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

[1]JC Davies, [2]S Robertson, [3]J Cooke, [3]M Higgins, [4]M Rosenfeld. [1]*Imperial College London and Royal Brompton and Harefield NHS Foundation Trust, London, UK*; [2]*Vertex Pharmaceuticals Incorporated, Boston, MA, USA*; [3]*Vertex Pharmaceuticals (Europe) Limited, London, UK*; [4]*Seattle Children's Hospital, Seattle, WA, USA*

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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.

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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)	20	−54.7 (26.0)
		$P < 0.0001$		$P < 0.0001$
FE-1, µg/g	27	99.8 (138.4)	17	128.8 (170.1)
		$P = 0.0009$		$P < 0.01$
IRT, ng/mL	25	−20.7 (24.0)	21	−15.9 (25.2)
		$P = 0.0002$		$P < 0.05$
Weight-for-age *z* score	33	0.2 (0.3)	28	0.2 (0.6)
		$P < 0.0001$		$P = 0.1$
BMI-for-age *z* score	32	0.4 (0.4)	28	0.3 (0.6)
		$P < 0.0001$		$P < 0.05$
Stature-for-age *z* score	32	−0.01 (0.3)	28	0.1 (0.4)
		$P = 0.84$		$P = 0.18$

[a]Patients 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

[1]D Ganmaa, [2]B Munkhsul, [1]S Bromage, [2]B Buyankhishig, [3]AR Martineau. [1]*Harvard School of Public Health, Boston, USA*; [2]*National Centre for Communicable Disease, Ulaanbaatar, Mongolia*; [3]*Queen Mary University of London, London, UK*

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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,