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HYPERTENSION

TREPROSTINIL THERAPY FOR PAH

Oral treprostinil—a prostacyclin analogue—is a potential initial therapy for patients with class II or III symptoms of pulmonary arterial hypertension (PAH). This finding comes from the international, double-blind, placebo-controlled FREEDOM-M trial, which was designed to assess the safety and efficacy of oral treprostinil therapy in patients with *de novo* PAH, who were not being treated with any other approved PAH therapy.

PAH is characterized by elevated pulmonary vascular resistance resulting in right ventricular failure and premature death. The clinical benefits of prostacyclin (improved haemodynamics, exercise capacity, and survival) have been shown. However, the complexity of intravenous or subcutaneous infusion of the drug restricts its use to the treatment of patients with advanced PAH. In the FREEDOM-M trial, investigators tested the safety and efficacy of the diolamine salt of treprostinil, which can be administered orally.

A total of 349 patients were randomly allocated to either treprostinil or placebo. Patients allocated to treprostinil initially received 1.0 mg of the drug twice daily. Owing to tolerability issues identified in the FREEDOM-C trial (a counterpart study involving patients already taking background therapy for PAH), the starting dose of the drug in the FREEDOM-M trial was amended to 0.25 mg twice daily, with an escalation by 0.25–0.50 mg every 3 days, to a maximum of 12.0 mg twice daily. Data quoted are for the 151 patients who started with a dose of 0.25 mg, compared with placebo ($n = 77$).

After 12 weeks, a significantly greater increase in the distance walked in 6 min compared with baseline (the primary end point) occurred with treprostinil than with placebo (23 m, 95% CI 4–41 m, $P = 0.0125$). Adverse events were common, with headache, nausea, or diarrhoea being reported by 63%, 30%, and 30% of patients taking treprostinil, and 19%, 18%, and 16% of those taking placebo, respectively.

The researchers believe that these data, and the ease of oral administration, make treprostinil diolamine suitable for the first-line treatment of patients with class II–III symptoms of PAH. They note, however, that "the long-term impact of oral treprostinil therapy on PAH disease progression" requires additional study.

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Original article Jing, Z.-C. *et al.* Efficacy and safety of oral treprostinil monotherapy for the treatment of pulmonary arterial hypertension: a randomized controlled trial. *Circulation* doi:10.1161/CIRCULATIONAHA.112.124388