|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **eTable 9** Multivariable models for disease worsening at two-year follow-up | | | | | | | |
|  | **All MS (n=140)** | | |  | **RRMS active treatment (n=62)** | | |
|  | **OR** | **95 % CI** | **p-value** |  | **OR** | **95 % CI** | **p-value** |
| **Model 1** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.90 | 0.93-3.89 | 0.078 |  | **3.22** | **1.02-10.20** | **0.047** |
| CD3+CD4+ | 1.01 | 0.98-1.03 | 0.665 |  | 0.99 | 0.94-1.03 | 0.523 |
| **Model 2** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 2.03 | 0.99-4.18 | 0.054 |  | **3.03** | **1.02-9.0** | **0.046** |
| CD3+CD8+ | 1.01 | 0.97-1.06 | 0.623 |  | 1.04 | 0.96-1.12 | 0.364 |
| **Model 3** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.99 | 0.98-4.04 | 0.056 |  | **3.28** | **1.08-9.92** | **0.036** |
| CD3+CD4+CCR6+CD161+CXCR3-CCR4+ (Th17) | 1.27 | 0.80-1.99 | 0.313 |  | 1.59 | 0.85-2.98 | 0.148 |
| **Model 4** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.89 | 0.93-3.84 | 0.078 |  | **2.98** | **1.01-8.83** | **0.049** |
| CD19+CD24highCD38low (B-memory) | 0.98 | 0.94-1.02 | 0.365 |  | 1.02 | 0.96-1.09 | 0.520 |
| **Model 5** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | **2.13** | **1.04-4.38** | **0.040** |  | **3.23** | **1.04-10.03** | **0.042** |
| CD19+CD24highCD38high (B-reg) | 1.02 | 0.99-1.05 | 0.172 |  | 1.03 | 0.95-1.12 | 0.422 |
| **Model 6** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.96 | 0.97-3.95 | 0.061 |  | 2.85 | 0.95-8.48 | 0.061 |
| Total CD3+ | 1.01 | 0.98-1.03 | 0.584 |  | 0.99 | 0.96-1.04 | 0.930 |
| **Model 7** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.95 | 0.95-3.96 | 0.067 |  | 2.99 | 0.98-9.20 | 0.055 |
| CD3+CD4+CD25+CD127- (CD4+T-reg) | 1.10 | 0.99-1.22 | 0.071 |  | **1.23** | **1.001-1.50** | **0.048** |
| **Model 8** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.89 | 0.93-3.85 | 0.077 |  | 2.77 | 0.95-8.07 | 0.061 |
| CD3+CD8+CD28-CD127- (CD8+T-reg) | 0.99 | 0.97-1.01 | 0.198 |  | 0.99 | 0.97-1.03 | 0.737 |
| **Model 9** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.86 | 0.91-3.78 | 0.089 |  | 2.82 | 0.97-8.21 | 0.057 |
| CD3+CD4+CCR6-CD161-CXCR3+ (Th1) | 1.05 | 0.99-1.11 | 0.069 |  | 0.99 | 0.92-1.08 | 0.970 |
| **Model 10** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.91 | 0.94-3.87 | 0.072 |  | 2.87 | 0.98-8.39 | 0.054 |
| CD3+CD4+CCR6+CD161+CxCR3highCCR4low (Th1/Th17) | 1.13 | 0.89-1.43 | 0.332 |  | 0.95 | 0.69-1.28 | 0.713 |
| **Model 11** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.92 | 0.95-3.89 | 0.069 |  | 2.68 | 0.91-7.89 | 0.073 |
| Total CD19+ | 0.98 | 0.92-1.05 | 0.528 |  | 0.92 | 0.79-1.05 | 0.207 |
| **Model 12** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.97 | 0.97-4.01 | 0.062 |  | 2.77 | 0.95-8.07 | 0.062 |
| CD19+CD24lowCD38low (B-mature) | 0.99 | 0.98-1.02 | 0.905 |  | 1.01 | 0.97-1.05 | 0.614 |
| **Model 13** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | **2.14** | **1.05-4.40** | **0.037** |  | 2.92 | 0.99-8.55 | 0.051 |
| CD19+CD24-CD38high (plasma B-cells) | 1.05 | 0.99-1.12 | 0.106 |  | 1.07 | 0.88-1.29 | 0.491 |
| **Model 14** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.92 | 0.95-3.90 | 0.071 |  | 2.85 | 0.97-8.38 | 0.057 |
| CD16+CD56low (CD56dim NK cells) | 0.99 | 0.97-1.01 | 0.213 |  | 1.002 | 0.98-1.03 | 0.886 |
| **Model 15** |  |  |  |  |  |  |  |
| sNfL ≥ 75 th\* | 1.97 | 0.97-4.03 | 0.063 |  | 2.84 | 0.97-8.27 | 0.056 |
| CD16+CD56high (CD56bright NK cells) | 1.01 | 0.91-1.12 | 0.906 |  | 1.01 | 0.86-1.20 | 0.893 |
| Abbreviations: RRMS = relapsing remitting MS; active treatment= interferon, glatiramer acetate, teriflunomide and dimethyl fumarate; 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. When analysing data from all MS patients together the multivariable analyses were adjusted for age, gender and treatment level (no treatment, active treatment and highly active treatment). Multivariable analyses in RRMS patients on active treatment were adjusted for age and gender. In bold are shown significant p-values, and the corresponding OR. None of the p-values survived multiple testing. \*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. | | | | | | | |