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Lung alert

When is it too EARLY to start bosentan in pulmonary arterial hypertension?

Pulmonary arterial hypertension is a debilitating progressive disease which eventually leads to right heart failure and death. Although observational studies indicate that early treatment initiation might be advantageous, previous clinical trials only looked at the use of bosentan (dual endothelin receptor antagonist) in patients with advanced symptomatic states (WHO functional class III and IV).

The EARLY trial enrolled 185 patients aged ⩾12 years with mildly symptomatic (WHO functional class II) pulmonary arterial hypertension who were randomised to receive either bosentan at an initial dose of 62.5 mg twice daily, up-titrated to 125 mg twice daily after 4 weeks, or placebo for 6 months. Treatment with other approved agents was prohibited with the exception of sildenafil. The primary end point was improvement in exercise capacity (reflected by 6 min walk distance), a surrogate for cardiopulmonary haemodynamics. Secondary end points included time to clinical worsening and change from baseline functional class. Analysis of the primary end points (in 168 patients) showed a reduction in the mean pulmonary vascular resistance (83.2% of baseline value). The initial increase in exercise capacity also seen in the bosentan group was not statistically significant at 6 months. The overall number of adverse effects was similar between groups, with syncope the most common serious adverse event in the bosentan group.

The study was not sufficiently powered to perform any subgroup analysis. The EARLY study showed the potential benefit of bosentan in mildly symptomatic patients with pulmonary arterial hypertension, as reflected by improvement in haemodynamics and the prevention of clinical deterioration.

► Galie N, Rubin LJ, Hoeper MM, *et al*. Treatment of patients with mildly symptomatic pulmonary arterial hypertension with bosentan (EARLY study): a double-blind, randomised controlled trial. *Lancet* 2008;**371**:2093–100

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