patients with prolonged drug-free remission dropped out of the study.

Table 1. Eight-Year Results.

	Group 1 (n=126)	Group 2 (n=121)	Group 3 (n=133)	Group 4 (n=128)	p value
DAS ≤2.4, (%)†	79	76	84	76	0.5
DAS <1.6, (%)†	49	56	57	47	0.5
DAS <1.6 drug free, (%)†	18	19	17	15	0.9
Still on initial treatment step, (%)†	29	22	45	66	<0.001
Mean HAQ over 8 years‡	0.69	0.71	0.63	0.57	<0.05*
IFX current use, (%)†	21	10	13	24	0.06
Lost to follow-up, n (%)‡	41 (33)	43 (36)	47 (35)	30 (23)	0.1
Missing data, no.	8	12	9	4	
SHS progression, median (mean)† year 0-8	3.0 (14.6)	4.3 (13.9)	2.0 (8.5)	2.0 (8.3)	0.6

DAS=Disease Activity Score; HAQ=Health Assessment Questionnaire; IFX=infliximab; SHS=Sharp-van der Heijde Score; †Completers analysis, ‡intention-to-treat. *LMM: Group 2 vs 4, p<0.05; Group 1 vs 4, p=0.055; all other, p>0.05.

After initial differences in Years 1 and 2 between the 4 groups, annual radiological damage progression rates were low and similar between all groups, reflecting the efficacy of DAS-steered therapy. Median (mean) total damage progression after 8 years was 3 (11) points SHS (nonsignificant between groups). Patients who were in sustained drug-free remission had a mean SHS progression of 0.1 [median (IQR) 0 (0–0.03)] per person-year drug-free.

The initial improvement of function, which occurred earlier in Groups 3 and 4 than in Groups 1 and 2, was maintained without deterioration over 8 years in all groups. No differences were found for functional ability over time, with the exception of better functional ability in Group 4 compared with Group 2 (mean HAQ 0.57 and 0.71, respectively). Toxicity was comparable between the groups (Table 2).

Table 2. Toxicity Over Eight Years.

	Sequential monotherapy n=126	Step-up comb n=121	Initial comb + PRED n=133	Initial comb + IFX n=128	p value
SAEs total number	99	84	104	102	0.5
Patients with ≥1 SAE (%)	55	46	53	59	0.6
Patients with serious infections (%)	21 (17)	10 (8)	11 (8)	14 (11)	0.1
Patients with malignancies (%)	10 (8)	4 (3)	12 (9)	10 (8)	0.3

PRED=prednisone; IFX=infliximab; SAE=serious adverse events.

Inflammation and Fatty Degeneration in New Bone Formation in Patients With AS Treated With Anti-TNF Agents

Written by Toni Rizzo

When the inflammation of ankylosing spondylitis (AS) subsides, it may be replaced by repair tissue and fatty lesions, a process that leads to osteoproliferation and development of syndesmophytes. Results from clinical trials suggest that new bone formation is not inhibited or enhanced by anti-tumor necrosis factor (TNF) therapy. Xenofon Baraliakos, MD, Rheumazentrum Ruhrgebiet Herne, Herne, Germany, presented results from the European Ankylosing Spondylitis Infliximab Cohort [EASIC] study, an open-label extension of the Ankylosing Spondylitis Study for the Evaluation of Recombinant Infliximab Therapy [ASSERT]. The objective of the EASIC study was to directly compare the effect of inflammation and fatty degeneration on the development of syndesmophytes in patients with AS after 5 years of anti-TNF therapy.

The aim of the ASSERT Study was to evaluate the effect of infliximab on the progression of structural damage over 2 years in patients with AS. A total of 279 patients participated. After a mean of 1.3±0.9 years, 103 patients from ASSERT were enrolled in the EASIC substudy. Complete magnetic resonance imaging (MRI) data at baseline and 2 years and x-ray data at baseline, 2 years, and 5 years were available for 73 EASIC patients. Assessments were blinded with respect to the time points of MRI and x-ray studies. Only the anterior edges of the cervical and lumbar spine were analyzed. Baseline lesions were compared with radiographic progression at 2 and 5 years after adjustment for within-patient variation.

At baseline, the mean (± standard deviation [SD]) age of patients was 40.5±10.5 years; 86.3% of patients were men, and the mean (±SD) disease duration was 10±8.4 years. Patients had mean (±SD) Bath Ankylosing Spondylitis (BAS) Disease Activity Index scores of 6.5±1.4, BAS Functional Index scores of 5.9±1.6, BAS Metrology Index scores of 4.1±1.7, and C-reactive protein (CRP) levels of 2.9±2.3 mg/dL, and 83.6% was human leukocyte antigen B27-positive.

