Long-term outcomes in newly diagnosed pulmonary arterial hypertension (PAH) patients receiving initial triple oral combination therapy: Insights from the randomised controlled TRITON study

Authors:
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Topic(s):
Pulmonary Hypertension

Introduction:
Long-term outcomes are important in PAH.

Purpose:
To evaluate the long-term efficacy and safety of initial triple oral therapy with selexipag, macitentan and tadalafil vs initial double oral therapy with macitentan and tadalafil in PAH.

Methods:
TRITON, a multicentre, double-blind, placebo-controlled, phase 3b study, randomised 1:1 newly diagnosed, treatment-naïve PAH patients to initial triple vs double therapy. Macitentan and tadalafil were initiated at randomisation and selexipag/placebo at day 15 (uptritated to wk 12). Efficacy and safety were assessed in a blinded manner until the last patient randomised completed wk 26 (end of observation period). Pulmonary vascular resistance (PVR; primary endpoint) and 6-minute walk distance (6MWD) were assessed at wk 26. Other secondary endpoints included time to first disease progression event (centrally adjudicated) to end of observation period +7 days. Time to all-cause mortality up to end of observation period was analysed post-hoc.

Results: 247 patients were randomised to initial triple (n=123) or initial double therapy (n=124); baseline characteristics were balanced between groups. Median follow-up was 77.6 (initial triple) and 75.8 wks (initial double). Initial triple and initial double therapy improved PVR (by 54% and 52%) and 6MWD (by 55 and 56 m), with no difference between groups. A 41% reduction in the risk of first disease progression event driven by PAH-related hospitalisation and all-cause death was observed with initial triple vs initial double therapy (hazard ratio 0.59, 95% CI 0.32–1.09, p=0.087; Figure). Two patients died in the initial triple vs 9 in the initial double therapy group (hazard ratio 0.23, 95% CI 0.05–1.04). Adverse events were consistent with the known safety profiles of the study drugs.

Conclusions: In TRITON, assessments at wk 26 showed marked improvements in both treatment arms, with no difference between groups. Exploratory analysis indicated a signal for improved long-term outcome with initial triple versus initial double therapy.
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