no significant difference in compensatory right ventricular hypertrophy when corrected for afterload while the correlation between ventricular mass index (right ventricular mass/left ventricular mass) and pulmonary vascular resistance was stronger in SSc-PAH.

Conclusion The reasons for poorer outcomes in SSc-PAH are likely to be multifactorial including, but not limited to, older age, increased pulmonary arterial stiffness and reduced gas transfer.

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Interventional Trials

S112 LONG-TERM SAFETY AND EFFICACY OF IVACAFTOR IN PAEDIATRIC PATIENTS AGED 2–5 YEARS WITH CYSTIC FIBROSIS AND A CFTR GATING MUTATION

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Background and objectives The 24-week open-label Phase 3 KIWI study demonstrated that the pharmacokinetics and safety of ivacaftor in patients aged 2–5 years with cystic fibrosis and a CFTR gating mutation are similar to those seen in older patients.¹ We report the final results from KLIMB, the long-term open-label extension of KIWI.

Methods Patients who completed KIWI Part B enrolled in KLIMB and received ivacaftor for an additional 84 weeks. Patients aged 2–5 years received weight-based dosing (50 mg q12h for weight < 14 kg; 75 mg q12 h for ≥14 kg); patients who turned 6 received 150 mg q12h. The primary endpoint was safety. Secondary endpoints included change from baseline (at the start of KIWI) in sweat chloride, weight, and body mass index (BMI). Exploratory endpoints included faecal elastase-1 (FE-1) and immunoreactive trypsinogen (IRT) levels.

Results Of 34 patients in KIWI Part B, 33 enrolled in KLIMB (mean age at KLIMB baseline, 3.7 years). Five patients discontinued study drug (1 for elevated alanine transaminase/aspartate transaminase [ALT/AST] levels, 2 switched to commercial ivacaftor, 2 for noncompliance). The most common adverse event (AE) of any grade was cough (73%). Eleven patients had serious AEs; 2 were considered related to ivacaftor (elevated ALT/AST levels). Ten patients had elevated ALT/AST levels > 3 × upper limit of normal (ULN). Of these, 4 had elevated ALT/AST levels > 8 × ULN in KIWI; ivacaftor was maintained or resumed in all patients except 1 who discontinued. Significant improvements in sweat chloride, FE-1 and IRT levels, and BMI z scores were observed at week 84 (Table 1).

Conclusion Ivacaftor demonstrated a stable safety profile during an extended 84-week follow-up period in patients with cystic fibrosis aged 2–5 years with a CFTR gating mutation. Reported AEs were consistent with the known safety profile; the incidence of elevated ALT/AST levels per 24-week period was consistent with that observed in KIWI. The improvements seen in KIWI in sweat

chloride, BMI z score, and measures of pancreatic function were maintained at the end of KLIMB.

Sponsored by Vertex Pharmaceuticals Incorporated

Please refer to page A270 for declarations of interest in relation to abstract S112.

Abstract S112 Table 1 Absolute Change From KIWI Baseline

Mean (SD)	n	KIWI Part B ^{1,2} (Week 24)	n	KLIMB (Week 84 ^a)
Sweat chloride, mmol/L	25	−46.9 (26.6) <i>P</i> < 0.0001	20	−54.7 (26.0) <i>P</i> < 0.0001
FE-1, µg/g	27	99.8 (138.4) <i>P</i> = 0.0009	17	128.8 (170.1) <i>P</i> < 0.01
IRT, ng/mL	25	−20.7 (24.0) <i>P</i> = 0.0002	21	−15.9 (25.2) <i>P</i> < 0.05
Weight-for-age z score	33	0.2 (0.3) <i>P</i> < 0.0001	28	0.2 (0.6) <i>P</i> = 0.1
BMI-for-age z score	32	0.4 (0.4) <i>P</i> < 0.0001	28	0.3 (0.6) <i>P</i> < 0.05
Stature-for-age z score	32	−0.01 (0.3) <i>P</i> = 0.84	28	0.1 (0.4) <i>P</i> = 0.18

^aPatients treated for a total of 108 weeks.

S113 HIGH-DOSE VITAMIN D3 DURING INTENSIVE PHASE TREATMENT OF PULMONARY TUBERCULOSIS IN MONGOLIA: A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL

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Introduction and objectives Existing trials of adjunctive vitamin D to enhance response to antimicrobial therapy for pulmonary tuberculosis are variously limited by relatively small sample sizes, inadequate dosing regimens and low baseline prevalence of vitamin D deficiency among participants. Our objective was to conduct a large randomised controlled trial of high-dose vitamin D in a setting where profound vitamin D deficiency was common in patients with pulmonary TB.

Methods We conducted a double-blind randomised placebo-controlled trial of high-dose adjunctive vitamin D3 in adults with sputum smear-positive pulmonary tuberculosis in Ulaanbaatar, Mongolia. 390 participants were allocated to receive 3.5 mg vitamin D3 (n = 190) or placebo (n = 200) at baseline and at 2, 4 and 6 weeks after starting standard tuberculosis treatment. The primary endpoint of the trial was time from initiation of antimicrobial therapy to sputum culture conversion. Secondary endpoints were time to sputum smear conversion, resolution of infiltrates on chest radiograph and serum 25-hydroxyvitamin D (25[OH]D) concentrations. This trial was registered with ClinicalTrials.gov (NCT01657656).

