defined as lumbar spine or hip BMD failing to increase by 2% or more, BMD remaining osteoporotic with a *t* score less than –2.5 or z-score less than –2.0, or development of new fragility vertebral or nonvertebral fractures during BSP treatment. Patients were randomly assigned to subcutaneous denosumab 60 mg every 6 months instead of BSPs or to continuation of BSPs; 21 patients were assigned to each treatment group, and 20 in each completed 12 months of therapy. There were no significant differences in clinical characteristics between treatment groups.

Patients receiving denosumab had a significant increase in lumbar spinal BMD, the primary endpoint, compared with the BSP group at 6 months (3.07% vs 0.56%; p=0.047) and at 12 months (3.39% vs 1.48%; p=0.026); these results were adjusted for baseline BMD, duration of disease and calcium and vitamin D use, osteoporosis risk factors, and cumulative dose of prednisolone. There were no significant differences in the secondary end point of changes in hip and femoral neck BMD at 6 and 12 months between treatment groups. No new fractures developed in any patients during the trial. Bone turnover marker assays are ongoing. Denosumab was well tolerated but was associated with increased infections. AEs are summarized in Table 1.

Table 1. Adverse Events

	Denosumab (n=21)	BSP (n=21)	p Value
Any AEs	18 (86%)	5 (24%)	<0.001
Fever after injection	1 (5%)	0 (0%)	>0.99
Infective episodes (eg, URI)	7 (33%)	1 (5%)	0.045
Dyspepsia, reflux	3 (14%)	0 (0%)	0.23
Dizziness/vertigo	2 (9.5%)	0 (0%)	0.49
High blood pressure	1 (5%)	1 (5%)	>0.99
Arthralgia	1 (5%)	1 (5%)	>0.99
Skin rash	1 (5%)	1 (5%)	>0.99
Alopecia	1 (5%)	0 (0%)	>0.99
Menorrhagia	0 (0%)	1 (5%)	>0.99
Keratitis	1 (5%)	0 (0%)	>0.99

No cases of hypocalcemia or cellulitis occurred; there were no withdrawals due to AEs.
AE=adverse events; BSP=bisphosphonate; URI=upper respiratory infection.

Although 12 months of therapy with denosumab was associated with increased lumbar spine BMD in patients receiving long-term GCs who did not respond to BSP therapy, there were no increases in hip or femoral neck BMD with denosumab. These results should be confirmed in a larger study.

Ultrasound Detects Early Involvement and Correlates With Other Techniques in SSc

Written by Lynne Lederman

Systemic sclerosis (SSc) is characterized by increased dermal thickness (DT); the severity and extent of skin involvement are used to establish the diagnosis and subclassify the disease. The modified Rodnan skin score (mRSS) is a validated method to evaluate skin involvement in SSc, and it is based on manual palpation of 17 areas of the skin. Alberto Sulli, MD, University of Genova, Genoa, Italy, discussed detection of subclinical diffuse dermal involvement by high-frequency ultrasound (US) in patients with limited cutaneous SSc (lcSSc) and presented a poster on the correlation among 3 different methods: mRSS, high-frequency ultrasound (US; a 18-MHz probe), and a plicometer skin test (plicometry) to evaluate skin involvement in patients with SSc [Ruaro B et al. EULAR 2014 (poster SAT0304)].

In patients with lcSSc, areas of skin that were normal according to mRSS were evaluated by high-frequency US. The aim of the study of mRSS, high-frequency US, and plicometry in patients with SSc was to identify possible correlations among these techniques to evaluate DT.

Prof. Sulli presented the results of a study in which 50 patients with lcSSc diagnosed by mRSS (a 5-year median duration of disease) were compared with 50 healthy subjects. DT was evaluated in the 17 standard skin areas (cheeks, fingers, dorsum of hands, forearms, arms, chest, abdomen, thighs, legs, and feet) in patients and healthy control subjects by both mRSS and high-frequency US. He then highlighted a comparative technique study by Ruaro and colleagues [EULAR 2014 (poster SAT0304)], in which the DT of 70 patients with SSc was compared with that of 63 healthy subjects using mRSS, high-frequency US, and plicometry on the standard 17 skin areas. The 3 techniques were performed on the same day for each subject and repeated by 2 blind operators to evaluate interobserver and intraobserver variability.

