

Long-term outcome with subcutaneous treprostinil sodium in pulmonary hypertension: a 10-year single-center study



Roela Sadushi-Kolici¹, Diana Bonderman¹, Nika Skoro-Sajer¹, Jutta Glatz², M.P. Kneussl³ and Irene M Lang¹
 From the Divisions of Cardiology¹, AOP Orphan Pharmaceuticals AG ² and Division of Pulmonary Disease³
 Medical University of Vienna¹, Wilhelminenspital³ Vienna, Austria

Study Objectives: The aim of this single center retrospective study was to investigate the long-term efficacy of subcutaneous (sc) treprostinil sodium in patients with severe precapillary pulmonary hypertension (PH).

Methods: Between 1998 and 2008, 79 PH patients (51 with pulmonary arterial hypertension, one PH associated with lung disease, 27 with inoperable chronic thromboembolic PH) were in World Health Organisation (WHO) classes III/IV, with a 6-minute walk distance (6-MWD) of <300m, a mean right atrial pressure (mRAP) of >10mmHg and/or a cardiac index (CI) of <2.2L/min/m² (Tables 1 and 2). Fifty-two (75%) patients were incident PH cases.

Patients who had been treated with sc treprostinil sodium for less than 6 months at the time of the analysis were not included (n=10, 12.6%). The follow-up hemodynamic assessment was after 3.2±2.8 years (mean±SD).

Fifty-nine (85.5%) patients were treated with first-line sc treprostinil and 10 (14.5%) patients were switched to sc treprostinil after oral therapy. Event-free status was defined as survival without hospitalisation for intravenous (iv) diuretics and/or vasopressors, switch to iv prostacyclin, combination therapy, balloon atrial septostomy (BAS) and double lung transplantation.

Results: During 3.85 (0.75 - 9.69) years of follow-up, significant improvements in 6-MWD [treatment effect (TE): +90m (95% CI: 18.5, 156); *p* < 0.001], WHO class (*p* < 0.001), mean pulmonary arterial pressure (mPAP) [TE: -7mmHg (95% CI: -15, +2); *p* = 0.002], cardiac output [TE: +0.20 L/min/m² (95% CI: -0.28, +1.03); *p* = 0.044] and pulmonary vascular resistance (PVR) [TE: -258.5 dynxsecxcm⁻⁵ (95% CI: -561, -29); *p* < 0.001] occurred under 41.76±23.43ng/kg/min (mean±SD; range 10-103) of sc treprostinil (Figure 1).

Six (8.8%) patients underwent double lung transplantation/BAS, and 10 (14.7%) patients died of right heart failure (Table 3).

Eighteen (26.1 %) patients survived non-PH related adverse events, e.g. organ biopsies, hip replacement, ureteral reconstruction, and aortic valve replacement.

At one, three and 10 years overall survival was 89%, 78% and 64%, and event-free status 87%, 68% and 34%, respectively (Figure 2).

Patients – no. (n=69)	
Sex – no. (%)	
Female	48 (69.6)
Age – yrs	
Mean± standard deviation	53±16
Range	19-86
Venice – Classification – no. (%)	
Venice I	45 (65.2)
Venice IV	23 (33.3)
6-min walking distance – meters	
Mean±SD	296±112
WHO functional class – no. (%)	
III	40 (58)
IV	29 (42)

Table 1 Demographics and clinical characteristics at baseline

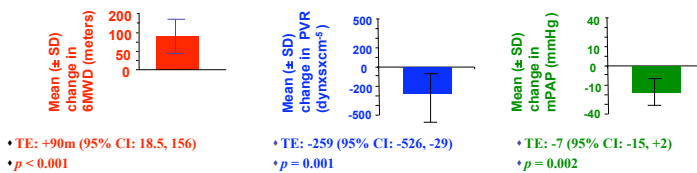


Figure 1 Effect of Treprostinil on Δ 6MWD (red bar), Δ PVR (blue bar), Δ mPAP (green bar).

Patients – no. (n=69)	
Cardiac output – liters/min	
Mean±SD	3.9±1.1
Cardiac index – liters/min/qm	
Mean±SD	2.2±0.6
Pulmonary Vascular Resistance – dynxsecxcm ⁻⁵	
Mean±SD	1078±583
Mean Pulmonary-artery pressure – mmHg	
Mean±SD	60±15
Mean Right atrial pressure – mmHg	
Mean±SD	10±6
Mixed venous saturation – (%)	
Mean±SD	60.6±10.2

Table 2 Hemodynamic parameters at baseline

Patients – no. (n=69)	
Time to Double Lung Transplantation-years	3.57(0.82-7.12)
Mean (Range)	
Time to Death from all causes-years	2.65 (0.95 – 6.64)
Mean (Range)	
Time to Death from Right Heart failure-years	2.11 (0.95-6.12)
Mean (Range)	
Double Lung Transplantation – no. (%)	6 (8.8)
Death from all causes – no. (%)	15 (22)
Death from Right Heart Failure – no. (%)	10 (14.7)

Table 3 Outcomes

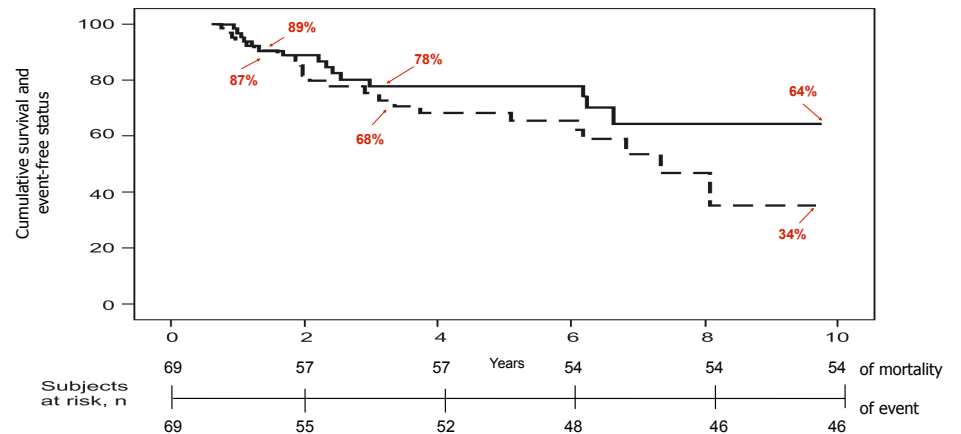


Figure 2 Kaplan-Meier estimates of overall survival (solid line) and event-free status (dashed line) in patients treated with subcutaneous treprostinil sodium.

Conclusion: Treatment with subcutaneous treprostinil remains efficacious over a ten-year period, and confers improvements of 6-MWD, WHO class and PVR, resulting in a significant survival benefit.