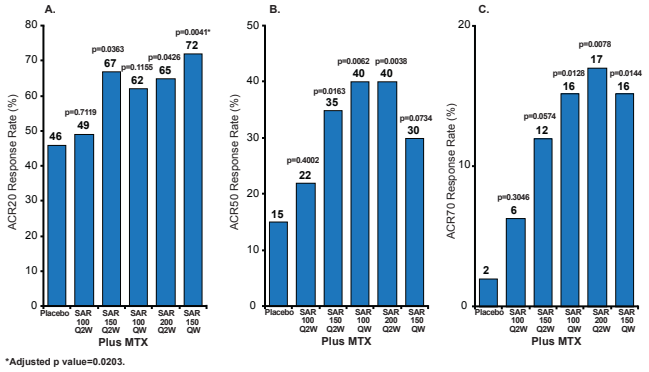
Choy EH. *Ther Adv Musculoskelet Dis* 2010], and work by a number of investigators has shown that blocking IL-6α with monoclonal antibodies (mABs) has been effective for some patients. A reduction in acute phase reactants has been shown with mABs in Phase I studies [Radin A et al. *Arthritis Rheum* 2010; Radin A et al. *Ann Rheum Dis* 2010].

This post hoc analysis was performed to evaluate the time-to-event of key outcomes by assessing differences in temporal patterns of the cumulative incidence of ACR20, ACR50, ACR70, and European League Against Rheumatology (EULAR) good plus moderate responses. A total of 306 adult patients with active RA for at least 3 months and with an inadequate response to methotrexate (MTX) in the Mobility Part A dose ranging study were included in this analysis. Baseline patient characteristics were similar among all groups (mean age at 52.2 years, 93.9% Caucasian, 79% women, mean disease duration of 7.8 years, and rheumatoid factor positivity 79.7%).

Researchers randomized the patients into 6 arms (n=51 or 52 each) to receive either SAR 100 mg Q2W plus MTX; SAR 150 mg Q2W plus MTX; SAR 100 mg QW plus MTX; SAR 200 mg Q2W plus MTX; SAR 150 mg QW plus MTX; or placebo plus MTX. All drug administration was subcutaneous. Figure 1 details the key results, including the primary endpoint of the ACR20 response rate at 12 weeks.

Figure 1. Primary and Secondary Outcomes (ACR Responses at Week 12)



ACR=American College of Rheumatology; Q2W=every other week; QW=weekly; SAR=sarilumab.

SAR doses of 150 mg Q2W or higher reduced RA signs and symptoms. Relative hazard ratios (HRs) favored 4 out of the 5 SAR doses compared with placebo, but not for 100 mg Q2W (Table 1). One death occurred from respiratory distress syndrome or a cerebrovascular accident in the SAR 100 mg Q2W group. Six of the 8 patients who experienced treatment-related adverse events in the two SAR groups discontinued treatment.

Table 1. Likelihood of Achieving Efficacy Outcome With Sarilumab Compared With Placebo

Placebo, n=52 (Reference arm)	n	Relative Hazard (95% CI)	p Value
ACR20			
100 mg Q2W	51	1.07 (0.66–1.75)	0.7816
150 mg Q2W	51	1.43 (0.89–2.30)	0.1378
100 mg QW	50	1.31 (0.80–2.12)	0.2815
200 mg Q2W	52	1.51 (0.95–2.41)	0.0848
150 mg QW	50	1.50 (0.93–2.41)	0.0939
ACR50			
100 mg Q2W	51	1.06 (0.45–2.46)	0.9
150 mg Q2W	51	2.15 (1.06–4.63)	0.04
100 mg QW	50	2.51 (1.25–5.36)	0.01
200 mg Q2W	52	3 (1.53–6.32)	<0.01
150 mg QW	50	2.19 (1.07–4.73)	0.04
ACR70			
100 mg Q2W	51	2.09 (0.38–11.39)	0.3957
150 mg Q2W	51	4.27 (0.91–20.10)	0.0664
100 mg QW	50	6.13 (1.36–27.66)	0.0183
200 mg Q2W	52	5.19 (1.14–23.70)	0.0335
150 mg QW	50	6.40 (1.42–28.88)	0.0157
EULAR (Good/Moderate)			
100 mg Q2W	51	1.12 (0.72–1.75)	0.6209
150 mg Q2W	51	1.79 (1.16–2.76)	0.0082
100 mg QW	49	2 (1.30–3.11)	0.0017
200 mg Q2W	50	2.05 (1.34–3.18)	0.0011
150 mg QW	50	1.99 (1.28–3.09)	0.0021

ACR=American College of Rheumatology; EULAR=European League Against Rheumatism; Q2W=every other week; QW=weekly.