In patients with lcSSc, DT measured by high-frequency US was significantly higher than DT in healthy subjects for all skin areas (p<0.0001) except the thighs. DT was significantly higher in patients with lcSSc than in healthy subjects in 4 out of 6 skin areas (the arms, chest,

and abdomen) in which the mRSS was normal, in agreement with the diagnosis of lcSSc.

In the comparative study, a significant positive correlation was found among the 3 methods used to evaluate DT in patients with SSc (mRSS vs US r=0.53, p<0.0001; mRSS vs plicometry r=0.98, p<0.0001; and US vs plicometry r=0.53, p<0.0001). DT in patients with SSc, including limited and diffuse SSc, was significantly higher (p=0.0001) than that of controls. Interobserver and intraobserver variability was small; variability and execution times for the 3 techniques are shown in Table 1.

Table 1. Interobserver and Intraobserver Variability and Execution Time for Dermal Thickness Assessment

	US	Plicometry	mRSS
Interobserver variability	5%	6%	8%
Intraobserver variability	3%	4%	5%
Running time, minutes	20	15	10

mRSS=modified Rodnan skin score; US=ultrasound.

These studies show that subclinical diffuse dermal involvement may be detectable by high-frequency US in patients with lcSSc. This may be useful in future disease subclassification and may explain the similar degree of organ involvement in patients with lcSSc and diffuse cutaneous SSc that has been seen in clinical studies. In nearly all 17 skin areas analyzed by high-frequency US, patients with SSc have a significantly higher DT than controls. The 3 techniques of mRSS, high-frequency US, and plicometry used to measure DT in patients with SSc show a high degree of correlation.

Forced Vital Capacity Is Inadequate for Assessing ILD in SSc

Written by Lynne Lederman

Interstitial lung disease (ILD) in patients with systemic sclerosis (SSc) frequently results in ventilatory restriction, a major cause of death in these individuals. Clinical trials in patients with SSc-related ILD have traditionally used forced vital capacity percentage (FVC%) predicted as a primary outcome measure [Hoyles RK et al. *Arthritis Rheum* 2006; Tashkin DP et al. *N Engl J Med* 2006]. Cyclophosphamide treatment of patients with SSc has been associated with improvements in clinically meaningful outcome measures other than FVC%. Elizabeth Volkmann, MD, University of California at Los Angeles, Los Angeles, California, USA, discussed the development of a composite outcome measure that included the FVC%, the computer-based quantitative lung fibrosis in the zone of maximum fibrosis (QLF-ZM) score from thoracic high-resolution computed tomography (CT) lung scans, the scleroderma modified Health Assessment Questionnaire Disability Index (HAQ-DI), and the Transition Dyspnea Index (TDI) for SSc-related ILD.

The objective of the analysis reported by Dr. Volkmann was to develop a composite outcome measure to assess treatment response in patients with SSc–ILD in clinical studies, and to create a more comprehensive measure than FVC% alone. The Scleroderma Lung Study I [SLSI; Tashkin DP et al. *N Engl J Med* 2006] compared oral cyclophosphamide with placebo in patients with active SSc and ILD. Of the 158 patients enrolled in the SLSI trial, 83 (41 treated with cyclophosphamide and 42 treated with placebo) had baseline and 12-month follow-up CT available and were analyzed for this presentation. There was no significant difference in baseline characteristics between the two treatment groups.

A univariate analysis that tested for treatment effects for individual outcomes, including FVC% predicted, total lung capacity predicted (TLC), QLF-ZM and whole-lung (WL) scores, quantitative interstitial lung disease (QILD)–ZM and –WL scores, HAQ-DI, TDI, and the visual analogue scale for breathing (VAS-B), was conducted to determine which variables had a significant treatment effect at 12 months. The results are shown in Table 1.

Table 1. Univariate Analysis for Treatment Effects

Predictor	p Value
FVC% predicted	p=0.04
TLC% predicted	NS
VAS-B	NS
TDI	p<0.0001
HAQ-DI	p=0.0002
QLF-ZM	p=0.003
QLF-WL	p=0.001
QILD-ZM	p=0.01
QILD-WL	p=0.05

FVC%=forced vital capacity percentage; HAQ-DI=scleroderma-modified Health Assessment Questionnaire Disability Index; NS=not significant; QILD=quantitative interstitial lung disease; QLF=quantitative lung fibrosis; TDI=Transition Dyspnea Index; TLC%=total lung capacity percentage; VAS-B=visual analogue score for breathing; WL=whole lung; ZM=zone of maximum fibrosis.