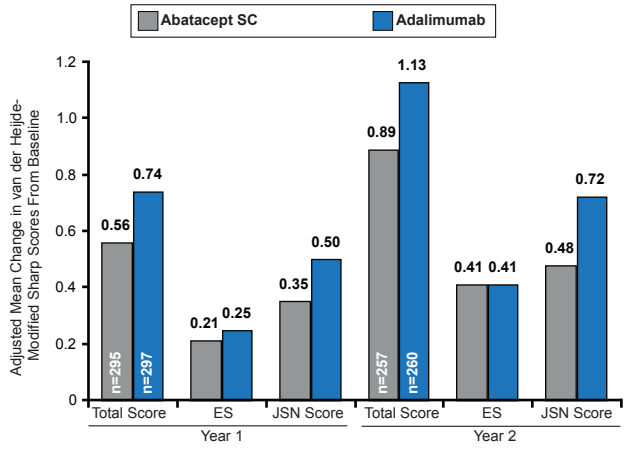
between the two groups were not statistically significant. The cumulative probability of change in mTSS from baseline to Year 2 was 84.8% in the ABA arm compared with 83.8% in the ADA arm.

Figure 2. Radiographic Outcomes at Years 1 and 2



ES=echographic score; JSN=joint-space narrowing.

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Adverse event (AE) rates were similar in both treatment groups, at 92.8% in the ABA arm and 91.5% in the ADA arm (Table 1). Serious AE (SAE) rates were 13.8% with ABA and 16.5% with ADA. Serious infections were reported in 3.8% of ABA and 5.8% of ADA patients. AEs leading to discontinuation occurred in 3.8% of patients treated with ABA and 9.5% of those treated with ADA. Two cases of tuberculosis were seen in Year 2 in the ADA+MTX arm.

Table 1. Adverse Events Through 2 Years of Treatment

	Number of Events (%)			
	AEs		AEs Leading to Discontinuation	
	ABA	ADA	ABA	ADA
Deaths	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)
AEs	295 (92.8)	300 (91.5)	12 (3.8)	31 (9.5)
SAEs	44 (13.8)	54 (16.5)	5 (1.6)	16 (4.9)
Serious infections	12 (3.8)	19 (5.8)	0	9 (2.7)
Opportunistic infections	4 (1.3)	4 (1.2)	0	9 (0.6)
Malignancies	7 (2.2)	7 (2.1)	4 (1.3)	4 (1.2)
Autoimmune SAEs	12 (3.8)	6 (1.8)	1 (0.3)	1 (0.3)
Injection-site reactions	13 (4.1)	34 (10.4)	0	3 (0.9)

ABA=abatacept; ADA=adalimumab; AE=adverse event; SAE=serious adverse event.

The AMPLE trial was the first study comparing two biologic agents in patients with RA who had an inadequate response to MTX. The 2-year efficacy results were similar to those reported at 1 year, with comparable responses in both treatment groups. The overall safety outcomes were similar in both groups but fewer patients treated with ABA discontinued treatment due to AEs, SAEs, and serious infections. The outcomes of the AMPLE trial demonstrate the comparable efficacy of ABA and ADA, and provide clinicians with evidence supporting the use of either biologic for the treatment of RA in patients with an inadequate response to MTX.

CV Risk Persists in RA Patients Despite Increased Medication Use for Both

Written by Larry Hand

Risk of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) persisted at similar rates at 3- and 10-year follow-ups, despite the increased use of statins, antihypertensive agents, and tumor necrosis factor-blocking agents, according to a 10-year prospective study. Alper M. van Sijl, MD, VU University Medical Center, Amsterdam, The Netherlands, presented data from the Cardiovascular Research and Rheumatoid Arthritis study [CARRÉ; Van Halm VP et al. *Ann Rheum Dis* 2009]. The CARRÉ investigators compared changes in CV risk factors, RA-related factors, and anti-inflammatory and cardioprotective medication use in RA patients who did or did not develop CVD over 10 years, starting in 2000 to 2001.

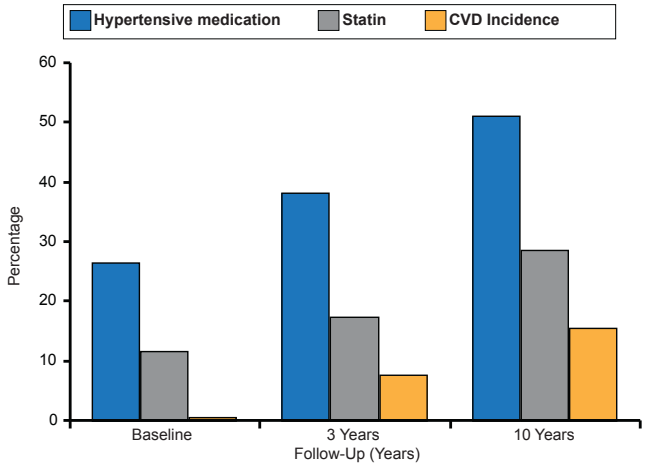
RA is associated with a 2-fold increased risk of CVD and up to a 2-fold increase in mortality [Peters MJL et al. *Arthritis Rheum* 2009]. The increased risk may be attributable to a patient's CV risk profile, chronic inflammation, or undertreatment [Solomon DH et al. *Ann Rheum Dis* 2010]. Most previous research accounts only for CV- and RA-related associations at baseline [del Rincón ID et al. *Arthritis Rheum* 2001].

