

Table S1 Clinical demographics of IFN- β -treated MS patients in the NEDA and EDA groups

	MS w/IFN- β			<i>p</i> value		
	NEDA (<i>n</i> = 8)	EDA (<i>n</i> = 13)	HCs (<i>n</i> = 44)	NEDA vs. HCs	EDA vs. HCs	NEDA vs. EDA
Female, <i>n</i> (%)	6 (75.0)	9 (69.2)	27 (61.4)	NS	NS	NS
Age at examination, years	47.0 [44.5-53.8]	44.0 [41.0-46.5]	35.0 [32.3-43.8]	0.004	0.010	NS
Age at disease onset, years	30.5 [25.5-34.8]	27.0 [23.5-34.0]	–	–	–	NS
Disease duration at INF- β initiation, years	6.83 [1.38-10.3]	6.50 [2.29-12.9]	–	–	–	NS
Disease duration at examination, years	15.8 [9.00-23.9]	15.2 [10.7-20.6]	–	–	–	NS
Subtype (RRMS / SPMS / PPMS), <i>n</i> (%)	7/1/0 (87.5/12.5/0.0)	6/6/1 (46.2/46.2/7.7)	–	–	–	NS
EDSS score at IFN- β initiation	3.0 [1.25-6.13]	2.5 [1.75-5.25]	–	–	–	NS
EDSS score at examination	2.0 [1.13-2.75]	4.5 [2.0-6.25]	–	–	–	NS (0.062)
Δ EDSS	–0.5 [–1.5-0.0]	1.0 [0.25-2.5]	–	–	–	0.003
MSSS at IFN- β initiation	4.89 [2.86-8.38]	6.00 [2.15-7.19]	–	–	–	NS
MSSS at examination	1.84 [0.57-3.65]	3.52 [1.99-7.39]	–	–	–	NS (0.060)
Δ MSSS	–2.69 [–5.16–1.16]	–0.20 [–1.69-0.96]	–	–	–	0.013
Years of IFN- β treatment	9.50 [5.50-14.5]	7.00 [4.50-8.50]	–	–	–	NS

Values are the median [IQR] or count (%). Δ EDSS was calculated as the difference between EDSS scores at IFN- β initiation and at examination. Δ MSSS was the difference between MSSS at IFN- β initiation and at examination.

EDA = evidence of disease activity; EDSS = Expanded Disability Status Scale; HCs = healthy controls; IFN- β = interferon- β ; IQR = interquartile ranges; MS = multiple sclerosis; MSSS = multiple sclerosis severity score; NEDA = no-evidence of disease activity; NS = not significant; PPMS = primary progressive MS; RRMS = relapsing-remitting MS; SPMS = secondary progressive MS; w/ = with.

Table S2 Clinical demographics of untreated MS patients in the NEDA and EDA groups

	Untreated MS			<i>p</i> value		
	NEDA (<i>n</i> = 19)	EDA (<i>n</i> = 13)	HCs (<i>n</i> = 44)	NEDA vs. HCs	EDA vs. HCs	NEDA vs. EDA
Female, <i>n</i> (%)	16 (84.2)	12 (92.3)	27 (61.4)	NS (0.086)	0.044	NS
Age at examination, years	52.0 [38.0-62.0]	49.0 [35.5-55.5]	35.0 [32.3-43.8]	<0.001	NS (0.054)	NS
Age at disease onset, years	31.0 [24.0-44.0]	31.0 [24.5-36.5]	–	–	–	NS
Disease duration at examination, years	13.9 [8.2-26.9]	13.0 [4.6-21.0]	–	–	–	NS
Subtype (RRMS/SPMS/PPMS), <i>n</i> (%)	14/3/2 (73.7/15.8/10.5)	10/2/1 (76.9/15.4/7.7)	–	–	–	NS
EDSS score at 2 years before examination*	2.0 [0.0-4.0]	1.0 [0.0-5.4]	–	–	–	NS
EDSS score at examination	2.0 [0.0-4.0]	2.0 [1.0-5.5]	–	–	–	NS
Δ EDSS*	0.0 [0.0-0.0]	1.00 [1.0-2.5]	–	–	–	<0.001
MSSS at 2 years before examination*	2.13 [0.25-5.44]	1.27 [0.06-6.16]	–	–	–	NS
MSSS at examination	1.80 [0.21-5.16]	2.85 [0.88-8.89]	–	–	–	NS
Δ MSSS*	-0.09 [-0.62--0.03]	1.18 [0.33-1.44]	–	–	–	<0.001

Values are the median [IQR] or count (%). Δ EDSS was calculated as the difference between EDSS scores at 2 years before examination and at examination.