The likelihood of achieving efficacy with an ACR50 response was high in 4 of 5 SAR doses but fell short for ACR20 responses.

Lower-Dose Etanercept Plus Methotrexate Shows Benefit for Early RA Patients in PRIZE Trial

Written by **Larry Hand**

In patient-reported outcomes for those with recently diagnosed rheumatoid arthritis (RA), treatment with etanercept 25 mg (ETN25) plus methotrexate (MTX) was superior to MTX plus placebo or placebo alone in maintenance of remission and therapeutic effect. Paul Emery, MD, University of Leeds, Leeds, United Kingdom, presented a poster of the results of A 3-Phase Study to Evaluate Sustained Remission and Productivity Outcomes in Subjects With Early Rheumatoid Arthritis Initiated on Treatment With Etanercept Plus Methotrexate [PRIZE;

EUCTR2008-00263-85-IT; Emery P et al. EULAR 2013 (poster 0543)].

The open-label, double-blind, 39-week Phase 2 study evaluated patients who had achieved remission by Week 52 in Phase 1 (28-joint disease activity score [DAS28] ≤3.2 at Week 39 and DAS28 <2.6 at Week 52), during which moderate to severe RA patients diagnosed within ≤1 year without previous MTX or biologic treatment were treated with ETN 50 mg plus MTX. Phase 2 patients were randomized 1:1:1 to ETN25 plus MTX (n=63), MTX plus placebo injection (n=65), or placebo capsules plus placebo injection at Week 52 (n=65). Patient-reportd outcomes in RA have shown significant improvement through treatment with biologic drugs [Bala S-V et al. *Musculoskeletal Care* 2010].

The patients entering Phase 2 were a mean 49.4 years and 64.8% were women. The mean disease duration was 6.8 months and the mean diagnosis duration was 2.3 months. Almost 41% had taken corticosteroids, 17.1% had taken disease-modifying antirheumatic drugs, and 66.3% had taken nonsteroidal anti-inflammatory drugs.

Of 193 patients entering Phase 2, 144 completed the trial, including 132 responders (ETN25+MTX=56; MTX=50; placebo=38), and 12 nonresponders (ETN25+MTX=3; MTX=4; placebo=35). For the noncompleters, three adverse events occurred in the ETN/MTX group and one occurred in the placebo group. Of the 28 noncompleters in the unsatisfactory response category, 17 were in the placebo group, 11 were in the MTX group, but none was in the ETN/MTX group. No significant radiographic disease progression was reported in any treatment group.

ETN/MTX patients reported significantly greater benefits in maintenance of health, quality of life (QoL), levels of fatigue, and activity impairment compared with placebo patients ($p<0.0001$), and maintenance of effect was significantly greater at the last observation carried forward for ETN/MTX patients compared with placebo patients. The ETN/MTX group also reported significantly greater low risk of work instability than the placebo group ($p=0.0011$).

Phase 2 patients reported several clinically meaningful improvements, including scoring 0 to 3 (clinically meaningful $\Delta \geq 0.22$) on the Health Assessment Questionnaire-Disability Index (HAQ-DI), scoring 0 to 52 (clinically meaningful $\Delta \geq 3.0$) on the Functional Assessment of Chronic Illness Therapy (FACIT-Fatigue) test, and scoring 0 to 1 (clinically meaningful $\Delta \geq 0.05$) for QoL on the EuroQoL-5 Dimensions (EQ-5D) utility score.

PRIZE Phase 2 patients report clinically relevant improvements in quality of life based on EQ-5D utility scores.

Of the responders, 131 entered Phase 3, during which the ETN/MTX dose was tapered for 2 to 4 weeks and the patients are to be observed for the remainder of the 121-week PRIZE trial.

PRIZE Phase 2 patients reported clinically relevant health improvements based on HAQ-DI scores.