

A COMPOSITE SCORE TO ASSESS TREATMENT RESPONSE IN PULMONARY SARCOIDOSIS: THE SARCOIDOSIS TREATMENT SCORE (STS)

Robert P. Baughman¹, Michael Tillinger², Yimin Qin², Nadera Sweiss³, Elyse E. Lower¹

¹University of Cincinnati Medical Center, Cincinnati, OH, USA; ²Mallinckrodt Pharmaceuticals, Bedminster, NJ, USA; ³University of Illinois Chicago, Chicago, IL, USA

TO THE EDITOR:

Assessing response to treatment for pulmonary sarcoidosis can be difficult (1). As more expensive agents are being considered for treatment of sarcoidosis, it is important that studies employ adequate and clinically relevant endpoints. A World Association of Sarcoidosis and other Granulomatous disease (WASOG) task force report on clinical trial endpoints examined those parameters reported in clinical trials of pulmonary sarcoidosis (2). The panel noted that several single endpoints had been used. With therapy, changes in forced vital capacity (3, 4) and DLCO (3) have been reported. Chest imaging has also been shown to improve with therapy (4). Two sarcoidosis specific quality of life instruments have been developed: the King's sarcoidosis questionnaire (KSQ) (5) and fatigue assessment scale (FAS) (6). In addition, some treatments have been shown to be steroid sparing (7). The task force recommended that a composite score be developed to capture the many facets of pulmonary sarcoidosis (2). To date, no reports utilize composite scores to assess treatment efficacy in pulmonary sarcoidosis. We recently reported a prospective study of repository corticotropin injection (RCI)

for chronic pulmonary sarcoidosis (8). In that study, many of the features were prospectively collected and allowed for the development of a composite score – Sarcoidosis Treatment Score (STS).

Sixteen patients were enrolled in a single blind, prospective study. They underwent physiological, imaging, patient reported quality of life questionnaires, and prednisone tapering evaluations. These included: forced vital capacity (FVC) and diffusion lung of carbon monoxide (DLCO) measurement, high resolution computer tomography (HRCT) scan, King's sarcoidosis health questionnaire - general health (KSQ-GH) (5), FAS, and prednisone dosage tapering at baseline and after 7 and 24 weeks of therapy. A composite score was developed (STS) using these parameters with scoring ranging from -6 to +6 points (Table 1). Absolute change of FVC and DLCO % predicted of both 5% and 10% were calculated. The composite score was then compared to the individual features of the composite score and to six minute walk distance (6MWD).

There was better correlation between the components of composite score and an absolute change of 5% versus 10% for FVC and DLCO percent predicted (data not shown). Therefore, further analysis used absolute change of 5%.

Response (R) was defined as scores of $\geq 3/6$ points; Partial Response (PR) was defined as scores of $2/6$ points or stable with corticosteroid reduction (i.e., a total score of +1 due to $\geq 50\%$ reduction in corticosteroid dosage); and Non Response (NR) was defined as scores of $\leq 1/6$ points without significant corticosteroid taper (stable or deterioration).

Received: 9 October 2018

Accepted after revision: 11 October 2018

Correspondence: Robert P Baughman,
University of Cincinnati Medical Center,
Cincinnati, OH, USA;
E-mail: baughmrp@ucmail.uc.edu

Supported in part by Mallinckrodt Pharmaceuticals

Table 1. Composite score and 6MWD determinations

Parameter	FVC	DLCO	HRCT	KSQ GH	FAS	Steroid Taper	Total Score
Improved							
+1 point	≥5%	≥5%	Improved	≥4	≤-4	≥50% reduction	
Unchanged							
0 point	>-5 to <5%	>-5 to <5%	Unchanged	>-4 to <4	>-4 to <4	<50% reduction or ≥5 mg increase for less than 2 weeks	
Deterioration							
-1 point	≤-5%	≤-5%	Worse	≤-4	≥4	≥5 mg increase for more than 2 weeks	
Patient number							
1-001	1	1	1	1	1	1	6 R
1-002	-1	1	1	1	0	0	2 PR
1-003	1	0	0	1	1	1	4 R
1-004	0	-1	0	0	0	1	0 NR
1-005	0	1	1	1	0	0	3 R
1-008	0	Not done	1	0	1	0	2 PR
1-009	-1	-1	0	0	0	1	-1 NR
1-010	0	-1	0	1	1	0	1NR
1-011	1	1	0	1	1	1	5 R
1-012	0	1	-1	1	0	1	2 PR
1-014	0	1	0	0	0	0	1 NR
1-015	1	1	0	0	1	0	3 R
1-016	0	0	0	1	1	1	3 R
2-001	0	1	1	1	1	1	5 R
2-002	0	0	0	1	0	0	1 NR

R=response; PR=partial response; NR=no response

Of the sixteen patients studied, fifteen patients had sufficient information available to be evaluated. Seven (46.6%) were responders, three (18.8%) were partial responders, and five (31.2%) were non responders. The final composite score and individual values are shown in Table 1.