Δ MSSS was the difference between MSSS at 2 years before examination and at examination.

*The data of 5 patients are missing because of a lack of data before the onset.

EDA = evidence of disease activity; EDSS = Expanded Disability Status Scale; HCs = healthy controls; IFN- β = interferon- β ; IQR = interquartile ranges; MS = multiple sclerosis; MSSS = multiple sclerosis severity score; NEDA = no-evidence of disease activity; NS = not significant; PPMS = primary progressive MS; RRMS = relapsing-remitting MS; SPMS = secondary progressive MS.

Table S3 Comparison of clinical demographics between RRMS and PMS patients

	Untreated MS			MS w/IFN- β		
	RRMS (<i>n</i> = 26)	PMS (<i>n</i> = 9)	<i>p</i> value	RRMS (<i>n</i> = 13)	PMS (<i>n</i> = 8)	<i>p</i> value
Female, <i>n</i> (%)	23 (88.5)	7 (77.8)	NS	9 (69.2)	6 (75.0)	NS
Age at examination, years	45.0 [36.5-54.0]	56.0 [46.5-67.5]	0.043	46.0 [43.0-47.0]	44.0 [40.8-51.5]	NS
Age at disease onset, years	31.0 [27.8-36.0]	29.0 [19.0-55.0]	NS	30.0 [25.0-34.0]	26.0 [21.0-36.8]	NS
Disease duration at examination, years	13.0 [7.6-18.3]	20.9 [10.7-28.1]	NS (0.086)	15.4 [11.1-21.7]	15.2 [10.2-20.8]	NS
EDSS score at examination	1.5 [0.0-3.0]	7.0 [6.25-7.25]	<0.001	2.0 [1.5-2.5]	6.25 [5.63-6.88]	<0.001
MSSS at examination	1.57 [0.24-2.99]	7.97 [6.56-8.60]	<0.001	1.64 [0.61-2.88]	7.24 [6.78-7.60]	<0.001
Disease duration at IFN- β initiation, years	–	–	–	7.1 [1.7-12.9]	5.8 [1.9-11.5]	NS
EDSS score at IFN- β initiation	–	–	–	2.0 [1.0-3.5]	4.0 [2.5-6.0]	NS (0.074)
MSSS at IFN- β initiation	–	–	–	3.69 [1.32-5.62]	7.19 [6.04-7.74]	0.015
Years of IFN- β treatment	–	–	–	7.0 [4.0-9.5]	8.5 [6.3-13.8]	NS

Values are the median [IQR] or count (%).

EDSS = Expanded Disability Status Scale; IFN- β = interferon- β ; IQR = interquartile ranges; MS = multiple sclerosis; MSSS = MS severity score; NS = not significant; PMS = progressive MS; RRMS = relapsing-remitting MS; w/ = with.

Table S4 Comparison of the percentages of CD4⁺ T cell subsets between the untreated MS group, IFN- β -treated MS group and healthy controls

In total CD4 ⁺ T cells	Untreated MS (<i>n</i> = 35)	MS w/ IFN- β (<i>n</i> = 21)	HCs (<i>n</i> = 44)	<i>p</i> value (K- W test)	<i>p</i> ^{adj} value		
					Untreated MS vs. HCs	MS w/ IFN- β vs. HCs	Untreated MS vs. MS w/ IFN- β
Tnaive (CCR7 ⁺ CD45RA ⁺)	45.3 [38.8-59.4]	51.2 [41.2-58.8]	49.4 [36.1-56.9]	NS	–	–	–
Tcm (CCR7 ⁺ CD45RA ⁻)	27.9 [21.7-33.7]	26.7 [21.0-32.0]	25.7 [23.2-33.6]	NS	–	–	–
Tem (CCR7 ⁻ CD45RA ⁻)	19.2 [12.5-24.7]	16.4 [13.9-26.8]	18.8 [15.3-28.8]	NS	–	–	–
Teff (CCR7 ⁻ CD45RA ⁺)	2.82 [1.74-3.87]	2.87 [2.20-4.58]	2.51 [1.99-3.67]	NS	–	–	–
Activated T (HLA-DR ⁺)	1.96 [1.50-3.07]	2.36 [1.72-3.02]	2.81 [1.59-3.57]	NS	–	–	–
Treg (CD25 ⁺ CD127 ^{low/-})	4.41 [2.83-5.95]	3.80 [3.50-5.82]	5.97 [4.34-6.87]	0.012	NS	NS (0.077)	NS

Values are the median [IQR]. Percentages of each population in total CD4⁺ T cells are shown.

p values (K-W test) were obtained by Kruskal-Wallis analyses, and if they were statistically significant, then *p*^{adj} values were calculated using multivariate linear regression analyses adjusted for age and sex.

