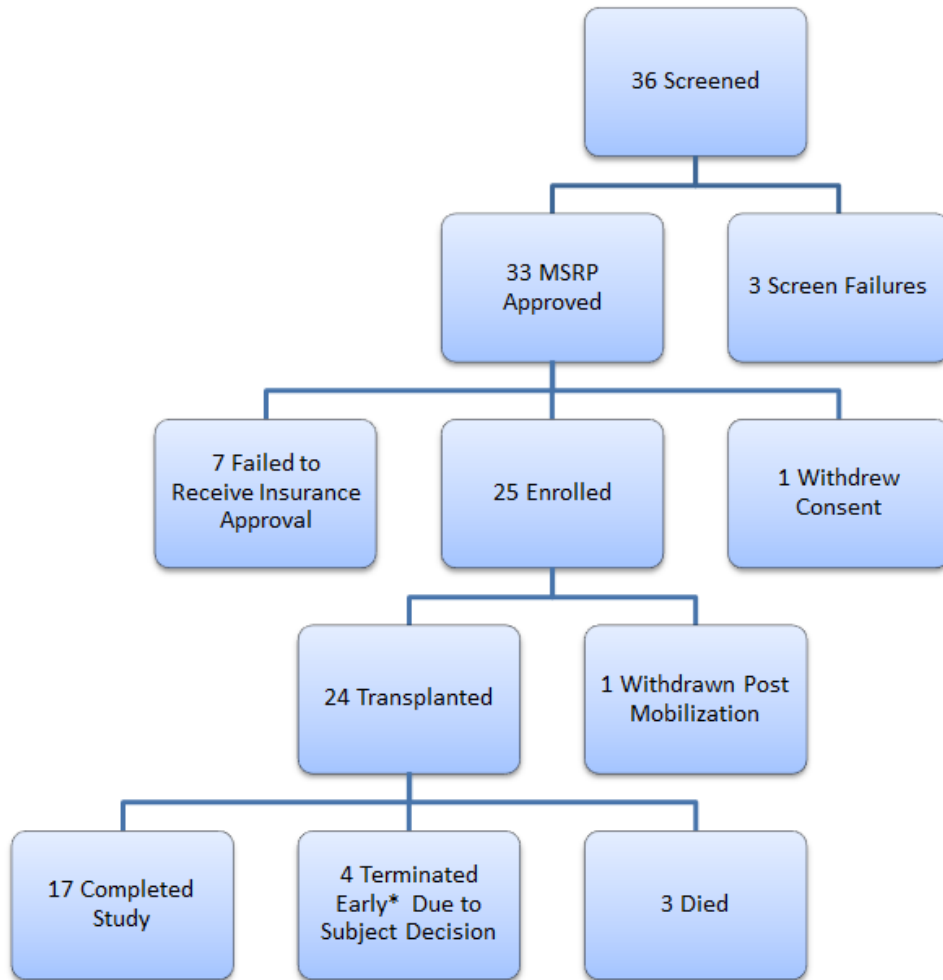
**Table e-3. Summary of EDSS, MSFC and MSIS-29 After Transplant**

**[a]** P-value from a Wilcoxon Signed Rank test. The null hypothesis tests whether the median difference between each post-baseline and baseline visit is zero. The z Scores are analyzed for the timed 25-foot walk, 9-hole peg test, and PASAT-29.

**[b]** The Multiple Sclerosis Functional Composite (MSFC) consists of results from the following tests: 1) Timed 25-Foot Walk; 2) 9 Hole Peg Test; and 3) Paced Auditory Serial Addition Test. Results from each test are transformed into a Z score using data from the task force database and averaged to yield a composite score for each subject at each timepoint. The MSFC is a relative measure that indicates how many standard deviations the current observation is from the mean of those in the task force data-base. Negative values indicate worse health.

