Supplementary Appendix: Statistical Methods

A mixed model for repeated measures (MMRM) including terms for treatment, visit, treatment-by-visit interaction, and region as fixed effects and baseline DAS28-ESR as a continuous covariate was used to assess difference between treatment groups in change from baseline in DAS28-ESR at week 24.

Secondary efficacy analyses of continuous variables were analyzed using MMRM as described above. Binary secondary efficacy variables were analyzed using a 2-sided Cochran-Mantel-Haenszel test stratified by region, and patients who discontinued treatment before week 24 were considered nonresponders. A hierarchical testing procedure predefined before unblinding was used to control type I error. A $P$ value of <0.05 was considered to be statistically significant when all preceding endpoints in the predefined hierarchy were statistically significant. For endpoints outside of the hierarchy, statistical significance is not claimed (nominal $P$ values provided).

Two sensitivity analyses were performed. In the first, all data (including assessments made after permanent treatment discontinuation) were included. In the second, all data after treatment discontinuation or adalimumab (or matching placebo) dose increase were set to missing and a multiple imputation approach was used. Subgroup analyses were performed using an MMRM approach as described above.