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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **eTable 6** Univariable models for disease worsening at two-year follow-up in subgroups of patients | | | | | | | | | | | | | | | |
|  | **RRMS patients no treatment (n=12)** | | | **RRMS patients active treatment (n=62)** | | | **RRMS patients highly active treatment (n=39)** | | | **PMS patients no treatment (n=16)** | | | **PMS patients active and highly active treatment (n=11)** | | |
|  | **OR** | **95 % CI** | **p** | **OR** | **95 % CI** | **p** | **OR** | **95 % CI** | **p** | **OR** | **95 % CI** | **p** | **OR** | **95 % CI** | **p** |
| sNfL ≥ 75 th\* | 0.45 | 0.02-9.95 | 0.609 | **2.90** | **1.02-8.21** | **0.046** | 2.11 | 0.518-8.603 | 0.298 | 2.50 | 0.19-32.19 | 0.482 | 0.63 | 0.06-7.23 | 0.713 |
| sNfL (pg/mL, continuous) | 1.37 | 0.85-2.19 | 0.195 | 1.08 | 0.97-1.20 | 0.155 | 1.20 | 0.959-1.491 | 0.113 | 0.82 | 0.52-1.28 | 0.371 | 0.68 | 0.32-1.43 | 0.310 |
| Age | 0.94 | 0.80-1.12 | 0.499 | 1.01 | 0.96-1.07 | 0.685 | 0.98 | 0.895-1.075 | 0.684 | 0.86 | 0.69-1.07 | 0.172 | 0.88 | 0.75-1.03 | 0.120 |
| Total CD3+ | 1.05 | 0.92-1.20 | 0.460 | 1.01 | 0.97-1.04 | 0.739 | 1.01 | 0.969-1.046 | 0.735 | 1.03 | 0.91-1.17 | 0.634 | 1.26 | 0.73-2.16 | 0.412 |
| CD3+CD4+ | 1.02 | 0.90-1.14 | 0.810 | 1.00 | 0.96-1.04 | 0.942 | 1.03 | 0.987-1.076 | 0.176 | 0.99 | 0.90-1.11 | 0.946 | 1.04 | 0.91-1.19 | 0.586 |
| CD4+CD25+CD127- (CD4+T-reg) | 5.05 | 0.68-37.51 | 0.114 | **1.24** | **1.01-1.52** | **0.045** | 0.95 | 0.796-1.114 | 0.613 | 0.89 | 0.53-1.50 | 0.662 | 0.77 | 0.30-2.01 | 0.595 |
| CD3+CD8+ | 1.05 | 0.88-1.26 | 0.570 | 1.03 | 0.95-1.11 | 0.516 | 0.94 | 0.865-1.031 | 0.203 | 1.05 | 0.91-1.22 | 0.505 | 1.21 | 0.93-1.53 | 0.167 |
| CD3+CD8+CD28-CD127- (CD8+T-reg) | 1.07 | 0.7-1.19 | 0.180 | 0.993 | 0.97-1.02 | 0.619 | 0.97 | 0.934-1.001 | 0.059 | 0.95 | 0.84-1.08 | 0.426 | 1.07 | 0.94-1.22 | 0.307 |
| CD3+CD4+CCR6-CD161-CXCR3+ (Th1) | 1.52 | 0.87-2.64 | 0.141 | 1.01 | 0.93-1.09 | 0.896 | 1.06 | 0.964-1.163 | 0.233 | 1.08 | 0.84-1.40 | 0.553 | 1.12 | 0.79-1.55 | 0.553 |
| CD3+CD4+CCR6+CD161+CXCR3-CCR4+ (Th17) | 11.68 | 0.48-286.00 | 0.132 | 1.42 | 0.78-2.62 | 0.255 | 0.60 | 0.171-2.071 | 0.415 | 0.05 | 0.000-58.11 | 0.407 | 0.19 | 0.001-36.81 | 0.540 |
