The primary efficacy endpoint was the proportion of patients with JIA American College of Rheumatology 30 (ACR30) flares on tocilizumab versus placebo in the 160 patients who completed Part 2 (Weeks 16 to 40). Significantly fewer patients randomized to tocilizumab had a JIA ACR30 flare compared with those randomized to placebo: 26% versus 48%, respectively. The adjusted difference in the mean risk of flares between groups was –0.21 (95% CI, –0.35 to –0.08; p=0.0024).

The percentage of patients who demonstrated improvements in JIA ACR30/50/70/90 responses at Week 16 was lower among the patients randomized to 8 mg/kg tocilizumab who weighed <30 kg compared with the other 2 tocilizumab treatment groups.

At Week 40, 74% of patients assigned to tocilizumab maintained a JIA ACR30 response, 73% maintained a JIA ACR50 response, 65% maintained a JIA ACR70 response, and 40% maintained a JIA ACR90 response.

Infections and infestations were the most common adverse event in patients on active treatment, occurring at a rate of 163.7 per 100 patient-years. There were no deaths during the study.

Autoantibodies Predict Treatment Response to Rituximab in Myositis

Written by Wayne Kuznar

The presence of myositis-associated autoantibodies is the strongest predictor of improvement in patients with adult and juvenile myositis treated with B-cell depletion.

Rohit Aggarwal, MD, MS, University of Pittsburgh, Pittsburgh, Pennsylvania, USA, described findings from the Rituximab for the Treatment of Refractory Adult and Juvenile Dermatomyositis (DM) and Adult Polymyositis (PM) [RIM] study, in which baseline clinical, laboratory, and serologic predictors of response were examined in rituximab-treated patients with refractory myositis, defined as failure of steroids and at least 1 other immunosuppressive agent. The study included 200 patients (76 with adult PM, 76 with adult DM, and 48 with juvenile DM) who were randomized to early (Weeks 0 and 1) or late (Weeks 8 or 9) rituximab with follow-up to 44 weeks.

The definition of improvement [Rider LG et al. *Arthritis Rheum* 2004] for this study is defined as improvement in 3 of any 6 core set measures (CSM) by ≥20%, with no more than 2 CSM worsening by ≥25% (excluding manual muscle testing) at 2 consecutive visits. The primary endpoint was to compare the time to improvement between the rituximab early and rituximab late groups. As reported previously [Oddis CV et al. *Arthritis Rheum* 2012], 83% of patients improved during the course of trial, with no difference in response between the 2 treatment groups.

For the current study, a list of the candidates' baseline clinical and laboratory parameters was compiled as potential predictor variables. All baseline variables were univariately assessed for association with time to improvement. All univariate variables that predicted or trended toward an association with time to improvement were then entered into a multivariate model. A final multivariate time-dependent Cox model was then created.

The final multivariate model consisted of global damage (high vs low) at Week 8 (p<0.01), disease subset (adult vs juvenile) at Week 8 (p<0.01), and myositis autoantibodies: Jo-1/other anti-syn (p<0.01) and Mi-2 (p<0.01) compared with no autoantibodies group. However, both global damage and disease subset washed out as significant predictive variables by Week 20, leaving anti-Jo-1 and anti-Mi-2 as the only significant markers of good prognosis and predictor of treatment response throughout the study.

In summary, the presence of juvenile DM and low global damage predicted a more rapid response than did adult onset myositis and high global damage, respectively. Although low global damage and juvenile DM were associated with more rapid improvement, there was no evidence that either predicts better prognosis if patients fail to improve early, said Dr. Aggarwal. The strongest predictor of improvement was the presence of myositis autoantibodies anti-Jo-1 and anti-Mi-2, which remained significant throughout the study period. In the future, myositis autoantibodies may serve as a prognostic marker and further investigation is needed for evaluation of anti-Jo-1 levels as a biomarker for myositis disease activity.

The Risk of Lymphoma in Patients Receiving Anti-TNF Therapy for RA: Results from the BSR Biologics Register

Written by Maria Vinall

Kimme L. Hyrich, MD, The University of Manchester, Manchester, United Kingdom, presented data from the British Society for Rheumatology Biologics Register, a large cohort study showing no evidence that antibody to tumor necrosis factor (anti-TNF) therapy increases the risk of lymphoma over the background risk associated with rheumatoid arthritis (RA).

The introduction of anti-TNF therapy almost 20 years ago led to a fundamental shift in the treatment paradigm for RA.

However, in 2002 concerns began to appear regarding the possibility of an association between anti-TNF therapy and an increased risk of lymphoma in this patient population [Brown SL et al. *Arthritis Rheum* 2002]. Assessing this risk is difficult because individuals with RA already have a 2 to 3 times higher risk of lymphoma compared with the general population, and this risk increases with increasing disease severity [Baecklund E et al. *Arthritis Rheum* 2006]. To date, neither clinical trials [Leombruno JP et al. *Ann Rheum Dis* 2009] nor observational studies [Setoguchi S et al. *Arthritis Rheum* 2006; Wolfe F and Michaud K. *Arthritis Rheum* 2007; Askling J et al. *Ann Rheum Dis* 2009] have shown such a relationship.

