**Supplementary**

**Supplementary Table 1.** Interaction analyses to compare the effect size between those with (N = 21) or without (N = 64) DMT treatment at baseline

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|  |  | **Received DMT at baseline (N = 21)** | **No DMT at baseline (N = 64)** |
| Baseline GCIPL thickness ~ Baseline OR lesion volume | β (95%CI) | -0.24 (-0.70 to 0.23) | -0.36 (-0.63 to -0.08) |
| *p*-value | 0.337 | 0.014 |
| ηρ2 for interaction with DMT, *p*-value | ηρ2 = 2.60e-4, *p* = 0.890 | |
| Baseline pRNFL thickness ~ Baseline OR lesion volume | β (95%CI) | -0.17 (-0.62 to 0.27) | -0.36 (-0.63 to -0.09) |
| *p*-value | 0.459 | 0.012 |
| ηρ2 for interaction with DMT, *p*-value | ηρ2 = 3.42e-4, *p* = 0.871 | |
| ΔGCIPL thickness ~ΔOR lesion volume | β (95%CI) | -0.11 (-0.69 to 0.46) | -0.28 (-0.53 to -0.03) |
| *p*-value | 0.713 | 0.034 |
| ηρ2 for interaction with DMT, *p*-value | ηρ2 = 1.20e-3, *p* = 0.782 | |
| ΔpRNFL thickness ~ ΔOR lesion volume | β (95%CI) | 0.38 (-0.03 to 0.78) | -0.09 (-0.13 to 0.61) |
| *p*-value | 0.088 | 0.204 |
| ηρ2 for interaction with DMT, *p*-value | ηρ2 = 0.02, *p* = 0.216 | |

Abbreviations: CI: confidence interval; DMT: disease-modifying therapies; ηρ2: partial eta-squared; GCIPL: combined macular ganglion cell and inner plexiform layer; OR: optic radiation; pRNFL: peri-papillary retinal nerve fiber layer; SD: standard deviation.

**Supplementary Table 2.** Comparison between ORL+ group and ORL– group (thinning rate and total change) only in pweMS without receiving DMT at baseline (N = 64)

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|  | **ORL+ (N = 24)** | **ORL– (N = 40)** | **ORL+ vs. ORL–** | |
|  | Annualized Thinning in Retinal Layer Thickness, µm/year, mean (SD) | | Annualized Thinning Rate Difference, µm/year, mean (SD) | Total Change Difference at 3rd year follow-up, µm, mean (SD) |
| GCIPL | -0.26 (0.07), p = 7.88e-4 | -0.08 (0.09), p = 0.380 | -0.18 (0.11), p = 0.115 | -0.83 (0.31), p = 0.013 |
| pRNFL | -0.32 (0.13), p = 0.037 | -0.19 (0.17), p = 0.277 | -0.12 (0.21), p = 0.502 | -0.23 (0.42), p = 0.441 |

Abbreviations: DMT: disease-modifying therapies; GCIPL: combined macular ganglion cell and inner plexiform layer; ORL+: presence of new or enlarging optic radiation lesion at maximum follow-up; ORL–: absence of new or enlarging optic radiation lesion at maximum follow-up; pRNFL: peri-papillary retinal nerve fiber layer; pweMS: people with early multiple sclerosis; SD: standard deviation.

**Supplementary Table 3.** Interaction analyses to compare the effect size between those who ever (N = 53) or never (N = 32) received DMT treatment before maximum follow-up

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|  |  | **Ever received DMT (N = 53)** | **Never received DMT (N = 32)** |
| ΔGCIPL thickness ~ΔOR lesion volume | β (95%CI) | -0.22 (-0.20 to 0.07) | -0.29 (-0.73 to 0.15) |
| *p*-value | 0.147 | 0.212 |
| ηρ2 for interaction with DMT, *p*-value | ηρ2 = 2.22e-3, *p* = 0.730 | |
| ΔpRNFL thickness ~ ΔOR lesion volume | β (95%CI) | 0.05 (-0.19 to 0.30) | -0.18 (-0.55 to 0.19) |
| *p*-value | 0.677 | 0.354 |
| ηρ2 for interaction with DMT, *p*-value | ηρ2 = 0.01, *p* = 0.438 | |

Abbreviations: CI: confidence interval; DMT: disease-modifying therapies; ηρ2: partial eta-squared; GCIPL: combined macular ganglion cell and inner plexiform layer; OR: optic radiation; pRNFL: peri-papillary retinal nerve fiber layer; SD: standard deviation.