HCs = healthy controls; IFN- β = interferon- β ; IQR = interquartile ranges; K-W = Kruskal-Wallis; MS = multiple sclerosis; NS = not significant; Tcm = central memory T cells; Teff = effector T cells; Tem = effector memory T cells; Tnaive = naïve T cells; Treg = regulatory T cells; w/ = with.

Table S5 Comparison of the percentages of CD8⁺ T cell subsets between the untreated MS group, IFN- β -treated MS group and healthy controls

In total CD8 ⁺ T cells	Untreated MS (<i>n</i> = 35)	MS w/ IFN- β (<i>n</i> = 21)	HCs (<i>n</i> = 44)	<i>p</i> value (K- W test)	<i>p</i> ^{adj} value		
					Untreated MS vs. HCs	MS w/ IFN- β vs. HCs	Untreated MS vs. MS w/ IFN- β
Tnaive (CCR7 ⁺ CD45RA ⁺)	28.1 [17.7-53.8]	46.0 [28.6-64.3]	44.4 [33.6-54.2]	0.035	NS	NS	0.031
Tcm (CCR7 ⁺ CD45RA ⁻)	5.14 [3.04-9.04]	8.68 [5.51-12.0]	5.55 [3.72-7.58]	0.017	NS	NS	0.013
Tem (CCR7 ⁻ CD45RA ⁻)	37.6 [26.7-46.6]	26.7 [16.9-45.3]	29.2 [23.9-44.0]	NS	–	–	–
Teff (CCR7 ⁻ CD45RA ⁺)	15.9 [8.70-25.2]	11.6 [6.68-17.4]	12.8 [8.16-22.8]	NS	–	–	–
Activated T (HLA-DR ⁺)	4.27 [2.72-6.83]	4.55 [2.79-6.58]	3.63 [2.07-6.17]	NS	–	–	–

Values are the median [IQR]. Percentages of each population in total CD8⁺ T cells are shown.

p values (K-W test) were obtained by Kruskal-Wallis analyses, and if they were statistically significant, then *p*^{adj} values were calculated using multivariate linear regression analyses adjusted for age and sex.

HCs = healthy controls; IFN- β = interferon- β ; IQR = interquartile ranges; K-W = Kruskal-Wallis; MS = multiple sclerosis; NS = not significant; Tcm = central memory T cells; Teff = effector T cells; Tem = effector memory T cells; Tnaive = naïve T cells; w/ = with.

Table S6 Comparison of the percentages of cytokine-producing $\alpha\beta$ T cell subsets between the untreated MS group, IFN- β -treated MS group and healthy controls

	Untreated MS (n = 35)	MS w/ IFN- β (n = 21)	HCs (n = 44)	p value (K-W test)	<i>p</i> ^{adj} value		
					Untreated MS vs. HCs	MS w/ IFN- β vs. HCs	Untreated MS vs. MS w/ IFN- β
In CD4⁺ T cells							
IL-17A ⁺	0.24 [0.16-0.58]	0.37 [0.27-0.61]	0.55 [0.25-1.11]	0.004	0.017	NS	NS
IFN- γ ⁺	5.77 [2.04-8.24]	6.70 [2.38-10.3]	9.42 [4.59-14.6]	NS (0.052)	–	–	–
IL-4 ⁺	1.70 [0.83-2.91]	1.64 [1.04-2.69]	2.76 [1.67-4.31]	0.018	0.011	NS	NS
GM-CSF ⁺	1.36 [0.76-3.19]	1.90 [1.56-3.71]	5.40 [1.19-7.91]	0.002	0.002	0.034	NS
IL-17A ⁺ IFN- γ ⁺	0.03 [0.01-0.08]	0.04 [0.02-0.08]	0.06 [0.02-0.14]	0.039	NS (0.093)	NS	NS
IL-17A ⁺ GM-CSF ⁺	0.04 [0.01-0.08]	0.05 [0.03-0.11]	0.15 [0.07-0.32]	<0.001	0.010	NS (0.081)	NS
In CD8⁺ T cells							
IL-17A ⁺	0.17 [0.08-0.28]	0.24 [0.14-0.39]	0.16 [0.10-0.31]	NS	–	–	–
IFN- γ ⁺	18.7 [10.1-37.6]	15.6 [4.97-33.0]	27.2 [16.1-38.3]	NS	–	–	–
IL-17A ⁺ IFN- γ ⁺	0.05 [0.02-0.10]	0.06 [0.02-0.07]	0.07 [0.02-0.14]	NS	–	–	–

Values are the median [IQR]. Percentages of each population are shown.

p values (K-W test) were obtained by Kruskal-Wallis analyses, and if they were statistically significant, then *p*^{adj} values were calculated using multivariate linear regression analyses adjusted for age and sex.

