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The BUILD-3 Trial: A Prospective, Randomized, Double-Blind, Placebo-Controlled Study of Bosentan in Idiopathic Pulmonary Fibrosis

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Abstract Body

Rationale: Idiopathic pulmonary fibrosis (IPF) is a progressive fibrosing disease with limited therapeutic options and a poor prognosis. In the randomized, double-blind, placebo-controlled, proof-of-concept BUILD-1 trial, a trend to delayed time to IPF progression or death and some improvements in health-related quality of life were observed in a subset of IPF patients treated with the dual endothelin receptor antagonist bosentan. Here we describe the design and preliminary, blinded baseline data from BUILD-3, a large-scale, morbidity/mortality, Phase III superiority trial of bosentan in IPF. The primary objective of BUILD-3 was to demonstrate that bosentan delays IPF progression or death.

Methods: The prospective, multicenter, randomized, double-blind, parallel-group, placebo-controlled, event-driven, BUILD-3 trial enrolled patients aged ≥18 years with a proven diagnosis of IPF according to ATS/ERS statement, of <3 years, with surgical lung biopsy. Patients with forced vital capacity (FVC) <50% of predicted, diffusing capacity for carbon monoxide (DL_{CO}) <30% of predicted, or extensive honeycombing on baseline high-resolution computed tomography (HRCT) were excluded. Patients were randomized 2:1 to receive oral bosentan (62.5 mg b.i.d. for 4 weeks, 125 mg b.i.d. thereafter) or placebo. The primary endpoint was time to IPF progression or death up to end of study. IPF progression was defined as either a worsening of pulmonary function tests (decrease from baseline in both FVC by ≥10% and DL_{CO} by ≥15%)—to be confirmed 4 weeks after identification—or acute exacerbation of IPF. BUILD-3 was designed to run until 202 cases of IPF progression or death were recorded. The safety and tolerability of bosentan in IPF patients were investigated.

Results: Enrollment was completed in October 2008 with 616 patients in North America, Europe, Israel, Australia, Japan, and South Korea. In preliminary, blinded analysis of baseline data from all randomized patients, the mean age was 63.6 years (standard deviation [SD], 8.6). In total, 429 patients (69.6%) were male and 510 patients (82.8%) were Caucasian. Mean baseline percent of predicted FVC was 74.3% (SD, 15.0) and mean baseline percent of predicted DL_{CO} was 47.8% (SD, 12.1).

Conclusion: The morbidity/mortality BUILD-3 trial of bosentan is one of robust design, performed in a homogenous IPF patient population without extensive honeycombing on baseline HRCT. Results from the BUILD-3 trial will be available for presentation at ATS 2010.

Trial registration: ClinicalTrials.gov, NCT00391443.

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