Triple Therapy Matches Etanercept in RA, New Option for PsA, and More

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From the top nonspecialty journals: Etanercept found no better than triple non-biologic therapy for RA when methotrexate fails; ustekinumab found effective for psoriatic arthritis, and how inflammation may trigger major mood disorders.

Last week's articles on rheumatology topics in the major non-specialty journals.

Rheumatoid Arthritis

Therapies for Active Rheumatoid Arthritis after Methotrexate Failure
N Engl J Med, June 11, 2013, online first. Full text $15

Making Rational Treatment Decisions in Rheumatoid Arthritis When Methotrexate Fails
N Engl J Med, June 11, 2013, online first. Full text $15

Triple therapy was noninferior to methotrexate plus etanercept for rheumatoid arthritis (RA) patients with inadequate response to methotrexate monotherapy. The improvement was about 2 points on the 28-joint Disease Activity Score (DAS28). A Veterans Affairs study randomized 353 patients with DAS28 ≥4.4 on methotrexate to 24 weeks of either triple therapy (methotrexate, sulfasalazine, and hydroxychloroquine), or to methotrexate and etanercept. After 24 weeks, the 27% of patients in each group who had no improvement (DAS28 <1.2) were switched to the other group, to match typical clinical use. Improvements were similar for patients who switched and those who did not. The primary outcome, improvement in DAS28 at 48 weeks, was noninferior but not significantly better, either statistically or clinically. There was a trend favoring etanercept for radiographic progression, as in two earlier trials comparing similar regimens (one, non-blinded, used infliximab rather than etanercept as anti-TNF therapy). Initial methotrexate monotherapy is successful in only about 30% of patients. This new information may arrive "too late to influence modern practice" for the remainder, says the commentary, as most doctors now prefer TNF inhibitors as the next step in therapy.

Psoriatic Arthritis

Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1 year results of the phase 3, multicentre, double-blind, placebo-controlled PSUMMIT 1 trial
Lancet, June 13, 2013, online first, $31.50

Ustekinumab for psoriatic arthritis: close to the PSUMMIT?
Lancet, June 13, 2013, online first, $31.50

Twice as many patients with active psoriatic arthritis (PsA) reached ACR20 (≥20% improvement in the American College of Rheumatology criteria) with ustekinumab than with placebo, so the drug may replace tumor necrosis factor inhibitors for treatment-resistant PsA.

In a phase 3 trial, 615 patients whose PsA was not controlled by either DMARDs or NSAIDs were randomized to placebo or to low or high doses of ustekinumab. At week 16, patients with <5% improvement were moved from the placebo group to the low-dose group or from low doses to high doses, and at 24 weeks all patients on placebo were moved to the low-dose group. At week 24, 50% of the high-dose group had achieved the primary endpoint of ≥ACR20, but only 42% of the low-dose group and 23% of those on placebo showed this improvement. Responses persisted through week 52.
Ustekinumab is a human monoclonal antibody that inhibits the p40 subunit common to IL(interleukin)-12 and IL-23, and single nucleotide polymorphisms in both have been identified as susceptibility loci in psoriasis and PsA. **Ustekinumab also showed efficacy in patients with coexistent spondyloarthritides, so the IL-23 pathway may also prove a therapeutic target in ankylosing spondylitis.**

**Mood Disorders and Immunity**

**Autoimmune Diseases and Severe Infections as Risk Factors for Mood Disorders: A Nationwide Study**
*JAMA Psychiatry*, June 12, 2013, online first. Full text $30

Autoimmune diseases and infections are risk factors for subsequent mood disorder diagnoses. A nationwide population-based prospective cohort study of 3.6 million people in Danish longitudinal registers found that a prior hospital contact for autoimmune disease increased the risk of a subsequent mood disorder by 45%, and hospitalization for infection increased the risk by 62%. **The two risk factors together increased the risk of a subsequent mood disorder by 235%**. Inflammation may increase the permeability of the blood-brain barrier, say the authors, and systemic inflammation can induce a “sickness behavior” of fatigue, reduced appetite, apathy, decreased social interaction, and sleep disturbances.

**Autoimmune Hepatitis**

**Seminar: Autoimmune hepatitis**
*Lancet*, June 14, 2013, online first, $31.50

Patients presenting with acute liver failure may have autoimmune hepatitis. Its symptoms are non-specific, and variants make it difficult to identify, but a **composite scoring system can diagnose patients into definitely, probably, or not having autoimmune hepatitis** (with a sensitivity of >80% and a specificity of >95%). This article describes serum markers and pathology, and outlines what is known about the molecular medicine, including descriptions of antibody types and specific HLA haplotypes that differentiate the two types of autoimmune hepatitis, as well as the standard of care for medical treatment. **Patients with cirrhosis who achieve remission have 10-year life expectancies of >90% in tertiary centers**, but those with the severe acute phenotype who do not respond to treatment within 7-14 days have a mortality of almost 50%. Liver transplant achieves 10-year survival rates >75%.

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