GM-CSF = granulocyte macrophage colony-stimulating factor; HCs = healthy controls; IFN = interferon; IL = interleukin; IQR = interquartile ranges; K-W = Kruskal-Wallis; MS = multiple sclerosis; NS = not significant; w/ = with.

Table S7 Comparison of the percentages of cytokine-producing $\gamma\delta$ T cell subsets in IFN- β -treated MS patients stratified to the NEDA or EDA groups

	MS w/IFN- β			<i>p</i> value (K-W test)	<i>p</i> ^{adj} value		
	NEDA (<i>n</i> = 8)	EDA (<i>n</i> = 13)	HCs (<i>n</i> = 44)		NEDA vs. HCs	EDA vs. HCs	NEDA vs. EDA
In Vδ1⁺ $\gamma\delta$T cells							
IL-17A ⁺	0.58 [0.10-1.04]	0.27 [0.00-1.20]	0.18 [0.01-0.72]	NS	–	–	–
IFN- γ ⁺	35.2 [17.7-56.9]	25.0 [5.75-34.3]	45.8 [24.4-60.8]	0.015	NS	0.001	NS (0.070)
IL-17A ⁺ IFN- γ ⁺	0.21 [0.04-0.75]	0.11 [0.00-0.55]	0.08 [0.00-0.31]	NS	–	–	–
IL-17A ⁻ IFN- γ ⁻	64.8 [42.9-82.0]	75.0 [65.3-93.2]	54.1 [39.1-75.5]	0.014	NS	0.001	NS (0.074)
In Vδ2⁺ $\gamma\delta$T cells							
IL-17A ⁺	0.00 [0.00-2.10]	0.00 [0.00-0.82]	0.13 [0.01-0.52]	NS	–	–	–
IFN- γ ⁺	39.9 [23.1-74.7]	32.4 [18.8-58.7]	83.6 [69.1-92.7]	<0.001	0.003	<0.001	NS
IL-17A ⁺ IFN- γ ⁺	0.00 [0.00-1.56]	0.00 [0.00-0.18]	0.11 [0.01-0.42]	NS	–	–	–
IL-17A ⁻ IFN- γ ⁻	60.1 [25.0-76.9]	67.6 [40.8-78.9]	16.0 [7.30-30.9]	<0.001	0.003	<0.001	NS
In Vδ1⁻Vδ2⁻ $\gamma\delta$T cells							
IL-17A ⁺	1.03 [0.39-2.13]	0.79 [0.31-1.87]	1.24 [0.66-2.81]	NS	–	–	–
IFN- γ ⁺	31.1 [14.6-52.8]	14.2 [8.88-27.3]	47.1 [32.5-58.2]	<0.001	NS	<0.001	0.033
IL-17A ⁺ IFN- γ ⁺	0.44 [0.19-0.80]	0.34 [0.00-0.65]	0.35 [0.19-1.22]	NS	–	–	–
IL-17A ⁻ IFN- γ ⁻	68.6 [46.4-84.7]	84.0 [72.2-88.6]	51.7 [41.3-66.9]	<0.001	NS	<0.001	0.038

Values are the median [IQR]. Percentages of each population are shown.

p values (K-W test) were obtained by Kruskal-Wallis analyses, and if they were statistically significant, then p^{adj} values were calculated using multivariate linear regression analyses adjusted for age and sex.

EDA = evidence of disease activity; HCs = healthy controls; IFN = interferon; IL = interleukin; IQR = interquartile ranges; K-W = Kruskal-Wallis; MS = multiple sclerosis; NEDA = no-evidence of disease activity; NS = not significant; w/ = with.

Table S8 Comparison of the percentages of $\gamma\delta$ T cell subsets in untreated MS patients stratified to the NEDA or EDA groups