The purpose of this prospective cohort study was to determine whether the use of anti-TNF therapy influences the risk of lymphoma. The study population comprised patients with RA but without prior lymphoproliferative malignancy who were being treated in routine clinical practice in the United Kingdom. Cohort 1 included patients newly exposed to anti-TNF therapy. Cohort 2 included biologic-naïve patients starting or changing to a disease-modifying antirheumatic drug (DMARD). Patient characteristics are shown in Table 1. All participants were followed with both physician and patient questionnaires and linked with the National Health Service cancer and death registry for lymphoma or death. The current results represent follow-up through September 30, 2010. The primary study outcome was risk of first lymphoma in patients ever exposed to anti-TNF therapy versus those exposed to nonbiologic DMARD only. The secondary outcome was the risk of non-Hodgkin lymphoma only.

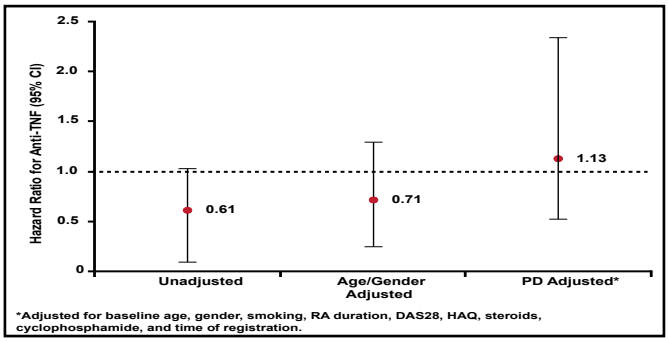
Table 1. Baseline Characteristics.

	nbDMARD n=3465	Anti-TNF n=11987
Follow-up (total patient-years)	13,186	66,353
Median follow-up, patient-years (IQR)	4.5 (2.6–5.9)	6.4 (4.8–7.4)
Mean age, years (SD)	60 (12)	56 (12)
Women, n (%)	2545 (73)	9145 (76)
Ever smoked, (%)	64	60
Median RA disease duration years (IQR)	6 (1–15)	11 (6–19)
Mean DAS score (SD)	5.3 (1.1)	6.6 (1.0)
Mean HAQ (SD)	1.5 (0.7)	2.0 (0.6)
Oral steroids (%)	23	44
Median # prior DMARDs (IQR)	2 (1, 3)	4 (3, 5)
Lymphoma, n Rate/100,000 person-years (95% CI)	20 152 (93–234)	64 96 (74–123)
Hodgkin lymphoma, n Non-Hodgkin lymphoma, n	4 16	9 55

DAS=Disease Activity Score; HAQ=Health Assessment Questionnaire; IQR=interquartile range; nbDMARD=nonbiologic disease-modifying antirheumatic drug; RA=rheumatoid arthritis; SD=standard deviation; TNF=tumor necrosis factor.

There was no increased risk for lymphoma with anti-TNF treatment compared with nonbiologic DMARD only. The adjusted HR for anti-TNF treatment was 1.13 (Figure 1). In the DMARD group 20% had Hodgkin lymphoma versus 14% in the anti-TNF group. A very similar pattern of risk was noted when limited to non-Hodgkin lymphoma (HR=1.26).

Figure 1. Hazard for Lymphoma (nbDMARD Referent).



DAS=Disease Activity Score; HAQ=Health Assessment Questionnaire; nbDMARD=nonbiologic disease-modifying antirheumatic drug; RA=rheumatoid arthritis; TNF=tumor necrosis factor.
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The strengths of the study include it being a large, national cohort with detailed patient data from the National Health Service registry and a propensity model that allowed for adjustment of a large number of covariates. It was limited by a reporting lag, possible screening bias, and the fact that it did not include data on changes in disease activity over time. Further follow-up is recommended to allow for longer latency.

Head-to-Head Biologics Trial Shows No Difference Between Abatacept and Adalimumab

Written by Rita Buckley

Outcomes from the Abatacept Versus Adalimumab Head-to-Head [AMPLE; NCT00929864] trial demonstrated comparable efficacy between subcutaneous (SC) abatacept and adalimumab on background methotrexate (MTX). Michael E. Weinblatt, MD, Brigham and Women's Hospital, Boston, Massachusetts, USA, presented key efficacy and safety results from the trial.

Dr. Weinblatt said that AMPLE is the first head-to-head study in rheumatoid arthritis (RA) patients that is powered to compare biologic disease-modifying antirheumatic drugs (DMARD) on a background of MTX in subjects who have failed MTX therapy and are naïve to biologic DMARD therapy. The hypothesis was that 12 months of treatment with SC abatacept would be noninferior to adalimumab. The primary endpoint was the proportion of subjects meeting the American College of Rheumatology 20% improvement criteria (ACR20) at 12 months.