**Supplemental Figure S1. FACS plots showing IL-3 expression by CD4+ T cells and IL-17 release by restimulated splenocytes.**

C57BL/6 mice were immunized with MOG-peptide 35-55 on day 0. Before immunization (day 0) or 14 and 21 days after immunization (3-5 mice / time point) splenocytes were analyzed. (A) Representative FACS-plots showing IL-3+CD4+ T cells on day 0 and 14 (upper panel). Co-staining of CD4+ T cells for expression of IL-3, IFN-γ, IL-17 and GM-CSF on day 14 (lower panel). (B) Total splenocytes (left) and splenocytes depleted of CD4+ or CD8+ T cells (right, day 21) were restimulated with MOG-peptide 35-55 or PBS as control for 3 days and IL-17 was measured in the supernatant. Data are represented as mean +/- SEM
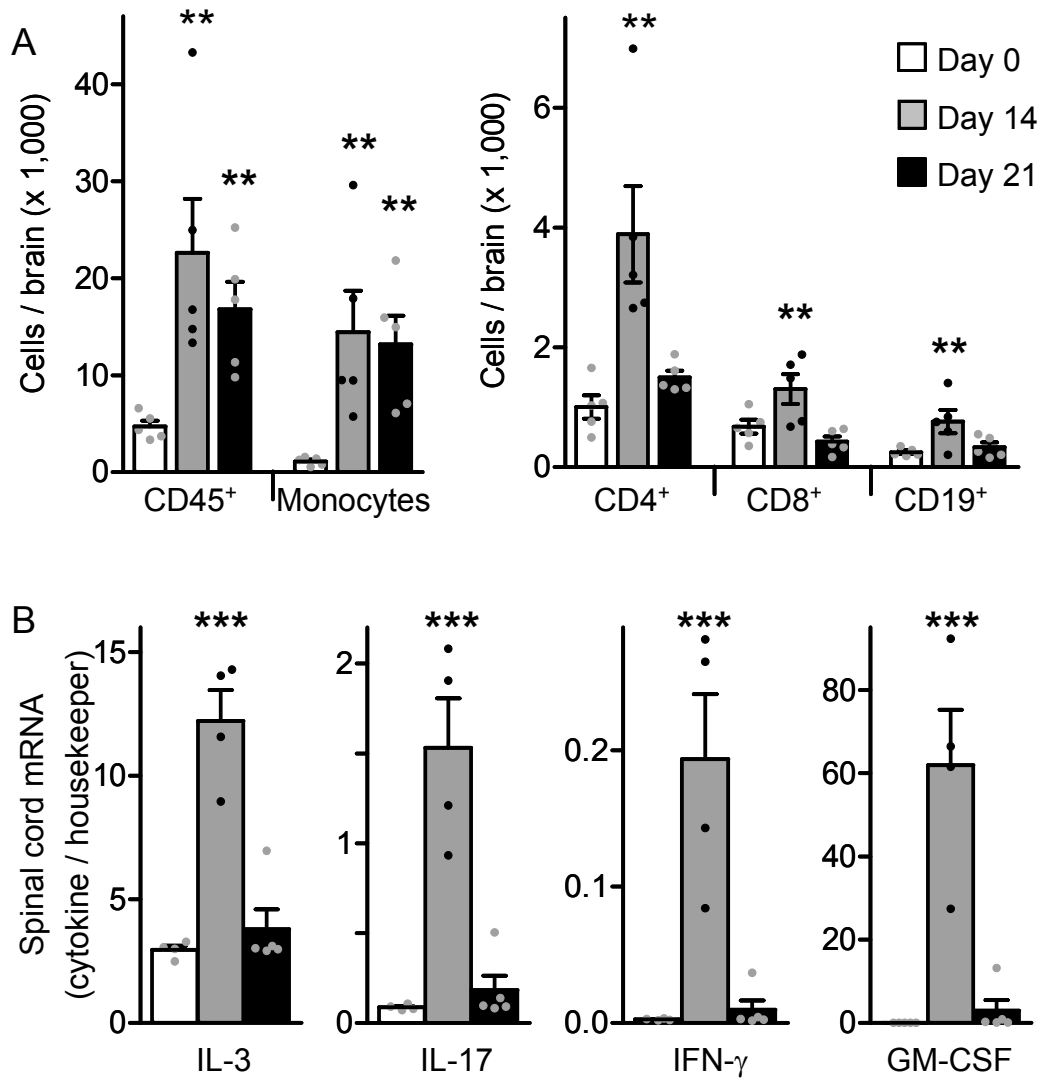
Supplemental Figure S2. Time course of leukocyte infiltration and cytokine expression in the CNS.

