Bosentan versus placebo in interstitial lung disease secondary to systemic sclerosis: The BUILD 2 study

**Abstract**

Rationale: Bosentan is a dual endothelin (ET1) receptor antagonist approved for pulmonary hypertension (PH) in SSc. The profibrotic effects of ET1 are relevant in the process of fibrosis. We report the BUILD 2 study, a double-blind, randomized, placebo-controlled study evaluating bosentan in subjects with idiopathic pulmonary fibrosis (IPF) and systemic sclerosis-ILD (SSc-ILD).

Study design and methods

**BUILD 2** was designed as part of a program to assess the effects of bosentan in IPF (BUILD 1) and SSc-ILD (BUILD 2). A sample of 132 patients with SSc-ILD, randomized placebo-controlled study in patients with SSc-ILD and was designed to select patients with progressive pulmonary hypertension. Patients with primary or secondary pulmonary hypertension and with a confirmed diagnosis of SSc-ILD were randomized in a 2:1 ratio to bosentan or placebo. The primary efficacy endpoint was change from baseline in 6 min walk test (6MW) between groups at month 12. Changes in % predicted FVC and DLco, are expected in January 2006.

**Results:**

- **Primary efficacy endpoint** was change from baseline in 6 min walk test (6MW) between groups at month 12 (SD = 75 m, two-sided p-value < 0.05).
- **Secondary endpoints** included time to death or worsening of pulmonary function tests (PFTs), defined as a decrease from baseline in % predicted FVC or a decrease from baseline in % predicted DLco. A total of 132 patients were randomized to receive a 45 m difference in the 6MW between groups after 1 year follow-up (p-value: 0.05).

**Conclusions:**

- **There were no statistically significant differences in primary outcome (6MW) or key secondary outcomes (PFTs, DLco), compared to bosentan and placebo-treated patients.**
- **Any one or both of these factors may have affected this result:**
  - use of 6MW may not be appropriate to assess treatment effects in parenchymal lung disease
  - this study failed to select a population with expected level of disease progression as shown by the stability of PFTs in both groups. Trials in SSc-ILD may require a longer period of observation

**References**