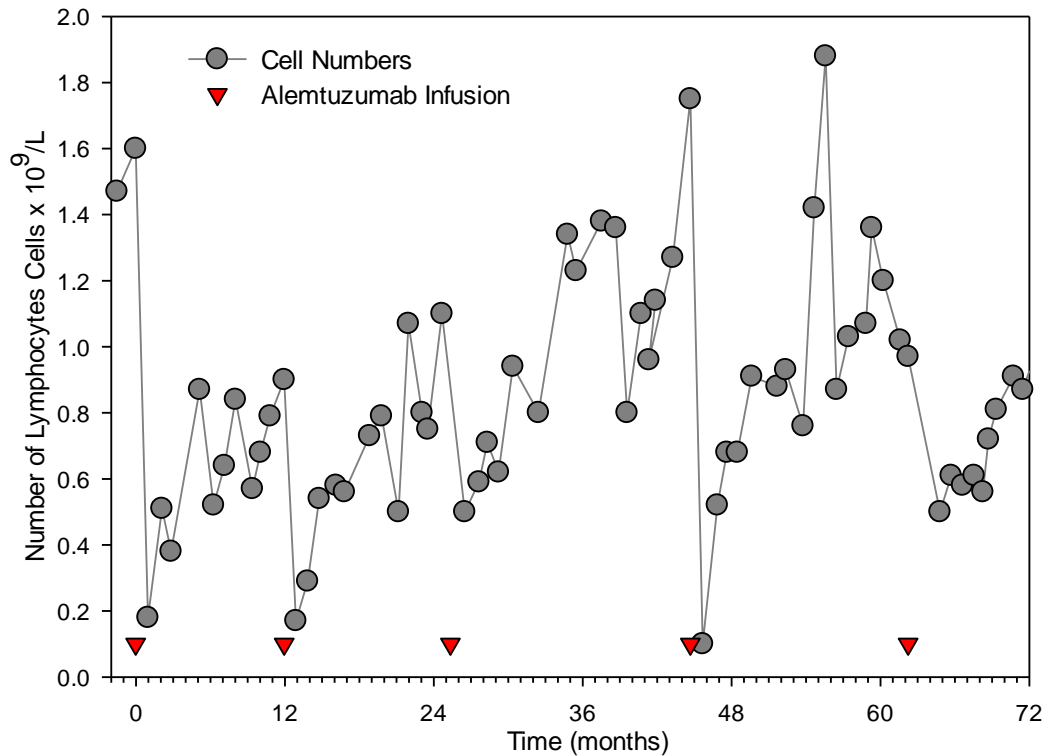


SUPPLEMENTARY TABLE S1. Influence of ever-positive alemtuzumab-specific binding and neutralizing antibodies on alemtuzumab-related adverse events