	Untreated MS			<i>p</i> value (K-W test)	<i>p</i> ^{adj} value		
	NEDA (<i>n</i> = 19)	EDA (<i>n</i> = 13)	HCs (<i>n</i> = 44)		NEDA vs. HCs	EDA vs. HCs	NEDA vs. EDA
V δ 1 ⁺	29.0 [14.0-71.5]	31.9 [17.5-51.8]	18.4 [11.6-34.2]	NS	–	–	–
V δ 1 ⁺ V γ 9 ⁺	4.00 [1.63-16.3]	3.91 [1.14-8.07]	2.15 [1.12-4.71]	NS	–	–	–
V δ 1 ⁺ V γ 9 ⁻	23.1 [10.2-42.3]	30.4 [15.0-41.4]	15.5 [8.47-31.5]	NS	–	–	–
V δ 2 ⁺	38.5 [5.30-56.2]	29.9 [15.6-51.7]	54.9 [31.7-65.9]	0.024	NS	NS (0.076)	NS
V δ 2 ⁺ V γ 9 ⁺	37.9 [5.16-55.9]	29.8 [14.5-51.0]	54.3 [31.1-65.7]	0.021	NS	NS (0.073)	NS
V δ 2 ⁺ V γ 9 ⁻	0.19 [0.11-0.46]	0.14 [0.03-0.67]	0.08 [0.03-0.29]	NS	–	–	–
V δ 1 ⁻ V δ 2 ⁻	21.1 [14.1-27.3]	28.2 [17.3-43.0]	22.8 [17.1-30.3]	NS	–	–	–
V δ 1 ⁻ V δ 2 ⁻ V γ 9 ⁺	1.61 [0.30-2.69]	1.10 [0.46-3.15]	2.42 [1.25-3.83]	NS (0.069)	–	–	–
V δ 1 ⁻ V δ 2 ⁻ V γ 9 ⁻	20.0 [11.0-25.7]	27.5 [17.2-36.9]	18.1 [10.7-26.4]	NS (0.065)	–	–	–

Values are the median [IQR]. Percentages of each population in total $\gamma\delta$ T cells are shown.

p values (K-W test) were obtained by Kruskal-Wallis analyses, and if they were statistically significant, then *p*^{adj} values were calculated using multivariate linear regression analyses adjusted for age and sex.

EDA = evidence of disease activity; HCs = healthy controls; IFN- β = interferon- β ; IQR = interquartile ranges; K-W = Kruskal-Wallis; MS = multiple sclerosis; NEDA = no-evidence of disease activity; NS = not significant.

Table S9 Comparison of the percentages of B cell subsets in untreated MS patients stratified to the NEDA or EDA groups

	Untreated MS			<i>p</i> value (K-W test)	<i>p</i> ^{adj} value		
	NEDA (<i>n</i> = 19)	EDA (<i>n</i> = 13)	HCs (<i>n</i> = 44)		NEDA vs. HCs	EDA vs. HCs	NEDA vs. EDA
Naïve (CD27 ⁻ IgD ⁺)	46.3 [27.1-54.0]	53.8 [38.8-59.5]	51.8 [41.4-60.6]	NS	–	–	–
Memory (CD27 ⁺)	13.4 [9.82-24.4]	19.9 [12.6-36.2]	22.7 [16.9-29.9]	0.024	NS	NS	NS
CS ⁺ Memory (CD27 ⁺ IgD ⁻)	11.2 [8.84-22.0]	18.0 [11.1-32.7]	18.8 [14.4-25.2]	NS (0.060)	–	–	–
CS ⁻ Memory (CD27 ⁺ IgD ⁺)	1.65 [0.72-2.68]	2.28 [1.86-3.80]	3.49 [2.49-4.67]	<0.001	0.043	NS	NS
Plasmablasts (CD38 ^{high} CD20 ⁻)	0.25 [0.12-0.49]	0.61 [0.28-1.48]	0.37 [0.24-0.67]	0.030	NS	NS (0.064)	0.008
Transitional (CD24 ^{high} CD38 ^{high})	3.16 [1.80-4.14]	2.50 [0.58-6.09]	3.14 [2.32-4.45]	NS	–	–	–

Values are the median [IQR]. Percentages of each population in total B cells are shown.

p values (K-W test) were obtained by Kruskal-Wallis analyses, and if they were statistically significant, then *p*^{adj} values were calculated using multivariate linear regression analyses adjusted for age and sex.

CS⁺ = class-switched; CS⁻ = non-class-switched; EDA = evidence of disease activity; HCs = healthy controls; IFN-β = interferon-β; IQR = interquartile ranges; K-W = Kruskal-Wallis; MS = multiple sclerosis; NEDA = no-evidence of disease activity; NS = not significant.

