Combination therapy with disease-modifying antirheumatic drugs in early rheumatoid arthritis is more effective than monotherapy in producing sustained remission, which in turn is associated with better radiographic outcomes, a Finnish study has found.

In a comparison of the rates of achieved and sustained remission and good treatment response among a cohort of early rheumatoid arthritis (RA) patients receiving either combination or single DMARD therapy, patients randomized to combination therapy were more than twice as likely to meet modified American College of Rheumatology (ACR) remission criteria at 2 years and were more than four times as likely to demonstrate sustained remission at each visit, compared with patients on monotherapy, reported Dr. Heidi Makinen of Jyväskylä Central Hospital (Finland) and colleagues in the Finnish RA Combination Therapy Trial (FIN-RACo).

The trial included 169 patients out of 195 included in the original FIN-RACo study for whom complete data were available. Patients were aged 18-65 years and had recent-onset RA, defined as less than 2 years’ duration of active disease with 3 or more swollen joints and three of the following: erythrocyte sedimentation rate (ESR) of at least 28 mm/hr or C-reactive protein (CRP) greater than 19 mg/L; morning stiffness lasting at least 29 minutes; more than 5 swollen joints; or more than 10 tender joints.

The 79 patients randomized to combination therapy initially received 2 g of sulfasalazine daily, which could be increased up to 3 g per day, and at the discretion of the treating rheumatologist, up to 10 mg of prednisolone daily. In the case of adverse events or lack of efficacy, sulfasalazine could be discontinued with monotherapy or other single DMARD. Intra-articular glucocorticoid injections were allowed in all patients at the treating physicians’ discretion.

Patient evaluations at baseline, 6, 12, and 24 months included assessments of tender joint count, swollen joint count, duration of morning stiffness, physician and patient overall assessment and pain on visual analog scale, physical function on patient self-report Health Assessment Questionnaire, ESR, and CRP. Radiographs of hands and feet were obtained at 6 and 24 months and were scored by radiologists blinded to the treatments according to the Larsen method.

Remission was defined based on modified ACR criteria, including no joint swelling or soft tissue swelling of tender or swollen joints, no joint tenderness or pain on motion, normal ESR, and morning stiffness lasting no longer than 15 minutes. Remission based on Disease Activity Score 28 (DAS28) was defined as a DAS28 score of less than 2.6. Sustained remission was defined as the presence of remission at 6, 12, and 24 months. Good treatment response was defined according to the European League Against Rheumatism (EULAR) treatment response criteria as a DAS28 score less than 3.2 and a decreased DAS28 score of more than 1.2 from baseline.

For Best Results, Consider Combining DMARDs

The authors noted that radiographic progression and the sustained remission and good treatment response showed markedly less deterioration in Larson score among patients in sustained remission, compared with those who achieved remission at the 6-month visit but did not sustain it, according to the investigators. Because sustained remissions were more common in the combination-therapy patients, it follows that such treatment would confer better radiographic outcomes, they said.

While the study was limited by its assessment of remission only at the 6-, 12-, and 24-month time points, leaving open the possibility that patients in remission at those time points could have experienced active disease flares between visits—previous studies have shown that such flares are often linked to discontinuation of therapy while in remission. “In our study, combination therapy was continued successfully for 2 years, and half the patients remained in sustained DAS28 remission,” the authors wrote.

The findings of this study suggest that sustained remission, rather than remission, should be the goal of DMARD therapy, the authors concluded.

**For Best Results, Consider Combining DMARDs**

**By Diana Mahoney New England Bureau**

**Image of the Month**

The patient’s twin brother and one sister had been diagnosed with rheumatoid arthritis (RA). On the basis of these findings and the physical evaluation, the primary care physician had diagnosed the man with RA and initiated treatment with nonsteroidal anti-inflammatory drugs for his twin brother and one sister had been diagnosed with RA, to his relief. He was advised to continue using them.