System	Cycle	Always Ab Negative		Ever Bab+/Nab Negative		Ever Bab/NAb Positive	
		N	N-AE (%)	N	N-AE (%)	N	N-AE (%)
Cardiac Disorders	O	49	7 (14.3%)	22	5 (22.7%)	305	43 (14.1%)
	C1	92	12 (13.0%)	68	7(10.3%)	216	25 (11.6%)
	C2	51	4 (7.8%)	18	1 (5.8%)	300	22 (7.3%)
Endocrine Disorders	O	49	0 (0%)	22	0(0%)	305	3 (1.0%)
Gastrointestinal Disorders	O	49	13 (26.5%)	22	3 (13.6%)	305	82 (26.9%)
	C1	92	17 (18.5%)	68	17 (25.9%)	216	39 (18.1%)
	C2	51	6 (11.8%)	18	2 (11.1%)	300	44 (14.7%)
Administration site Issues	O	49	26 (53.1%)	22	13 (59.1%)	305	164 (53.8%)
	C1	92	36 (39.1%)	68	27(39.7%)	216	91 (42.1%)
	C2	51	12 (23.5%)	18	5 (27.8%)	300	92 (30.7%)
Immune System Disorders	O	49	1 (2.0%)	22	0 (0.0%)	305	7 (2.3%)
	C1	92	2 (2.2%)	68	1 (1.5%)	216	5 (2.3%)
	C2	51	1 (2.0%)	18	0 (0.0%)	300	1 (1.3%)
Infection & Infestations	O	49	4 (8.2%)	22	0 (0.0%)	305	20 (6.6%)
	C1	92	5 (5.4%)	68	3 (4.4%)	216	11 (5.1%)
	C2	51	1 (2.0%)	18	0 (0.0%)	300	5 (1.7%)
Metabolism Disorder	O	49	0 (0.0%)	22	0 (0.0%)	305	2 (0.7%)
	C1	92	0 (0.0%)	68	1 (1.5%)	216	1 (0.5%)
	C2	51		18		300	
Muscular Skeletal Disorder	O	49	6 (12.2%)	22	4 (18.4%)	305	60 (19.7%)
	C1	92	7 (7.6%)	68	10 (14.7%)	216	34 (15.7%)
	C2	51	4 (7.8%)	18	3 (16.7%)	300	26 (8.7%)
Nervous System Disorders	O	49	26 (53.1%)	22	6 (27.3%)	305	149 (48.9%)
	C1	92	30 (32.6%)	68	33(48.5%)	216	93 (43.1%)
	C2	51	16 (31.4%)	18	3 (16.7%)	300	96 (32.0%)
Psychiatric Disorders	O	49	5 (10.2%)	22	3 (13.6%)	305	40 (13.1%)
	C1	92	6 (6.5%)	68	7 (10.3%)	216	18 (8.3%)
	C2	51	1 (2.0%)	18	2(11.1%)	300	19 (6.3%)
Renal Disorders	O	49	0 (0.0%)	22	0 (0.0%)	305	1 (0.3%)
Reproductive Disorders	O	49	1 (2.0%)	22	0 (0.0%)	305	2 (0.7%)
	C1	92	1 (1.1%)	68	0 (0.0%)	216	2 (0.9%)
	C2	51	0 (0.0%)	18	0 (0.0%)	300	1 (0.3%)
Respiratory Disorders	O	49	7 (14.3%)	22	4 (16.2%)	305	54 (17.7%)
	C1	92	11 (12.0%)	68	11 (16.2%)	216	30 (13.9%)
	C2	51	2 (3.9%)	18	2 (11.1%)	300	20 (6.7%)
Skin Disorders	O	49	29 (59.2%)	22	15 (68.2%)	305	205 (67.2%)
	C1	92	50 (54.3%)	68	49 (72.1%)	216	140 (64.8%)
	C2	51	13 (25.5%)	18	5 (27.8%)	300	81 (27.0%)
Vascular Disorders	O	49	8 (16.3%)	22	3 (13.6%)	305	59 (19.3%)
	C1	92	8 (8.7%)	68	11 (16.2%)	216	33 (15.3%)
	C2	51	5 (9.8%)	18	0 (0/0%)	300	23 (7.7%)

The adverse events were assessed overall (O) with the 2 year trial or the year following the first cycle (C1) or the year following the second cycle (C2). The results show the total number (N) within the no alemtuzumab-specific antibodies, ever binding antibody (Bab) positive always neutralizing antibody (Nab) negative or ever Nab and Bab positive groups and the number showing and adverse event (N-AE).

