

## SUPPLEMENTARY MATERIAL

### MRI protocols

Spinal cord: a) sagittal proton density (PD) weighted turbo-spin-echo (TSE) of the cervical and thoracic segments (two separate acquisitions) (repetition time (TR)=2000 ms, echo time (TE)=9 ms, slice thickness=3 mm, slice gap = 10%; in-plane voxel size=0.42x0.42mm<sup>2</sup>); b) axial T2-weighted multi-echo gradient echo in the cervical segment (TR=510 ms, TE=14 ms, slice thickness=3 mm, slice gap=10%, in-plane voxel size=0.4x0.4mm<sup>2</sup>) and TSE in the thoracic segment (TR=3500 ms, TE=103 ms, slice thickness=3 mm, slice gap=10%, voxel size=0.31x0.31mm<sup>2</sup>).

Brain: a) axial dual-echo TSE (TR=2670 ms, TE=24/120 ms, slice thickness=3 mm, gap=0%, acquisition parallel to the AC-PC plane, voxel size=0.98x0.98x3.3 mm<sup>3</sup>); and b) sagittal 3D T1-weighted MPRAGE (TR=2300 ms, TE=2.81 ms, FA=9°, TI=900 ms, matrix=256x256, slice thickness=0.9 mm, slice number=192, voxel size=0.93x0.93x0.9 mm<sup>3</sup>).

## Supplementary tables

Supplementary table 1: Univariate Cox regression testing the association between presence at T2 of a-SL, a-BL, either a-SL or a-BL as well as additional covariates with time to EDSS progression after T2.

| Variables                                       | Time to EDSS progression |         |
|---|--------------------------|---------|
|   | HR (95%CI)               | p-value |
| a-SPL   | 1.00 (0.42-2.38)         | 0.995   |
| a-BL  | 1.23 (0.57-2.67)         | 0.593   |
| a-BL or a-SPL                                   | 1.14 (0.59-2.24)         | 0.693   |
| Age at MS onset, years                          | 1.03 (1.00-1.05)         | 0.052   |
| Disease duration, years                         | 0.98 (0.94-1.02)         | 0.356   |
| Gender (male vs female)                         | 1.08 (0.57-2.03)         | 0.815   |
| EDSS score                                      | 1.00 (0.82-1.22)         | 0.996   |
| Treatment history (previously treated vs naive) | 0.58 (0.24-1.39)         | 0.223   |
| Relapsing Remitting (as reference)              | -                        |         |
| Primary Progressive                             | 3.98 (1.72-9.21)         | 0.001   |
| Secondary Progressive                           | 2.31 (1.11-4.79)         | 0.001   |

Supplementary table 2: Univariate Cox and Poisson regressions testing within RRMS patients the association between presence at T2 of a-SL, a-BL, either a-SL or a-BL and additional covariates with annualized relapse rate (ARR) between T2 and T3 and time to first relapse (TTFR) after T2.

| Variables                                       | ARR              |         | TTFR              |         |
|---|------------------|---------|-------------------|---------|
|   | RR (95%CI)       | p-value | HR (95%CI)        | p-value |
| a-SPL   | 0.80 (0.17-2.76) | 0.757   | 0.83 (0.19-3.62)  | 0.800   |
| a-BL  | 1.42 (0.49-3.78) | 0.514   | 1.35 (0.44-4.14)  | 0.597   |
| a-BL or a-SPL                                   | 1.15 (0.42-2.91) | 0.780   | 1.12 (0.40-3.18)  | 0.824   |
| Age at MS onset, years                          | 1.00 (0.96-1.04) | 0.967   | 1.02 (0.97-1.06)  | 0.437   |
| Disease duration, years                         | 0.98 (0.91-1.04) | 0.500   | 0.99 (0.93-1.06)  | 0.841   |
| Gender (male vs female)                         | 0.80 (0.28-2.11) | 0.675   | 0.94 (0.34-2.65)  | 0.914   |
| EDSS score                                      | 0.69 (0.46-1.00) | 0.056   | 0.83 (0.56-1.23)  | 0.350   |
| Treatment history (previously treated vs naive) | 1.00 (0.26-4.98) | 0.997   | 2.04 (0.27-15.38) | 0.488   |

Supplementary table 3: Univariate and multivariate Poisson regression testing the association between presence at T2 of a-SL, a-BL, either a-SL or a-BL as well as additional covariates with annualized brain lesion rate between T2 and T3.

| Variables  | Univariate analysis |         | Multivariate analysis |         |
|--|---------------------|---------|-----------------------|---------|
|  | RR (95%CI)          | p-value | RR (95%CI)            | p-value |
| <b>a-SPL</b>   | 1.38 (0.85-2.14)    | 0.169   |                       |         |
| <b>a-BL</b>  | 1.66 (1.08-2.48)    | 0.016   |                       |         |
| <b>a-BL or a-SPL</b>                                   | 2.00 (1.39-2.84)    | 0.0001  | 1.81 (1.25-2.60)      | 0.001   |
| <b>Age at MS onset, years</b>                          | 0.96 (0.94-0.97)    | <0.0001 | 0.97 (0.95-0.99)      | 0.009   |
| <b>Disease duration, years</b>                         | 0.97 (0.94-0.99)    | 0.008   |                       |         |
| <b>Gender (male vs female)</b>                         | 0.60 (0.39-0.88)    | 0.012   |                       |         |
| <b>EDSS score</b>                                      | 0.67 (0.58-0.77)    | <.0001  | 0.80 (0.67-0.95)      | 0.012   |
| <b>Treatment history (previously treated vs naive)</b> | 1.36 (0.73-2.88)    | 0.378   |                       |         |
| <b>Disease phase (RRMS vs progressive)</b>             | 0.28 (0.14-0.50)    | 0.0001  | 0.53 (0.24-1.03)      | 0.076   |

Supplementary table 4: Univariate and multivariate Poisson regression testing the association between presence at T2 of a-SL, a-BL, either a-SL or a-BL as well as additional covariates with annualized spinal lesion rate between T2 and T3.

| Factors  | Univariate analysis |         | Multivariate analysis |         |
|--|---------------------|---------|-----------------------|---------|
|  | RR (95%CI)          | p-value | RR (95%CI)            | p-value |
| <b>a-SPL</b>   | 5.45 (2.64-11.04)   | <0.0001 |                       |         |
| <b>a-BL</b>  | 2.01 (0.84-4.31)    | 0.089   |                       |         |
| <b>a-BL or a-SPL</b>                                   | 3.08 (1.51-6.26)    | 0.002   | 2.63 (1.27-5.45)      | 0.009   |
| <b>Age at MS onset, years</b>                          | 0.98 (0.94-1.01)    | 0.181   |                       |         |
| <b>Disease duration, years</b>                         | 0.94 (0.87-0.99)    | 0.044   |                       |         |
| <b>Gender (male vs female)</b>                         | 1.02 (0.46-2.11)    | 0.961   |                       |         |
| <b>EDSS score</b>                                      | 0.68 (0.52-0.89)    | 0.007   | 0.74 (0.53-1.00)      | 0.059   |
| <b>Treatment history (previously treated vs naive)</b> | 1.02 (0.36-4.27)    | 0.972   |                       |         |
| <b>Disease phase (RRMS vs progressive)</b>             | 0.53 (0.16-1.36)    | 0.238   |                       |         |