CHEST Online Supplement

Riociguat for Sarcoidosis-Associated Pulmonary Hypertension

Results of a 1-Year Double-Blind, Placebo-Controlled Trial

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e-Table 1. Study Design

	Screen	0	2	4	6	8	10	12	16	24	32	40	48	52
Focused history and physical exam		X	X	X	X	X	X	X	X	X	X	X	X	X
Sarc organ assessment		X												
Chest roentgenogram		X							X					
HRCT	X													
Vital capacity measurement	X	X				X			X		X		X	
DLCO measurement		X							X					
Six minute walk	X	X				X			X	X	X	X	X	
QOL (SF-36, SGRQ, SHQ,FAS)		X				X			X		X		X	
Blood for cytokines, BNP		X							X				X	
Pregnancy test		X		X		X		X	X	X	X	X	X	X
Drug dispense		X	X	X	X	X	X	X	X	X	X	X		

The focused physical examination included vital signs, a cardiopulmonary exam, and examination of any other abnormal areas.

The sarcoidosis assessment score is a previously defined score to determine organ involvement with the disease (15).

Routine PA chest roentgenogram was performed within three months prior to entry and at the specified follow up point. An initial high resolution computer tomography (HRCT) scan was performed to assess for aspergilloma and to determine the degree of fibrosis and emphysema.

Pulmonary function studies included spirometry performed without bronchodilators. In addition, the DLCO was measured at two time points, using the single breath technique.

The six minute walk test recorded the distance walked in six minutes and the level of oxygenation using a finger tip oximeter and the level of dyspnea using a ten point dyspnea scale (Borg score). A standardized protocol for the six minute walk was be done for all the institutions (8,24).

At the baseline testing, patients used the level of supplemental oxygen they have been using for exercise. This level of oxygen supplementation was noted and employed at all the follow-up six minute walk tests.

Patients performed 2 six minute walks (screening and randomization) prior to first drug. The 6MWD was within 15% of each other prior to patient entry.

A right heart catheterization performed within twelve months of entry into the study and the patient in a stable clinical status will be used as the baseline hemodynamic values.

Medication for sarcoidosis (prednisone, methotrexate, etc) were kept constant through the study unless the PI feels that modification is needed to treat the sarcoidosis. Reasons for changing medicine doses was noted.

Quality of life was determined by several scores: the short form 36 (SF-36); the disease specific King's college sarcoidosis health questionnaire (SHQ) (20); and a fatigue assessment score (FAS) (10).

Women of reproductive potential underwent pregnancy testing prior to and monthly during the study using a urine pregnancy test.

Patients were block randomized to each institution to receive either drug or placebo for the full 48 weeks of the study.

Patients received their first dose of riociguat in the clinic setting and will be monitored for hypotension.

Patients were provided each month with a known number of pills including an extra 5 days of medicine to allow for unexpected events delaying return visit. When the patient returned for their follow up visit, they brought their unused medicines and a pill count was performed.