266. Treatment of pulmonary hypertension

P2378

Late-breaking abstract: Short term improvement in 6 minute walk distance predicts long term survival in *incident* idiopathic pulmonary arterial hypertension. Results from the Pulmonary Hypertension Registry of the United Kingdom and Ireland

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Background: Improvement in 6 minute walk distance (6MWD) after 12-16 weeks of treatment has been used as the primary end point in many pivotal pulmonary arterial hypertension (PAH) clinical trials. However, the consensus view is that although baseline 6MWD predicts survival, *change* in 6MWD (Δ6MWD) does not.

Aim: To determine whether Δ6MWD after 3 months of disease targeted therapy predicts long term survival in patients from the Pulmonary Hypertension Registry of the UK and Ireland.

Methods: Retrospective observational study of all *incident* cases of idiopathic (IPAH), heritable and anorexigen-associated PAH diagnosed in the UK and Ireland between 1st January 2001 and 31st December 2009. Patients were divided into low and high baseline 6MWD by the median 6MWD (295 m).

Results: Total of 646 patients were diagnosed. After 3 months of disease targeted therapy, patients with absolute 6MWD >353 m (corresponding to the median value at 3 months) had better survival than those with 6MWD < 353 m. Mean improvement in 6MWD after 3 months of therapy was 42.4±75.8 m (median 37.5 m). Patients with greater increase in 6MWD from baseline to 3 months had better post-3 months survival (hazard ratio 0.65, 95% confidence interval 0.42 to 0.99 per 100 metres improvement). In patients with low baseline 6MWD, Δ6MWD at 3 months of > 37.5 m had better survival compared to those with Δ6MWD at 3 months of < 37.5 m (Log-rank, p=0.03). This is not seen in patients with high baseline 6MWD.

Conclusion: *Change* in 6MWD after 3 months of treatment predicts long term survival in patients with low baseline 6MWD.

P2379

Comparison of hemodynamic effects of inhaled nitric oxide (iNO) and inhaled epoprostenol (iEPO) in patients with pulmonary hypertension (PH)

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Rationale: Acute vasodilator testing with iNO during right heart catheterization in pulmonary arterial hypertension predicts suvival and response to calcium channel blockers. iEPO is less expensive than iNO with fewer systemic effects than intravenous EPO. We hypothesized that iEPO has similar vasodilatory efficacy as iNO and their combination has additive effects.

Methods: Prospective double-blinded study of PH treatment-naïve consecutive patients. Patients >18 years, WHO Group1-5 with pulmonary capillary wedge pressures ≤ 20 were included. Patients received iNO, iEPO and their combination in random order, with a washout phase between treatments. Hemodynamics at baseline and treatments were reported as%change, means±SD. Correlation was assessed with regression analysis. $p<0.05$ was significant.

Results: Patients enrolled: Group 1 (11), Group 2 (9), Group 3 (1), Group 4 (1), Group 5 (1). 2 did not complete the study (hypoxemia and dyspnea respectively). Mean pulmonary artery pressures (mPAP) in Groups 1, 2 and other groups were 47±12, 35±7 and 35±9.2. Mean pulmonary vascular resistances (PVR) were

Mean (SD)	iNO 20PPM	iEPO 50mcg/kg/min	R^2	p value
Group 1				
%ΔmPAP	-11.9(6.6)	-11.5(9.3)	0.57	0.006
%ΔPVR	-18.9(22.9)	-16.6(21.7)	0.58	0.006
%ΔCO	4.1(21.5)	7.5(19.5)	0.52	0.01
Group 2				
%ΔmPAP	-6.1(9.6)	-8.4(11.1)	0.59	0.014
%ΔPVR	-25.8(24.6)	-25.2(27.2)	0.55	0.021
%ΔCO	12.2(26.5)	6.4(18.2)	0.43	ns

628±352, 416±323 and 397±80. Mean cardiac outputs (CO) were 5.0±1.3, 4.7±1.3 and 4.9±0.6. The 2 vasodilators correlated significantly and did not have additive effects.
Conclusions: iNO and iEPO have similar effects on hemodynamics in PH patients. iEPO may be a less expensive alternative.

