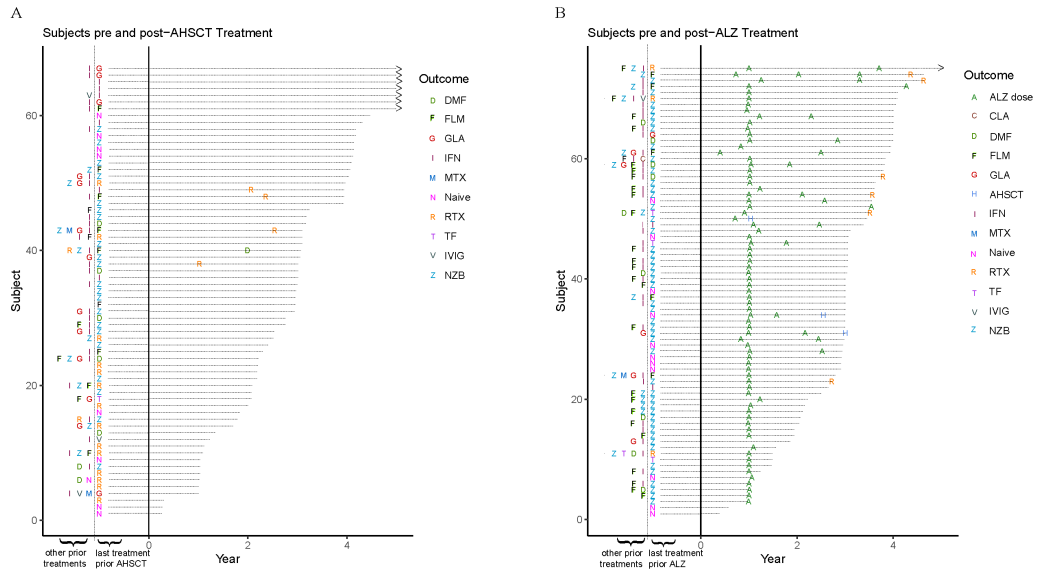
APPENDIX

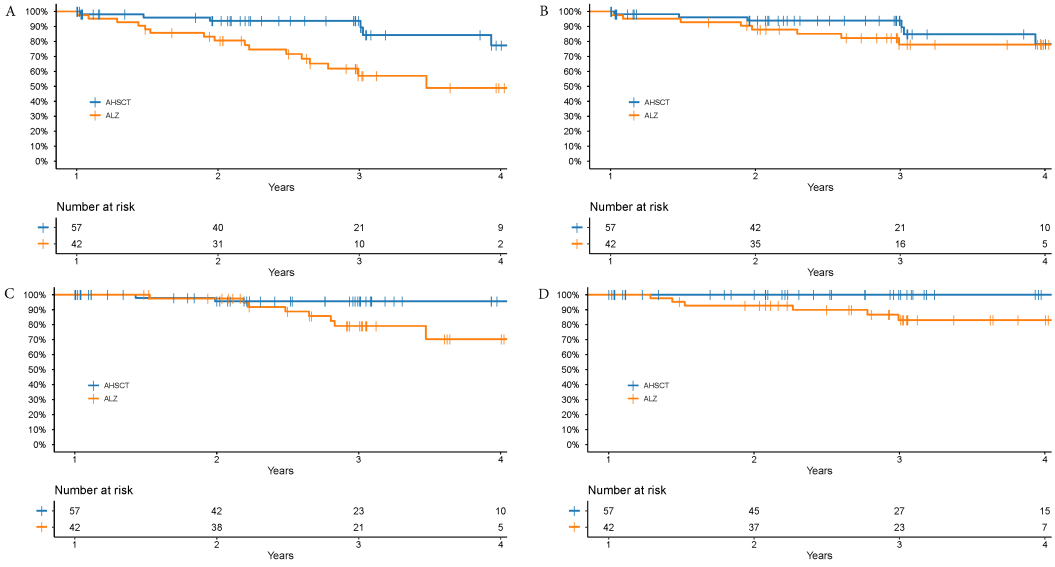
Supplementary Figure 1. Disease modifying drugs prior to and after therapeutic intervention with autologous hematopoietic stem cell transplantation and alemtuzumab.



Abbreviations: CLA, cladribine; DMF, dimethyl fumarate; FLM, fingolimod; GLA, glatiramer acetate; IFN, interferon beta; MTX, mitoxantrone; Naive, treatment naïve; RTX, rituximab; TF, teriflunomide; NZB, natalizumab.

Each line summarizes changes in treatment for individual patients treated with (A) autologous hematopoietic stem cell transplantation and (B) alemtuzumab. Additional treatments with ALZ are also shown in (B). The lines continue until the latest follow-up assessment or until five years after treatment. To the left of the baseline are two columns; one summarizing the last treatment before AHSCT or ALZ and furthest left column summarizing all other treatments prior to AHSCT or ALZ.

Supplementary Figure 2. No evidence of disease activity (NEDA), MRI progression, clinical relapses and freedom from confirmed disability worsening after a new baseline was set one year after therapeutic intervention.



A new baseline after one year was made. Thereafter Kaplan–Meier estimates of (A) no evidence of disease activity (p=0.003), (B) freedom from MRI events (p= 0.5), (C) freedom from clinical relapses (p= 0.04), and (D) freedom from confirmed disability worsening (p= 0.008) at four years were compared.

Supplementary Table 1. Adverse events in patients treated with autologous hematopoietic stem cell transplantation from mobilization to day +100 after AHSCT.

