



Abatacept and Adalimumab Equally Effective for Rheumatoid Arthritis

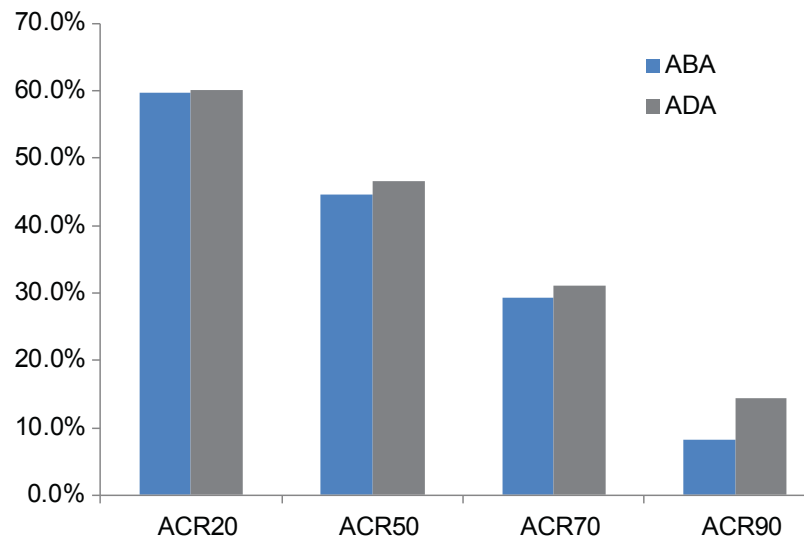
Written by Toni Rizzo

To date, few direct comparisons of biologic agents for the treatment of rheumatoid arthritis (RA) have been conducted, resulting in a lack of evidence-based guidance for selection of biologic therapy. The Abatacept Versus Adalimumab Comparison in Biologic-Naïve RA Subjects With Background Methotrexate trial [AMPLE; NCT00929864] was the first powered head-to-head study comparing two biologic disease-modifying antirheumatic drugs (DMARDs), abatacept (ABA) and adalimumab (ADA), with the standard of care, methotrexate (MTX). Each was administered with MTX in patients without prior biologic DMARD therapy. The 1-year results of this blinded 2-year study showed comparable efficacy, radiographic progression, and safety for patients treated with ABA versus ADA [Weinblatt ME et al. *Arthritis Rheum* 2013].

The objective of the AMPLE Phase 3b trial, presented by Michael Schiff, MD, University of Colorado, Denver, Colorado, USA, was to compare the efficacy and safety of ABA versus ADA after 2 years of treatment in biologic DMARD-naïve patients with RA. A total of 646 patients were randomized to treatment with subcutaneous (SC) ABA 125 mg weekly plus MTX (n=318) or SC ADA 40 mg biweekly plus MTX (n=328). All patients had active RA for ≤ 5 years and an inadequate response to MTX. The primary endpoint was the American College of Rheumatology 20% improvement criteria (ACR20) response at 1 year. The secondary endpoints were injection-site reactions at 1 year and ACR responses, 28-joint disease activity score (DAS28) based on C-reactive protein (CRP), and radiographic inhibition, safety, and retention at 2 years.

After 2 years, ACR responses with ABA versus ADA were as follows: ACR20, 59.7% versus 60.1%; ACR50, 44.7% versus 46.6%; ACR70, 29.3% versus 31.1%; ACR90, 8.2% versus 14.5% (Figure 1).

Figure 1. ACR Response Through 2 Years

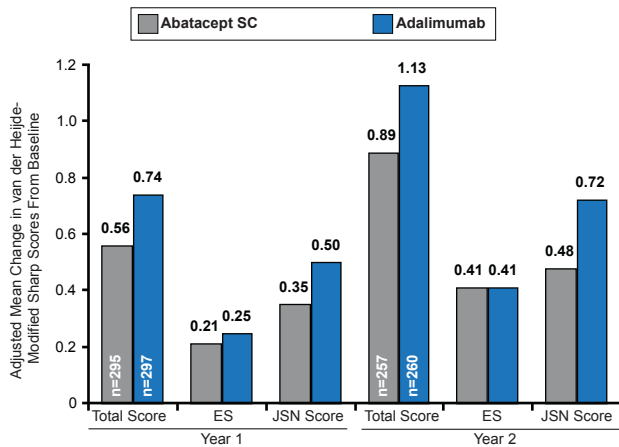


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The adjusted mean change in DAS28-CRP at 2 years was <2.6 in both treatment groups. Radiographic outcomes showed an adjusted mean change in the modified total Sharp score (mTSS) of 0.89 with ABA treatment versus 1.13 with ADA therapy (Figure 2). The adjusted mean change in erosion score was 0.41 in both treatment groups and the adjusted mean change in joint space narrowing was 0.48 with ABA versus 0.72 with ADA. The differences in radiographic outcomes

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. Reproduced with permission from M Schiff, MD.

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