P2380
Pulmonary artery diameter and pulsatility did not decrease after vasodilator therapy lasting two years
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Background: In Pulmonary Hypertension (PH) the Pulmonary Artery (PA) dilates proportionally with pulmonary artery mean pressure (PAPx) and resistance (PVR) together with a reduced pulsatility.
Aim of the study: Our aim was to assess effect of vasodilator therapy (eg Bosentan) upon diameter and pulsatility of PA during PH.
Methods: Twenty patients affected by PH were studied by means of whole body pletismography, haemodynamics, and HRCT. Bosentan (125mg bid) was administered for two years and examination were repeated again on 10 patients still alive.
Results: In survivors Bosentan diminished pulmonary artery pressure and vascular resistance; pulmonary artery diameter and pulsatility did not change significantly with a modest worsening.
Conclusion: The lack of changes of diameter, despite the decrease of pressures, indicate that progressive intrinsic wall vessel changes took place. Pulmonary artery diameter and pulsatility do not allow to assess the response to the therapy.

P2381
The use of perioperative intravenous sildenafil in patients with mitral valve disease and co-existent pulmonary hypertension during cardiac surgery
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Introduction: Patients who have mitral valve (MV) disease with associated pulmonary hypertension (PH) may develop acute rises in pulmonary vascular resistance (PVR) perioperatively.Such pulmonary hypertensive crises may significantly increase perioperative morbidity and mortality. Although there is limited experience with agents to reduce the PVR, their use may be associated with systemic hypotension.
Aim: To evaluate the safety and haemodynamic effects of intravenous (IV) sildenafil perioperatively, in patients with PH and MV disease undergoing cardiac surgery.
Method: Nine patients, two males and seven females, age range 64 to 81 (median 76) years, with PH, mean pulmonary artery pressure range 30 to 56 (median 43) mmHg, associated with MV disease, who had MV surgery, received IV sildenafil (1mg/ml) at a rate of 1mg/kg for one hour in the immediate post operative period.Pulmonary and systemic haemodynamic measurements were recorded at ten-minute intervals.
Results: A statistically significant reduction (p=0.006) in PVR was observed.There was a trend towards improvement in the cardiac index (CI), although it did not reach statistical significance (p=0.059).Mean systemic arterial pressure remained stable and no detrimental effect on other haemodynamic parameters was noted.
Discussion: Our study suggests that perioperative use of IV sildenafil is safe and not associated with systemic hypotension.We observed a favourable response in PVR and a trend towards improvement in CI.We suggest that IV sildenafil should be considered for selected patients with MV disease and PH who require MV surgery.

P2382
Current epoprostenol use in patients with severe pulmonary hypertension (PH): Data from the French PH registry
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The management of pulmonary arterial hypertension (PAH) has evolved since the early 2000s with the introduction of oral therapies, and consequently data on the current use of epoprostenol (epo) are scarce.
Methods: Patients (pts) with a newly diagnosed PH treated with epo were analysed from the prospective French PH Registry launched in Nov. 2006. The cut-off date was 1 Sept. 2010.
Results: 177 adult pts were identified for analysis. 127 (72%) had PAH (group 1) and among them, 81 (64%) had idiopathic, heritable or anorexigen-associated PAH (IHAr-PAH), 17 (13%) connective tissue disease and 17 (13%) portopulmonary hypertension. 6% of patients received epo for pulmonary veno-occlusive disease, 8% for PH with lung diseases, 12% for chronic thromboembolic PH and 2% for miscellaneous PH. At the time of epo initiation, mean (±SD) age was 51±17 yrs. 7%, 43% and 50% of pts were in NYHA class II, III, IV, respectively, and 47% were naive to PAH specific therapy. The 6-min walk distance was 309±131 m. Haemodynamic measures confirmed severe impairment with mean PAP 56±13 mmHg, right atrial pressure 10±6 mmHg, cardiac index 2.0±0.6 L/min/m^2 and pulmonary vascular resistance 1194±571 dyn s cm^{-5}. In the overall PH population, survival estimates following epo commencement were 77%, 63% and 54% at 1, 2 and 3 years, respectively, and 82%, 72% and 69% in the subgroup of pts with IHAr-PAH.
Conclusion: Epo is still used as first-line therapy in severe forms of PAH. It is notably prescribed in non-group 1 PH in 28% of cases. In incident pts with IHAr-PAH, 1- and 2-year survival is similar to that of historical cohorts, despite the prior use of an oral treatment in 48% percent of them.

