New Scleroderma-Modifying Therapies Emerging

BY PATRICE WENDLING

CHICAGO — Several pioneering treatment approaches have emerged to modify the vascular and fibrotic disease in scleroderma, Dr. Frederick Wigley said at a symposium sponsored by the American College of Rheumatology.

Dr. Wigley, director of the scleroderma center at Johns Hopkins University in Baltimore, discussed several of these novel therapies that are being studied and/or are in use, including the following six:

► **Bosentan.** This endothelial inhibitor is approved in the United States and Europe to manage the symptoms of pulmonary artery hypertension (PAH). Two trials in scleroderma show that bosentan (Tracleer) reduces digital ulcers but has no benefit on Raynaud's attacks, Dr. Wigley said.

► **Tyrosine kinase inhibition with imatinib mesylate.** Industry-sponsored trials are underway evaluating imatinib (Gleevec) in systemic sclerosis and PAH, and dasatinib (Sprycel) in scleroderma pulmonary fibrosis.

► **Immunoablation with and without stem cell transplantation.** This should be looked at as "an experiment in progress," Dr. Wigley said.

In a pilot study of 34 patients with poor prognosis for systemic sclerosis, major improvements in skin and overall function were reported in 17 of 27 evaluable patients who survived 1 year after high-dose immunosuppressive treatment and autologous hematopoietic cell transplantation (Blood 2007;110:1388-96).

These results came at a cost, however, with relapse occurring in 10 survivors and 23% of the 34 patients dying as a result of the procedure.

► **Statins.** These drugs have shown some benefit in early trials, possibly because they display pleiotropic effects on endothelial function that could potentially delay vascular injury.

Levels of circulating endothelial precursor cells, reduced in scleroderma, were increased up to eightfold after 12 weeks of therapy with atorvastatin (Lipitor) 10 mg/day in 14 patients with systemic sclerosis in an open-label pilot study (Arthritis Rheum. 2006;54:1946-51).

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Endothelial markers improved and fewer new digital ulcers occurred with atorvastatin 40 mg/day for 16 weeks vs. placebo in 86 patients with scleroderma (J. Rheumatol. 2008;35:1801-8).

► **ACE inhibitors.** These agents have been shown to improve 12-month survival in patients with systemic scleroderma-induced renal disease, which is often associated with corticosteroids. ACE inhibitors can be used with angiotensin II receptor blockers (ARBs), calcium channel blockers, and prostaglandins when full doses of an ACE inhibitor do not control a crisis.

The true benefits and risks of combining an ACE inhibitor with other agents in scleroderma have not been fully studied, he said.

ONTARGET (Ongoing Telmisartan Alone and in Combination With Ramipril Global End Point Trial), which did not include scleroderma patients, showed that the use of combined ARBs and ACE inhibitors was associated with worse renal outcomes in high-risk patients, Dr. Wigley added.

► **Prostaglandins.** When administered intravenously, prostaglandins are an option for reducing digital ulcers, Raynaud's attacks, and PAH associated with scleroderma. Two trials are underway to evaluate oral formulations of iloprost and treprostinil in vascular scleroderma and Raynaud's, he said.

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