



Arthritis News

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POTENTIAL NEW TREATMENT MAY HELP THOUSANDS WHO SUFFER FROM PULMONARY HYPERTENSION AS A COMPLICATION OF LUPUS, SCLERODERMA

SAN ANTONIO, TEXAS—An investigational new drug for pulmonary hypertension may improve the quality of life for thousands of patients with scleroderma, lupus, and other associated connective tissue diseases, according to research presented this week at the American College of Rheumatology Annual Scientific Meeting in San Antonio, Texas.

Lupus, scleroderma and related connective tissue diseases are chronic inflammatory autoimmune diseases that can damage the blood vessels of the lung and other organs. Pulmonary hypertension, which is high blood pressure in the lungs, is a common and potentially devastating complication of these diseases that causes heart failure, inability to exercise and ultimately to the death of about half of the patients with this complication within two to three years after diagnosis. Patients with pulmonary hypertension have elevated levels of endothelin, a powerful blood vessel constrictor, in their plasma and lung tissue.

Researchers conducted a multicenter, randomized, double-blind, placebo-controlled trial of sitaxsentan, a once-daily oral endothelin receptor antagonist which blocks the action of endothelin on blood vessels to determine whether it could improve the ability of pulmonary hypertension patients to exercise without difficulty. This 12-week trial involved 178 patients with pulmonary hypertension, 42 of whom had pulmonary hypertension related to a connective tissue disease. Patients received either 100mg or 300 mg of sitaxsentan, or placebo, for 12 weeks. All patients participated in the 6-minute walk test, the standard test for treatments for pulmonary hypertension that measures how far an individual can walk in six minutes, before the treatment began and again at the end of the 12-week trial. Researchers found that patients with pulmonary hypertension related to connective tissue disease who were taking either the 100mg or 300mg dosage significantly improved their walking distance as compared to those taking placebo (whose time actually worsened).

“Sitaxsentan was shown to significantly improve six-minute walk distance, as well as hemodynamics such as cardiac index and pulmonary vascular resistance for patients with pulmonary hypertension related to connective tissue disease,” said lead investigator Vallerie McLaughlin, MD, University of Michigan Hospital, Ann Arbor, Michigan. “The first therapy shown to improve key efficacy variables in this population was epoprostenol, a prostacyclin therapy that requires a central catheter and continuous intravenous infusion that is often difficult for patients to tolerate. Thus, the ability of an oral, once daily therapy such as sitaxsentan sodium to improve key efficacy variables represents an important treatment advance.”

The American College of Rheumatology is the professional organization for rheumatologists and health professionals who share a dedication to healing, preventing disability and curing arthritis and related rheumatic and musculoskeletal diseases. For more information on the ACR’s annual meeting, see www.rheumatology.org/annual.

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Editor’s Notes: Dr. McLaughlin will present this research during a scientific session at the ACR Annual Scientific Meeting from 9:15–9:30 AM CT (10:15–10:30 AM ET) on Thursday, October 21 in Room 217 of the Henry B. González Convention Center. She will be available for media questions during a briefing at 1:30 PM CT (2:30 PM ET) on Monday, October 18, in the on-site Press Conference Room, Room 218.

Sitaxsentan Improves 6MW in Patients with Pulmonary Arterial Hypertension (PAH) Related to Connective-Tissue Diseases (CTD)

Vallerie V. McLaughlin¹, Nicholas Hill², Victor F. Tapson³, Adaani E. Frost⁴, David Langleben⁵, Ronald Oudiz⁶, Shelley Shapiro⁷, Ivan M. Robbins⁸, Robyn J. Barst⁹, on behalf of the STRIDE-1 Study Group. ¹University of Michigan Hospital, Ann Arbor, MI; ²Tufts-New England Medical Center, Boston, MA; ³Duke University Medical Center, Durham, NC; ⁴Baylor College of Medicine, Houston, TX; ⁵Sir Mortimer B. Davis Jewish General Hospital, Montreal, PQ, Canada; ⁶Harbor-UCLA Medical Center, Torrance, CA; ⁷University of Southern California, Los Angeles, CA; ⁸Vanderbilt University Hospital, Nashville, TN; ⁹Columbia University College of Physicians and Surgeons, New York, NY

PURPOSE: PAH related to CTD is progressive and difficult to manage. The multicenter, randomized, placebo (PBO) controlled bosentan BREATHE-1 PAH trial reported a trend towards a 6MW treatment effect in the CTD subgroup (47 of the 213 patients in BREATHE-1 had PAH related to CTD). However, this was due to deterioration in the PBO group rather than an improvement in the bosentan treatment group. Sitaxsentan (SITAX) is a selective (6500:1) once daily oral endothelin A receptor antagonist in clinical development for the treatment of PAH.

METHODS: The Sitaxsentan to Relieve Impaired Exercise trial (STRIDE-1) was a multicenter, randomized, double-blind, placebo-controlled, 12 week trial evaluating SITAX 100mg, 300 mg, and PBO in 178 patients with PAH. A post hoc analysis was performed to evaluate the effect of SITAX in the intent-to-treat CTD subgroup (42 of the 178 patients had PAH related to CTD). Due to similar treatment effects in total ITT population, the SITAX 100mg and 300mg groups were pooled.

RESULTS: All CTD patients were NYHA class II or III at baseline (BL). BL 6MW distance was 356 meters. 6MW treatment effect was 58m ($p=0.0274$), due to both an increase in 6MW in the SITAX group from BL (+20m; $p=0.0327$) and a decrease in 6MW in the PBO group from BL (-38m). 8/33 (24%) SITAX patients improved by one NYHA functional class on SITAX compared with 1/9 (11%) PBO patients. SITAX was well tolerated. No patients experienced LFT abnormalities and no patients discontinued due to adverse events.

CONCLUSIONS: SITAX improves 6MW and NYHA functional class in PAH related to CTD.

Disclosure: V.V. McLaughlin, Encysive Pharmaceuticals 2, 5; Actelion 2, 5, 8; N. Hill, None; V.F. Tapson, None; A.E. Frost, None; D. Langleben, None; R. Oudiz, None; S. Shapiro, None; I.M. Robbins, None; R.J. Barst, None.

Author disclosure legend—Authors' disclosures of third-party relationships are listed in numeric format according to the following listing:

None—Nothing to disclose; 1—Stock options or bond holdings in a for-profit corporation or self-directed pension plan; 2—Research grants; 3—Employment (full or part-time); 4—Ownership or partnership; 5—Consulting fees or other remuneration (payment); 6—Non-remunerative positions of influence such as officer, board member, trustee or public spokesperson; 7—Receipt of royalties; 8—Speakers bureau.