P2383
Effectiveness of "Korargin" in the therapy of pulmonary arterial hypertension in patients with systemic lupus erythematosus
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Introduction: Pulmonary arterial hypertension (PAH) in systemic lupus erythematosus (SLE) is a complex therapeutic problem and occurs from 5 to 14%. The main pathophisiological mechanism of PAH is an endothelium dysfunction with abnormality of nitric oxide synthesis (Ghofrani H.A. et al. J. Am. Coll. Cardiol. 2004; 43; 68S-72S).
Objective was to examine the efficacy of the "Korargin" (1 tabl. contains 0.1g L-arginine and 0.1g inosine), production of "Korargin", Uman, Ukraine in SLE patients with PAH.
Methods: 30 SLE patients with PAH (mean age is 48.3±1.7 y.)were studied, whom to conventional therapy was added "Korargin" 2 tablets 3 times a day for 8 weeks. The object of the effectiveness were increased distance of 6-minute walk (6MW), changes in pulmonary artery pressure and improvement of functional class (FC) PAH on WHO.
Results: II FC PAH was diagnosed in 80% patients. Patients with III FC was 20%. From the 4th week and untill the end of the initial study, the patients demonstrated a significant increase in the distance test of 6MW an average of 61.2±3.2 m compared with the baseline data. In addition, it was observed decrease in pulmonary arterial pressure on 11% in 37% of patients. 64% patients improved their FC.
Conclusion: Despite of the fact, that insufficient long-term follow-up period and relatively non-severe population of SLE patients with PAH, having taken "Korargin", patients has improved tolerance to phisical activity, FC PAH on WHO and hemodynamic parameters.

P2384
Impact of functional class change on survival in patients with pulmonary arterial hypertension in the REVEAL registry
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Introduction: The Registry to EValuate Early And Long-term PAH Disease Management (REVEAL), a 55-center observational, US-based study, describes current demographic, clinical, and treatment patterns in PAH patients (pts).
Objective: Determine if pts who improve from functional class (FC) III at enrollment to FC I/II at follow-up (f/u) have a better 2-year survival than pts who remain FC III.
Methods: 1,082 adults enrolled in REVEAL were assessed as FC III at enrollment (based on most recent pre-enrollment evaluation) and had ≥1 f/u FC assessment within the first year after enrollment. We classified pts based on their first FC f/u assessment after enrollment as: 1) improved if FC improved to FC I/II; 2) unchanged if remained FC III; or 3) deteriorated if worsened to FC IV. We compared survival (estimates±SE) of these 3 subgroups from the first f/u FC assessment (log-rank test).
Results: FC improved in 26% (n=281) of pts, was unchanged in 66% (n=718) and deteriorated in 8% (n=83). At enrollment, there were no differences in gender, PAH subgroup, right atrial pressure, or cardiac index; significant differences were observed in age, proportion of newly diagnosed (diagnostic confirmatory cardiac catheterization ≤3 months before enrollment) pts, and 6-minute walk distance among groups. Two-year survival was 88±2%, 76±2%, and 34±6% for FC I/II, FC III, and FC IV pts, respectively (P<0.001 for all pairwise comparisons). Results are similar for both newly and previously diagnosed pts who were FC III at enrollment.
Conclusions: Pts who improve from FC III to FC I/II appear to have a better

2-year survival than those who remain FC III.

P2385

Inhaled treprostinil therapy in patients with pulmonary hypertension and parenchymal lung disease

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The treatment of patients with Parenchymal Lung Disease (PLD) and Pulmonary Hypertension (PH) is challenging. PLD is characterized by an imbalance between alveolar ventilation and pulmonary blood flow. The ability to deliver therapy to areas of lung that are well ventilated would utilize preserved V/Q matching and improve drug delivery. This would reduce undesirable alterations in perfusion caused by a systemic vasodilator and provide a more effective way of treating these patients. We examined the response of patients with PLD and PH receiving Inhaled Treprostinil. We followed eight patients with NYHA Functional Class IIIB to IV symptoms with a mean PAP >25mmHg and PCWP of <15mmHg for at least 3-months. Five subjects had Obstructive Lung Disease and three were classified as having Restrictive Lung Disease. All followed the usual protocol starting with three breaths four times a day and gradually increased to the goal of nine breaths a day. Two patients had to be reduced to six breaths a day due to throat irritation but were able to increase back to nine breaths a day. One patient stopped the Inhaled Treprostinil one week after starting therapy for worsening symptoms of shortness of breath. Two patients were on a background PDE5 Inhibitor prior to starting the inhaled treatment. All but one patient reported less shortness of breath after initiation of treatment. The majority of patients had an improvement in 6-MWD and Borg Dyspnea Scale. Our experience suggests that patients with PLD and PH can be safely treated with inhaled Treprostinil. Inhaled Treprostinil may offer an effective and well tolerated treatment in subjects with PLD and shortness of breath exacerbated by PH.

