Lung function and structure in CF infants diagnosed through newborn screening (NBS)

L.P. Thia1, A. Calder2, C. Owens2, A.F. Hoo3, T.T.D. Nguyen1, C. Wallis3, A. Bush5, J. Stocks1, London Cystic Fibrosis Collaboration. 1University College London, Institute of Child Health, Portex Respiratory Unit, London, United Kingdom; 2Great Ormond Street Hospital for Children, Paediatric Radiology, London, United Kingdom; 3Great Ormond Street Hospital for Children, Respiratory Unit, London, United Kingdom; 4Royal Brompton Hospital, Respiratory Unit, London, United Kingdom

Introduction: Computed tomography (CT) of chest is increasingly used as a sensitive measure of early lung disease in CF children; showing correlation between Brody-II CT scores and pulmonary function tests (PFTs) with greatest correlation seen in lung clearance index (LCI) [1,2]. This relationship has yet to be established during infancy.

Aim: To explore the relationship between PFTs and CT scans in NBS CF infants.

Method: CF infants underwent PFTs at ~1 year old, followed by volumetric inspiratory and expiratory high resolution CT scan of the chest under general anaesthesia within 2 weeks of the PFTs. Scans were anonymised and scored using Brody-II.

Results: Of 62 CF infants tested, 16% (10/61) had elevated LCI, 15% (9/60) elevated plethysmographic lung volume and 17% (10/59) diminished forced expiratory volume or flow. Bronchial dilatation present in 8% (5/62) of the HRCT scans. Although gas trapping was seen in 24% (15/62), only 2% had significant involvement. Total CT score was not correlated with LCI or forced expiratory volumes and flows. Gas trapping sub-score revealed significant but weak correlation with LCI (Spearman correlation, R = 0.3).

Conclusions: In early infancy, few abnormalities were detected by CT with minimal correlation to lung function. Further study is required to establish the evidence for routine use of CT in monitoring early lung disease in CF infants diagnosed through NBS.

Reference(s)

Effect of ivacaftor on lung function in subjects with CF who have the G551D-CFTR mutation and mild lung disease: a comparison of lung clearance index (LCI) vs. spirometry

J.C. Davies1,2, H. Sheridan1, P.-S. Lee4, T. Song4, A. Stone4, F. Ratjen5, on behalf of the VX10–770–106 Study Group. 1Royal Brompton Hospital, London, United Kingdom; 2Imperial College, London, United Kingdom; 3University of Edinburgh, Edinburgh, United Kingdom; 4Vertex Pharmaceuticals Incorporated, Cambridge, United States; 5The Hospital for Sick Children, Toronto, Canada

Objectives: It can be difficult to demonstrate that drugs targeting CFTR benefit patients with mild disease. If FEV1 is in the normal range, it may be of limited value. A more sensitive test such as LCI may be useful.

Methods: This Phase 2, randomized, double-blind, placebo-controlled, multicenter, crossover study evaluated the effect of ivacaftor on LCI derived from multibreath washout of SF6 using an Innocor device. Subjects were ⩾6 years with the G551D-CFTR mutation, FEV1 >90% predicted, and LCI >7.4 (the upper limit of normal). Ivacaftor 150 mg or placebo was administered q12h for two 4-week periods with a 4-week washout in between. Enrollment is complete (n=21); results reported here are from the interim analysis of the first 7 subjects to have completed both periods.

Results: Mean (SD) age was 14.0 (8.6) years. Mean (SD) baseline LCI was 9.2 (1.9). The treatment effect of ivacaftor for adjusted mean change from baseline in LCI at Day 29 was −2.22 (P=0.0097). Mean (SD) baseline FEV1 was 98.5% predicted (6.4%). The treatment difference for the mean change from baseline in FEV1 was 7.2% (P=0.1264). The treatment difference for the mean change from baseline in sweat chloride was −48.3 mmol/L (P=0.0086). 6 subjects reported AEs in the ivacaftor period vs. 5 in the placebo period. 1 SAE was reported (constipation).

Conclusions: Treatment with ivacaftor significantly improved LCI. Trends were seen for FEV1, but these were not statistically significant. These preliminary results suggest that LCI is more sensitive than FEV1 in detecting treatment effect among CF subjects with minimal lung disease and should be considered as an endpoint in future trials.

Sponsored by Vertex