## 36 The effect of ivacaftor therapy on clinical and PCR-identified microbial diversity of cystic fibrosis lung infection

H. Green[1,2], C. Paisey[3], A. Smith[3], P. Barry[1], W. Flight[1], A. Jones[1,2], J. Marchesi[3], A. Horsley[1,2], E. Mahenthiralingam[3]. [1]*University Hospital of South Manchester NHS Foundation Trust, Manchester Adult Cystic Fibrosis Centre, Manchester, United Kingdom;* [2]*University of Manchester, Institute of Inflammation and Repair, Manchester, United Kingdom;* [3]*Cardiff University, Cardiff School of Biosciences, Cardiff, United Kingdom*

**Objectives:** Ivacaftor is licensed for CF patients with the G551D mutation. Clinical benefits of ivacaftor have been demonstrated, but its impact on microbial diversity of chronic lung infection has not. The aim of this study was to investigate whether expected rapid improvement in FEV1 from restoring CFTR function using ivacaftor is associated with early changes in airway microbiology.
**Methods:** Paired sputum samples were obtained from 13 of 14 recruited adult CF patients immediately prior to ivacaftor therapy, and after 1 and/or 3 months of treatment. Samples underwent routine microbiology, and extraction of total nucleic acids using a standardised automated method. Ribosomal Intergenic Spacer Analysis (RISA) qualitatively investigated sputum bacterial diversity and 16s rRNA gene pyrosequencing used for detailed analysis. FEV1 was measured at each visit, and sweat chloride (a marker of CFTR function) was assessed pre-treatment and at 2 months.
**Results:** 10 of 14 subjects had samples at all three timepoints. Mean FEV1 percent predicted improved from 56 to 63% at 1 month ($p < 0.01$). Mean sweat chloride improved from 115 to 54 mmol/L ($p < 0.01$). Culture, RISA and pyrosequencing analysis demonstrated no major changes in microbial diversity, especially with regards to the dominant pathogen, pre- and post-treatment. However, 10 patients had a reduction in the number pyrosequencing reads attributable to *Streptococcus* for the 3 month samples ($p < 0.05$).
**Conclusion:** Airway microbiology was largely unaltered in the 3 months after starting ivacaftor. These findings suggest that the improvement of FEV1 seen is not due to changes in airway pathogens.

## 37 Clinical outcomes of real world Kalydeco (CORK) study

N.J. Ronan[1,2], G. O'Callaghan[1,2], M.J. Harrison[1,2], C. Shortt[1], M. McCarthy[1], C. Hickey[1], C. Fleming[1], K. Cronin[1], R. Jennings[1], D. O'Donovan[1], P. Shanahan[1], M. Ni Chroinin[1], D.M. Murphy[1,2], D. Mullane[1], B.J. Plant[1,2]. [1]*Cork Cystic Fibrosis Centre, Cork University Hospital, Cork, Ireland;* [2]*HRB Clinical Research Facility, University College Cork, Cork, Ireland*

**Objectives:** Ivacaftor (Kalydeco™) produces significant benefit in patients with cystic fibrosis with the G551D mutation. Cork University Hospital (CUH) has the highest worldwide prevalence for this mutation at 21% making it uniquely placed to provide single centre insight into real world response to treatment.
**Methods:** With Irish reimbursement of ivacaftor resolved in March 2013, 29 ivacaftor-naive patients with cystic fibrosis (age $\geqslant 6$) consented and completed 6 months prospective routine clinical quarterly follow up where change pre and post ivacaftor were recorded.
**Results:** At 3 months a significant absolute improvement in mean FEV1 percent predicted of 10.35% ($P < 0.001$), 2.73 kg mean increase in weight ($P < 0.001$), 0.83 kg/m$^2$ increase in BMI ($P < 0.001$), 57.97 mmol/l mean reduction in sweat chloride ($P < 0.001$) and a 147.4 metre increase in walk test ($P = 0.001$) were observed. Benefits were maintained at 6 months. CFQ-R increased for respiratory (mean 16.55, $P = 0.005$), weight (mean 31.1, $P = 0.019$), and body image (mean 17.79, $P = 0.009$) domains at 3 months. Improvements were significantly maintained at 6 months. Care givers completed care-giver CFQ-R for patients younger than 14 years with similar results. There was a significant reduction in the likelihood of requiring intravenous antibiotics (Relative Risk = 0.069, CI 0.001 to 0.49) in the 6 months post-Ivacaftor compared to the corresponding 6 month period pre-Ivacaftor.
**Conclusion:** In a large single centre cohort with the G551D mutation we report real world sustained efficacy, tolerability and satisfaction with ivacaftor at 6 months.

