Patients aged 40 to 70 old (n=126) with daily knee pain ≥40 mm on a 1- to 100-mm visual analog scale (VAS) during a PF activity (eg, climbing or descending stairs, kneeling, prolonged sitting or squatting) for 3 months, a radiographic Kellgren-Lawrence Grade 2 or worse in the PF joint or PF OA worse than tibiofemoral disease, and confirmed PF joint tenderness on clinical examination were randomized to 6 weeks of treatment with a PF brace or no treatment.

The primary symptom outcome was the change in pain as measured on the VAS during nominated aggravating activity. The primary structural outcome was bone marrow lesion volume in the PF joint as assessed on contrast-enhanced magnetic resonance imaging. Tibiofemoral bone marrow lesion volume served as an untreated control region. In the treatment group, braces were worn for a mean of 7.35 hours per day. Five patients in the bracing group and one in the no-treatment group withdrew from the trial before completion.

In the bracing group, pain on the VAS during the nominating activity decreased by 18.16 mm, compared with a 1.29-mm reduction in the no-treatment group (p<0.001). Improvements in the Knee Injury and Osteoarthritis Outcome Score pain subscale and activities of daily living subscale were also significantly superior in the bracing group (p=0.02 for each vs no treatment; Table 1).

Table 1. Randomized Trial Results

Variable	No Brace Group	Brace Group	Between Groups Difference	
Change @ 6 weeks	Mean change (95% CI)	Mean change (95% CI)	Mean difference in change (95% CI)	p
Primary Symptom Outcome: Nominated VAS (0–100)	–1.29 (–6.39, 3.80)	–18.16 (–23.88, –12.44)	16.87 (9.30, 24.43)	<0.001
Primary Structural Outcome: BML Volume in PF joint (in mm^3)	102.66 (–292.80, 498.12)	–554.92 (–964.02, –145.82)	–657.58 (–1226.57, –88.59)	0.02
Secondary Structural Outcome: BML Volume in TF Joint (in mm^3)	1.79 (–492.67, 496.26)	198.08 (–313.44, 709.60)	196.29 (–515.15, 907.73)	0.59

BML=bone marrow lesion; PF=patellofemoral; VAS=visual analog scale.

PF bone marrow lesion volume decreased by a mean of 554.92 mm^3 in the bracing group, compared with a mean increase of 102.66 mm^3 in the no-treatment group (p=0.02). There was no significant difference between groups in the mean change in tibiofemoral bone marrow lesion volume or in synovitis volume.

The reduction in the size of bone marrow lesion volumes in the PF but not the tibiofemoral joint is consistent with a compartment-specific effect of the brace, concluded Prof. Felson.

Higher Incremental Cost-Effectiveness Ratios Seen With Biologics in the TEAR Trial

Written by Muriel Cunningham

As additional treatments have been approved for rheumatoid arthritis (RA), researchers have used clinical trial data to analyze the cost effectiveness of these new drugs. Since 1998, more than 30 cost-effectiveness analyses (CEAs) have been conducted, with highly variable results. Kaleb Michaud, PhD, National Data Bank for Rheumatic Diseases and the University of Nebraska Medical Center, Omaha, Nebraska, USA, presented the CEA results of patient-level data from the Treatment of Early Aggressive Rheumatoid Arthritis trial [TEAR; NCT00259610], a large, randomized, double-blind clinical study.

The objective of the TEAR trial was to determine the best strategy for treating patients with early RA [Moreland LW et al. *Arthritis Rheum* 2012]. Eligible patients were adults who had RA for <3 years, limited exposure to disease-modifying antirheumatic drugs, seropositivity or erosions, and at least 4 swollen and 4 tender joints on the 28-joint count. At baseline, patients were randomized to 1 of 4 treatments:

1. immediate treatment with methotrexate (MTX) plus etanercept (IE)
2. immediate triple therapy (IT) consisting of MTX plus sulfasalazine plus hydroxychloroquine
3. MTX monotherapy with a step-up to MTX plus etanercept (SE)
4. MTX monotherapy with a step-up to triple therapy (ST)

Step-up occurred at Week 24 in patients with active disease, defined as Disease Activity Score in 28 joints using the erythrocyte sedimentation rate (DAS28-ESR) ≥3.2. Patients were followed for up to 2 years. The primary outcome measure was the mean DAS28-ESR score from Weeks 48 to 102.