| CD3+CD4+CCR6+CD161+CxCR3highCCR4low (Th1/Th17) | 2.48 | 0.74-8.32 | 0.143 | 0.97 | 0.73-1.30 | 0.851 | 1.18 | 0.548-2.555 | 0.669 | 1.51 | 0.25-9.19 | 0.656 | 1.81 | 0.66-4.97 | 0.247 |
| Total CD19+ | 0.82 | 0.53-1.26 | 0.358 | 0.91 | 0.80-1.04 | 0.158 | 1.04 | 0.958-1.123 | 0.371 | 0.84 | 0.54-1.30 | 0.423 | 0.40 | 0.08-1.98 | 0.259 |
| CD19+CD24highCD38low (B-memory) | 0.93 | 0.80-1.09 | 0.359 | 1.01 | 0.9-1.08 | 0.731 | 0.93 | 0.839-1.040 | 0.213 | 1.15 | 0.90-1.49 | 0.269 | 1.09 | 0.89-1.33 | 0.407 |
| CD19+CD24lowCD38low (B-mature) | 1.01 | 0.92-1.10 | 0.887 | 1.01 | 0.98-1.05 | 0.528 | 1.01 | 0.964-1.050 | 0.796 | 0.94 | 0.84-1.04 | 0.233 | 0.94 | 0.84-1.05 | 0.240 |
| CD19+CD24highCD38high (B-reg) | 1.17 | 0.85-1.61 | 0.339 | 1.01 | 0.94-1.09 | 0.813 | 1.00 | 0.958-1.045 | 0.983 | 0.92 | 0.43-1.99 | 0.834 | 0.99 | 0.91-1.1 | 0.957 |
| CD19+CD24-CD38high (plasma B-cells) | 0.96 | 0.49-1.86 | 0.912 | 1.05 | 0.87-1.27 | 0.602 | 1.11 | 0.897-1.377 | 0.335 | 2.64 | 0.23-31.99 | 0.445 | 1.0 | 0.96-1.18 | 0.268 |
| CD16+CD56low (CD56dim NK cells) | 1.03 | 0.92-1.14 | 0.632 | 0.99 | 0.97-1.02 | 0.872 | **0.94** | **0.884-0.994** | **0.031** | 0.95 | 0.85-1.07 | 0.411 | 1.00 | 0.90-1.13 | 0.989 |
| CD16+CD56high (CD56bright NK cells) | 0.98 | 0.63-1.52 | 0.933 | 0.99 | 0.85-1.17 | 0.963 | 0.99 | 0.850-1.167 | 0.960 | 1.14 | 0.65-2.00 | 0.651 | 0.83 | 0.35-1.95 | 0.665 |
| Abbreviations: RRMS = relapsing remitting MS; PMS = progressive MS; active treatment= interferon, glatiramer acetate, teriflunomide and dimethyl fumarate; highly active treatment = fingolimod, natalizumab, alemtuzumab, rituximab and ocrelizumab. sNfL= serum neurofilament light chain; disease worsening = ≥ 3 new cerebral MRI lesions and/or confirmed Expanded Disability Status Score (EDSS) progression and/or evidence of a new clinical relapse. Results are presented with odds ratio (OR), 95% confidence interval (CI) and p-value. In bold are shown significant p-values, and the corresponding OR. The analyses were adjusted for age and gender \*Cut off 75th percentile: 20-29 years ≥ 4.325 pg/ml, 30-34 years ≥ 6.60 pg/ml, 35-39 years ≥ 7.05 pg/ml, 40-44 years ≥ 6.825 pg/ml, 45-49 years ≥ 7.075 pg/ml, 50-54 years ≥ 8.225 pg/ml, 55-59 years ≥ 11.15 pg/ml, 60-69 years ≥ 12.95 pg/ml. None of the p-values survived multiple testing. | | | | | | | | | | | | | | | |