The 353 study participants had a mean age of 63 years and 34% were men. Median disease duration was 7 years. Medication use at baseline was biologicals by only 1% of participants, methotrexate 60%, prednisone 17%, nonsteroidal anti-inflammatory drugs 69%, statins only 12%, and antihypertensives only 26%. The baseline incidence of CVD was 16.1%, the mean RA disease activity score at 28 joints (DAS28) was 3.91±1.36, and the health assessment questionnaire score was 0.75 (0.25 to 1.13).

The first follow-up was conducted in 2004 to 2005 and the second in 2010 to 2011. The incidence of CVD

and events did not change substantially at Years 3 and 10 (Figure 1), while the use of statins and antihypertensives increased substantially at those time points.

Figure 1. Incidence of CVD and CV Events



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In women, baseline systolic blood pressure, the use of antihypertensive drugs, and the estimated renal function were significantly associated with developing CVD (Table 1). No association between RA-related factors and the development of CVD was found in women.

Table 1. RA-Related and CV-Related Factors Associated With CVD Incidence

RA-Related Factors	Males (n=111)	Females (n=218)
RA disease duration, years	0.98 (0.87-1.11)	1.08 (0.97-1.21)
RF positivity, %	1.02 (0.42-2.47)	1.91 (0.64-5.71)
Nodular disease, %	2.04 (0.87-4.77)	0.75 (0.24-2.29)
DAS28	1.02 (0.79-1.32)	1.16 (0.82-1.66)
Use of NSAIDs, %	1.66 (0.60-4.59)	0.81 (0.33-1.96)
CV Risk Factors		
Systolic BP, mm Hg	1.00 (0.98-1.03)	1.03 (1.01-1.05)
Antihypertensives, %	1.14 (0.42-3.11)	3.41 (1.38-8.42)
Renal function, mL/min	0.98 (0.95-1.02)	0.95 (0.92-0.99)
Total cholesterol, mmol/L	1.17 (0.78-1.77)	0.66 (0.42-1.02)
Prior CVD, %	1.52 (0.59-3.92)	2.43 (0.93-6.30)

BP=blood pressure; CV=cardiovascular; CVD=cardiovascular disease; DAS28=disease activity score at 28 joints; NSAIDs= nonsteroidal anti-inflammatory drugs; RA=rheumatoid arthritis; RF=rheumatoid factor.

The erythrocyte sedimentation rate, an RA-related factor, increased in patients who developed CVD, while there was little change in those without CVD. A similar pattern was seen for the DAS28, which declined initially, but increased in patients who developed CVD. The use of biologicals was substantially increased in patients free of CVD.

Generalized estimating equations evaluated whether changes in RA-related factors or CV-related factors are associated with the incidence of CVD. The CV risk factors played a role in developing CVD at baseline. However, the change in DAS28 was significantly and more strongly associated with developing CVD (HR, 2.03; 95% CI, 1.33 to 3.09) than the traditional CV-related factors in women (Table 2). When adjusting for the use of biologicals, this association was completely negated, which may point out a protective role for biologicals, said Prof. van Sijl.

Table 2. The Effect of RA- and CV-Related Factors on CVD in Women

RA-Related Factors	Adjustment for Age	Additional Adjustment for Use of Biologicals
DAS28	2.03 (1.33-3.09)	0.85 (0.44-1.65)
Use of NSAIDs, %	0.44 (0.03-7.56)	0.12 (0.01-1.02)
CV Risk Factors		
Systolic BP, mm Hg	1.03 (1.01-1.05)	—
Antihypertensives, %	2.47 (0.44-13.90)	—
Renal function, mL/min	1.05 (1.03-1.07)	—

BP=blood pressure; CV=cardiovascular; CVD=cardiovascular disease; DAS28=disease activity score at 28 joints; NSAIDs= nonsteroidal anti-inflammatory drugs; RA=rheumatoid arthritis.

The changes in the RA-related factors during follow-up were associated with increased risk of CVD. The presenters concluded that there is a strong indication that improving disease activity and inflammatory markers may positively influence the CV risk in patients with RA.

Efficacy Maintained When Transitioning Directly From TNF Inhibitor to Tofacitinib in RA

Written by Wayne Kuznar

Patients with rheumatoid arthritis (RA) who transition directly from adalimumab (ADA) to tofacitinib (TOFA) maintained a clinical response. Mark Genovese, MD, Stanford University, Stanford, California, USA, presented results from the open-label extension Oral Rheumatoid Arthritis Phase 3 Trials Sequel study [ORAL; NCT00413699] of the randomized, double-blind, placebo-controlled ORAL Standard study in which the two treatments were compared in patients with active RA [NCT00853385].

TOFA is a novel oral Janus kinase inhibitor that has been approved by the United States Food and Drug Administration for the treatment of RA. In ORAL Standard, in subjects with RA (n=717) receiving stable doses of methotrexate, the addition of TOFA 5 or 10 mg twice daily significantly performed better than placebo and was