C57BL/6 mice were immunized with MOG-peptide 35-55 on day 0. (A) Before immunization (day 0) or 14 and 21 days after immunization (5 mice / time point) cells infiltrating the brain were quantified by flow cytometry. CD4+ T cells, CD8+ T cells and CD19+ B cells were markedly increased at day 14, but returned to baseline levels again on day 21. Monocytes largely outnumbered the T cells and remained high in the brain until day 21. (B) Cytokine mRNA levels were quantified in the spinal cord by RT-PCR (4-5 mice / time point). Data are represented as mean +/- SEM. ANOVA test of day 14 or day 21 vs. day 0: **P<0.01, ***P<0.01.
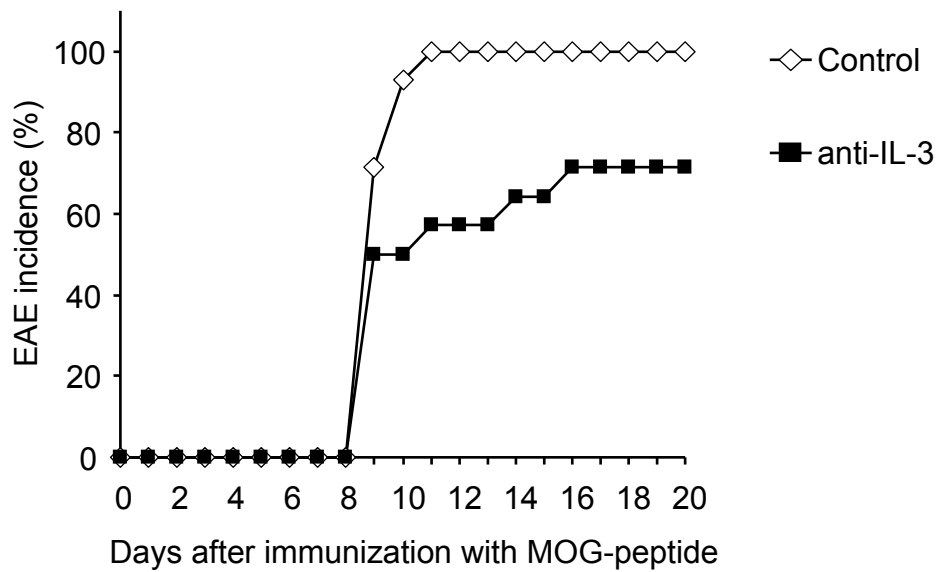
**Supplemental Figure S3. Blockade of IL-3 delays the onset and reduces the incidence of EAE.**

EAE was induced in C57BL/6 mice by immunization with MOG-peptide 35-55 on day 0. From day 0-19 mice were treated with an intact anti-IL-3 antibody (anti-IL-3, 50 µg/day) or purified rat IgG (Control, 50 µg/day) (n = 14 / group). The incidence (%) of EAE (EAE score >0) is depicted. One out of 2 representative experiments is shown.
