Efficacy Sustained Over 2 Years

Abatacept *from page 1*

group and 0.75 in the placebo group, Dr. Genant reported.

Measures of clinical efficacy also showed durable responses during the second year of therapy, Dr. Joel M. Kremer reported in a poster session at the meeting, sponsored by the European League Against Rheumatism.

At year 1, 82% of patients who had received abatacept plus methotrexate achieved American College of Rheumatology (ACR) 20 responses, 54% achieved ACR 50 responses, and 32% achieved ACR 70 responses.

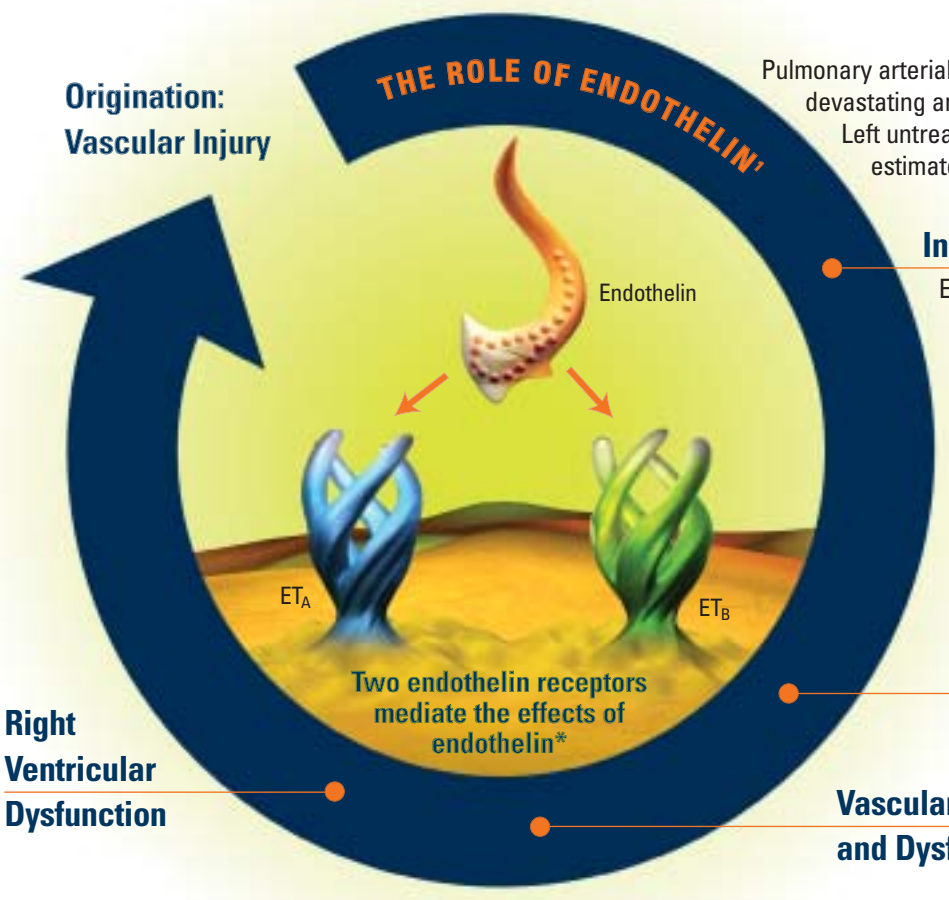
The corresponding numbers at year 2 were 80%, 56%, and 34%, according to Dr. Kremer of Albany (N.Y.) Medical College.

By the end of the long-term extension phase of the trial, patients who initially got placebo but had been receiving abatacept for 1 year had similar clinical responses to those who had been receiving the active treatment for 2 years, with 78% achieving ACR 20 responses, and 58% and 32% achieving ACR 50 and 70 responses, respectively.

Remission, defined as a score of less than 2.6 on the Disease Activity Score (DAS 28), was reached by 25.4% of patients in the abatacept group at year 1, compared with 2.5% of those in the placebo group, according to Dr. Kremer. By the end of year 2, rates of remission were similar in the two groups, regardless of initial randomization, at 30.9% and 32.6% in the active treatment and placebo groups, respectively.

