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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **eTable 8** Univariable models for disease worsening at two-year follow-up in RRMS patients on different treatments at baseline | | | | | | | | | | | | | | | | | | |
|  | Interferon (n=16) | | | Glatiramer acetate (n=13) | | | Teriflunomide (n=11) | | | Dimethyl fumarate (n=22) | | | Fingolimod (n=16) | | | Natalizumab (n=16) | | |
|  | OR | 95 % CI | p-value | OR | 95 % CI | p-value | OR | 95 % CI | p-value | OR | 95 % CI | p-value | OR | 95 % CI | p-value | OR | 95 % CI | p-value |
| sNfL ≥ 75 th\* | 3.16 | 0.24-41.9 | 0.383 | 6.00 | 0.22-162.5 | 0.287 | 8.00 | 0.50-127.9 | 0.141 | 0.96 | 0.14-6.38 | 0.963 | 4.10 | 0.32-52.6 | 0.279 | 1.00 | 0.10-10.17 | 1.000 |
| sNfL (pg/mL, continuous) | 0.91 | 0.61-1.35 | 0.635 | 1.19 | 0.71-1.99 | 0.505 | 1.09 | 0.88-1.34 | 0.420 | 1.06 | 0.80-1.40 | 0.672 | 1.21 | 0.84-1.75 | 0.310 | 1.27 | 0.89-1.82 | 0.190 |
| Age | 1.00 | 0.88-1.14 | 0.981 | 1.13 | 0.94-1.37 | 0.197 | 1.03 | 0.90-1.17 | 0.695 | 0.97 | 0.90-1.06 | 0.521 | 1.09 | 0.94-1.27 | 0.241 | 0.92 | 0.80-1.07 | 0.274 |
| Total CD3+ | 0.98 | 0.89-1.08 | 0.624 | 1.17 | 0.93-1.47 | 0.179 | 0.83 | 0.59-1.18 | 0.304 | 0.99 | 0.94-1.05 | 0.791 | 1.02 | 0.95-1.09 | 0.584 | 1.03 | 0.89-1.20 | 0.703 |
| CD3+CD4+ | 1.03 | 0.92-1.15 | 0.619 | 1.12 | 0.94-1.34 | 0.191 | 0.94 | 0.72-1.21 | 0.612 | 0.98 | 0.92-1.03 | 0.385 | 1.04 | 0.97-1.11 | 0.239 | 1.09 | 0.94-1.27 | 0.232 |
| CD3+CD4+CD25+CD127- (CD4+T-reg) | 1.11 | 0.76-1.63 | 0.588 | 0.99 | 0.90-1.09 | 0.790 | 15.24 | 0.11-2172.3 | 0.282 | 1.21 | 0.89-1.64 | 0.217 | 0.79 | 0.57-1.09 | 0.145 | 1.08 | 0.44-2.65 | 0.873 |
| CD3+CD8+ | 0.93 | 0.78-1.10 | 0.407 | 1.00 | 0.70-1.44 | 0.983 | 0.94 | 0.66-1.35 | 0.753 | 1.07 | 0.93-1.23 | 0.338 | 0.87 | 0.71-1.06 | 0.171 | 0.93 | 0.78-1.12 | 0.456 |
| CD3+CD8+CD28-CD127- (CD8+T-reg) | 0.96 | 0.91-1.03 | 0.264 | 0.99 | 0.90-1.09 | 0.790 | 0.76 | 0.53-1.08 | 0.126 | 1.04 | 0.99-1.09 | 0.144 | 0.95 | 0.90-1.01 | 0.101 | 0.93 | 0.83-1.05 | 0.262 |
| CD3+CD4+CCR6-CD161-CXCR3+ (Th1) | 0.99 | 0.82-1.19 | 0.894 | 0.88 | 0.73-1.07 | 0.207 | 2.08 | 0.85-5.08 | 0.108 | 0.91 | 0.74-1.11 | 0.403 | 1.08 | 0.95-1.23 | 0.243 | 0.99 | 0.77-1.27 | 0.929 |
| CD3+CD4+CCR6+CD161+CXCR3-CCR4+ (Th17) | 1.60 | 0.35-7.26 | 0.542 | 0.62 | 0.06-6.73 | 0.697 | 3.21 | 0.23-44.21 | 0.383 | 1.66 | 0.70-3.92 | 0.249 | 0.33 | 0.04-3.13 | 0.334 | 1.26 | 0.10-16.61 | 0.862 |
| CD3+CD4+CCR6+CD161+CxCR3highCCR4low (Th1/Th17) | 0.66 | 0.29-1.52 | 0.330 | 0.44 | 0.12-1.59 | 0.212 | 2.14 | 0.44-10.52 | 0.348 | 0.81 | 0.30-2.18 | 0.669 | 1.94 | 0.43-8.85 | 0.393 | 0.96 | 0.16-5.66 | 0.961 |
| Total CD19+ | 0.71 | 0.41-1.24 | 0.228 | 2.01 | 0.77-5.27 | 0.156 | 0.93 | 0.65-1.32 | 0.681 | 0.87 | 0.68-1.11 | 0.261 | 1.14 | 0.71-1.82 | 0.589 | 1.11 | 0.89-1.38 | 0.371 |
| CD19+CD24highCD38low (B-memory) | 1.02 | 0.92-1.13 | 0.717 | 0.96 | 0.75-1.24 | 0.778 | 0.05 | 0.00-34.06 | 0.361 | 0.99 | 0.89-1.12 | 0.989 | 0.93 | 0.70-1.25 | 0.639 | 0.81 | 0.63-1.04 | 0.099 |
| CD19+CD24lowCD38low (B-mature) | 1.02 | 0.95-1.10 | 0.545 | 1.15 | 0.86-1.53 | 0.345 | 2.04 | 0.65-6.40 | 0.223 | 1.001 | 0.95-1.06 | 0.963 | 0.95 | 0.83-1.08 | 0.409 | 1.06 | 0.96-1.17 | 0.272 |
| CD19+CD24highCD38high (B-reg) | 1.03 | 0.91-1.18 | 0.628 | 1.05 | 0.72-1.54 | 0.802 | 1.53 | 0.70-3.32 | 0.284 | 1.03 | 0.90-1.18 | 0.641 | 1.03 | 0.96-1.12 | 0.409 | 1.51 | 0.85-2.71 | 0.162 |
| CD19+CD24-CD38high (plasma B-cells) | 0.59 | 0.22-1.60 | 0.299 | 9.93 | 0.23-423.07 | 0.231 | 0.81 | 0.37-1.76 | 0.587 | 1.18 | 0.91-1.53 | 0.221 | 1.49 | 0.68-3.24 | 0.319 | 0.001 | 0.000-3.90 | 0.101 |
| CD16+CD56low (CD56 dim NK cells) | 0.99 | 0.94-1.034 | 0.561 | 1.03 | 0.94-1.12 | 0.568 | 0.98 | 0.87-1.10 | 0.685 | 0.99 | 0.96-1.04 | 0.950 | 0.95 | 0.89-1.02 | 0.161 | 0.89 | 0.78-1.02 | 0.099 |
| CD16+CD56high (CD56 bright NK cells) | 0.82 | 0.57-1.19 | 0.297 | 6.58 | 0.35-124.9 | 0.210 | 1.09 | 0.76-1.58 | 0.633 | 0.84 | 0.48-1.47 | 0.544 | 0.94 | 0.38-2.29 | 0.883 | 0.99 | 0.61-1.61 | 0.971 |
| Abbreviations: RRMS = relapsing remitting MS; 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 75 th 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. | | | | | | | | | | | | | | | | | | |