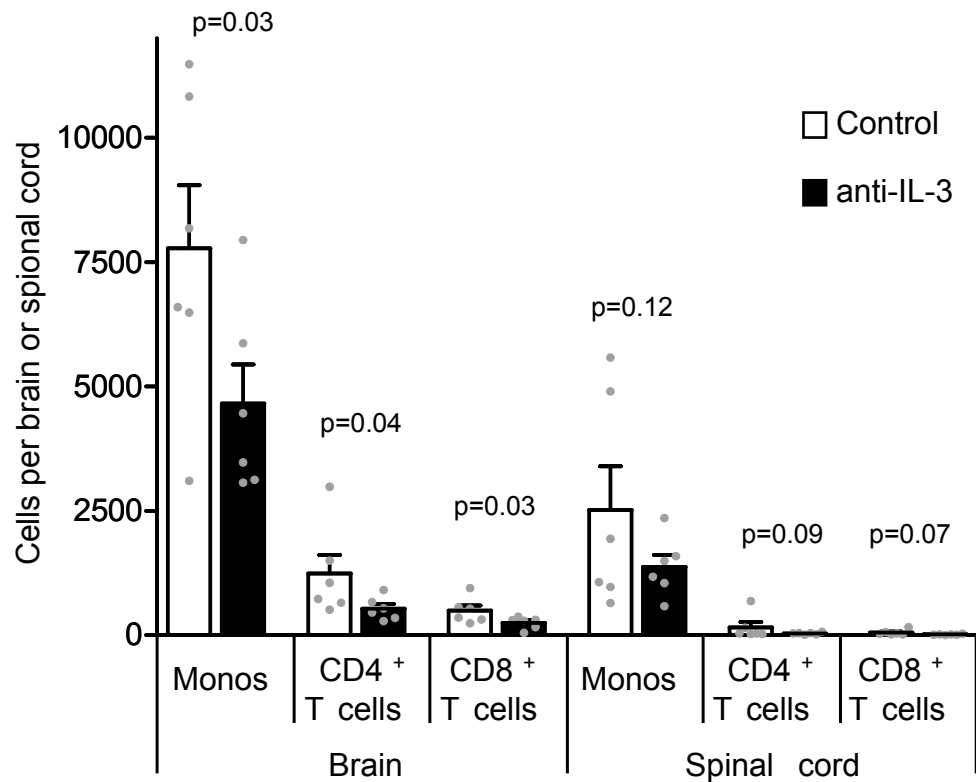
Supplemental Figure S4. Blockade of IL-3 reduces the immune cell infiltrate in the brain and spinal cord.

EAE was induced in C57BL/6 mice by immunization with MOG-peptide 35-55 on day 0. From day 0-12 mice were treated with a neutralizing anti-IL-3 antibody (anti-IL-3, 50 µg/day) or purified rat IgG (Control, 50 µg/day) (n = 6 / group). Leukocytes infiltrating the brain and the spinal cord were quantified by flow cytometry on day 13. Infiltrating monocytes (Monos), CD4+ T cells and CD8+ T cells were significantly reduced in the brain of mice treated with anti-IL-3. There was also a trend for reduced infiltrates in the spinal cord. Data are represented as mean +/- SEM. Student's T test of anti-IL-3 vs. Control.
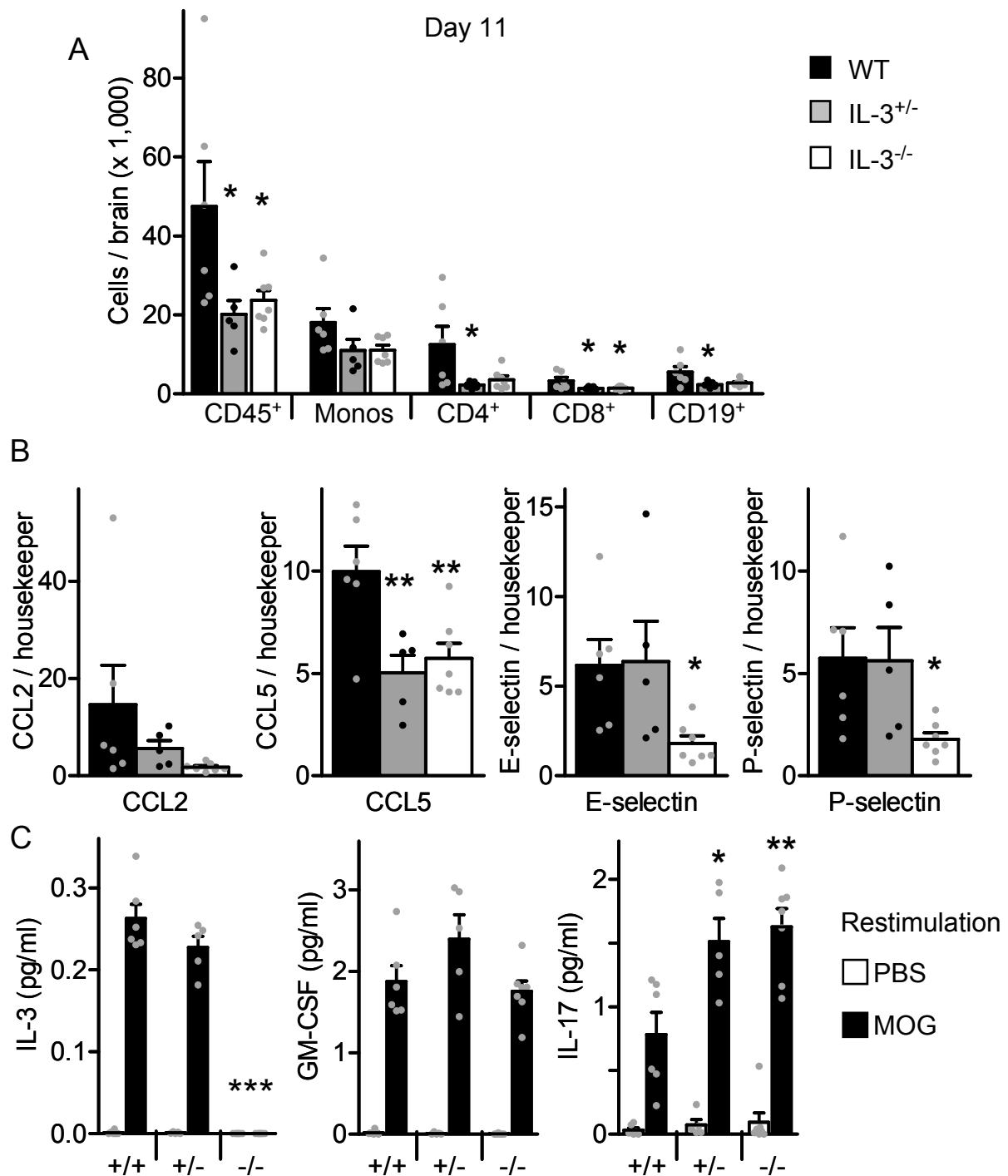
Supplemental Figure S5. Analysis of IL-3 deficient mice on day 11 after induction of EAE. EAE was induced in C57BL/6 wild type (IL-3$^{+/+}$, n=6), heterozygous IL-3 deficient (IL-3$^{+/-}$, n=5) and homozygous IL-3 deficient (IL-3$^{-/-}$, n=7) littermates by immunization with MOG-peptide 35-55 on day 0. (A) The immune cell infiltrate was quantified in the brain by flow cytometry on day 11. (B) The expression of CCL2, CCL5, E- and P-selectin was quantified in the spinal cord. (C) Splenocytes were restimulated with MOG-peptide 35-55 or PBS for 3 days and the release of IL-3, GM-CSF and IL-17 was measured in the supernatant by ELISA. Data are represented as mean +/- SEM. ANOVA test of IL-3$^{+/-}$ or IL-3$^{-/-}$ vs. IL-3$^{+/+}$: *$P \leq 0.05$, **$P < 0.01$.