A total of 755 patients were randomized in the trial. At baseline, participants had a mean duration of RA of 3.6 months (range, 0 to 41.4), a mean (standard deviation [SD]) DAS28 of 5.8 (1.1), and an average of 14.3 (6.8) painful joints with 12.8 (6.0) swollen joints. At the Week 24 time point, both immediate treatment groups had significant decreases in DAS28 compared with the SE and ST groups (p<0.0001). However, in the primary analysis of results from Weeks 48 to 102 the four treatment arms had comparable improvement (p=0.55) [Moreland LW et al. *Arthritis Rheum* 2012].

A Markov simulation model with a societal perspective was utilized to estimate the costs and quality-adjusted life years (QALYs). The following inputs

were used in the model: discontinuation rate for triple therapy [0.22, (range, 0.11 to 0.46)] and etanercept [0.10 (range, 0.07 to 0.15)], annual cost of triple therapy [$791 (range, $500 to $1200)] and etanercept [$24,446 (range, $12,000 to $26,000)], mean income [$45,552 (range, $30,000 to $60,000)], discounting of 3% (0% to 5%), and quality-of-life mapping using the EQ-5D. At both 1 and 2 years the IT group had the lowest cost and greatest effectiveness. When the model was extended to lifetime, both the IT and IE treatment groups were cost effective, with an incremental cost effectiveness ratio (ICER) of ~$840,000/QALY.

A sensitivity analysis indicated that the results were the most sensitive to etanercept cost and decreases in the discontinuation rates of triple therapy, but these findings did not change the overall conclusions. "The benefits from all strategies were comparable, but biologics strategies were almost twice as expensive as triple strategies, producing ICERs greater than what most healthcare settings find acceptable," concluded Dr. Michaud.

Early Results Indicate Rituximab Effective in the Treatment of IgG4-Related Disease

Written by **Muriel Cunningham**

Immunoglobulin G4-related disease (IgG4-RD) is a fibro-inflammatory disorder that was first described 10 years ago. IgG4-RD may affect multiple organs and resembles other diseases such as Sjögren's syndrome, lupus, sarcoidosis, lymphoma, and idiopathic membranous glomerulonephropathy. This disorder is typically treated with steroids but the response is mixed: some patients experience a complete response but others cannot completely discontinue steroid therapy. John H. Stone, MD, MPH, Massachusetts General Hospital, Boston, Massachusetts, USA, gave an overview of the results of a prospective open-label investigator-initiated trial of rituximab in the treatment of IgG4-related disease [NCT1584388].

Thirty patients were enrolled at two centers and received rituximab 1000 mg intravenously in two doses. The use of steroids was minimized by having patients taking steroids at baseline and taper off within the first 2 months. The primary outcome measure was the disease response at 6 months, defined as a decline in the IgG4-RD Responder Index (IgG4-RD RI) of at least 2 points without concomitant prednisone use. Flow cytometry analyses were also conducted at one of the sites.

The mean age of the patients was 63 years (range, 42 to 82 years) and 26 (87%) were male. Ten of 30 (33%) had normal serum IgG4 concentrations at baseline with a wide range in obtained values (26 to 4780 mg/dL). The most common organs involved (≥50%) were the pancreas, salivary glands, and lymph nodes. Twenty-six patients were followed for 6 months and were included in the primary analysis. Of these 26 patients, 24 (92%) met the primary outcome. The mean IgG4-RD RI score at baseline fell from 12 to 2.1 at 6 months ($p<0.01$). The mean Physician's Global Assessment (PGA) at baseline was 63 mm and, by the 6-month time point, 73% of completed patients had improved to a PGA of 0 mm. In addition, a significant decrease of serum IgG4 concentration was observed, from a baseline mean of 609 to 293 mg/dL ($p<0.001$).

Overall, 90% of patients had controlled disease without prednisone and three patients achieved disease control by adding prednisone. Of the three that added prednisone, two achieved complete remission and the remaining patient was unable to completely discontinue prednisone. Five patients relapsed, one occurring before the 6-month time point. Seven serious adverse events were reported but none were considered related to rituximab.

The flow cytometry results were striking, showing a large peripheral plasmablast expansion at baseline in all IgG4-RD patients that were tested. These increases occurred even when serum IgG4 concentrations were within the normal range. The number of plasmablasts decreased dramatically within 4 weeks of rituximab treatment.

The results from this mechanistic study suggest that plasmablast elevations may be a useful biomarker in monitoring patients with IgG4-RD. "Rituximab appears to be a highly effective therapy for IgG4-RD. This medication has an important role in IgG4-RD that is refractory to steroids and for patients in whom steroids are contraindicated," concluded Dr. Stone.