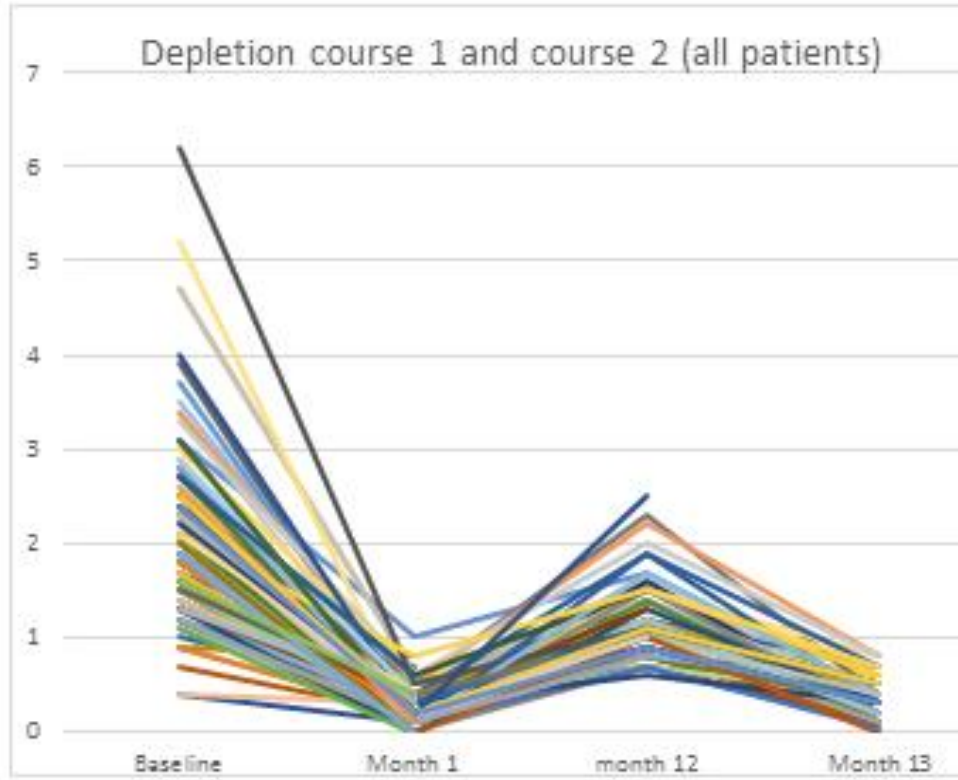
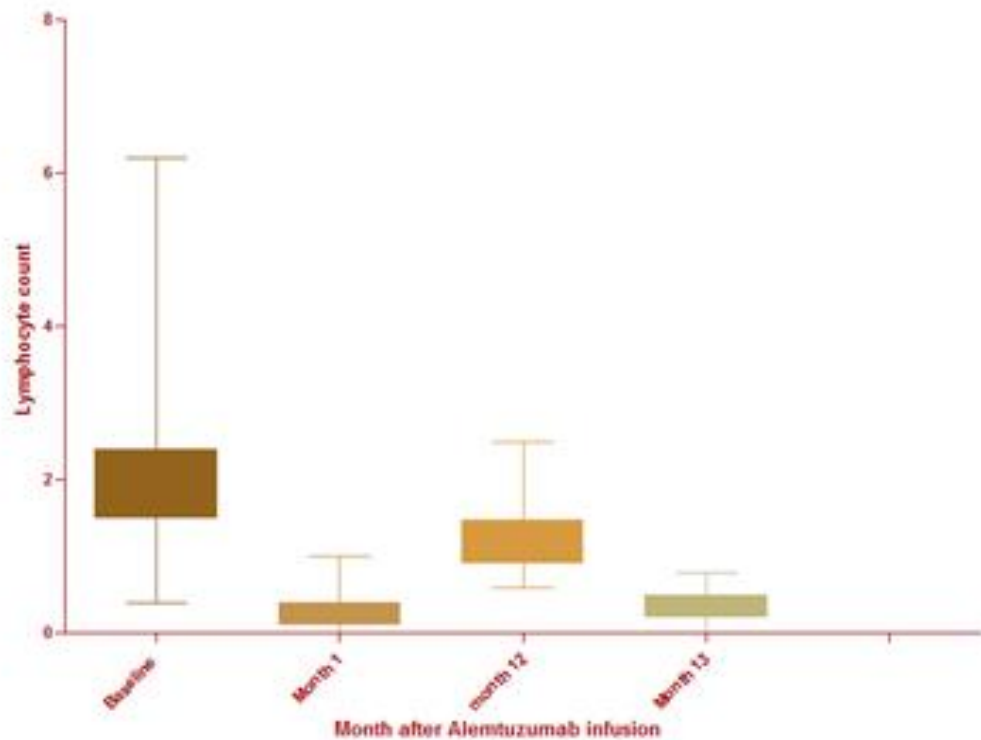
SUPPLEMENTARY FIGURE S1. *Blunted lymphocyte depleting response in a person with MS who received multiple alemtuzumab infusion cycles.*



An individual who was a participant in the MS-CARE-1 trial and extension programme received multiple treatment cycles due to MS disease activity. Regular lymphocyte levels were assessed. A third cycle was administered due to MRI activity, but lymphocyte depletion was modest. The patient had a subsequent clinical relapse at (16 months), which triggered a fourth cycle of treatment. Ongoing MRI activity subsequently triggered a fifth cycle, which resulted in limited lymphocyte depletion. Following specific requests, the manufacturer confirmed this individual had binding and neutralizing antibodies with titres that were boosted after each treatment cycle. The robust depletion by the fourth cycle could reflect the increased time interval between cycles, allowing elimination of neutralizing antibodies.

SUPPLEMENTARY FIGURE S2

Lymphocyte count profile on people with MS treated with alemtuzumab treated with alemtuzumab in the post-marketing setting.

(A)**(B)**

(A) Absolute lymphocyte counts and (B) a box (25-50% quartile) and whisker plot (25-75% quartile) of people treated with alemtuzumab at the Royal London Hospital in the post-marketing setting (n=126). 8