Dr. Genant has received consulting fees from Synarc, and Dr. Kremer has received research grants and consulting fees from Bristol-Myers Squibb. ■

Endothelin's Role in the Rapid Progression of Pulmonary Arterial Hypertension



Pulmonary arterial hypertension (PAH) is a devastating and rapidly progressing disease. Left untreated, PAH patients have an estimated 5-year survival rate of 34%.[2]

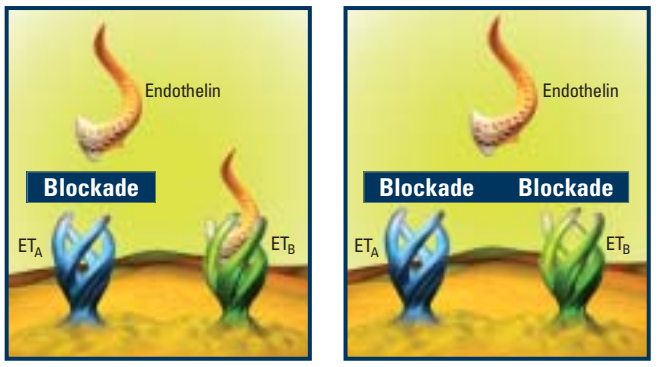
Increase in Endothelin

Endothelin, a neurohormonal mediator produced by the endothelium, is overproduced in PAH.[3] This excess endothelin is associated with dramatic structural changes in the pathology of PAH vasculature, including inflammation,[4] vasoconstriction,[3] cell proliferation,[5] and fibrosis.[6]

Blockade of Both ET_A and ET_B Receptors Is Critical

ET_A Activity in PAH*
Cell proliferation[5]
Vasoconstriction[3]
Inflammation[4]

ET_B Activity in PAH*
Cell proliferation[5]
Vasoconstriction[3]
Inflammation[4]
Fibrosis[6]
Hypertrophy[6]



To learn more about the effects of endothelin in pulmonary arterial hypertension, please visit www.endothelinscience.com

*Statements are based on observations reported from in vitro or animal trials.

1. Gaine SP, Rubin LJ. Primary pulmonary hypertension. *Lancet.* 1998;352:719–725. **2.** D'Alonzo GE, Barst RJ, Ayres SM, et al. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. *Ann Intern Med.* 1991;115:343–349. **3.** Miyauchi T, Masaki T. Pathophysiology of endothelin in the cardiovascular system. *Annu Rev Physiol.* 1999;61:391–415. **4.** Muller DN, Mervaala EM, Schmidt F, et al. Effect of bosentan on NF-kappaB, inflammation, and tissue factor in angiotensin II-induced end-organ damage. *Hypertension.* 2000;36:282–290. **5.** Davie N, Haleen SJ, Upton PD, et al. ET(A) and ET(B) receptors modulate the proliferation of human pulmonary artery smooth muscle cells. *Am J Respir Crit Care Med.* 2002;165:398–405. **6.** Giaid A, Yanagisawa M, Langleben D, et al. Expression of endothelin-1 in the lungs of patients with pulmonary hypertension. *N Engl J Med.* 1993;328:1732–1739.

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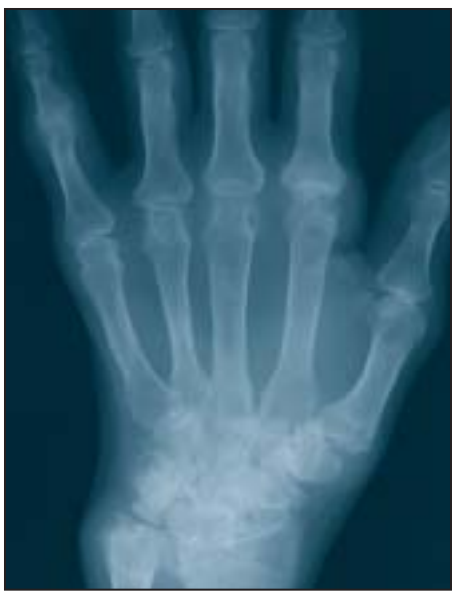
THE ERA OF ENDOTHELIN SCIENCE



Photos courtesy Dr. Harry K. Genant

Figures, from top to bottom, represent a single abatacept-treated patient's radiographs of the left hand at day 1 (baseline), day 365 (year 1), and day 730 (year 2), showing moderate joint damage, which is stable or non-progressive over the 2-year interval.

Online Epocrates Rx Drug Guide Available

Physicians can access an online version of the Epocrates Rx mobile drug and formulary guide. The guide provides information on more than 3,300 drugs, including dosing, pricing, potential drug interactions, and Medicare Part D formulary coverage. For more information, contact Epocrates Inc. by visiting www2.epocrates.com (registration required for use) or by calling 650-227-1700. ■

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