Results At baseline, 81% of participants had profound vitamin D deficiency (serum 25[OH]D <25 nmol/L). Vitamin D supplementation elevated 8-week serum 25(OH)D concentrations to high-physiological levels (154.5 in intervention arm vs. 15.2 nmol/L in placebo arm, 95% CI: for difference 125.9 to 154.7 nmol/L, *P* < 0.001), but did not influence time to sputum culture conversion (adjusted hazard ratio 1.11, 95% CI: 0.88 to 1.39,

$P = 0.39$). Allocation to vitamin D was associated with accelerated sputum smear conversion (adjusted HR 1.47, 95% CI: 1.09 to 1.98, $P = 0.01$) and a small but statistically significant reduction in the mean number of zones affected on chest radiograph at 8 weeks (5.48 vs. 5.69, 95% CI: for difference 0.06 to 0.77 zones, $p = 0.02$).

Conclusions This is the largest randomised controlled trial to investigate effects of adjunctive vitamin D on time to sputum culture conversion in pulmonary tuberculosis conducted to date. Adjunctive high-dose vitamin D was effective in elevating serum 25(OH)D concentrations to high-physiological levels, but did not influence time to sputum culture conversion.

S114 PREDICTORS OF PRIMARY TREATMENT FAILURE IN CHILDREN WITH EMPYEMA

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Introduction and objectives Empyema is a relatively rare but severe form of respiratory infection in childhood associated with significant morbidity. A decade long prospective observational study of paediatric empyema – the UK-ESPE study – completed recruitment in April 2016. This preliminary analysis focused on identification of predictors of primary treatment failure.

Methods Data were available from 23 UK centres on 542 patients aged 0–16 years, admitted between December 2006 to December 2015, who were diagnosed with empyema and required pleural drainage. A standard logistic regression approach was used to evaluate the influence of age, sex, pre-hospital illness length, total illness length, time from admission to pleural drainage, length of pleural drainage, length of hospital stay, primary treatment modality and co-morbidity on the risk of primary treatment failure. Variables were investigated using univariate analysis and those that were significant were included in a multivariate model. Stepwise removal was then used to generate a parsimonious final multivariate model. The primary outcome measure was treatment failure as defined by a second procedure carried out >24 hours after the primary pleural drainage procedure.

Results The study group was 56% male, median age was 4 years (IQR 2–7). Recorded pre-hospital illness length was a median of 7 days (IQR 4–10) and total hospital length of stay 12 days (IQR 9–16). 34.7% of children had a co-morbidity recorded. Baseline characteristics were similar in children who did ($n = 37$) or did not fail ($n = 505$) primary treatment. There was substantial variation in the choice of primary treatment; chest drainage alone (20.1%), chest drainage with fibrinolytics (58.4%), video-assisted thoracoscopic surgery (12.1%), decortication (8.9%) and other treatments (0.3%). Treatment failure occurred in 6.9% of children and no demographic factor was found to influence treatment failure. The only significant predictor of treatment failure was primary method of treatment (Table). The relative risk of treatment failure was highest in children who received chest drainage alone (OR = 3.04 (95% CI: 1.47–6.27)).

Conclusions In this large cohort no predictors of treatment failure other than primary treatment modality were identified and those who had chest drainage alone had the highest risk of failure.

Abstract S114 Table 1 Parsimonious multivariate model of potential predictors of treatment failure

Covariant	OR	95% CI	P value
Drainage and fibrinolysis	Standard for comparison		
Drainage alone	3.04	1.47–6.27	0.003*
Video-assisted thoracoscopic surgery	1.14	0.32–3.20	0.821
Decortication	1.53×10^{-7}	N/A ¹	0.987
Other procedure	1.53×10^{-7}	N/A ¹	0.987

OR = Odds ratio CI = Confidence interval *p-value > 0.05

¹N/A 95% CI values were too small to compute

S115 HOT-HMV UK TRIAL SECONDARY OUTCOME ANALYSIS: EARLY READMISSION IS REDUCED BY THE ADDITION OF HOME MECHANICAL VENTILATION TO HOME OXYGEN THERAPY IN COPD PATIENTS WITH CHRONIC RESPIRATORY FAILURE FOLLOWING A LIFE-THREATENING EXACERBATION

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Introduction Hospital readmission following treatment for a life-threatening exacerbation of COPD with acute NIV is frequent and associated with an adverse impact in terms of lung function and health related quality of life. They have been identified as a priority area in the NHS with financial penalties for any patient readmitted within 28 days following discharge.

Method A multicentre open labelled randomised controlled trial recruited patients with persistent hypercapnia ($\text{PaCO}_2 > 7 \text{ kPa}$) 2–4 weeks following resolution of acute acidosis. Patients were randomised to either home oxygen therapy (HOT) or HOT and home mechanical ventilation (HOT-HMV). HMV was titrated overnight to control nocturnal hypercapnia. Follow up was for 12 months. The primary outcome, 12-month admission free survival, has been reported previously demonstrating a significant treatment effect (ERS 2016). Secondary outcome analysis included 28-day all-cause hospital readmission and 12 month exacerbation rate.

Results 116 patients were randomised (HOT = 59, HOT-HMV = 57), age 67 ± 10 years, FEV1 $0.6 \pm 0.2 \text{ L}$, PaCO_2 $7.9 \pm 0.9 \text{ kPa}$. 28-day readmission was 22 (37%) in the HOT and 7 (12%) in the HOT-HMV arm (unadjusted HR 0.27, 0.12 to 0.63, $p = 0.003$; adjusted HR 0.26, 0.11 to 0.61, $p = 0.002$) (Figure 1). 12 month exacerbation rate was reduced from median 5 (1 to 9) per year in the HOT arm to 4 (2 to 6) in the HOT-HMV arm (unadjusted HR 0.64 (0.44 to 0.94); $p = 0.022$; adjusted HR 0.66, 0.46 to 0.95, $p = 0.026$).

Conclusion The addition of HMV to HOT in patients with persistent hypercapnia following an acute life-threatening exacerbation of COPD reduces both 28-day readmission and 12 month exacerbation frequency. These data strongly support a change in