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Upfront triple combination therapy with ambrisentan, tadalafil and subcutaneous treprostinil in incident patients with severe pulmonary arterial hypertension

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Aim.
Current treatments strategies for high-risk patients with pulmonary arterial hypertension (PAH) are based on the use of parenteral prostanoids. The evidence to support triple upfront combination therapy remains largely based on expert consensus or small studies. Aim of this study was to evaluate the efficacy and safety of an upfront triple combination therapy with ambrisentan, tadalafil and subcutaneous (sc) treprostinil in patients with severe PAH.

Methods.
This is a multi-center retrospective analysis of patients with newly diagnosed severe PAH treated with upfront triple combination therapy with ambrisentan, tadalafil and sc treprostinil between 2014 and 2018. Clinical evaluations, WHO functional class (FC), 6-min walk distance, biomarkers and right heart catheterization were collected from the patients’ medical records at baseline and during the follow-up.

Results.
Overall, 20 patients (mean age 44±15 years, 15 female) were included. Over a median follow-up of 12 months, all patients were still alive on triple combination therapy. At baseline 11 patients were in WHO-FC 3 and 9 patients in WHO-FC 4. At follow-up, WHO-FC (2.0±0.5 vs 3.5±0.5, p<0.001, improved in all: 2, 16, and 2 patients in FC 1, 2 and 3, respectively), exercise capacity (431±67 vs 152±130 m, p<0.001), NT-proBNP (423±260 vs 3492±1864 pg/ml; p<0.001), and haemodynamics (right atrial pressure 5±2 vs 13±3 mmHg, p<0.001; mean pulmonary artery pressure 42±5 vs 60±9 mmHg, p<0.001; cardiac index 3.5±0.8 vs 1.8±0.3 l/min/m2, p<0.001; pulmonary vascular resistance 5.5±1.3 vs 16.4±4.4 Wood units, p<0.001; pulmonary arterial compliance 2.5±0.9 vs 0.8±0.3 ml/mmHg, p<0.001) significantly improved compared with baseline. No patient discontinued the therapy due to serious adverse events.

Conclusions.
Triple upfront combination therapy with ambrisentan, tadalafil and sc treprostinil is safe and offers clinical and haemodynamics benefits in incident patients with severe PAH.