

**Survival in patients with class III idiopathic pulmonary arterial hypertension treated with oral bosentan compared with an historical cohort of patients started on IV epoprostenol**

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**On-line Methods Supplement**

*Matched-patient analysis:* To reduce any inherent differences between groups, matched cohorts of bosentan- and epoprostenol-treated patients were identified using a conservative, systematic procedure from among all patients in the two groups who had valid baseline assessments for cardiac index, mean pulmonary arterial pressure, and mean right atrial pressure. Percentiles of the range of values for each variable were computed and used to construct a series of cell sets ( $1^3$ – $10^3$  cells/set, corresponding to 100% to tenth percentiles within each cell) that contained patients with appropriate values for each of the three hemodynamic variables. Within each cell, the numbers of hemodynamically matched patients per treatment were equalized by removing patients in the over-represented group using a procedure biased against bosentan. Patients were excluded in order, based on the longest survival time or follow-up if on bosentan and on the shortest survival time or follow-up if on epoprostenol. Because the bosentan cohort was smaller, the larger the percentile included in the cell, the more biased the output in favor of epoprostenol (the worst epoprostenol patients eliminated), and the smaller the percentile, the more accurate the match but the smaller the number of patients included (all unmatched patients excluded). In the absence of known criteria, the set containing  $6^3$  cells was chosen as providing the best match while preserving around 80 patients per

set (see results). Kaplan-Meier survival estimates and hazard ratio with 95% confidence limits were computed for the resulting matched cohorts.