Clinical Outcomes of Real-World Kalydeco (CORK) study – Investigating the impact of CFTR potentiation on the intestinal microbiota, exocrine pancreatic function and intestinal inflammation prospectively over 12 months

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Objectives: Ivacaftor is effective in the treatment of patients with CF and the G551D gating mutation. We present faecal analysis results of the CORK cohort, a single-centre, adult (n = 20), prospective, longitudinal study of G551D clinical responders (median follow-up 12 months), examining the gut microbiota, exocrine pancreatic function and intestinal inflammation on a 3 monthly basis after commencing treatment.

Methods: Stool samples pre- and 3 monthly post commencement of ivacaftor in 20 adult patients underwent metagenomic profiling of faecal microbiota. Faecal elastase-1 (FE-1), faecal calprotectin (FC) and faecal lactoferrin (FL) were measured using commercially available ELISA kits.

Results: Ivacaftor did not significantly alter gut microbial diversity, as measured by chao1 (p = 0.886). At phylum, family and genus levels significant increases were observed in Bacteroidetes (p = 0.048), Bacteroidaceae (p = 0.021) and Bacteroides (p = 0.021). Significant decreases were observed in Microbacteriaceae (p = 0.003) and Enterobacteriaceae (p = 0.014). A positive significant correlation was seen between FE1, and gut microbiota diversity following treatment (r = 0.4, p = 0.002). No significant difference was measured in levels of FE-1 (p = 0.267), FC (p = 0.496) or FL (p = 0.779).

Conclusion: Ivacaftor therapy has a normalisation effect on the gut microbiota, directing the microbiota towards a non-CF profile. Despite this elevated intestinal inflammation. Lack of exocrine pancreatic recovery may reflect established exocrine pancreatic dysfunction in an adult cohort. On-going longitudinal prospective data may demonstrate further improvements in the gut health of this cohort.

Oral Presentations

WS16.2 The prevalence of gastro-oesophageal reflux disease in infants with cystic fibrosis diagnosed by newborn screening and the relationship with lung infection

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Gastro-oesophageal reflux disease (GORD) has been implicated in the respiratory symptoms of CF. Studies in small populations suggest GORD may be present in up to 40% of these infants.

Aim: To describe the prevalence of GORD in a large cohort of infants with CF diagnosed by NBS. The secondary aim was to look for an association with bacterial infection.

Methods: Our NBS surveillance programme includes a 24 hr dual probe pH study and BAL for microbiology. Results were collected on infants over a 6 year period. GORD was diagnosed using ENSPHAG criteria: corrected reflux index (RI) >12%, reflux episodes >72, length of longest reflux episode >41 minutes. An association between GORD and positive bacterial samples was explored.

Results: Infants: n = 117, median age: 4.1 months (range 1.8–9.7 mo), 57 males (48%), 15 pancreatic insufficient (13%). 103 had valid pH studies (88%). RI >12% n = 44 (43%), reflux episodes >72 n = 55 (53%), reflux episodes >41 min n = 2. Positive bacteria at BAL n = 29%. Including: PA = 3, SA = 8, H1 = 5, coliforms = 7, other = 8 (some with mixed growths). There was no statistical difference in bacteria between those with and without GORD. There was a significant difference in wt z score -0.98 vs -0.2 p = 0.02. A scatter plot showed no significant reduction in RI with age.

Discussion: This large study confirms the high prevalence of GORD in infants with CF which was RI above 43%, the true prevalence may be higher. 53% showed an abnormally high number of reflux episodes. No association with bacterial infection was found.

In conclusion: GORD appears more prevalent than thought in infants with CF and the significantly lower weight in this group needs further exploration.

WS16.3 Consecutive transient elastography measurements to detect cystic fibrosis liver disease

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Background: Cystic fibrosis (CF) related liver disease (CFLD) is diagnosed using a combination of criteria. Transient elastography (TE) (ultrasoundographic method evaluating liver stiffness) differentiates CF patients with and without liver disease (CFLD) and identifies patients with an increased risk for portal hypertension.

Aim: Detect evolving CFLD using TE measurements.

Method: Retrospective study (2007–2013) including all patients with TE measurements, performed by the same operator. Measurement was correlated to the presence or development of CFLD based on the medical files.

Results: 150 CF patients [median age 17 (9–24) years] were included, 118 with repeated TE: 20 (14%) had CFLD at the first TE measurement, 4 (3%) developed CFLD during follow-up. The median TE value in CFLD was 14 (8.9–32.2) compared to 5.3 (4.9–5.7) in CF no LD (P = 0.0001). The intra-individual differences between 2 consecutive measurements [median interval between measurements 1 yr (1–2)] was 0.05 (–1.1, 1.2) in CF no LD and 0.55 (–1.68, 1.53) in the CFLD patients. The area under the receiver operating curve for TE predicting CFLD was 0.985. TE measurements above 6.53 kPa predicted CFLD with a specificity of 94.7% and a specificity of 90.8% according to the AUROC. In CF <14 years a TE measurement above 6.5 kPa had a positive predictive value of 83%, decreasing to 60% for the total group and a negative predictive value of 100%. Patients with developing CFLD had progressively increasing TE measurements.

Conclusion: TE measurements progressively increased in CF patients developing CFLD. A prospective study is needed to evaluate whether TE will be able to detect CFLD before it becomes clinically apparent.