Table S10 Comparison of the percentages of $\gamma\delta$ T cell subsets between RRMS and PMS patients

	Untreated MS			MS w/IFN- β		
	RRMS (<i>n</i> = 26)	PMS (<i>n</i> = 9)	<i>p</i> value	RRMS (<i>n</i> = 13)	PMS (<i>n</i> = 8)	<i>p</i> value
V δ 1 ⁺	27.0 [13.3-47.4]	49.7 [16.8-77.2]	NS	29.6 [14.9-52.0]	24.5 [12.7-43.6]	NS
V δ 1 ⁺ V γ 9 ⁺	3.26 [0.93-5.31]	11.1 [2.64-20.9]	NS (0.062)	3.22 [1.88-6.70]	2.68 [1.52-3.90]	NS
V δ 1 ⁺ V γ 9 ⁻	22.5 [9.64-38.0]	36.7 [10.6-51.2]	NS	23.5 [9.18-42.7]	21.9 [11.4-35.3]	NS
V δ 2 ⁺	37.0 [18.6-54.8]	7.34 [2.11-54.3]	NS	11.0 [3.75-24.2]	33.4 [11.2-44.5]	NS (0.076)
V δ 2 ⁺ V γ 9 ⁺	36.0 [18.0-54.6]	7.34 [1.87-54.0]	NS	10.6 [3.55-23.8]	32.2 [11.1-44.4]	NS (0.089)
V δ 2 ⁺ V γ 9 ⁻	0.20 [0.11-0.51]	0.06 [0.00-0.27]	NS	0.21 [0.11-0.72]	0.06 [0.00-0.20]	NS (0.099)
V δ 1 ⁻ V δ 2 ⁻	26.2 [16.4-42.9]	22.7 [14.5-38.7]	NS	43.6 [22.8-63.4]	32.3 [27.7-43.2]	NS
V δ 1 ⁻ V δ 2 ⁻ V γ 9 ⁺	1.89 [0.38-3.57]	0.66 [0.10-1.31]	0.050	2.22 [0.33-2.82]	0.88 [0.25-1.48]	NS
V δ 1 ⁻ V δ 2 ⁻ V γ 9 ⁻	23.8 [15.4-34.8]	21.3 [13.8-37.0]	NS	41.4 [19.5-60.1]	31.7 [25.4-42.5]	NS

Values are the median [IQR]. Percentages of each population in total $\gamma\delta$ T cells are shown.

IFN- β = interferon- β ; IQR = interquartile ranges; MS = multiple sclerosis; NS = not significant; PMS = progressive MS; RRMS = relapsing-remitting MS; w/ = with.

Table S11 Comparison of the percentages of CD4⁺ T cell subsets between RRMS and PMS patients

In total CD4 ⁺ T cells	Untreated MS			MS w/IFN- β		
	RRMS (<i>n</i> = 26)	PMS (<i>n</i> = 9)	<i>p</i> value	RRMS (<i>n</i> = 13)	PMS (<i>n</i> = 8)	<i>p</i> value
Tnaive (CCR7 ⁺ CD45RA ⁺)	55.8 [43.4-66.2]	38.8 [32.9-41.8]	0.002	51.9 [44.4-57.1]	44.6 [33.2-60.6]	NS
Tcm (CCR7 ⁺ CD45RA ⁻)	25.3 [21.2-33.5]	30.4 [28.0-38.0]	NS	26.7 [19.4-34.1]	27.5 [21.7-31.6]	NS
Tem (CCR7 ⁻ CD45RA ⁻)	17.6 [12.1-22.1]	26.4 [20.8-35.0]	0.004	16.4 [14.7-19.0]	22.8 [10.7-34.7]	NS
Teff (CCR7 ⁻ CD45RA ⁺)	2.75 [1.73-3.52]	2.85 [1.77-7.60]	NS	2.87 [2.19-5.39]	2.76 [2.15-3.03]	NS
Activated T (HLA-DR ⁺)	1.86 [1.31-2.86]	2.55 [1.84-4.01]	NS (0.070)	2.36 [1.83-2.91]	2.05 [1.06-4.73]	NS
Treg (CD25 ⁺ CD127 ^{low/-})	4.16 [2.39-5.85]	5.21 [4.05-6.12]	NS	3.83 [3.57-5.82]	3.66 [2.30-6.13]	NS

Values are the median [IQR]. Percentages of each population in total CD4⁺ T cells are shown.

IFN- β = interferon- β ; IQR = interquartile ranges; MS = multiple sclerosis; NS = not significant; PMS = progressive MS; RRMS = relapsing-remitting MS; Tcm = central memory T cells; Teff = effector T cells; Tem = effector memory T cells; Tnaive = naïve T cells; Treg = regulatory T cells; w/ = with.

