# Supplementary Tables

**eTable 1** Characteristics of the MS-STAT per-protocol trial cohort and descriptive statistics for serum NFL and serum NFH across timepoints

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Placebo**  **(n=49)** | **Simvastatin (n=52)** | **All**  **(n=101)** |
| **Baseline characteristics** |  |  |  |
| Gender: N (%) female | 31 (63%) | 36 (69%) | 67 (66%) |
| Ethnicity: N (%) white | 44 (90%) | 52 (100%) | 96 (95%) |
| Relapse in last 24 months: N (%) | 12 (24%) | 5 (10%) | 17 (17%) |
| Age (years): mean (SD) | 50.4 (7.1) | 52.0 (7.1) | 51.2 (7.1) |
| MS duration (years): mean (SD) | 19.6 (9.4) | 23.1 (8.0) | 21.4 (8.9) |
| SPMS duration (years): mean (SD) | 6.2 (4.1) | 7.2 (5.6) | 6.7 (4.9) |
| EDSS: median (IQR) | 6.0 (6.0 to 6.5) | 6.0 (5.5 to 6.5) | 6.0 (5.5 to 6.5) |
| Previous use of interferon: N (%) | 11 (16%) | 6 (9%) | 17 (12%) |
|  |  |  |  |
| **Serum NFL (pg/ml)** |  |  |  |
| Baseline: median  (IQR) | 16.2 (11.3 to 23.4) | 14.5 (11.3 to 20.2) | 15.6 (11.3 to 21.3) |
| N | 43 | 49 | 92 |
| Month 6: median  (IQR) | 15.1 (11.1 to 23.7) | 16.2 (11.8 to 23.7) | 15.4 (11.8 to 23.7) |
| N | 44 | 47 | 91 |
| Month 12: median  (IQR) | 16.6 (11.0 to 22.3) | 17.9 (13.7 to 24.3) | 17.1 (12.9 to 23.9) |
| N | 45 | 48 | 93 |
| Month 24: median  (IQR) | 18.5 (14.0 to 23.6) | 16.2 (12.0 to 24.8) | 17.0 (12.4 to 24.6) |
| N | 41 | 50 | 91 |
|  |  |  |  |
| **Serum NFH (pg/ml)** |  |  |  |
| Baseline: median  (IQR) | 68.7 (24.0 to 164.8) | 57.8 (21.3 to 110.6) | 63.3 (23.9 to 118.5) |
| N | 43 | 48 | 91 |
| Month 6: median  (IQR) | 87.3 (34.5 to 139.5) | 53.1 (18.1 to 105.5) | 63.4 (21.3 to 118.5) |
| N | 39 | 43 | 82 |
| Month 12: median  (IQR) | 74.6 (22.6 to 144.4) | 63.4 (20.2 to 107.1) | 67.2 (20.2 to 118.5) |
| N | 44 | 47 | 91 |
| Month 24: median  (IQR) | 73.4 (42.2 to 119.9) | 57.4 (24.1 to 114.3) | 67.8 (24.8 to 116.2) |
| N | 42 | 50 | 92 |

Abbreviations: MS = multiple sclerosis; SPMS = secondary progressive multiple sclerosis; EDSS = Expanded Disability Status Scale; NFL = serum neurofilament light; NFH = serum phosphorylated neurofilament heavy; IQR = interquartile range; N = number.

**eTable 2** Effect of high dose simvastatin on serum NFL and serum NFH, per-protocol analysis

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Adjusted difference in geometric mean (%)\*** | **95% CI** | **p-value** |
| **Serum NFL (pg/ml)** |  |  |  |
| Month 6 | -2.0 | -17.3 to 16.1 | 0.815 |
| Month 12 | 13.6 | -1.1 to 30.4 | 0.071 |
| Month 24 | -0.9 | -15.1 to 15.6 | 0.905 |
| Mean treatment effect | 3.3 | -7.7 to 15.6 | 0.570 |
| **Serum NFH (pg/ml)** |  |  |  |
| Month 6 | -15.0 | -37.6 to 15.9 | 0.305 |
| Month 12 | 2.7 | -20.6 to 33.0 | 0.837 |
| Month 24 | -6.8 | -28.1 to 20.8 | 0.594 |
| Mean treatment effect | -6.6 | -27.0 to 19.5 | 0.586 |

\* Percentage difference in geometric mean serum neurofilaments, simvastatin versus placebo, adjusted for age, sex, dichotomised EDSS (4.0-5.5, 6.0-6.5) and study site. Differences are shown for each follow-up visit, and also the average treatment effect across all follow-up visits. Abbreviations: NFL = serum neurofilament light; NFH = serum phosphorylated neurofilament heavy; CI = confidence interval.

**eTable 3** Effect of high dose simvastatin on serum NFL and serum NFH, adjusted for baseline lesion volume and relapses in the last 24 months in addition to age, sex, dichotomised EDSS (4.0-5.5, 6.0-6.5) and study site

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Adjusted difference in geometric mean (%)\*** | **95% CI** | **p-value** |
| **Serum NFL (pg/ml)** |  |  |  |
| Month 6 | -0.6 | -13.7 to 14.6 | 0.939 |
| Month 12 | 7.9 | -5.3 to 22.9 | 0.254 |
| Month 24 | -4.3 | -16.8 to 10.2 | 0.544 |
| Mean treatment effect | 0.9 | -8.8 to 11.6 | 0.863 |
| **Serum NFH (pg/ml)** |  |  |  |
| Month 6 | -8.7 | -29.6 to 18.4 | 0.491 |
| Month 12 | 4.8 | -15.8 to 30.4 | 0.674 |
| Month 24 | 2.0 | -18.6 to 27.8 | 0.863 |
| Mean treatment effect | -0.8 | -19.3 to 21.9 | 0.938 |

\* Percentage difference in geometric mean serum neurofilaments, simvastatin versus placebo, adjusted for baseline lesion volume, relapses in the last 24 months, age, sex, dichotomised EDSS (4.0-5.5, 6.0-6.5) and study site. Differences are shown for each follow-up visit, and also the average treatment effect across all follow-up visits. Abbreviations: NFL = serum neurofilament light; NFH = serum phosphorylated neurofilament heavy; CI = confidence interval.