P2386

Parenteral treprostinil for significant pulmonary arterial hypertension associated with pulmonary fibrosis: A safety study

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Objectives: Safety & efficacy of treprostinil (IV/SQ) in patients with pulmonary fibrosis (PF) and PAH.
Methods: Prospective, open label trial of patients referred for lung transplantation with PF/PAH (mean PA >35 mmHg & PVR >3 WU), treated treprostinil × 12 weeks.
Results: N=14 received treprostinil (18-97 ng/kg/min). The hemodynamics, 6MW, BNP, and UCSD/SF 36 significantly improved. No significant changes were seen in peripheral oxygen at rest or during 6MW.

Table 1 Baseline characteristics

Age years (SD)		63 (14)
NYHA Class (n=14)	III	7/14 (50%)
	IV	7/14 (50%)
Race	Hispanic	8/14 (57%)
	Caucasian	4/14 (29%)
	Middle Eastren	1/14 (7%)
	Filipino	1/14 (7%)
Diffuse Lung Disease	Idiopathic Pulmonary Fibrosis (IPF)	4 (29%)
	NSIP fibrosis	3 (21%)
	Chronic Hypersensitivity Pneumonitis	2 (14%)
	Pulmonary Fibrosis, unknown	1 (7%)
	IPF/Emphysema (CPFE)	4 (29%)
Baseline Therapy (n)	Phosphodiesterase-5 Inhibitors (PDE5-I)	5
	Endothelin Antagonists (ERA)	3
	ERA/PDE5-I	3
	None	3

Table 2: Baseline		12-weeks	
Pulmonary Function: (SD)		Pulmonary Function: (SD)	
FVC (% Pred)	64 (20)	FVC (% Pred)	65 (18)
FEV1 (% Pred)	63 (17)	FEV1 (% Pred)	65 (16)
FEV1/FVC	76 (11)	FEV1/FVC	79 (12)
DLCO (% Pred)	25 (13)	DLCO (% Pred)	25 (13)
FVC%/DLCO%	3.31 (2.22)	FVC%/DLCO%	3.09 (1.11)
6-minute walk (meters)	165 (94)	6-minute walk (meters)	227 (118)*
Room Air saturation, %	82 (7)	Room Air, %	80 (11)
10L face mask, %	98 (2)	10L face mask, %	97 (4)
10L face mask nadir, %	84 (9)	10L face mask nadir, %	81 (10)
Borg Score	13.8 (2.4)	Borg Score	13.0 (2.6)

*p<0.05

Table 3: Baseline		12-weeks		p-value
Hemodynamics		Hemodynamics		
mean RA (right atrial), mmHg	9.8 (3.4)	mean RA, mmHg	6.0 (3.7)	0.002
mean PA (pulmonary artery), mmHg	48.0 (7.6)	mean PA, mmHg	39.3 (13.8)	0.007
mean Pcw (pulmonary wedge), mmHg	12.6 (4.2)	mean Pcw, mmHg	10.9 (6.1)	0.17
Cardiac Output (L/min)	4.3 (1.2)	Cardiac Output (L/min)	4.9 (1.1)	0.00
Cardiac Index (L/min/m$_2$)	2.3 (0.6)	Cardiac Index (L/min/m$_2$)	2.7 (0.6)	0.04
PVR (dyn*sec*cm-5)	708 (286)	PVR (dyn*sec*cm-5)	495 (238)	0.0004
Mixed Venous Saturation (%)	64.9 (7.2)	Mixed Venous Saturation (%)	71.2 (7.5)	0.04
PC (pulmonary capacitance)	1.26 (0.55)	PC, mL/mmHg	1.57 (0.98)	0.02
Stroke Volume Index, mL/m^2	24.5 (4.9)	Stroke Volume Index, mL/m^2	21.2 (4.0)	0.30
SBP (systolic blood pressure), mmHg	125 (22)	SBP, mmHg	113 (13)	0.03
HR (heart rate), bpm	70 (13)	HR, bpm	96 (16)	0.01
SVR (dyn*sec*cm-5)	1595 (500)	SVR	1299 (370)	0.02
PVR/SVR	0.47 (0.13)	PVR/RS, mmHg	0.39 (0.16)	0.01
TPG (transpulmonary gradient)	35.4 (8.6)	TPG	28.4 (10.7)	0.01
BNP (pg/mL)	540 (888)	BNP (pg/mL)	227 (352)	0.005

