HLA-B27 Predicts TNF-Inhibitor Response

Costly agents reduce symptoms of AS, but not everyone benefits.

BY SARA FREEMAN

FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

LONDON – In the everyday setting, HLA-B27 positivity is the strongest predictor of an early, good response to the first use of an anti–tumor necrosis factor agent in patients with ankylosing spondylitis, according to the results of a longitudinal, observational study.

Other "real-world" and independent predictors of a good response using the ankylosing spondylitis disease activity score (ASDAS) are younger age, male sex, a higher baseline C-reactive protein (CRP) level, and a higher baseline patient global assessment score.

"TNF [tumor necrosis factor] inhibitors are effective in reducing symptoms in ankylosing spondylitis [AS], but not all patients have a response, and [they] sometimes have side effects, and the medication is expensive," said Karen Fagerli, Ph.D., of the department of rheumatology at Diakonhjemmet Hospital in Oslo.

"So we want to identify characteristics of patients who will have a response in order to potentially utilize this knowledge when selecting patients for TNF-inhibitor therapy, and [therefore] treat patients with an optimized benefit-to-risk ratio," Dr. Fagerli added. ASDAS was used as the main outcome measure, which may be the first time it has been used in an observational study setting.

Using data from the NOR-DMARD (Norway–Disease-Modifying Antirheumatic Drug) register, researchers identified a study population of 171 patients with AS who were starting a TNF inhibitor for the first time.

NOR-DMARD is a large, observational register that includes all patients with inflammatory arthropathies who are starting treatment with a DMARD for the first time at five rheumatology centers in Norway. Patients are routinely assessed at baseline, then after 3, 6, and 12 months, and then annually.

ASDAS major improvement was defined as a change in score of 2 or more; this was achieved by 32.7% of patients after 3 months of anti-TNF therapy.

Several parameters that had been identified as predictors of response in univariate analysis did not hold up as being statistically significant in a multivariate analysis model; these included the number of swollen joints, physician's global score, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and the Bath Ankylosing Spondylitis Functional Activity Index (BASFAI).

Patients who were HLA-B27 positive had a much higher chance of achieving ASDAS major improvement at 3 months than did those who were HLA-B27 negative (odds ratio, 6.72; 95% confidence interval, 1.33-33.87; $P = .02$).

Baseline CRP levels higher than 10 mg/L were also significantly predictive of an early treatment response (OR, 5.31; 95% CI, 2.23-12.42; P less than .001).

The next strongest predictor was male sex, with men almost three times more likely than women to show a benefit of anti-TNF treatment at 3 months (OR, 2.69; 95% CI, 1.04-7.00; P less than .04). However, the majority of the study population (73.4%) was male.

For every 1-year increase in age, the likelihood of achieving ASDAS major improvement declined, with young patients faring the best overall (OR, 0.95; 95% CI, 0.91-1.00; P less than .03). Furthermore, for every 10-mm increase in a 0- to 100-mm visual analog scale of patient global assessment, the chance of a good response improved (OR, 1.75; 95% CI, 1.40-2.19; P less than .0001).

Taken together, these data could help clinicians to identify patients who not only may respond to anti-TNF inhibitors but also should be prioritized for such treatment. However, "this is on a crude level; we don't know to what extent we can use [this information] on an individual level," Dr. Fagerli said in an interview.

"We know for certain that there are patients who have none of these characteristics that I've talked about, who do get a response, so this is not the full truth; this is a little piece of the puzzle." ■

VITALS

Major Finding: The odds ratio for patients who were HLA-B27 positive and achieved ASDAS major improvement (greater than or equal to 2.0) at 3 months was 6.72, compared with those who were not (95% CI, 1.33-33.87; $P = .02$).

Data Source: Longitudinal, observational study of 171 patients with AS who were treated with an anti-TNF agent for the first time and were enrolled in NOR-DMARD, a register of adult patients with inflammatory arthropathies who were treated at five rheumatology centers in Norway.

Disclosures: Dr. Fagerli disclosed receiving a speaker's fee from Pfizer in the past.

COPD Prevalence Is Doubled With Rheumatoid Arthritis

BY SARA FREEMAN

FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

LONDON – Patients with rheumatoid arthritis have a high risk of concomitant chronic obstructive pulmonary disease, according to data from two studies.

VITALS

Major Finding: COPD was a comorbid condition in 8.9% of patients with RA compared with 4.4% of controls from the general population in one study (P less than .001), with 7.3% of the Norfolk Arthritis Register study population also found to have the respiratory disease.