**Knuckle pads** are commonly seen in patients with and without Dupuytren’s disease in a small series of patients. Dr. Alarcón and Dr. Lopez noted a difference in the sonographic appearance of knuckle pads in patients with and without Dupuytren’s in a small series. These two patients showed diffuse areas of lower echo signal and skin thickening, whereas the affected PIP joints with a linear hypoechoic band paralleling the epidermis layer. Focal subcutaneous areas of lower echo signal are more suggestive of rheumatoid nodules and neurofibromas.

No sonographic evidence of synovitis was identified in this patient, but there were clear subcutaneous areas of lower echo signal. With arthritis, the joint capsule would appear distended and the cortical surface would be irregular, while the soft tissue would appear normal.

This image shows that “the joint is fine. This person does not have an inflammatory arthritis. What he has is this condition that infiltrates the skin,” said Dr. Lopez. The pressure of the patient’s case on the withhold use of anti-rheumatic arthritis, to his relief. He was advised to continue using anti-inflammatory drugs on an as-needed basis but was strongly encouraged not to take them routinely. He was not referred for surgery because the patient who were not causing significant functional impairment and if removed, they are likely to return.

—Kerri Wachter

**Periarticular soft-tissue fullness is visible on x-ray.**

**Longitudinal ultrasound of the fourth PIP shows diffuse areas of low echo signal.**

**Image of the Month**

The term ‘knuckle pad’ is most often used to describe benign cutaneous lesions of the extensor surfaces of the fingers. However, the lesions most commonly affect the PIP joint, rather than the entire extensor surface. These discrete, round skin nodules are usually soft and free moving.

Many physicians are unfamiliar with this diagnostic condition; ultrasound examination confirmed the absence of synovitis and the presence of periarticular soft-tissue fullness in this case and several others reported by Dr. Alarcón and her colleagues (Skeletal Radiol. 2006;35:942-7). This may be important to reassure patients and physicians that they are not dealing with RA.

Knuckle pads are commonly associated with palmar and plan tar fibromatoses, occurring in up to 20% of patients with Dupuytren’s contracture. Less well-defined or softer knuckle pads may be confused with more common causes of soft-tissue swelling, such as inflammatory arthritis. The presence of knuckle pads may lessen the accuracy of the physical exam when assessing the presence of underlying synovitis.

The radiograph shows periarticular soft-tissue fullness, which can sometimes be seen in RA, leaving the diagnosis unclear, said Dr. Robert Lopez, a radiologist at the University of Alabama, Birmingham, who specializes in musculoskeletal imaging.

Ultrasound is demonstrably better than standard clinical joint assessment for synovitis and is more sensitive than radiography in identifying erosive disease in inflammatory arthritis. Another advantage of ultrasound is that it allows physicians to quickly see in the office what the likely causes are, said Dr. Lopez.

In their small series of patients, Dr. Alarcón and Dr. Lopez noted a difference in the sonographic appearance of knuckle pads in patients with and without Dupuytren’s in a small series. These two patients showed diffuse areas of lower echo signal and skin thickening, whereas the affected PIP joints with a linear hypoechoic band paralleling the epidermis layer. Focal subcutaneous areas of lower echo signal are more suggestive of rheumatoid nodules and neurofibromas.

No sonographic evidence of synovitis was identified in this patient, but there were clear subcutaneous areas of lower echo signal. With arthritis, the joint capsule would appear distended and the cortical surface would be irregular, while the soft tissue would appear normal.

This image shows that “the joint is fine. This person does not have an inflammatory arthritis. What he has is this condition that infiltrates the skin,” said Dr. Lopez. The pressure of the patient’s case on the withhold use of anti-rheumatic arthritis, to his relief. He was advised to continue using anti-inflammatory drugs on an as-needed basis but was strongly encouraged not to take them routinely. He was not referred for surgery because the patient who were not causing significant functional impairment and if removed, they are likely to return.

—Kerri Wachter