RA: right atrial pressure; PA: pulmonary artery pressure; Pcw: pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance
PC: pulmonary capacitance; SVR: systemic vascular resistance; TPG: transpulmonary gradient

Conclusions: Chronic administration of treprostinil is well tolerated in patients with PF/PAH. Prospective, multicenter, randomized-controlled studies are warranted to verify these results

P2387

Cardiotonic agents affect pulmonary vessels in precision-cut lung slices (PCLS)

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Introduction: Cardiotonic agents play a major role in the therapy of heart failure. Apart from their effects on ventricular contractility and systemic afterload, they may affect the tone of pulmonary arteries (PAs) and pulmonary veins (PVs). However, in particular the responses of PVs to cardiotonic agents are only poorly defined.
Aims and objectives: We investigated the effects of α- and β-adrenergic agents as well as vasopressin in PAs and PVs to clarify their potential role in pulmonary hypertension (PH) or lung edema and coexisting heart failure.
Methods: After terminal anaesthesia with pentobarbital, PCLS were prepared from female Dunken Hartley guinea pigs and investigated by video microscopy. Concentration-response curves of various cardiotonic drugs were analyzed in PAs and PVs.
Results: After stimulation with α1-adrenergic agents, PAs contracted up to 80.5% ± 3, in respect to the initial vessel area, whereas β2-adrenergic agents showed only little effect. In contrast, after stimulation of α1-receptors PVs contracted up to 77% ± 2.6 and relaxed due to activation of β2-receptors up to 124.7% ± 2.8. Notably, inhibition of β2-receptors unmasked the α1-mimetic effect of (nor)epinephrine. Vasopressin contracted PVs up to 76.4% ± 7.4, without any effect on PAs.
Conclusion: Thus, vasoconstriction of PVs enhances capillary and venous hydrostatic pressures and promotes the development of lung edema. Our findings suggest that (nor)epinephrine in combination with unselective β-blockers and vasopressin might be harmful in patients with left heart failure. Further, α1-mimetic agents might exacerbate a pre-existing PH and a failing right ventricle by contracting PAs, whereas vasopressin might not.

P2388

Stability and microbial properties of reconstituted and diluted epoprostenol with expanded stability

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Microbial activity and stability of epoprostenol with expanded stability (EPO-ES, Veletri®) were investigated at 5°C and 25°C over a range of concentrations. EPO-ES was reconstituted and immediately diluted with sterile Water for Injection (WFI) or Sodium Chloride 0.9% Injection (NaCl). Stability for up to 72 hours (h) at 25°C was measured immediately following dilution (A), and after 1 (B) or 7 days (C) storage at 5°C. Shelf-life was assessed by determining the time over which potency ≥90% was maintained. For microbiological testing, diluted samples of EPO-ES were inoculated with S. aureus, P. aeruginosa, E. coli, C. albicans, A. niger or C. sporogenes and incubated for up to 14 days at 5°C or 4 days at 25°C. Potency of EPO-ES 6,000 ng/mL at 12h under test condition B was 92% for both diluents.
Potency of EPO-ES 9,000 ng/mL under test condition C was 91% for WFI and 87% for NaCl at 12h, and ≥90% for both diluents at 12 and 24 h at 12,000

Table 1. Potency of EPO-ES over time (Condition A)

