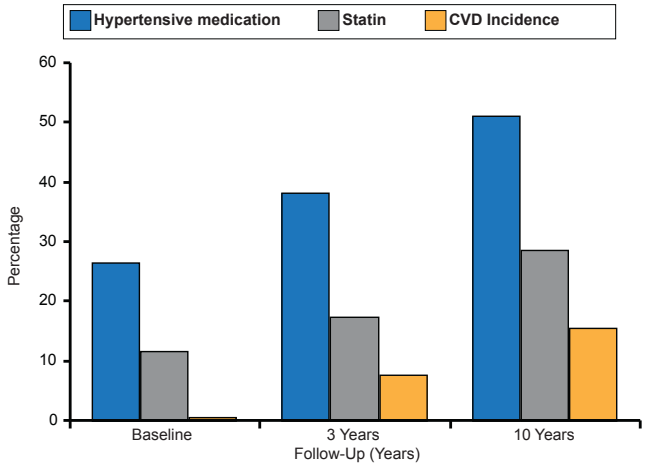
and events did not change substantially at Years 3 and 10 (Figure 1), while the use of statins and antihypertensives increased substantially at those time points.

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

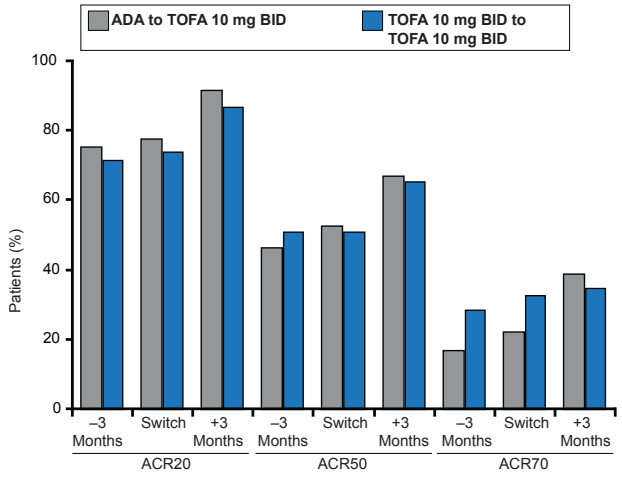
numerically similar to ADA 40 mg Q2W on three primary outcome measures: 20% improvement at Month 6 in the American College of Rheumatology scale (ACR20); the change from baseline to Month 3 in the score on the Health Assessment Questionnaire-Disability Index (HAQ-DI); and the percentage of patients at Month 6 who had a Disease Activity Score for 28-joint counts based on the erythrocyte sedimentation rate (DAS28-4[ESR]) of <2.6 [van Vollenhoven RF et al. *N Engl J Med* 2012].

Subjects who completed ORAL Standard were eligible to enroll in ORAL Sequel, receiving TOFA 10 mg BID, without a washout, with the timing of the first TOFA dose ≤1 week following the last dose of ADA in ORAL Standard. The goal was to define the efficacy and safety of transitioning from ADA to TOFA without a washout.

Of the 204 subjects randomized to ADA, 145 enrolled in ORAL Sequel and 125 of them began TOFA without a washout ≤1 week after their last dose of ADA in Oral Standard. Of the 201 subjects randomized to TOFA, 148 enrolled in ORAL Sequel and 124 took their first dose of TOFA ≤1 week after their last dose of TOFA in Oral Standard.

Results were reported for subjects randomized to ADA 3 months before the end of ORAL Standard, at the end of ORAL Standard, and 3 months after the transition to TOFA in ORAL Sequel. Data for TOFA 10 mg BID, during each phase were reported for the same time points. The ACR20 response rate in patients randomized to ADA were 74.2% at 3 months before the end of ORAL Standard, 76.6% at the end, and 90.5% at 3 months after the transition to TOFA in ORAL Sequel. A similar pattern was observed for ACR50 and ACR70 responses (Figure 1).

Figure 1. Efficacy: ACR Responses in Last 3 Months of ORAL Standard and First 3 Months of ORAL Sequel Study



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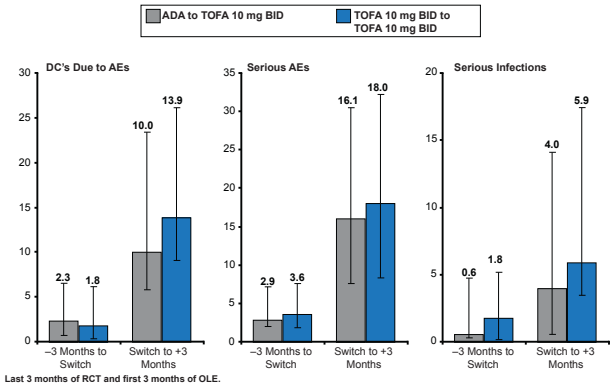
Mean change from baseline in HAQ-DI in patients transitioning from ADA to TOFA was -0.55, -0.60, and -0.70 at these same three time points. Efficacy results in patients who continued on TOFA were similar at the same time points and showed a similar pattern of increases from ORAL Standard to ORAL Sequel. The rate of serious adverse events increased post transition in both groups, when analyzed per 100 patient-years (Figure 2). The overlapping immunomodulatory effects of ADA and TOFA did not appear to be the cause of the increase in safety-related events, because they were increased in both groups.

Figure 2. Safety: Incidence Rates per 100 Patient-Years



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MOBILITY Part A Hones in on Effective Dosing for Sarilumab in RA

Written by **Larry Hand**

Rheumatoid arthritis (RA) patients treated with sarilumab (SAR) 150 or 200 mg Q2W or 100 or 150 mg QW were more than twice as likely to achieve an American College of Rheumatology 50 (ACR50) response after 12 weeks, compared with patients treated with placebo, and the benefit started appearing as early as 2 weeks. Roy Fleischmann, MD, Metroplex Clinical Research Center, Dallas, Texas, USA, presented a poster of a post hoc analysis from the Evaluation of SAR153191 (REGN88; Sarilumab) on Top of Methotrexate in Rheumatoid Arthritis Patients study [RA-MOBILITY; NCT01061736; Fleischmann R et al. EULAR 2013 (poster 0136)].

The need for new therapies is known, with only a minority of RA patients achieving a sustained clinical remission, despite the current treatment options [Kavanaugh A et al. *Ann Rheum Dis* 2013]. It has been shown that an elevated level of interleukin 6 (IL-6) drives inflammation in RA [Srirangan S,