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LUMACAFTOR/IVACAFTOR IS ASSOCIATED WITH HIGH DISCONTINUATION RATES IN PATIENTS WITH BASELINE SEVERE LUNG FUNCTION BUT ALSO BENEFITS IN THOSE WHO TOLERATE THERAPY

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10.1136/thoraxjnl-2017-210983.389

Lumacافتor/ivacافتor (LUM/IVA) is a combination CFTR modulator which is licensed for patients with cystic fibrosis homozygous for the Phe508del mutation. In clinical trials, use of LUM/IVA resulted in modest improvements in lung function, a reduction in pulmonary exacerbations and small increases in nutritional parameters. Although these trials excluded patients with FEV1 <40%, licensing does not restrict therapy on this basis. In the UK, LUM/IVA is only available on a managed access programme for patients with low lung function. We aimed to examine the safety, tolerability and effectiveness of LUM/IVA in patients with severe lung disease. 32 patients were admitted to commence LUM/IVA and 8 (25%) permanently discontinued therapy. One patient successfully recommenced therapy after discontinuation. Adverse event rate was 88%, with 87% related to respiratory symptoms. Therapy initiation was associated with significant relative falls in both FEV1 ($-14 \pm 11.6\%$) and FVC ($-11.6 \pm 13.1\%$) at 24 hours. A significant increase in CRP (mg/L) was identified at both day 3 [18 (7–40) $p < 0.001$] and day 7 [16.5 (5–49), $p = 0.038$] compared to baseline [7.5 (4–18.8)]. Those patients who discontinued therapy had a higher increase in CRP at day 3 ($p = 0.01$), a lower baseline pO₂ ($p = 0.013$) in the preceding year, and were more likely to complain of dyspnoea ($p = 0.017$). For those who continued therapy, FEV1 increased compared to day 0 values ($32.0\% \pm 6.9\%$ v. $29.5\% \pm 6.7\%$, $p = 0.01$) but not compared to best FEV1 in the preceding 3 months ($31.1\% \pm 6.5\%$, $p = 0.23$). A 2 kg increase in weight from day 0 was identified in those who continued LUM/IVA ($p < 0.001$). In 14 patients who had at least 6 months therapy there was a reduction in the annualised rate of pulmonary exacerbations requiring iv antibiotics compared to the preceding year (3.2 ± 2.8 v. 5.2 ± 2.5 , $p = 0.001$) and days on iv antibiotics (47 ± 33 v. 69 ± 39 , $p = 0.026$). We report a very high adverse events rate associated with the initiation of LUM/IVA which was associated with adverse changes in objective markers. In those who tolerate therapy benefits may be similar to those reported in clinical trials.

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CFRD IS NOT AN INDEPENDENT RISK FACTOR FOR STENOTROPHOMONAS MALTOPHILIA ACQUISITION – 5 YEAR ANALYSIS OF UK CF REGISTRY DATA

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10.1136/thoraxjnl-2017-210983.390

Introduction Recently, *Stenotrophomonas maltophilia* (SM) has been shown to have an increased prevalence in the sputum of

people with CF-related diabetes (CFRD), raising the question as to whether CFRD is a risk factor for its acquisition. We investigated this at a population level by looking at UK CF Registry data.

Methods We analysed national UK CF Registry data for 2011–2015, looking at demographics, lung function and sputum microbiology, using descriptive and multivariable strategies to establish independent predictors for SM culture and associated outcomes. 6234 people with CF older than age 12 (mean 26 years, CFRD 26%, SM 15%, 54% male) with more than 3 years complete sputum microbiology and lung function data were included.

Results Although on univariate analysis those with SM were more likely to have CFRD (odds ratio [95% CI] 1.18 [1.01–1.39] $p < 0.0001$), lower lung function (mean FEV1 [% predicted] 66.6 vs. 74.15, $p < 0.001$) and more IV days (24 vs. 10, $p < 0.0001$), multivariate logistic regression analysis showed no independent association for CFRD or Hba1c but IV antibiotic use and *Aspergillus* culture independently demonstrated an increased likelihood of SM growth (see Table 1). Furthermore, longevity of SM growth showed weak but statistically significant correlations with poorer FEV1 ($\rho = -0.2$, $p < 0.0001$) and more IV days ($\rho = 0.1$, $p < 0.0001$) but no association with CFRD (OR 1.09 [0.98–1.21]) or Hba1c ($\rho = -0.001$, $p = 0.94$).

Conclusion Our data suggests CFRD is not an independent risk factor for SM growth in CF. The increased prevalence of SM in CFRD may be explained by increased intravenous antibiotic pressure in this group.

Acknowledgement We would like to thank the CF Registry Research Committee for releasing the data used in this analysis.

Abstract P248 Table 1 Multivariate analysis of potential predictors of SM growth

Variable	Odds Ratio (95% CI)	
Age (years)	0.99 (0.98–1.00)	NS
>18		
FEV1 (% predicted)	1.22 (0.92–1.64)	NS
<50	1.28 (0.82–2.01)	NS
<30		
IV antibiotics (days/year)	0.41 (0.31–0.52)	***
0	1.46 (1.05–2.02)	***
>0	1.64 (1.06–2.23)	**
>14		
Dysglycaemia	1.08 (0.80–1.46)	NS
CFRD	0.98 (0.62–1.58)	NS
Hba1c >48		
Microbiology		
<i>Pseudomonas aeruginosa</i>	0.69 (0.55–0.87)	**
<i>Aspergillus</i>	3.76 (2.93–4.82)	***
<i>Burkholderia Cepacia Complex</i>	0.59 (0.34–1.03)	1.46 (1.18–1.83) NS **
<i>Staphylococcus aureus</i>		

NS=not statistically significant *= <0.05 **= <0.01 ***= <0.001