Evaluation of the long-term treatment effect of teriflunomide on cognitive outcomes and association with brain volume change: data from TEMSO and its extension study

S. Cavalier[7], T. Sprenger[1,2], M. P. Sormani[3], J. S. Wolinsky[4], J. Wuerfel[5], K. Thangavelu[6], M. Mandel[8], L. Kappos[9]
[1]*Department of Neurology, University Hospital Basel, Switzerland*
[2]*Department of Neurology, DKD HELIOS Klinik, Germany*
[3]*Department of Health Sciences, University of Genoa, Italy*
[4]*McGovern Medical School, UTHealth, USA*
[5]*Medical Image Analysis Center (MIAC AG), University of Basel, Switzerland*
[6]*Department of Biostatistics, Sanofi, USA*
[7]*MS Global Scientific Communications, Sanofi, USA*
[8]*Department of Neurology, Sanofi, USA*
[9]*Neurologic Clinic and Policlinik, University Hospital Basel, Switzerland*

Introduction: In a blinded SIENA (Structural Image Evaluation using Normalization of Atrophy) analysis of TEMSO (NCT00134563), teriflunomide significantly reduced brain volume loss (BVL) over 2 years vs placebo. Here, we explore the relationship between BVL and long-term changes in cognitive function in TEMSO and its extension (NCT00803049). Methods: Effect of teriflunomide on cognitive function was assessed by change from baseline in Paced Auditory Serial Addition Test (PASAT)-3 scores in the TEMSO core (N=1086) and extension (N=740) studies. To evaluate change in PASAT-3 scores over 5 years, the TEMSO population was categorized into groups defined by percentage brain volume change from baseline to Year 2 (assessed by SIENA). Results: Adjusted mean changes from baseline to Week (W)96 in PASAT-3 Z-score were –0.022 and 0.073 for placebo and teriflunomide 14 mg, respectively (difference vs placebo: *P*=0.0435). Over the long term, improvements in mean (SD) changes from baseline in PASAT-3 scores were observed with teriflunomide 14 mg treatment (Z-scores: W156, 0.194 [0.634]; W276, 0.200 [0.677]. Raw scores: W156, 2.36 [7.73]; W276, 2.43 [8.24]). In an association analysis, the group with least BVL from baseline to Year 2 demonstrated a significant improvement in PASAT-3 score with teriflunomide treatment over 5 years vs the group with most BVL. Conclusions: Teriflunomide significantly improved PASAT-3 performance vs placebo over 5 years in the TEMSO core and extension studies. Significant association of early BVL with long-term cognitive changes was observed, suggesting that BVL earlier in the disease course predicts longer term cognitive function.