EPO-ES, ng/mL	Diluent	Potency, %				
		0 hour	8 hours	12 hours	24 hours	72 hours
3,000	WFI	100	92	88	75	–
	NaCl	100	91	86	72	–
6,000	WFI	100	96	93	87	–
	NaCl	100	94	93	86	–
9,000	WFI	100	–	–	90	–
	NaCl	100	–	–	90	–
12,000	WFI	100	–	–	91	–
	NaCl	100	–	–	93	–
30,000	WFI	100	–	–	97	91
	NaCl	100	–	–	97	90

Table 2. Shelf-life (hours) of reconstituted and immediately diluted EPO-ES at 25°C based on potency and microbiological testing

Epoprostenol ES, ng/mL	Condition A	Condition B	Condition C
≥3,000 – <6,000	12	Do not use	Do not use
≥6,000 – <9,000	24	12	Do not use
≥9,000 – <12,000	24	12	12
≥12,000 – <30,000	24	24	12
≥30,000	72	48	24

and 30,000 ng/mL. No microbial proliferation occurred in any diluted solution of EPO-ES.

P2389

WITHDRAWN

P2390

Cardiac output measured by rebreathing nitrous oxide for the follow-up of patient with pulmonary hypertension

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Introduction: Careful and frequent assessment is important for management of patient with pulmonary hypertension (PH). Cardiac output (CO) is one of the most relevant indexes to be assessed but cannot be performed routinely because of invasive determination. A simple non-invasive method, such as nitrous oxide inert gas rebreathing (REB) could be performed at every clinic visit.
Aims and objective: To evaluate the possibility to follow up CO by REB against thermodilution (TD) in patients with severe PH. (Dana Point class 1 and 4)
Methods: CO and Stroke volume (SV) were determined via TD and REB at two different visits and spearman correlation were applied.
Results: Good correlations were found between TD and REB Δ (visit 1 – visit 2) CO and ΔSV. TD and REB ΔCO and ΔSV correlated similarly with other indexes of clinical assessment.

Correlation between TD and REB ΔCO and ΔSV and other Δ indexes

n		17 ΔCO TD	17 ΔSV TD	25 Δ6MWD	23 ΔQOL	6 ΔNT-proBNP	21 ΔWHO
29	ΔCO REB	0.8	0.67	0.58	–0.46	–0.99	–0.19
17	ΔCO TD		0.93	0.66	–0.44	–0.99	–0.26
29	ΔSV REB	0.76	0.79	0.64	–0.49	–0.96	–0.27
17	ΔSV TD	0.93		0.64	–0.45	–0.92	–0.23

n: number of patient; 6MWD: 6 minutes walk distance; QOL: quality of life,; NT-proBNP: N-terminal fragment of pro-brain natriuretic; WHO: functional classification following the world health organisation.

Conclusions: Nitrous oxide rebreathing CO measurement can be used as a monitioring tool of disease monitoring and potentially reduce the need for invasive CO measurement in patients with pulmonary hypertension.

P2391

Use of non invasive gas exchange to track pulmonary vascular responses to exercise in heart failure

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Simple metrics to quantify severity of pulmonary hypertension (PH) are lacking, particularly with exercise. Studies have suggested that end tidal CO_2 ($PetCO_2$) and ventilatory efficiency (V_E/VCO_2) may be good indicators of the pulmonary vascular (PV) response to exercise in patients with PH. In addition, measures of PV capacitance (stroke volume/pulmonary arterial pressure, Pv_{CAP}) are predictive of survival in the PH population and may potentially be estimated with gas exchange. PH is common in heart failure (HF) and appears to have both passive and reactive components. However, HF is associated with a number of gas exchange abnormalities that could limit the ability of using $PetCO_2$ or V_E/VCO_2 to estimate the presence of PH. The focus of this study was, a) determine how well non-invasive gas exchange tracks the PV response to exercise and b) test a non-invasive estimate of Pv_{CAP}. Forty-two patients with HF (age 54±9, LVEF 20±6, NYHA class 3±1) undergoing rt.-hrt catheterization as part of a pre-transplant evaluation were studied. PV pressures (Ppa/Ppw), cardiac output and PV resistance (PVR) were obtained with simultaneous measures of gas exchange. $PetCO_2$ and V_E/VCO_2 obtained during moderate exercise (VO_2 9±2ml/kg/mn, 37±13W) were highly correlated (r -0.95) and thus data were analyzed in tertiles according to $PetCO_2$ (mean 23±3, 29±2, 36±4mmHg). PVR followed a decreasing trend from low to high $PetCO_2$ groups (365±256, 282±162, 188±91WU, $p<0.01$, r-0.47). Pv_{CAP} from catheter measures was highly associated with a value estimated from O_2pulse/($1/PetCO_2$), (r=0.84). Non invasive gas exchange measures may represent a relatively simple way to track PV response to exercise in HF.
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P2392

