Slowing of cortical gray matter atrophy with teriflunomide is associated with delayed conversion to clinically definite MS

R. Zivadinov[1,2], M-G. Dwyer[1], E. Carl[1], K. Thangavelu[3], S. Cavalier[4], N. Bergsland[1]
[1]*Buffalo Neuroimaging Analysis Center, University at Buffalo, USA*
[2]*Center for Biomedical Imaging at Clinical Translational Science Institute, University at Buffalo, USA*
[3]*Department of Biostatistics, Sanofi, USA*
[4]*MS Global Scientific Communications, Sanofi, USA*

Introduction: In TOPIC (NCT00622700), teriflunomide significantly reduced risk of conversion to clinically definite MS (CDMS) vs placebo in patients with a first clinical episode suggestive of MS. Gray matter (GM) atrophy after a first clinical event is associated with conversion to CDMS and disability accumulation. Here, we explore the effect of cortical GM volume (CGMV) change on risk of conversion to CDMS in the TOPIC study. Methods: Patients received placebo (n=197) or teriflunomide 14 mg (n=214) for ≤108 weeks. CGMV change was evaluated using the SIENAX-MTP (Structural Image Evaluation using Normalization of Atrophy, Cross-sectional, multi–time-point) analysis. Data at Month (M)6, M12, M18, and M24, standardized for follow-up duration, were analyzed relative to baseline. Statistical models were used to assess treatment effects (nonparametric ANCOVA) and relationship of CGMV loss to CDMS conversion (Cox proportional hazards models). Results: Teriflunomide 14 mg reduced CGMV change vs placebo by ≥40% (*P*P=0.0052 for cumulative difference over 2 years). For every 1% decrease in CGMV, there was a 12.4% increased risk of conversion to CDMS at M12 (*P*=0.0099), 14.2% at M18 (*P*=0.0009), and 14.5% at M24 (*P*=0.0005). Teriflunomide 14 mg also reduced risk of CDMS vs placebo: 46.3% (*P*=0.0220) at M12, 42.1% (*P*=0.0260) at M18, and 46.6% (*P*=0.0085) at M24. Conclusions: Consistent effects of teriflunomide on reducing CGMV loss, together with the correlation between conversion to CDMS and CGMV loss indicate how teriflunomide may favorably impact early inflammatory and neurodegenerative components of MS.