

High CRP Levels, ESR Warrant Infliximab Add-On

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Patients with early rheumatoid arthritis who are most likely to benefit from immediate introduction of infliximab plus high-dose methotrexate are those with high C-reactive protein levels, a high erythrocyte sedimentation rate, or persistent disease activity, as well as greater initial joint damage, according to a new analysis of trial data reported Dr. Josef S. Smolen, and his associates in Europe and the United States.

The 54-week trial showed that overall, combination therapy with methotrexate and infliximab provided greater clinical, radiographic, and functional benefits than treatment with methotrexate alone for patients with active, early-stage RA (Arthritis Rheum. 2006;54:702-10).

The new findings build on results from the ASPIRE study (Active-Controlled Study of Patients Receiving Infliximab for

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the Treatment of Rheumatoid Arthritis of Early Onset), the investigators reported. Patients in the trial had RA for no longer than 3 years; the 1,049 patients were randomized to receive titrating doses of methotrexate up to 20 mg/wk plus placebo or infliximab at weeks 0, 2, and 6, and then every 8 weeks through week 46, Dr. Smolen, of the Medical University of Vienna, and his colleagues reported.

In the new analysis, the investigators looked for predictors of radiographic joint damage in order to identify subgroups of patients who would likely improve with methotrexate alone and those who would most benefit from the more expensive and potentially toxic combination therapy.

To do so, Dr. Smolen and his colleagues looked at the relationship between disease activity measures taken at baseline and at week 14, as well as those averaged over time, with changes in radiographic joint damage.

Radiographs were obtained within 4 weeks of the start of treatment and at weeks 30 and 54. Joint damage was assessed by changes in modified Sharp/van der Heijde scores (SHS).

The investigators found that methotrexate alone failed to prevent the progression of joint damage among patients with the highest C-reactive protein (CRP) levels, erythrocyte sedimentation rate (ESR), and swollen joint counts, as well as the highest levels of joint damage at baseline.

Infliximab in combination with methotrexate, on the other hand, inhibited radiographic progression regardless of baseline and early disease activity or joint damage.

Patients in the highest baseline tertile of

CRP (3 mg/dL or greater) and ESR (52 mm/hour or greater) who were treated only with methotrexate had mean increases in the SHS for joint damage of 5.62 and 5.89, respectively, from baseline to week 54. In patients who were treated with methotrexate plus infliximab, these changes were 0.73 and 1.12, respectively.

Also, patients receiving methotrexate alone who had persistently active disease—higher disease activity scores (DAS28)—at week 14 showed greater pro-

