Supplementary Methods

Pulse Wave Velocity Assessments

The SphygmoCor system (AtCor, Inc., San Jose, CA)—including computer, software, relevant supplies and user's manual—was provided to each site. Pulse wave velocity (PWV) measurements were obtained during baseline assessment and at weeks 2, 12 and 24. During the open-label follow-up, PWV measurements were obtained during weeks 36, 52 and 104. A detailed instruction manual was provided by AtCor to each site.

Patients were required to be supine quietly for 10 minutes before measurements were obtained. No interruptions or other study procedures were allowed during this 10-minute period. First, the patient's supine blood pressure, measured by sphygmomanometry, was entered into the SphygmoCor system. A three-lead electrocardiogram was attached to the patient (each wrist, left leg), and the quality of the electrocardiogram was checked. Then carotid and femoral sites were palpated to determine the location of the strongest pulse, and distances from the suprasternal notch to the carotid pulse and to the femoral pulse were measured and entered into the SphygmoCor system. The tonometer was placed over the site, and its position was adjusted until a good-quality waveform was obtained. When a waveform signal of consistent pressure was obtained, the tonometer was held in position for at least 12 seconds; the data were then transferred to the system.

Quality indices indicated by the SphygmoCor system were assessed during the decision-making about whether to accept the measurement. The first PWV measurement that met quality control criteria was printed and retained as a source document. The distance from the center of the suprasternal notch directly to the carotid measurement site was measured; this was followed by similar measurement of the distance from the center of the suprasternal notch to the femoral measurement site. These values were entered into the system for calculation of the PWV values. The SphygmoCor database was then archived to a compact disk. Data were transferred to AtCor Medical (West Ryde, NSW, Australia) for quality control review. The initial data transfer took place immediately on the receipt and assembly of the SphygmoCor system. Ongoing data transfers occurred quarterly thereafter.

Biomarker assays

Secretory Phospholipase 2-IIA (sPLA2-IIA), oxidised LDL and D-dimer were determined using enzyme immunoassay (EIA) kits. For sPLA2-IIA (Cayman Chemical, Ann Arbor, MI, USA), a monoclonal capture antibody was coupled with detection by acetylcholinesterase (AChE)/Fab conjugate and DTNB detection. Oxidised LDL was measured by competitive assay (Mercodia, Uppsala, Sweden). The method makes use of a biotin-labeled monoclonal antibody, 4E6, first described by Holvoet,[1] and detection by horseradish peroxidase (HRP)-conjugated streptavidin with 3,3',5,5'-tetramethylbenzidine (TMB). D-dimer (American Diagnostica, Stamford, CT, USA) was assayed using D-dimer monoclonal capture and HRP-conjugated monoclonal with TMB detection. EDTA plasma fibrinogen (Kamiya Biomedical, Seattle, WA, USA), lipoprotein(a) (Denka Seikin, Niigata, Japan), hs-CRP (Roche Diagnostics, Indianapolis, IN, USA) and serum haptoglobin (Roche Diagnostics, Mannheim, Germany) were quantified using immunoturbidimetric assay kits. These assays were performed using a Roche Modular P autoanalyzer (Roche Diagnostics). For determination of HDL-associated SAA, serum HDL particles were isolated by polyethylene glycol 8000 (PEG-8000; Promega, Madison, WI) precipitation, as described by Chiba et al.[2] Briefly, equal volumes of 13.0% PEG (P-4463; Sigma-Aldrich, St. Louis, MO) were mixed to precipitate non-HDL proteins and lipoproteins. After centrifugation for 5 minutes at 18,000*g*, supernate serum amyloid A was determined by EIA (Abazyme; Needham, MA, USA). An anti-SAA monoclonal capture and an HRP-conjugated polyclonal antibody were used with TMB detection. Paraoxonase activity was measured by modification of the method described by Haagen and Brock.[3] The assay was performed using the Roche Modular P autoanalyzer, and enzyme activity was determined as the initial rate of p-nitrophenol formation from diethyl p-nitrophenyl phosphate at 415 nm.

References

1. **Holvoet P,** Donck J, Landeloos M, et al. Correlation between oxidized low density lipoproteins and von Willebrand factor in chronic renal failure. *Thromb Haemost* 1996;**76**:663-9.
2. **Chiba H**, Akizawa K, Fujisawa S-I, et al. A rapid and simple quantification of human apolipoprotein E-rich high-density lipoproteins in serum. *Biochem Med Metab Biol* 1992;**47**:31-7.
3. **Haagen L**, Brock A. A new automated method for phenotypingarylesterase (EC 3.1.1.2) based upon inhibition of enzymatic hydrolysis of 4-nitrophenyl acetate by phenyl acetate. *Eur J Clin Chem Clin Biochem* 1992;**30**:391-5.

Supplementary Figure 1. Change in (A) ACR 20/50/70 response and (B) DAS28 response* at 12 and 24 weeks (TCZ vs placebo). ACR, American College of Rheumatology; DAS28, Disease Activity Score at 28 joints; MTX, methotrexate; TCZ, tocilizumab. *Data are presented as mean (SE).