At 2 years, radiographic progression had occurred in 0.7% (n=10) of patients with baseline inflammation and 0.9% (n=13) of patients with baseline fatty degeneration. At 5 years, radiographic progression was present in 1.0%

(n=14) of patients with baseline inflammation and 1.4% (n=21) of those with fatty degeneration. Among patients with both inflammation and fatty degeneration at baseline, radiographic progression was present in 2.1% (n=20) at 2 years and 3.7% (n=35) at 5 years.

Bone formation in the cervical and lumbar spine was limited in patients with AS who received anti-TNF therapy for 5 years. Bone inflammation and fatty changes at baseline appear to influence new bone formation. The combination of inflammatory lesions and fatty lesions is most likely to lead to development of new syndesmophytes. Numerically, most new syndesmophytes could not be explained by baseline inflammation or fatty changes. The author concluded that early treatment of active lesions should be the aim of anti-TNF therapy for regression of syndesmophytes in patients with AS.

Lung Ultrasound for Screening Interstitial Lung Disease

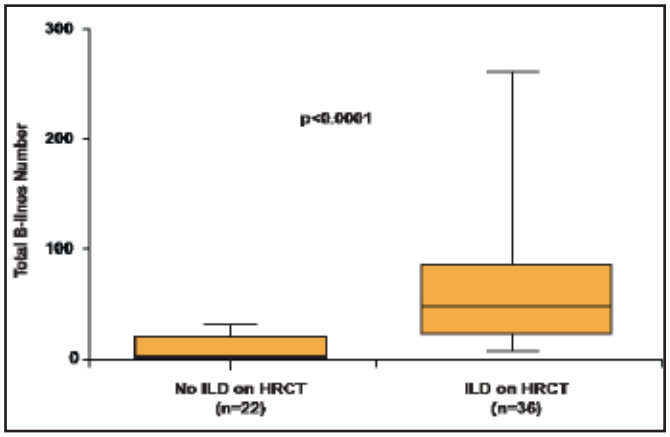
Written by Toni Rizzo

Approximately two-thirds of patients with systemic sclerosis develop interstitial lung disease (ILD). High-resolution computed tomography (HRCT) of the chest is the gold standard for diagnosing ILD, but it cannot be used often because of the risks that are associated with radiation exposure and cost concerns. Recent data have suggested that lung ultrasound (LUS) can aid in the detection of ILD by evaluating B-lines, the sonographic marker of pulmonary interstitial syndrome. The aims of this study [Barskova T et al. *Ann Rheum Dis* 2012] were to verify the correlation between HRCT detection of ILD and B-lines and to evaluate the reliability of LUS as a screening tool in patients with very early systemic sclerosis.

A total of 58 consecutive patients (54 women, mean age 51±14 years) with systemic sclerosis were evaluated with chest HRCT and LUS. LUS was performed on the right and left hemithoraces to evaluate the location and number of B-lines. A B-line was defined as an echogenic coherent wedge-shaped signal with a narrow origin in the near field of the image [Volpicelli et al. *Intensive Care Med* 2012]. The number of B-lines in the intercostal spaces was recorded and totaled to produce a score that denoted the extent of ILD. ILD was diagnosed when ≥3 B-lines were found in at least 2 adjacent scanning sites or when >5 B-lines were present.

Among the total population, 32 patients (29 women, mean age 51±15 years) were diagnosed with very early systemic sclerosis. HRCT and LUS were performed a mean of 42±46 days (median 27 days) apart. ILD was found on HRCT in 88% of the total population and in 41% of the very early systemic sclerosis population (p<0.01). Significantly more B-lines were found in patients with HRCT-detected ILD (mean 57±53, median 43) versus those without (mean 9±9, median 5; p<0.0001; Figure 1). Patients with ground glass on HRCT (n=13; 63±47) had a higher total number of B-lines than patients without ground glass (33±40; p<0.05). There was no statistically significant difference in the number of B-lines that were detected between younger (≤50 years) and older (>50) patients or between patients with shorter (<1 year) or longer (>1 year) disease duration.

Figure 1. Difference in Number of B-Lines in Patients With and Without ILD on HRCT.



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Analysis of individual patients in the overall population showed 83% concordance between LUS and HRCT, with 100% sensitivity, 100% negative predictive value, 55% specificity, and 78% positive predictive value. All 10 discordant cases were false positive on LUS. Receiver operating characteristic (ROC) curve analysis confirmed the analytical relationship between the number of B-lines and the presence of ILD on HRCT (area under curve, 0.94; 95% CI, 0.89 to 0.99; p<0.0001). The presence of >5 B-lines had 100% sensitivity and 59% specificity. The presence of ≥20 B-lines had 83% sensitivity and 96% specificity.

This study shows that LUS is highly sensitive for detecting ILD in patients with very early systemic sclerosis. The presence of B-lines on LUS examination correlates with detection of ILD on HRCT. LUS appears to be a reliable screening tool to determine which patients should be evaluated further with HRCT.