heart block with maternal fluorinated or nonfluorinated steroids [Shinohara K et al. *Obstet Gynecol* 1999] and a review that failed to find utility of prophylactic treatment of congenital heart block [Costedoat-Chalumeau N et al. *Rev Med Interne* 2003].

Given the uncertainty over the benefit of fluorinated steroids and the maternal and fetal risks associated with these agents, the use of fluorinated steroids on the survival of fetuses with cardiac-NL and the protection from recurrent disease was investigated by Peter M. Izmirly, MD, New York University School of Medicine, New York, New York, USA. Data sources for the investigation were the Research Registry for Neonatal Lupus (RRNL) and an international historical control of 257 pregnancies following the birth of a child with cardiac-NL (which comprised cases in the US-based RRNL, France, and the United Kingdom). The outcomes assessed were fetal survival at 6 months and the recurrence rate of cardiac-NL.

Of the 276 cardiac-NL pregnancies in families enrolled in the RRNL, 150 were treated with fluorinated steroids and 126 were not. Gestational age at detection was 22.1 weeks in those treated with fluorinated steroids versus 24.4 weeks in those not treated ($p<0.0001$). The average dose of dexamethasone in those treated was 4.1 mg for an average duration of 10.9 weeks. Of fetuses with isolated third-degree block at presentation, there were 2 deaths at 6 months in the 78 treated with fluorinated steroids and no deaths in the 74 not treated with fluorinated steroids.

Any benefit to fluorinated steroids appeared to be restricted to those cases associated with hydrops: 13 of 27 (48.1%) with hydrops who were treated with fluorinated steroids were alive at 6 months compared with 1 of 10 (10.0%) not treated with fluorinated steroids ($p=0.059$).

There was no difference in the case fatality rate among treated and nontreated patients with at least 2 poor prognostic risk factors (heart rate ≤50 beats/minute, dilated cardiomyopathy, or endocardial fibroelastosis; Table 1).

Table 1. Effect of Fluorinated Steroids on Case Fatality Rate in Cardiac NL with Associated Poor Prognostic Factors.

Associated Manifestation	Fluorinated Steroids (Case Fatality Rate)	No Fluorinated Steroids (Case Fatality Rate)
DCM	1/4	1/5
EFE	1/11	0/1
≥2 Poor prognostic factors (HR ≤50 bpm, DCM, EFE)	1/6	2/6

bpm=beats per minute; DCM=dilated cardiomyopathy; EFE=endocardial fibroelastosis.

Among the international historical controls of pregnancies following the birth of a child with cardiac-NL, the overall recurrence rate was 19.1%, with no significant difference in the recurrence rate between those treated and not treated with fluorinated steroids (14.3% vs 19.3%; $p=0.58$; Table 2).

Table 2. Exposure to Fluorinated Steroids Does Not Reduce the Recurrence Rate of Cardiac NL.

	Fluorinated Steroids	No Fluorinated Steroids
Unaffected	12	196
Cardiac Neonatal Lupus	2 2/14 (14.3%)	47 47/243 (19.3%)

p=0.58.

Tocilizumab Significantly Reduces Flares in Polyarticular Juvenile Idiopathic Arthritis

Written by Wayne Kuznar

Treatment with tocilizumab, a humanized monoclonal antibody that interrupts interleukin-6-mediated signaling, results in meaningful improvement of polyarticular-course juvenile idiopathic arthritis (pcJIA) following methotrexate failure, with treatment responses maintained to at least 40 weeks, said Hermine I. Brunner, MD, MSc, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA.

The finding comes from A Study of Tocilizumab in Patients with Active Polyarticular-Course Juvenile Idiopathic Arthritis [CHERISH; NCT00988221], a 3-part trial in which patients aged 2 to 17 years with pcJIA who had at least 5 joints with active arthritis were randomized to treatment with tocilizumab 8 mg/kg or 10 mg/kg, depending on body weight, or placebo after an open-label run-in. To be eligible, patients had to have an inadequate response to or an inability to tolerate methotrexate and had to be on a maximum stable dose of oral corticosteroids (10 mg/day or 0.2 mg/kg/day—whichever was lower).

In Part 1 of the study, 188 patients received intravenous infusion of tocilizumab (8 mg/kg for patients ≥30 kg, 8 mg/kg or 10 mg/kg for patients <30 kg) in an open-label fashion for 16 weeks. In Part 2, 166 patients who had an adequate response in Part 1 were randomized to receive either tocilizumab at the same dosage as in Part 1 or placebo, every 4 weeks for up to 24 weeks. In Part 3, patients will receive tocilizumab at the same dosage as in Part 1, every 4 weeks for up to another 64 weeks. Standard-of-care therapy was continued throughout the study. Data from Parts 1 and 2 were presented by Dr. Brunner.

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.