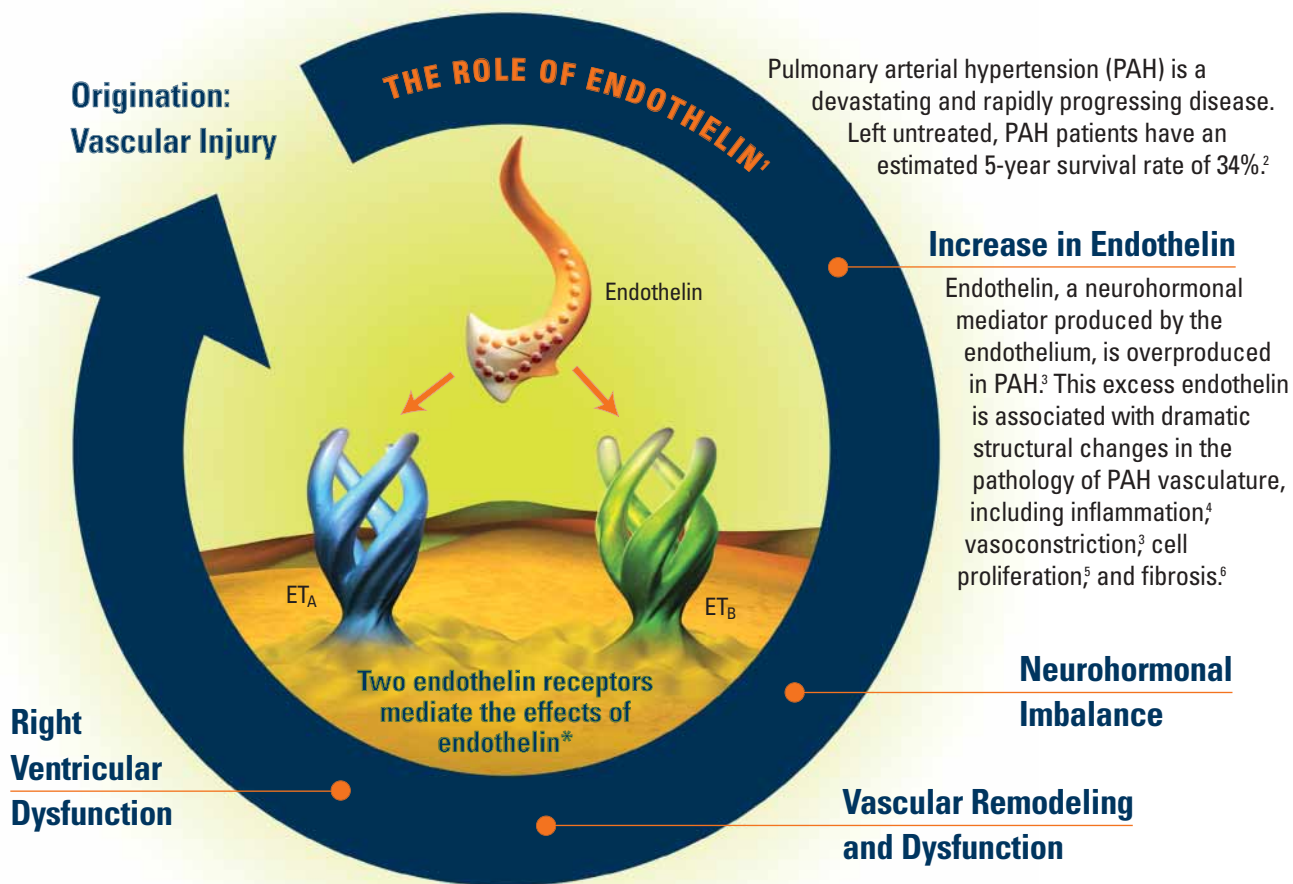
gression of joint damage from baseline to week 54 than those with lower DAS28 scores. Combination treatment led to significantly less joint damage regardless of disease activity at this time.

"This finding is of particular importance, since physicians generally prescribe [methotrexate] as initial [disease modifying-antirheumatic drug therapy] and then assess the adequacy of response [some] 3-6 months later," the investigators said. The results "suggest that con-

tinuation of [methotrexate] alone in patients with a DAS28 of [greater than] 4.02 (or a simplified Disease Activity Index of [greater than] 23.8) at week 14 carries with it a significant risk of progressive joint damage."

Overall, they said, the new analysis shows that "it is especially important to identify patients whose disease is rapidly advancing and who have the greatest potential to benefit from more intensive therapy." ■

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



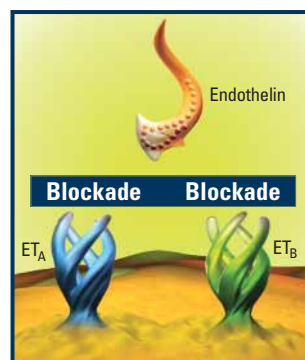
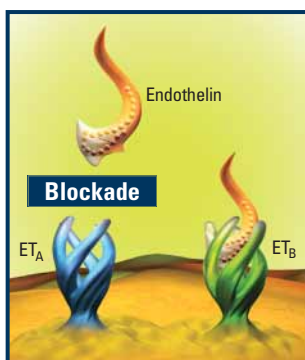
Blockade of Both ET_A and ET_B Receptors Is Critical

ET_A Activity in PAH*

- Cell proliferation⁵
- Vasoconstriction²
- Inflammation⁴

ET_B Activity in PAH*

- Cell proliferation⁵
- Vasoconstriction²
- Inflammation⁴
- Fibrosis⁶
- Hypertrophy⁶



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.

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