Table S12 Comparison of the percentages of CD8⁺ T cell subsets between RRMS and PMS patients

In total CD8 ⁺ T cells	Untreated MS			MS w/IFN- β		
	RRMS (<i>n</i> = 26)	PMS (<i>n</i> = 9)	<i>p</i> value	RRMS (<i>n</i> = 13)	PMS (<i>n</i> = 8)	<i>p</i> value
Tnaive (CCR7 ⁺ CD45RA ⁺)	31.7 [19.6-58.2]	21.9 [6.77-28.7]	NS (0.052)	52.1 [43.0-64.3]	28.6 [16.4-70.9]	NS
Tcm (CCR7 ⁺ CD45RA ⁻)	5.22 [3.03-7.81]	3.45 [2.28-9.97]	NS	9.97 [7.87-13.1]	6.15 [3.41-11.0]	NS (0.076)
Tem (CCR7 ⁻ CD45RA ⁻)	36.4 [25.0-46.0]	43.5 [34.8-55.6]	NS	21.1 [16.9-30.6]	45.3 [14.5-64.8]	NS
Teff (CCR7 ⁻ CD45RA ⁺)	15.9 [7.62-26.5]	19.4 [12.0-41.1]	NS	11.6 [6.18-17.4]	12.7 [7.29-23.0]	NS
Activated T (HLA-DR ⁺)	4.11 [2.71-7.25]	4.27 [2.85-6.43]	NS	4.77 [4.12-6.58]	3.07 [1.67-6.43]	NS

Values are the median [IQR]. Percentages of each population in total CD8⁺ T cells are shown.

IFN- β = interferon- β ; IQR = interquartile ranges; MS = multiple sclerosis; NS = not significant; PMS = progressive MS; RRMS = relapsing-remitting MS; Tcm = central memory T cells; Teff = effector T cells; Tem = effector memory T cells; Tnaive = naïve T cells; Treg = regulatory T cells; w/ = with.

Table S13 Comparison of the percentages of B cell subsets between RRMS and PMS patients

	Untreated MS			MS w/IFN- β		
	RRMS (<i>n</i> = 26)	PMS (<i>n</i> = 9)	<i>p</i> value	RRMS (<i>n</i> = 13)	PMS (<i>n</i> = 8)	<i>p</i> value
Naïve (CD27 ⁻ IgD ⁺)	45.5 [27.7-56.3]	52.0 [29.6-60.7]	NS	55.6 [50.3-63.2]	35.1 [18.0-40.9]	<0.001
Memory (CD27 ⁺)	17.3 [11.4-29.2]	11.3 [8.47-19.8]	NS	8.81 [6.12-12.5]	14.0 [8.42-23.8]	NS (0.065)
CS ⁺ memory (CD27 ⁺ IgD ⁻)	15.3 [10.2-25.6]	10.7 [7.72-18.1]	NS	6.93 [5.31-11.3]	13.2 [7.48-20.9]	NS (0.060)
CS ⁻ memory (CD27 ⁺ IgD ⁺)	2.27 [0.98-2.78]	1.65 [0.57-2.50]	NS	1.13 [0.89-1.67]	0.92 [0.64-2.86]	NS
Plasmablasts (CD38 ^{high} CD20 ⁻)	0.28 [0.11-0.59]	0.49 [0.16-1.65]	NS	0.36 [0.21-0.47]	0.31 [0.28-1.14]	NS
Transitional (CD24 ^{high} CD38 ^{high})	2.83 [1.88-6.00]	3.20 [0.48-7.00]	NS	6.36 [4.16-10.5]	1.52 [1.05-5.14]	0.015

Values are the median [IQR]. Percentages of each population in total B cells are shown.

CS⁺ = class-switched; CS⁻ = non-class-switched; IFN- β = interferon- β ; IQR = interquartile ranges; MS = multiple sclerosis; NS = not significant; PMS = progressive MS; RRMS = relapsing-remitting MS; w/ = with.

Table S14 Comparison of the percentages of cytokine-producing $\gamma\delta$ T cell subsets between RRMS and PMS patients