Data Source: A case-control study of more than 30,000 individuals with or without rheumatoid arthritis and data from a 15-year follow up of 435 patients with inflammatory polyarthritis or RA in the Norfolk Arthritis Register.

Disclosures: NOAR is funded by Arthritis Research UK. Dr. Verstappen and Dr. Amital and colleagues had no conflicts of interest to declare.

In one of the studies – which involved more than 15,000 patients with rheumatoid arthritis (RA) and 15,000 healthy individuals as case-matched controls – the risk of the long-term lung condition was 8.9% and 4.4%, respectively (P less than .001).

Other data, from the Norfolk Arthritis Register (NOAR) showed that the prevalence of chronic obstructive pulmonary disease (COPD) in patients with inflammatory polyarthritis (IP) or RA was 7.3% (n = 425) at 15 years' follow-up. Prevalence of the respiratory disease was again doubled when compared to the general population.

"Lung involvement is a common extra-articular manifestation in rheumatoid arthritis," said Dr. Suzanne Verstappen, who presented the findings from the NOAR at the congress.

"As could be expected, age and gender were associated with obstructive and restrictive lung disease," said Dr. Verstappen, a research fellow at the Arthritis Research UK Epidemiology Unit at the University of Manchester, England, where the NOAR is coordinated.

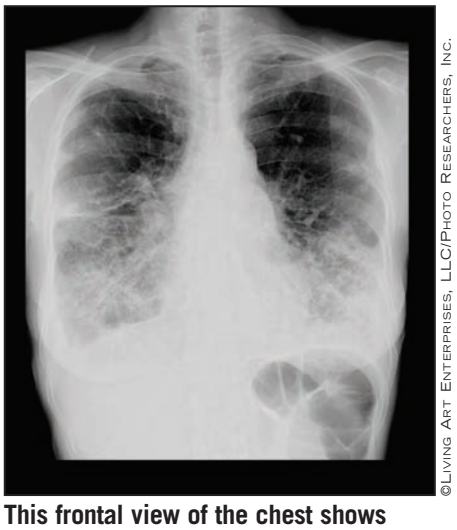
Validated spirometry parameters and the Medical Research Council respiratory symptoms questionnaire were used to identify patients with IP or RA who also had COPD. The latter was distinguished from restrictive lung disease. The prevalence of restrictive lung disease was 9.7%.

COPD was observed in 7.3% of the population at 15 years, with higher prevalence rates found in men versus women over the age of 45 years (12.7% vs. 6%, respectively) in a crude comparison.

Published rates for the U.K. general population without IP or RA are 6.8% and 3.9% (Popul. Health Metr. 2007;5:8).

Like RA, COPD is a chronic and often debilitating disease. The disease manifests later in life and treatment is symptomatic rather than curative, as the obstruction in the airways is permanent and not usually reversible with bronchodilator therapy.

Unlike RA, however, which has multiple etiologic factors and autoimmunity at its root, COPD is almost always caused by smoking.



©Living Art Enterprises, LLC/Photo Researchers, Inc.

This frontal view of the chest shows chronic obstructive pulmonary disease.

In the NOAR analysis, 53% of the 425 patients were ex-smokers and 13% were current smokers; 34% had never smoked.

Data from the first study, presented during a poster session by Dr. Howard Amital of Sheba Medical Centre in Tel Hashomer, Israel, showed, however, that even with smoking out of the equation, the risk of COPD in patients with RA was higher than in the general population.

Indeed, multivariate analysis demonstrated that RA was associated with COPD after the researchers controlled for confounding factors such as age, gender, smoking, obesity, and socioeconomic status.

"The strength of the association increased," Dr. Amital and colleagues reported, with an adjusted odds ratio of 2.015 (95% confidence interval 1.83-2.22; P less than .001) and an unadjusted OR of 1.89 (95% CI 1.74-2.05, P less than .0001).

The case-control study involved 15,766 patients with RA and 15,240 age- and sex-matched healthy individuals without RA.

The study also found higher rates of other chronic disease in patients versus controls, including diabetes (23.9% vs. 19.8%, P less than .0001), ischemic heart disease (19.5% vs. 15.4%, P less than .0001), and heart failure (6.3% vs. 4.3%, P less than .0001).

"This study corroborates the hypothesis that COPD and RA are closely interrelated," Dr. Amital and his team concluded. ■