Is flying safe for individuals with pulmonary arteriovenous malformations and hereditary haemorrhagic telangiectasia? A questionnaire-based study

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Background: Flight-related complications reported in individuals with pulmonary arteriovenous malformations (PAVMs) and hereditary haemorrhagic telangiectasia (HHT) have included deep venous thrombosis (DVT), ischaemic stroke, and haemorrhage from PAVMs. In addition there are concerns that the reduced barometric pressure associated with flying might exacerbate PAVM-induced hypoxaemia.
Methods: With ethical approval (NRES 10/H0806/8), individuals with PAVMs and/or HHT were sent a questionnaire to document flights they had taken, and symptoms experienced during or shortly afterwards. Responses were correlated with sea level erect oxygen saturations (SaO_2), and haemoglobin (Hb).
Results: 159 replies were received (response rate 52%). 147 individuals had flown, 97 (66%) with PAVMs. The median number of flights per individual was 25, totalling 18,943 flight hours in 3,950 flights. 111 (77%) respondents reported no complications. Six (4%) reported dyspnoea, two (1%) had a deep vein thrombosis, and one had an ischaemic stroke whilst flying. However the most common in-flight complications were HHT-related nosebleeds, reported by 26 (18%). There was no difference in SaO_2 at sea level between those who reported dyspnoea, and those who did not (medians 93 [range 85–96]%; 94 [84–99]%). There was

also no difference in Hb measured in clinic between the groups that developed complications, and those who did not.
Conclusion: Flight appears safe for the majority of individuals with PAVMs and HHT. It is difficult to predict who will experience complications. Recognition of potential thrombotic and haemorrhagic sequelae should influence pre-flight advice.

P2393
Is there an association between hyperthyroidism and PAH and, if yes, is pulmonary pressure decreasing after hyperthyroidism treatment?
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Rationale: About 30-40% of patients of idiopathic pulmonary arterial hypertension (IPAH) have thyroid dysfunction, in particular hypothyroidism. Pulmonary vascular remodeling in PAH is characterized by proliferation of vascular cells and thyroid hormones are known to promote angiogenesis (Mousa et al J Cardiovasc Pharmacol, 2005). We therefore hypothesized that hypothyroidism would improve pulmonary vascular remodeling in a model of angioproliferative pulmonary hypertension (SuHx model).
Objectives: To clarify the effect of thyroid hormone on pulmonary vascular remodeling in SuHx treated rats.
Methods: PAH was induced by the combined exposure of rats to the VEGF receptor blocker SU5416 and hypoxia (SuHx). Hypothyroidism was induced by PTU (10mg/kg, 5times a week), two weeks after the initial SU5416 dose (SuHx) rats. RV function was determined by echocardiography. Right ventricular pressure was measured by direct insertion of a conductance catheter into the heart.
Results: In SuHx rats, pulmonary vascular remodeling and pulmonary hypertension were decreased after PTU treatment and completely suppressed after thyroidectomy.
Conclusions: Thyroid dysfunction may affect the progression of pulmonary vascular cell proliferation in patients with PAH.

P2394
Immunosuppression in systemic lupus erythematosus associated pulmonary arterial hypertension (SLE-APAH): Improvement in exercise and functional capacity
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Evidence suggests that inflammation plays a role in the pathogenesis of SLE-APAH. We aimed to assess the effect of aggressive immunosuppression (IMM) added to PAH-specific therapy in SLE-APAH. Stanford's PAH database was searched for patients who met American College of Rheumatology (ACR) criteria for SLE and had PAH by right heart catheterization. Those who met ACR criteria for other connective tissue diseases or had <6 months of follow-up were excluded. Patients given IMM for >3 months were compared to those on PAH-specific therapy only (non-IMM). Cumulative probability of freedom from worsening New York Heart Association functional class (FC) was calculated with the Kaplan-Meier estimator and compared by the log-rank test. Mean changes in parameters between groups were compared by Student's t-test. Thirteen patients met inclusion criteria; 6 were treated with IMM (3:high dose steroids+mycophenolate mofetil, 2:intravenous cyclophosphamide, 1:hematopoietic stem cell transplant). Mean follow-up was 12.9 months. There was no significant difference in baseline demographics, SLE features, duration of PAH, hemodynamics, FC, 6 minute walk distance (6MWD) or PAH-specific therapy between IMM and non-IMM groups. At follow-up, hemodynamics and PAH-specific therapy did not differ between groups. Mean improvements in FC (-1.2 vs 0.1, p=0.06) and 6MWD (+231 vs -20 m, p=0.02) were higher in the IMM group. The IMM group had more infections (1.8 vs 0.3, p=0.05), but the percent of patients with serious infections did not differ (33% vs 14%, p=0.56). IMM added to PAH-specific therapy may improve functional and exercise capacity in SLE-APAH.

