

**EudraCT number:** 2009-012005-19

**Title:** Eficacia de Revatio en el test vasodilatador agudo realizado en pacientes con hipertensión pulmonar al menos moderada secundaria a enfermedad valvular corregida con prótesis normofuncionante

**Code:** DOM-SIL-2009

**Sponsor:** HOSPITAL VALL DE HEBRON

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**End of Trial:** 31/05/2013

### SUMMARY OF RESULTS

**Objectives:** Persistent pulmonary hypertension (P-PH) leads to poor outcomes after mitral (MVR) and aortic (AVR) valve replacement. We analysed the effects of sildenafil (SILD) in patients with P-PH after left prosthetic valvular replacement at rest and during dobutamine stress according to the haemodynamic phenotype.

**Methods:** We assessed the mean and pulse pulmonary artery pressure (mPAP, pPAP), pulmonary artery wedge pressure (PAWP), mPAP/mean aortic pressure ratio (mPAP/mAoP), cardiac output (CO), peripheral and total pulmonary vascular resistance (PVR, TVR) and pulmonary arterial capacitance (PAC) of 15 stable patients ( $72 \pm 7$  ys, 2 males, 13 females) who underwent successful MVR at least one year before, presenting PH by echo in the follow-up (7 of them underwent a concomitant AVR). Haemodynamic measurements were made at basal state, after breathing 20ppm of NO gas for 10 min (iNO), after washout of 10 min, 30 min (20mg oral) or 10 min (10 mg i.v.) after SILD treatment at rest, and during dobutamine infusion (up to  $20 \mu\text{g}/\text{kg}/\text{min}$ ) plus  $30^\circ$  leg trendelenburg (SILD + stress).

**Results:** Eight patients had Cpc-PH (combined pre- and post-capillary PH,  $\text{DFG} \geq 7\text{mm Hg}$  and/or  $\text{PVR} > 3\text{Wu}$ ), 6 patients had lpc-PH (isolated post-capillary PH,  $\text{DPG} < 7\text{mm Hg}$  and/or  $\text{PVR} \leq 3\text{Wu}$ ) and one patient had pre-capillary PH. CpC-PH patients had higher mPAP, pPAP, PVR, TPR, and lower PAC than lpc-PH patients ( $p < 0.05$ ). iNO increased CO, stroke volume and PAC, and decreased TPR and mPAP/mPAo ( $< 0.05$ ). After SILD treatment the haemodynamic variables did not change significantly. SILD+stress increased CO and heart rate and decreased TPR ( $p < 0.05$ ),

with no change of mPAP/mPAo ratio. Patients with pre-capillary PH had a behaviour similar to Cpc-PH, except for a lower increase in CO during SILD+stress (0.3 L/min).

**Conclusions:** At rest, SILD treatment, similarly to iNO, improves PAC and TPR in Cpc-PH patients. However, iNO acts preferentially on CO and SV, while SILD decreases mPAP and pPAP. During stress, SILD allows to increase CO in both Cpc-PH and lpc-PH groups, with no changes of mPAP, pPAP, PAC, and TPR values at rest.

**Table 1.** Summary of results of the study

Comparison between Cpc-PH and lpc-PH						
	$\Delta$ iNO lpc-PH	$\Delta$ iNO Cpc-PH	$\Delta$ Sild lpc-PH	$\Delta$ Sild Cpc-PH	$\Delta$ Sild+stress lpc-PH	$\Delta$ Sild+stress Cpc-PH
mPAP, mmHg	1.8±3.3	-2.8±3.9	0.5±1.2	-7±3‡	4±1.7	-7.5±2.2‡
pPAP, mmHg	-5.2±2.7	-0.4±5	8±6.5	-8±4‡	13.5±7.6	-6±3.6‡
CO, L/min	0.7±0.25	2.1±0.4‡*	-0.2±0.2	0.1±0.2	1.7±0.3*§	1.6±0.2*
SV, mL	-0.4±3	31±9‡*	0.3±3	0.6±3	0.1±5	4±5§
Heart Rate, bpm	4±5	-0.5±3	-4±2	1±2	26±9§	26±9*§
TPR, Wood units	-1.3±1.1	-6±2.8	0.6±0.4	-3±1.7‡	-1.3±0.4	-6±1.6‡
PAC, mL/mmHg	1.04±0.6	2.7±0.8*	-0.3±0.3	0.2±0.1‡	-0.6±0.3§	0.3±0.1‡§

Mean ± SEM. \*p<0.05 vs  $\Delta$ Sild and §p<0.05 vs  $\Delta$ iNO in the same PH phenotype. ‡p<0.05 Cpc-PH vs lpc-PH in the same state.