Supplementary Table 1. Demographic and clinical characteristics of our patient cohorts.

Subjects RRMS Discovery	Naïve N=47	FAE N=35	GA N=16		Subjects RRMS Validation	FAE N=7
Age (SD)	38.4 (10.7)	42.3 (9.8)	43.4 (10.9)	ANOVA $F_{(2,95)}=2.143$ $p=0.123$	Age (SD)	41.2 (8.3)
Gender	F: 31 (66%)	F: 21 (60%)	F: 9 (56%)	chi-squared $Xsq_2=0.59539$ $p=0.7425$	Gender	F: 3 (42.9%)
Race	Caucasian: 32 (68.1%) NonCaucasian: 15 • Asian: 0 • Black: 9 • Black-Caucasian: 2 • Caucasian-Hispanic: 0 • Hispanic: 4	Caucasian: 29 (82.9%) NonCaucasian: 6 • Asian: 1 • Black: 1 • Black-Caucasian: 0 • Caucasian-Hispanic: 2 • Hispanic: 2	Caucasian: 11 (69.8%) NonCaucasian: 5 • Asian: 0 • Black: 4 • Black-Caucasian: 0 • Caucasian-Hispanic: 0 • Hispanic: 1	chi-squared $Xsq_2=2.4643$ $p=0.2917$	Race	Caucasian: 3 (42.9%) NonCaucasian: 4 • Asian: 0 • Black: 2 • Black-Caucasian: 1 • Caucasian-Hispanic: 0 • Hispanic: 1
BMI (SD)	25.7 (5.5)	25.3* (4.9)	25.6 (4.3)	ANOVA $F_{(2,95)}=0.061$ $p=0.941$	BMI (SD)	26.6 (5.8)
Disease Duration-months (SD)	40.4 (57.1)	130.0 (90.2)	100.0 (73.0)	ANOVA $F_{(2,95)}=15.65$ $p<0.0001$	Disease Duration-months (SD)	68.5 (71.7)
EDSS Median (Range)	1.5 (0-3.5)	1 (0-3.5)	1.25 (0-2.5)	ANOVA $F_{(2,95)}=1.423$ $p=0.246$	EDSS median (Range)	2 (1-3)
Treatment Duration-months (SD)	0	18.0 (8.3)	56.8 (52.9)	Welch t-test; $t_{15.337}=-2.9171$ $p=0.01043$	Treatment Duration-months (SD)	10.5 (2.9)

*One missing BMI value in FAE group: replaced by BMI median

We recruited 47 treatment-naïve RRMS patients, 35 FAE-treated patients and 16 GA-treated patients in our discovery cohort and 7 RRMS patients in our prospective validation cohort. The three cross-sectional groups were similar in demographic and disease characteristics except

disease duration between treatment-naïve and all treated patients (ANOVA; $F_{(2,95)}$=15.65, p<0.0001). GA-treated patients also had a longer treatment duration compared to FAE-treated patients (Welch‘s t-test; $t_{15.337}$=-2.9171, p=0.0104). RRMS: relapsing remitting multiple sclerosis, FAE: fumaric acid esters, GA: glatiramer acetate, SD: standard deviation, F: female, BMI: body mass index

Supplementary Table 2. T cell antibody cocktail used for immunophenotyping. Whole blood was collected from each participant at study enrollment and was processed within 3 hours by the Mount Sinai's Human Immune Monitoring Core. Cells were stained with a pre-optimized T-cell antibody cocktail that contained anti-CD45, anti-CD3, anti-CD4, anti-CD8, anti-CCR4 and anti-CCR6 antibodies.

Antigen	Fluorochrome
CD45	Pacific Orange
CD3	BV650
CD4	AlexaFluor 700
CD8	PECF594
CCR4	BV605
CCR6	AlexaFluor 488