The mean composite post treatment score was 3, with only five patients having a composite score of -1 to 1. There was a significant correlation between the composite score and all of its components. A significant positive correlation existed between change in 6MWD at week 7 with composite score ($\rho=0.588$, $p=0.0344$), change in FVC % predicted ($\rho=0.628$, $p=0.0216$) and KSQ-GH ($\rho=0.583$, $p=0.0364$). For change in 6MWD at 24 weeks, there was a borderline correlation with composite score ($\rho=0.523$, $p=0.0666$) and borderline negative correlation with change in prednisone dose ($\rho=-0.542$, $p=0.0566$). No correlation existed at either time point for changes in DLCO % predicted, HRCT, or FAS.

A composite score to assess the value of angiotensin converting enzyme in monitoring sarcoidosis was used by DeRemee et al (9). To date, compos-

ite scores have not been employed as end points of clinical trials. In this study, we examined a composite score which consisted of physiology, radiology, quality of life, and steroid sparing parameters. The composite score confirmed the value of the RCI in treating advanced sarcoidosis. In a prospective study (8), RCI treatment was associated with significant steroid sparing, improvement in DLCO, and KSHQ-GH and FAS scores. In addition, some patients had improvement of their HRCT when scored in a blinded fashion. The composite score mirrored the positive results seen for the individual parameters. As none of the previous randomized clinical trials in sarcoidosis have collected all of these parameters, validating the STS would require future studies. We also compared the composite score to the 6MWD. Previous studies in sarcoidosis have demonstrated that 6MWD is independently affected by lung function and patient's reported quality of life (10). In this study, we found that the composite score was associated with changes in 6MWD at 7 and 24 weeks of treatment.

Using a composite score consisting of physiology, radiology, and quality of life parameters as well

as changes in prednisone dosing, as recommended by WASOG (2), may prove useful in assessing treatment for pulmonary sarcoidosis. This endpoint is being explored in an upcoming double blind placebo controlled trial of RCI which may help to validate the STS.

REFERENCES

1. Valeyre D, Prasse A, Nunes H, Uzunhan Y, Brillet PY, Muller-Quernheim J. Sarcoidosis. *Lancet* 2014; 383: 1155-1167.
2. Baughman RP, Drent M, Culver DA et al. Endpoints for clinical trials of sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis* 2012; 29: 90-98.
3. Gibson GJ, Prescott RJ, Muers MF et al. British Thoracic Society Sarcoidosis study: effects of long term corticosteroid treatment. *Thorax* 1996; 51: 238-247.
4. Baughman RP, Drent M, Kavuru MS, et al. Infliximab therapy in patients with chronic sarcoidosis and pulmonary involvement. *Am J Respir Crit Care Med* 2006; in press.
5. Patel AS, Siegert RJ, Creamer D, et al. The development and validation of the King's Sarcoidosis Questionnaire for the assessment of health status. *Thorax* 2013; 68: 57-65.
6. de Vries J, Michielsen H, van Heck GL, Drent M. Measuring fatigue in sarcoidosis: the Fatigue Assessment Scale (FAS). *Br J Health Psychol* 2004; 9: 279-291.
7. Park MK, Fontana JR, Babaali H, et al. Steroid sparing effects of pentoxifylline in pulmonary sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis* 2009; 26: 121-131.
8. Baughman RP, Sweiss N, Keijsers R et al. Repository corticotropin for Chronic Pulmonary Sarcoidosis. *Lung* 2017; 195: 313-322.
9. DeRemee RA, Rohrbach MS. Serum angiotensin-converting enzyme activity in evaluating the clinical course of sarcoidosis. *Ann Intern Med* 1980; 92: 361-365.
10. Alhamad EH. The six-minute walk test in patients with pulmonary sarcoidosis. *Ann Thorac Med* 2009; 4: 60-64.