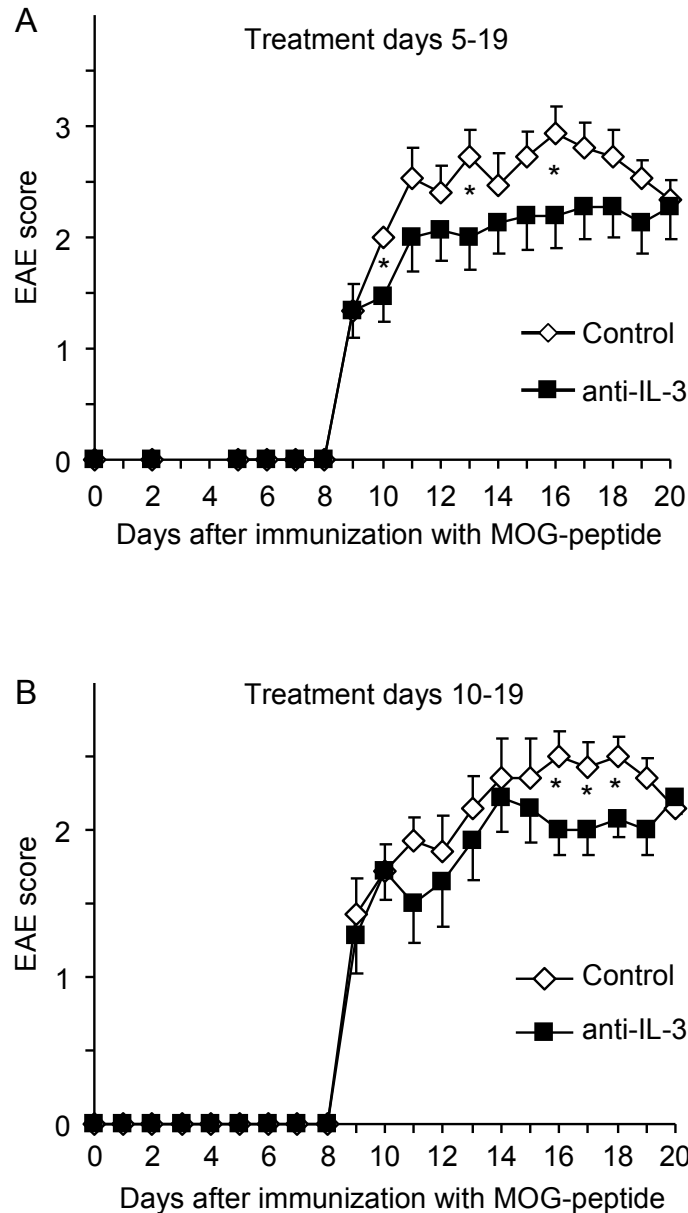
Supplemental Figure S6. Late blockade of IL-3 has less impact on the development of EAE.

EAE was induced in C57BL/6 (H-2b) mice by immunization with MOG-peptide 35-55 on day 0. (A) From day 5-19 mice were treated with a neutralizing anti-IL-3 antibody (anti-IL-3, 50 μg/day) or purified rat IgG (Control, 50 μg/day) (n = 15 / group). (B) From day 10-19 mice were treated with a neutralizing anti-IL-3 antibody (anti-IL-3, 50 μg/day) or purified rat IgG (Control, 50 μg/day) (n = 14 / group). Data are represented as mean +/- SEM, Student's T test of anti-IL-3 vs. Control: *P≤0.05.