P2395
Monitoring of liver function in patients with pulmonary hypertension treated with endothelin receptor antagonists: The value of a novel monitoring system
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Background: Endothelin receptor antagonists are used for treatment of pulmonary arterial hypertension (PAH). However, these drugs have been associated with liver injury and patients require regular monitoring of liver function (LFT). We introduced a postal system whereby patients receiving these therapies had blood taken by their local practitioner and sent pre packaged boxes to our centre for analysis and monitoring on a monthly basis.
Aim: We audited effectiveness of this system with respect to frequency of blood sampling and compliance with accepted guidelines for monitoring of LFT derangements.
Results: Data on 181 patients aged mean 61.6 was collected with mean duration of therapy of 1.81 years representing a total of 327.61 patient years. Over this period, 2181 LFT's were performed representing an mean 6.66 samples per patient year. Of 181 patients 32.0% had ≥10 samples per year, 59.1% ≥ 8 samples per year, 72.9% ≥ 6 samples per year and 82.3% ≥ 4 samples per year. All patients had LFT's performed prior to commencing ERA therapy. Over this period 21 (11.6%) had LFT > 3 ULN and 10 (5.5%) ≥ 8 ULN. Of these patients 48.4% of patients with > 3 ULN had their ERA stopped and 19.4% of patients were re-challenged. Of 10 (5.5%) of patients with LFT> 8 ULN 3 (30%) were re-challenged with ERA. During follow up 87 patients died, of which 2 had LFT > 3 ULN. Data for LFT's was not available for 6 patients who died.
Conclusion: A novel system using pre-packaged boxes with prescribing centre laboratory monitoring and supervision by specialist nursing staff is capable of providing an acceptable level of compliance with recommended LFT monitoring.

P2396
Is there a link between long-term endothelial receptor antagonists therapy and carcinogenesis in PAH: A case series?
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Objective: Endothelial receptor antagonists (ETRAs) are commonly used agents in the treatment of pulmonary arterial hypertension (PAH). Data suggest a carcinogenetic potential of ETRA in animals treated with long-term high dose ETRA. However, there is no such reported data on patients exposed to long-term ETRA therapy. We report our novel data in five PAH patients who developed cancer while on an ETRA.
Material and methods: Retrospective chart review conducted at Baylor College of Medicine from 01/2005 to 12/2010 identified 5 patients who developed cancer while on an ETRA. Demographic data, NYHA/WHO functional class, six-minute walk distance (6MWD), type of cancer, echocardiogram, and survival data was collected.
Results: Mean age was 55.4±8.6 years (Mean±SD). All were female and duration of PAH was 6.80±1.92 years. Mean duration of ETRA therapy was 4.6±0.89 years. Four patients had idiopathic PAH and one patient had connective tissue disease associated PAH. At the time of cancer diagnosis, BNP levels were 123.74±65.3 pg/ml, 6MWD was 390.25±75.3 meters, right ventricular systolic pressure was 83±21.4 mm Hg, RAP was 11±2.23 mm Hg and CO was 4.12±.45 L/min. Follow-up duration after cancer diagnosis was 0.74±1.6 years. One patient developed bronchoalveolar lung cancer, two patients had infiltrating ductal cancer, one had malignant melanoma and one had multiple myeloma. One patient had died while the other four patients are alive at the time of last follow-up.
Conclusion: Carcinogenetic potential of ETRA should be considered in PAH patients who are on long-term ETRA therapy. Further studies are needed to confirm these findings.