

| | naïve | "BASIC"-Cohort | | | | | |
|--|------------|----------------|------------|------------|------------|--------------------|------------|
| | | IFN | GLAT | DMF | TERI | <i>p</i> | total |
| Patients, No. | 35 | 22 | 7 | 19 | 4 | - | 52 |
| Age at baseline ALEM infusion, years, median (IQR) | 27 (22-36) | 31 (27-35) | 28 (22-34) | 33 (25-40) | 35 (27-38) | 0.554* | 32 (25-36) |
| Male patients, No. (%) | 17 (49) | 7 (32) | 3 (43) | 10 (52) | 2 (50) | 0.343 [#] | 23 (44) |
| Baseline-ARR, median (IQR) | 1 (1-2) | 1 (1-2) | 1 (1-2) | 1 (1-2) | 1.5 (1-2) | 0.937* | 1 (1-2) |
| Baseline-EDSS, median (IQR) | 2 (1-2.5) | 2 (1-3) | 1.5 (1-2) | 2.5 (2-3) | 2 (2-3) | 0.150* | 2 (1-3) |
| Disease duration since onset, years, median (IQR) | 1 (0-2) | 6 (4-9) | 4 (1-6) | 4 (2-10) | 6 (2-7) | 0.162* | 5 (3-8) |
| Treatment duration of last previous DMT (non-naïve pat.), months, median (IQR) | - | 33 (9-49) | 19 (10-31) | 17 (12-33) | 21 (11-33) | 0.203* | 14 (7-34) |
| Previous DMT | | | | | | | |
| 0 (No. (%)) | 35 (100) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0.137 [#] | 0 (0) |
| 1 (No. (%)) | 0 (0) | 12 (55) | 7 (100) | 6 (32) | 4 (100) | | 29 (56) |
| 2 (No. (%)) | 0 (0) | 5 (23) | 0 (0) | 4 (21) | 0 (0) | | 9 (17) |
| 3 (No. (%)) | 0 (0) | 3 (14) | 0 (0) | 7 (37) | 0 (0) | | 10 (19) |
| ≥4 (No. (%)) | 0 (0) | 2 (9) | 0 (0) | 2 (10) | 0 (0) | | 4 (8) |
| washout duration of last previous DMT, (non-naïve pat.), days, median (IQR) | - | 0 (0-3) | 0 (0-0) | 14 (0-36) | 43 (35-50) | - | 0 (0-14) |
| Follow-up duration, months, median (IQR) | 44 (36-53) | 47 (36-53) | 34 (20-46) | 39 (29-48) | 39 (29-44) | 0.250* | 42 (32-50) |

Table S1 Distribution of baseline data in the PROGRAMMS cohort: ALEM: alemtuzumab, DMT: disease-modifying treatment, IFN: beta-interferon; GLAT: glatiramer acetate; DMF: dimethyl fumarate; TERI: teriflunomide; IQR: interquartile range; ARR: annualized relapse rate; EDSS: expanded disability status scale. Significance levels were calculated using Kruskal-Wallis test for continuous data (*) or Fisher's exact test for categorical data (#).

