

BUILD-1: A Randomized Placebo-controlled Trial of Bosentan in Idiopathic Pulmonary Fibrosis 177:75-81

Rationale: Idiopathic pulmonary fibrosis (IPF) is a progressive, fatal lung disease lacking effective treatment.

Objectives: To determine the effects of bosentan on exercise capacity and time to disease progression in patients with IPF.

Methods: In a double-blind, multicenter trial, patients with IPF were randomized to receive oral bosentan 62.5 mg twice daily for 4 weeks, increased to 125 mg twice daily thereafter, or placebo, for 12 months or longer. The primary efficacy endpoint was change from baseline up to Month 12 in exercise capacity, as measured by a modified six-minute-walk test. Secondary endpoints were time to death or disease progression (worsening pulmonary function tests [PFTs] or acute decompensation), change in PFT scores, and quality of life (QOL) assessed using Short-Form 36 and St. George's Respiratory Questionnaire.

Measurements and Main Results: A total of 158 patients randomly received bosentan ($n = 74$) or placebo ($n = 84$). Bosentan showed no superiority over placebo in six-minute-walk distance (6MWD) up to Month 12, the primary efficacy endpoint. A trend in favor of bosentan was observed in the secondary endpoint of time to death or disease progression (hazard ratio [HR], 0.613; 95% confidence interval [CI], 0.328–1.144; $P = 0.119$), which was more pronounced in a patient subgroup diagnosed using surgical lung biopsy (*post hoc* analysis; HR, 0.315; 95% CI, 0.126–0.789; $P = 0.009$). Changes from baseline up to Month 12 in assessments of dyspnea and QOL favored treatment with bosentan. No unexpected adverse events were reported.

Conclusions: Bosentan treatment in patients with IPF did not show superiority over placebo on 6MWD. A trend in delayed time to death or disease progression, and improvement in QOL, was observed with bosentan. The more pronounced treatment effect in patients with biopsy-proven IPF warrants further investigation.

Clinical trial registered with www.clinicaltrials.gov (NCT 00071461). **AM J RESPIR CRIT CARE MED 2008.**