## 38 Cayston® in clinical practice – experiences from a UK adult CF unit

E.A. Lloyd[1], R. Sapina-Vivo[1], M. Jackson[1], E. Spencer-Clegg[1], M. Walshaw[1], C. Whitty[1]. [1]*Adult CF Unit, Liverpool Heart & Chest Hospital NHS FT, Liverpool, United Kingdom*

**Objectives:** Aztreonam lysine (Cayston®) was funded by NHS England as a third-line inhalation antibiotic in February 2013, and since then we have used it in selected adult CF patients who fulfil the prescription protocol. We report our experience with this expensive drug to date.
**Method:** We reviewed clinical parameters including lung function, other inhaled antibiotics used, use of IV antibiotics, adherence to treatment (from pharmacy dispensing records), and patient reported outcomes (PROM).
**Results:** Following a test dose, 24 patients (mean FEV1 34.7% predicted [range 17–77], 8.4% of our clinic) commenced Cayston®. However, 3 developed subsequent chest tightness and stopped the medication (at 3–21 days), and a further 3 have died. 14 alternate with inhaled tobramycin, 3 with colomycin, and 2 use it alone. For 8 patients with more than 6 months data, 6 have improved spirometry and 7 a reduction in the requirement for IV therapy. Pharmacy dispensing records show high adherence to collection. 19/24 completed a PROM. Whilst only 1 reported a significant decrease in sputum or breathlessness, all report feeling better in the Cayston® month. Only minimal side effects are reported from the 19 who continue to use, mainly cough. All 8 in the >6 month group report an improved quality of life reflected in increased or stabilised FEV1 and reduction in IV days.
**Conclusions:** Cayston® seems to be a well-tolerated medication which has improved the clinical state of a selected group of our adult CF patients and improved their quality of life. We will continue to monitor the use of this expensive therapy in our clinic.

## 39 'Real world' tolerability, ease of use, patient satisfaction and reported adherence in CF adults commencing Colobreathe®

S. Cameron[1], J. Choyce[1], B. Ahitan[1], C. Brown[1], R. Rashid[1], J.L. Whitehouse[1], E.F. Nash[1]. [1]*West Midlands Adult Cystic Fibrosis Centre, Heart of England NHS Foundation Trust, Birmingham, United Kingdom*

**Objectives:** Colobreathe® dry powder inhaler (CSDPI) is a new inhaled formulation of colistimethate sodium, recently introduced for CF patients infected with *P. aeruginosa*. We conducted this study to assess our initial clinical experience with CSDPI at a large regional UK adult CF centre.
**Methods:** Demographics and reason for switching to CSDPI were recorded at test dose. Spirometry and side effects were recorded at test dose and 1-month review. Patients rated: ease of use, time taken, satisfaction, effectiveness and estimated adherence to nebulised colistimethate sodium (NCS) compared with CSDPI, as well as their likelihood to continue with CSDPI and their treatment preference.
**Results:** 13 patients (6 male) with median age 33 yrs, $FEV_1$ 63% predicted were recruited. 8 patients trialled CSDPI due to intolerance of NCS (INTOL group) and 5 patients due to poor adherence to NCS (ADH group). At 1-month review, 6/8 patients in the INTOL group successfully tolerated CSDPI and planned to continue. In the ADH group, reported adherence at 1-month review was higher with CSDPI (median 100% of doses) compared with NCS (50% of doses, $p = 0.02$). Combining both groups, $FEV_1$ did not change from baseline to 1-month visits ($p = 0.4$). CSDPI was reported to be easier to use than NCS, less time consuming and all patients, despite some initial reports of device functioning issues, expressed a preference for CSDPI.
**Conclusion:** Early 'real world' evidence suggests that CSDPI is well tolerated, easier to use, less inconvenient and associated with improved adherence. Longer-term outcomes are needed to assess whether these benefits are maintained and are associated with improved clinical outcomes.