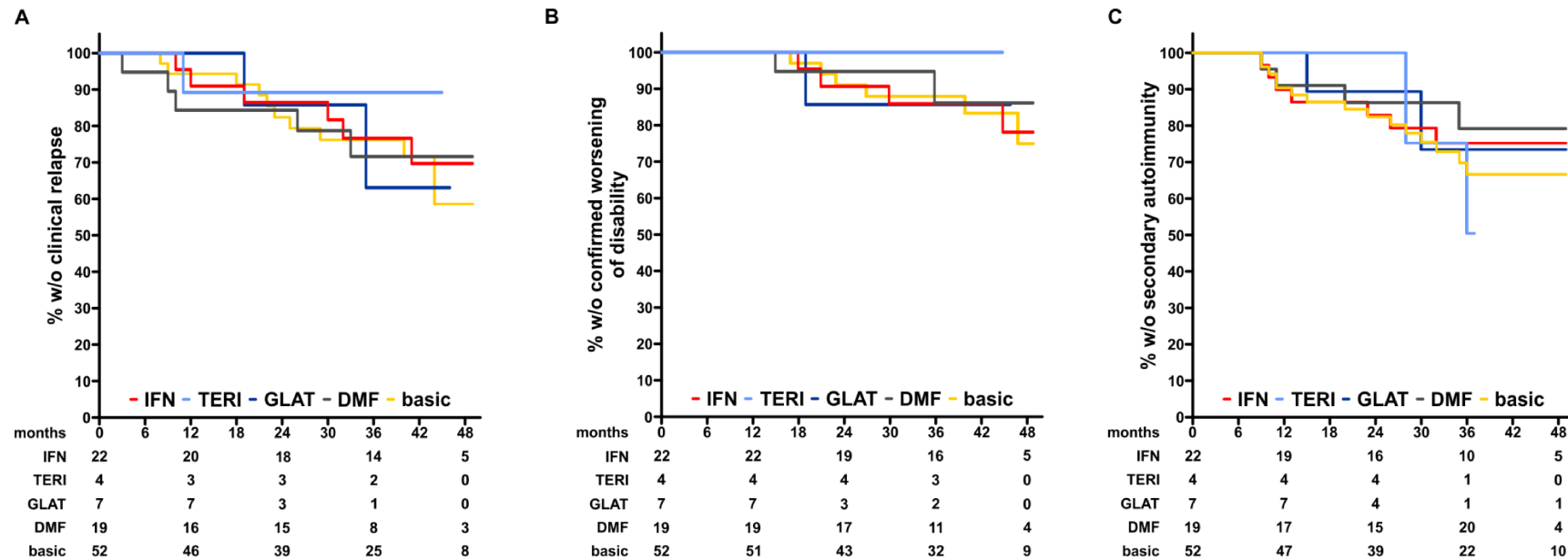


Figure S1 Analysis of efficacy outcomes in the PROGRAM^{MS} cohort: (A) Kaplan-Meier plot depicting time to first clinical relapse of patients stratified to last previous disease-modifying treatment. Numbers below the x-axis indicate patients at risk at the respective time point. (B) Kaplan-Meier plot depicting time to first three months confirmed progression of disability. (C) Kaplan-Meier plot depicting time to onset of (first) secondary autoimmune disorder.

| Time to first relapse | Hazard ratio | 95%-confidence interval | p-value |
|--|---------------------|--------------------------------|---------------------|
| Sex (male vs. female (ref.)) | <i>0.654</i> | <i>0.389-1.099</i> | <i>0.109</i> |
| Age (<34yrs (ref.) vs ≥34yrs) | <i>1.229</i> | <i>0.752-2.010</i> | <i>0.410</i> |
| Annualized relapse rate at baseline | <i>1.230</i> | <i>0.967-1.563</i> | <i>0.092</i> |
| Baseline-EDSS | <i>1.109</i> | <i>0.891-1.381</i> | <i>0.353</i> |
| Disease duration since onset (yrs) | <i>0.941</i> | <i>0.887-1.098</i> | <i>0.141</i> |
| ALEM treatment position (first-line=ref.) | | | |
| second-line | <i>1.493</i> | <i>0.674-3.308</i> | <i>0.323</i> |
| third-line | <i>2.651</i> | <i>1.279-5.497</i> | <i>0.009</i> |

Table S2A Regression model for analyzing time to first clinical relapse: Results from our Cox proportional hazard model using an enter method to integrate all the covariates in the final analysis. For analysis of age as a covariate, we split our group according to the median. Reference categories are indicated for categorical covariates.

| Time to first confirmed progression of disability | Hazard ratio | 95%-confidence interval | p-value |
|--|---------------------|--------------------------------|----------------|
| Sex (male vs. female (ref.)) | <i>0.713</i> | <i>0.373-1.363</i> | <i>0.306</i> |
| Age (<34yrs (ref.) vs ≥34yrs) | <i>1.288</i> | <i>0.694-2.391</i> | <i>0.423</i> |
| Annualized relapse rate at baseline | <i>1.285</i> | <i>0.963-1.714</i> | <i>0.089</i> |
| Baseline-EDSS | <i>1.030</i> | <i>0.787-1.350</i> | <i>0.827</i> |
| Disease duration since onset (yrs) | <i>0.971</i> | <i>0.909-1.038</i> | <i>0.386</i> |
| ALEM treatment position (first-line=ref.) | | | |
| second-line | <i>1.714</i> | <i>0.610-4.811</i> | <i>0.306</i> |
| third-line | <i>2.527</i> | <i>0.961-6.649</i> | <i>0.060</i> |

Table S2B Regression model for analyzing time to confirmed progression of disability: Results from our Cox proportional hazard model using an enter method to integrate all covariates in the final analysis. For analysis of age as a covariate, we split our group according to the median. Reference categories are indicated for categorical covariates.

| Time to first development of secondary autoimmunity | Hazard ratio | 95%-confidence interval | p-value |
|--|---------------------|--------------------------------|----------------|
| Sex (male vs. female (ref.)) | 1.274 | 0.689-2.358 | 0.440 |
| Age (<34yrs (ref.) vs ≥34yrs) | 0.803 | 0.432-1.493 | 0.488 |
| Annualized relapse rate at baseline | 0.884 | 0.561-1.200 | 0.430 |
| Baseline-EDSS | 1.042 | 0.791-1.371 | 0.771 |
| Disease duration since onset (yrs) | 0.977 | 0.912-1.047 | 0.509 |
| ALEM treatment position (first-line=ref.) | | | |
| second-line | 2.512 | 0.941-6.709 | 0.066 |
| third-line | 2.805 | 1.060-7.424 | 0.038 |

Table S2C Regression model for analyzing time to first secondary autoimmune disorder: Results from our Cox proportional hazard model using an enter method to integrate all the covariates in the final analysis. For analysis of age as a covariate, we split our group according to the median. Reference categories are indicated for categorical covariates.