**[c]** Average of trials from the dominant and non-dominant hands

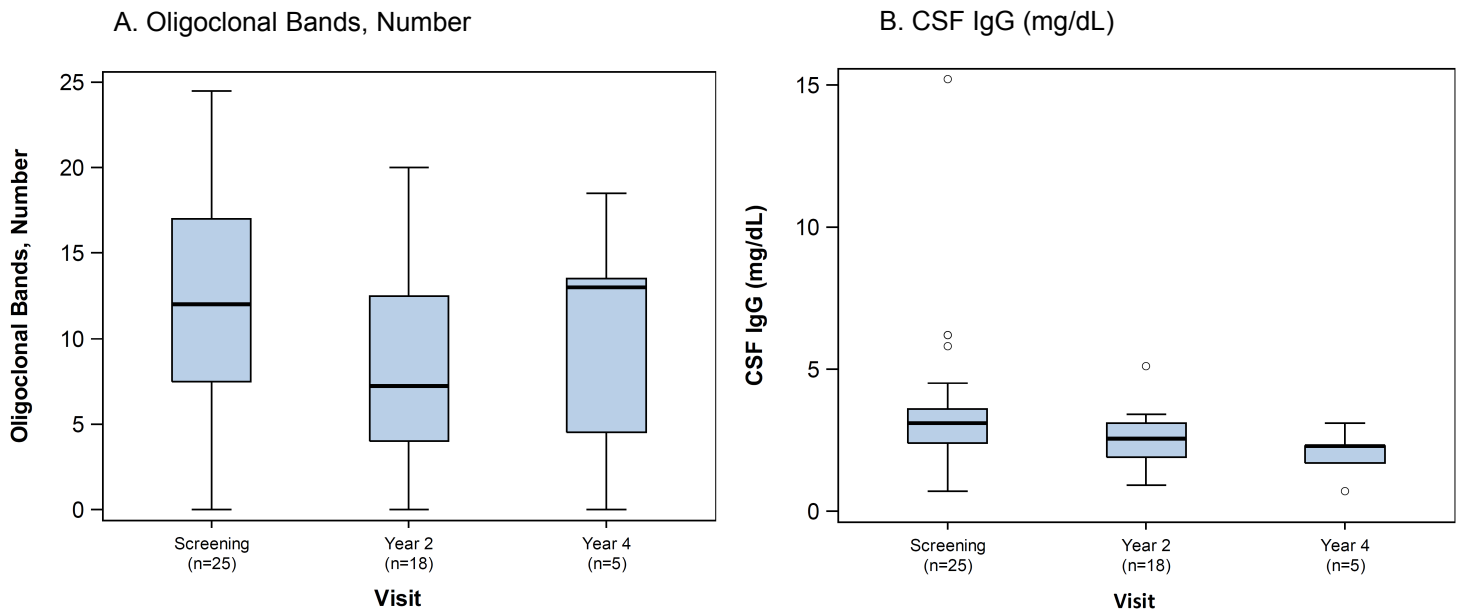
**[d]** The Multiple Sclerosis Impact Scale (MSIS) is a 29-item questionnaire that assesses physical and psychological impact. The score is a sum of the 29 questions, each that range in value from 1 to 5. The total score can range from 29 to 145, with high scores indicating worse health.



**Figure e-1: Screening, Enrollment and Follow-up**

Participant flow diagram illustrating subject disposition from screening through follow-up. An MS Review Panel (MSRP) consisting of 2 neurologists and a transplant physician from an outside site independently assessed the eligibility of each potential participant.

\*The last follow-up time on the 4 subjects who terminated early was: 12, 41, 48, and 56 months.



**Figure e-2: Oligoclonal Bands**

A, Number of oligoclonal bands present at visit. A change in the number of bands from screening was detected at Year 2 ( $p < 0.001$ ). B, CSF IgG (mg/dL) at visit. A change in CSF IgG from screening was detected at Year 2 ( $p < 0.001$ ). Change from screening was assessed at Year 2 using a Wilcoxon signed-rank test. This change was not assessed at Year 4 due to sample size. The presence of OCB in the CSF are a marker of brain inflammation, and consistent with the diagnosis of MS. OCB while reduced in number after transplant continue to be present, consistent with persistence of plasma cells producing these bands. Other studies have previously demonstrated persistence of OCB in CSF after HDIT/HCT but the numbers of patients were small and most analyses were performed early after HDIT/HCT.<sup>e1,e2,e3</sup>

Electronic References

- e1. Nash RA, Bowen JD, McSweeney PA, et al. High-dose immunosuppressive therapy and autologous peripheral blood stem cell transplantation for severe multiple sclerosis. *Blood* 2003;102:2364-2372.
- e2. Bowen JD, Kraft GH, Wundes A, et al. Autologous hematopoietic cell transplantation following high-dose immunosuppressive therapy for advanced multiple sclerosis: long-term results. *Bone Marrow Transplant.* 2012;47:946-951.
- e3. Saiz A, Carreras E, Berenguer J, et al. MRI and CSF oligoclonal bands after autologous hematopoietic stem cell transplantation in MS. *Neurology* 2001;56:1084-1089.