

Treatment with oral treprostinil is associated with improved survival in pulmonary arterial hypertension participants from the FREEDOM-EV Study

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Oral treprostinil (TRE) has been shown to improve exercise capacity in patients with pulmonary arterial hypertension (PAH). A post-hoc analysis of AMBITION suggests an association between randomized therapy and survival.

In this global, event-driven study, eligible participants taking one approved oral PAH medication were randomized to TRE or placebo (PBO), allowing doses up to 12 mg three times daily. Primary objective was to determine the effect of TRE on time to first adjudicated clinical worsening (CW) event (death, hospitalization due to worsening PAH, initiation of inhaled/infused prostacyclin, disease progression, or unsatisfactory long-term clinical response). We analyzed mortality at end of randomized treatment (EOT) and end of study (EOS), which included open-label treatment. Vital status was assessed at 6-month intervals for consenting individuals who discontinued participation.

690 participants were randomized (346 TRE, 344 PBO); 89% were included in the mortality analysis at EOS. Participants were predominantly female and <65 yrs with idiopathic/heritable PAH; median time on approved therapy at randomization was 6 months. The majority had FC II symptoms; median 6MWD was 396 m. There were 90 and 124 CW events with TRE and PBO, respectively (HR 0.74; 95% CI 0.56-0.97; p=0.039). While mortality was similar between groups at EOT (4.9% TRE, 5.2% PBO), mortality at EOS was lower with TRE (11% TRE, 17.4% PBO; HR 0.63; 95% CI 0.42-0.95; log-rank p=0.032). Vital status was unknown for 43 TRE and 31 PBO participants. 108 PBO participants began therapy with open-label TRE after a CW event, but were included in the mortality analysis according to initial treatment assignment. Prostacyclin AEs were more common with TRE; 18.9% TRE and 4.1% PBO permanently discontinued treatment for AEs.

TRE added on to background PAH monotherapy significantly reduced the risk of a CW event at EOT and was associated with improved survival at EOS.

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