	Untreated MS			MS w/IFN- β		
	RRMS (<i>n</i> = 26)	PMS (<i>n</i> = 9)	<i>p</i> value	RRMS (<i>n</i> = 13)	PMS (<i>n</i> = 8)	<i>p</i> value
In Vδ1⁺$\gamma\delta$ T cells						
IL-17A ⁺	0.13 [0.00-0.41]	0.12 [0.00-0.50]	NS	0.54 [0.02-1.03]	0.33 [0.04-1.16]	NS
IFN- γ ⁺	35.9 [16.5-40.8]	36.6 [12.4-54.9]	NS	25.0 [7.14-45.2]	32.7 [11.9-37.9]	NS
IL-17A ⁺ IFN- γ ⁺	0.03 [0.00-0.14]	0.00 [0.00-0.12]	NS	0.17 [0.00-0.66]	0.18 [0.00-0.58]	NS
IL-17A ⁻ IFN- γ ⁻	64.1 [58.5-81.8]	63.4 [45.0-87.4]	NS	75.0 [54.8-91.9]	66.8 [62.1-87.7]	NS
In Vδ2⁺$\gamma\delta$ T cells						
IL-17A ⁺	0.07 [0.00-0.45]	0.00 [0.00-0.47]	NS	0.00 [0.00-2.63]	0.00 [0.00-1.15]	NS
IFN- γ ⁺	51.5 [12.7-85.1]	37.5 [6.33-62.4]	NS	38.1 [24.6-56.3]	49.2 [11.4-71.9]	NS
IL-17A ⁺ IFN- γ ⁺	0.00 [0.00-0.29]	0.00 [0.00-0.06]	NS	0.00 [0.00-1.06]	0.00 [0.00-0.47]	NS
IL-17A ⁻ IFN- γ ⁻	48.5 [14.9-87.3]	62.5 [36.8-93.2]	NS	61.9 [43.4-75.4]	50.4 [27.2-88.5]	NS
In Vδ1⁻Vδ2⁻$\gamma\delta$ T cells						
IL-17A ⁺	0.63 [0.27-1.38]	0.53 [0.25-1.43]	NS	0.73 [0.40-1.72]	1.22 [0.20-1.93]	NS
IFN- γ ⁺	29.3 [14.0-40.7]	23.9 [6.52-41.7]	NS	15.8 [11.6-42.4]	24.8 [7.81-31.7]	NS
IL-17A ⁺ IFN- γ ⁺	0.23 [0.03-0.53]	0.17 [0.00-0.51]	NS	0.34 [0.18-0.48]	0.65 [0.00-0.92]	NS
IL-17A ⁻ IFN- γ ⁻	70.6 [58.9-85.6]	75.8 [57.9-93.5]	NS	83.9 [56.7-87.8]	75.1 [67.3-91.9]	NS

Values are the median [IQR]. Percentages of each population are shown.

IFN = interferon; IL = interleukin; IQR = interquartile ranges; MS = multiple sclerosis; NS = not significant; PMS = progressive MS; RRMS = relapsing-remitting MS; w/ = with.

Table S15 Comparison of the percentages of cytokine-producing $\alpha\beta$ T cell subsets between RRMS and PMS patients

	Untreated MS			MS w/IFN- β		
	RRMS (<i>n</i> = 26)	PMS (<i>n</i> = 9)	<i>p</i> value	RRMS (<i>n</i> = 13)	PMS (<i>n</i> = 8)	<i>p</i> value
In CD4⁺ T cells						
IL-17A ⁺	0.24 [0.15-0.61]	0.29 [0.11-0.47]	NS	0.39 [0.27-0.57]	0.33 [0.27-0.62]	NS
IFN- γ ⁺	4.42 [2.01-7.32]	8.20 [3.19-9.98]	NS	6.70 [2.38-8.74]	8.22 [2.57-16.0]	NS
IL-4 ⁺	1.48 [0.80-2.81]	2.46 [1.06-3.85]	NS	1.64 [1.04-2.44]	2.12 [1.06-3.55]	NS
GM-CSF ⁺	1.47 [0.76-3.22]	1.36 [0.48-4.01]	NS	2.59 [1.78-4.12]	1.68 [1.28-2.13]	NS
IL-17A ⁺ IFN- γ ⁺	0.03 [0.01-0.06]	0.03 [0.01-0.05]	NS	0.04 [0.02-0.09]	0.04 [0.02-0.08]	NS
IL-17A ⁺ GM-CSF ⁺	0.04 [0.01-0.10]	0.04 [0.01-0.05]	NS	0.08 [0.03-0.15]	0.04 [0.02-0.05]	NS (0.089)
In CD8⁺ T cells						
IL-17A ⁺	0.19 [0.10-0.37]	0.13 [0.06-0.17]	NS	0.25 [0.16-0.63]	0.18 [0.13-0.25]	NS
IFN- γ ⁺	16.8 [9.97-29.1]	37.6 [8.73-50.7]	NS	15.3 [4.97-20.9]	33.0 [7.12-41.5]	NS
IL-17A ⁺ IFN- γ ⁺	0.05 [0.02-0.12]	0.04 [0.01-0.08]	NS	0.06 [0.02-0.13]	0.04 [0.03-0.06]	NS

Values are the median [IQR]. Percentages of each population are shown.

GM-CSF = granulocyte macrophage colony-stimulating factor; IFN = interferon; IL = interleukin; IQR = interquartile ranges; MS = multiple sclerosis; NS = not significant; PMS = progressive MS; RRMS = relapsing-remitting MS; w/ = with.