Adverse event, n (%)	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Total**
INFECTIONS					
Febrile neutropenia			**38** (55)	**2** (2.9)	**40** (58)
Catheter related infection			**3** (4.3)		**3** (4.3)
Pneumonia			**1** (1.4)		**1** (1.4)
Skin infection	**1** (1.4)	**1** (1.4)	**1** (1.4)		**3** (4.3)
UTI		**7** (10)			**7** (10)
CMV reactivation‡	**2** (2.9)	**3** (4.3)			**5** (7.2)
EBV reactivation‡	**11** (16)	**1** (1.4)			**12** (17)
GASTROINTESTINAL					
Nausea	**19** (28)	**29** (42)	**4** (5.8)		**52** (75)
Oral mucositis	**12** (17)	**10** (14)	**4** (5.8)		**26** (38)
Elevated AST or ALT	**46** (67)	**8** (12)	**2** (2.9)		**56** (81)
Diarrhea	**7** (10)	**9** (13)			**16** (23)
Vomiting	**7** (10)	**3** (4.3)			**10** (14)
Dyspepsia	**3** (4.3)	**1** (1.4)			**4** (5.8)
Constipation	**15** (22)				**15** (22)
ALLERGIC REACTIONS					
Allergic reaction	**6** (8.7)	**3** (4.3)			**9** (13)
Serum sickness			**2** (2.9)		**2** (2.9)
Cytokine release syndrome	**1** (1.4)		**1** (1.4)		**2** (2.9)
Urticaria			**1** (1.4)		**1** (1.4)
CARDIAC					
Atrial fibrillation			**1** (1.4)		**1** (1.4)
Pericarditis			**1** (1.4)		**1** (1.4)
METABOLIC					
Hypokalemia	**24** (35)	**25** (36)	**13** (19)		**62** (90)
Hypoalbuminemia*	**23** (34)	**44** (66)			**67** (100)
Hyponatremia	**25** (36)	**2** (2.9)			**27** (39)
Hypernatremia	**10** (14)				**10** (14)
NEUROLOGICAL					
Seizure			**1** (1.4)		**1** (1.4)
Headache	**12** (17)	**4** (5.8)			**16** (23)
PAIN					
Myalgia			**1** (1.4)		**1** (1.4)
Bone pain	**12** (17)	**2** (2.9)			**14** (20)
Abdominal pain	**3** (4.3)	**5** (7.2)			**8** (12)
Oral pain	**4** (5.8)	**3** (4.3)			**7** (10)
Non-cardiac chest pain	**5** (7.2)	**2** (2.9)			**7** (10)
GENERAL					
Fatigue	**22** (32)	**5** (7.2)	**2** (2.9)		**29** (42)
Hypotension	**3** (4.3)	**3** (4.3)	**2** (2.9)		**8** (12)

Syncope			**1** (1.4)	**1** (1.4)
Anorexia			**1** (1.4)	**1** (1.4)
Generalised edema	**3** (4.3)	**11** (16)		**14** (20)
Insomnia	**3** (4.3)	**4** (5.8)		**7** (10)
PSYCHIATRIC				
Mania			**1** (1.4)	**1** (1.4)
Anxiety	**2** (2.9)	**2** (2.9)		**4** (5.8)
MISCELLANEOUS				
Elevated glucose during steroids			**4** (5.8)	**4** (5.8)
Leukocytosis			**1** (1.4)	**1** (1.4)
Vaginal haemorrhage	**2** (2.9)	**8** (12)		**10** (14)
Amenorrhea	**1** (1.4)	**3** (4.3)		**4** (5.8)

The table displays all grade 3 and 4 adverse events, and all grade 1 and 2 occurring more than three times (according to CTCAE v5.0).

The total number of patients is 69.
*Not available for two patients
[t]CMV and EBV reactivations were reported if the number of virus copies were quantifiable, i.e. 1000 virus copies/mL or more.

Supplementary Table 2. Long-term adverse events.

	ALZ, n=75	**AHSCT, n=69**
Adverse events		
Grade 2, autoimmune events, No. of events	36	16
Grade 2, infectious events, No. of events	9	8
Grade 3, No. of events	5	1
	No. of patients treated with ALZ (%)	**No. of patients treated with AHSCT (%)**
Adverse events		
Grade ≥2, autoimmune events	35 (47)	14 (20)
Grade ≥2, infectious events	10 (13)	7 (10)
Grade 3 (any)	5 (6.7)	1 (1.4)
Autoimmune events (grade 2 or higher)		
Autoimmune hemolysis (grade 2)	1 (1.3)	0 (0)
Hypogammaglobulinemia (grade 2)	0 (0)	1 (1.4)
Immune thrombocytopenia (grade 3)	4 (5.3)	0 (0)
Psoriasis vulgaris (grade 2)	0 (0)	1 (1.4)
Thyroid disease (grade 2)	31 (41)	13 (19)
Hyperthyroidism	29 (39)	5 (7.2)
Hypothyroidism	0 (0)	7 (10)
Thyroiditis	2 (2.7)	1 (1.4)
Breast cancer (grade 3)	1 (1.3)	0 (0)
Infections (grade 2 or higher)		
Herpes zoster (grade 2)	5 (6.7)	4 (5.8)
Lyme neuroborreliosis (grade 3)	0 (0)	1 (1.4)
Otitis media (grade 2)	0 (0)	1 (1.4)
Respiratory tract infection (grade 2)	1 (1.3)	1 (1.4)
Sinusitis (grade 2)	1 (1.3)	0 (0)
Urinary tract infection (grade 2)	2 (2.7)	0 (0)

Adverse events were graded according to CTCAE v5.0