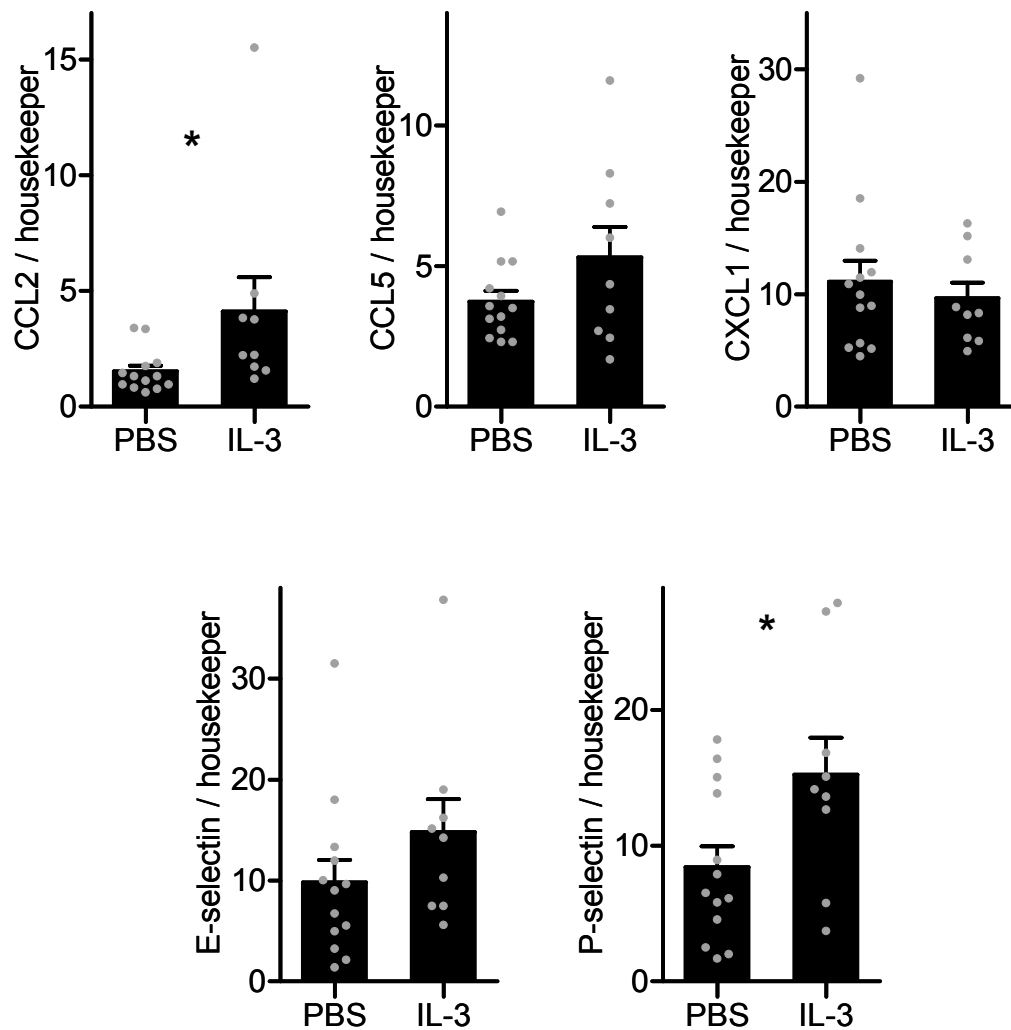
Supplemental Figure S7. Impact of IL-3 on the expression of chemokines and selectins in the brain.

EAE was induced in C57BL/6 (H-2b) mice by immunization with MOG-peptide 35-55 on day 0. From day 0-10 mice were treated by daily i.p. injection of 200 ng recombinant murine IL-3 (IL-3, n=9) or PBS as control (PBS, n=13) and analysed on day 11. Expression of CCL2, CCL5, CXCL1, E-selectin and P-selectin was quantified in the brain by RT-PCR. Data are represented as mean +/- SEM, Student's T test of IL-3 vs. PBS: *$P \leq 0.05$.

Supplemental Table 1. Characteristics of MS patients and controls

