Figure e-1. MRI lesion number outcomes at 2 years – results of primary and sensitivity analyses

Sensitivity analyses, illustrating outcomes based on all observed data alongside those based on observed data prior to starting alternative MS medication.

Abbreviations: BID = twice daily; DMF = delayed-release dimethyl fumarate (also known as gastro-resistant DMF); GA = glatiramer acetate; Gd+ = gadolinium-enhancing; ITT = intent-to-treat; MS = multiple sclerosis; OR = odds ratio; TID = three times daily.

^aRatios shown are lesion mean ratios, from baseline to 2 years; 95% CI and *p*-value for comparison between active and placebo groups, based on negative binomial regression, adjusted for region and baseline lesion volume.

^bPrimary MRI analyses – excluded observed data obtained after switch to alternative MS medications. Missing data prior to alternative MS medications and visits after switch are imputed using the constant rate assumption.

°Odds ratio, 95% CI and *p*-values for comparison between active and placebo groups at 2 years, based on ordinal logistic regression, adjusted for region and baseline number of Gd+ lesions.

| | Treatment | (placebo, active) | | (95% CI) | p-value |
|--|----------------------------|----------------------------------|--|--|-------------------------------|
| Number of new/enlarging T2 lesions ^a | | | | | |
| ITT MRI cohort ^b | DMF* BID DMF* TID GA | 139, 140 139, 140 139, 153 | * * | 0.29 (0.21–0.41) 0.27 (0.20–0.38) 0.46 (0.33–0.63) | <0.0001 <0.0001 <0.0001 |
| Observed data prior to switch | DMF* BID DMF* TID GA | 107, 121 107, 120 107, 131 | - - - - - | 0.26 (0.18-0.37) 0.33 (0.23-0.46) 0.42 (0.30-0.59) | <0.0001 <0.0001 <0.0001 |
| All observed data | DMF* BID DMF* TID GA | 126, 128 126, 132 126, 142 | - - - - - - - | 0.27 (0.19-0.38) 0.32 (0.23-0.45) 0.47 (0.34-0.64) | <0.0001 <0.0001 <0.0001 |
| Number of new T1-hypointense lesions | Sª | | | | |
| ITT MRI cohort ^b | DMF* BID DMF* TID GA | 139, 140 139, 140 139, 154 | _ ← | 0.43 (0.30-0.61) 0.35 (0.24-0.49) 0.59 (0.42-0.82) | <0.0001 <0.0001 0.0021 |
| Observed data prior to switch | DMF* BID DMF* TID GA | 107, 120 107, 120 107, 131 | - ← - ★ - - # - | 0.43 (0.29-0.62) 0.43 (0.30-0.63) 0.59 (0.41-0.85) | <0.0001 <0.0001 0.0043 |
| All observed data | DMF* BID DMF* TID GA | 124, 127 124, 131 124, 142 | <u>→</u> + | 0.43 (0.30-0.62) 0.40 (0.28-0.58) 0.58 (0.41-0.81) | <0.0001 <0.0001 0.0018 |
| Number of Gd+ lesions at 2 years ^c | | | | | |
| ITT MRI cohort ^b | DMF* BID DMF* TID GA | 144, 147 144, 144 144, 161 | | 0.26 (0.15-0.46) 0.35 (0.20-0.59) 0.39 (0.24-0.65) | <0.0001 0.0001 0.0003 |
| Observed data prior to switch | DMF* BID DMF* TID GA | 107, 120 107, 120 107, 131 | | 0.26 (0.14-0.50) 0.40 (0.22-0.73) 0.37 (0.21-0.67) | <0.0001 0.0027 0.0011 |
| All observed data | DMF* BID DMF* TID GA | 124, 127 124, 132 124, 142 | | 0.27 (0.15-0.49) 0.44 (0.25-0.76) 0.36 (0.21-0.64) | <0.0001 0.0034 0.0004 |
| | | | 0.01 0.1 | 10 | |
| | | | OR or lesion mean ratio | (95% CI) | |
| *DMF, delayed-release DMF (also known as gastro-re | esistant DMF) | | | | |

No. of patients

Favors active treatment Favors placebo

OR or lesion mean ratio