Case	Sex	Type of disease	Age (years)	Years since diagnosis	EDSS	Immunmodulation
1	M	Control	49	n.a.	n.a.	n.a.
2	F	Control	22	n.a.	n.a.	n.a.
3	F	Control	22	n.a.	n.a.	n.a.
4	M	Control	21	n.a.	n.a.	n.a.
5	F	Control	18	n.a.	n.a.	n.a.
6	M	Control	23	n.a.	n.a.	n.a.
7	F	Control	49	n.a.	n.a.	n.a.
8	M	Control	46	n.a.	n.a.	n.a.
9	F	Control	41	n.a.	n.a.	n.a.
10	F	Control	31	n.a.	n.a.	n.a.
11	F	Control	28	n.a.	n.a.	n.a.
12	F	Control	48	n.a.	n.a.	n.a.
13	F	Control	35	n.a.	n.a.	n.a.
14	F	Control	25	n.a.	n.a.	n.a.
15	M	Control	32	n.a.	n.a.	n.a.
16	F	Control	48	n.a.	n.a.	n.a.
17	M	Control	26	n.a.	n.a.	n.a.
18	F	Control	23	n.a.	n.a.	n.a.
19	F	Control	23	n.a.	n.a.	n.a.
20	F	Control	22	n.a.	n.a.	n.a.
21	M	Control	24	n.a.	n.a.	n.a.
22	F	RRMS active disease	43	1	4	None
23	M	RRMS active disease	42	0	1	None
24	M	RRMS active disease	44	0	1	None
25	F	RRMS active disease	32	7	2.5	Natalizumab (Tysabri^{TM})
26	F	RRMS active disease	42	0	2	None
27	M	RRMS active disease	26	0	3.5	None
28	M	RRMS active disease	32	1	2	Interferon-beta-1a (Avonex^{TM})
29	F	RRMS active disease	19	4	2	None
30	F	RRMS active disease	23	1	3	Dimethlyfumarate (Tecfidera^{TM})
31	F	RRMS active disease	36	0	2	None
32	F	RRMS active disease	26	11	2	None
33	F	RRMS active	33	0	2	None

		disease				
34	F	RRMS active disease	29	6	2	Glatirameracetate (Copaxone^{TM})
35	F	RRMS active disease	24	0	4.5	None
36	M	RRMS active disease	50	0	2	None
37	F	RRMS active disease	23	0	2	None
38	F	RRMS active disease	54	4	5.5	Dimethlyfumarate (Tecfidera^{TM})
39	F	RRMS active disease	47	0	2	None
40	M	RRMS active disease	42	0	2	None
41	F	RRMS inactive disease	23	0.5	0	Interferon-beta-1a (Avonex^{TM})
42	F	RRMS inactive disease	43	0.5	0	Glatirameracetate (Copaxone^{TM})
43	F	RRMS inactive disease	51	2	2.5	Interferon-beta-1a (Rebif^{TM})
44	F	RRMS inactive disease	50	3	1.5	Interferon-beta-1b (Extavia^{TM})
45	F	RRMS inactive disease	38	1	3	None
46	F	RRMS inactive disease	46	0.5	2	None
47	F	RRMS inactive disease	45	0.5	0	None
48	F	RRMS inactive disease	42	0.5	2.5	Interferon-beta-1a (Avonex^{TM})
49	M	RRMS inactive disease	54	0.5	1.5	None
50	M	RRMS inactive disease	27	0.5	1.5	Natalizumab (Tysabri^{TM})
51	M	RRMS inactive disease	36	0.5	2	Interferon-beta-1a (Rebif^{TM})
52	F	RRMS inactive disease	35	7	0	Glatirameracetate (Copaxone^{TM})
53	F	RRMS inactive disease	55	11	3	Glatirameracetate (Copaxone^{TM})
54	F	RRMS inactive disease	33	2	1.5	Glatirameracetate (Copaxone^{TM})
55	F	RRMS inactive disease	42	12	3	Interferon-beta-1b (Extavia^{TM})
56	F	RRMS inactive disease	19	4	1	Dimethlyfumarate (Tecfidera^{TM})
57	F	RRMS inactive disease	38	13	1.5	None

58	M	RRMS inactive disease	55	8	3	None
59	F	RRMS inactive disease	26	10	1.5	None
60	F	RRMS inactive disease	33	0.5	0	Dimethlyfumarate (Tecfidera^{TM})
61	F	RRMS inactive disease	36	10	0	Dimethlyfumarate (Tecfidera^{TM})
62	F	RRMS inactive disease	49	15	2	None
63	F	RRMS inactive disease	64	18	3.5	None
64	F	RRMS inactive disease	44	12	1.5	None
65	F	RRMS inactive disease	31	15	3.5	Dimethlyfumarate (Tecfidera^{TM})
66	F	RRMS inactive disease	43	19	2	Interferon-beta-1a (Rebif^{TM})
67	M	RRMS inactive disease	57	12	3.5	None
68	F	RRMS inactive disease	45	15	0	Interferon-beta-1b (Extavia^{TM})
69	F	RRMS inactive disease	33	15	1.5	Dimethlyfumarate (Tecfidera^{TM})
70	M	RRMS inactive disease	50	0.5	2	Teriflunomide (Aubabio^{TM})