CLINICAL OUTCOMES OF ASPERGILLUS DISEASE MANAGEMENT IN ADULT CYSTIC FIBROSIS PATIENTS

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Objectives Aspergillus disease in cystic fibrosis (CF) patients has been proposed to encompass 4 classes: Class 1; No disease, Class 2; Allergic Bronchopulmonary Aspergillosis (ABPA), Class 3; Aspergillus sensitised, Class 4; Aspergillus Bronchitis. The clinical consequence of non-ABPA Aspergillus disease in CF is not fully understood. We evaluated the survival of patients with different classes of Aspergillus disease who were diagnosed as part of Baxter’s work between 2008–2011 in order to determine the clinical consequences of the different phenotypes of disease.

Methods A retrospective case note analysis was undertaken for all 129 patients from the Baxter et al. patient cohort. Survival outcomes were documented for all patients, and baseline demographics including age, gender, FEV1, BMI and co-pathogens were collected. Any patients who received double lung transplantation or who moved away from the unit during this time were identified. The best FEV1 for each year of follow up, FEV1 closest to annual consent date, and BMI were collected. There was no statistical significance in survival rates for normality and between group comparisons were calculated using one-way anova. Survival was assessed with Kaplan Meier monitoring and reclassify disease phenotype in this patient population. LUM/IVA was associated with improved BMI and maintenance of lung function.

Results There was no statistical significance in survival rates between the 4 classes of Aspergillus disease (P value 0.521). The sole predictor of survival was baseline FEV1% predicted at time of diagnosis (P value<0.001).

Conclusions There was no statistically significant difference in survival for CF patients with Aspergillus disease over 6–8 years follow up. Further work is being undertaken to continue monitoring and reclassify disease phenotype in this patient cohort.

REFERENCE

AN OPEN-LABEL EXTENSION (EXT) STUDY OF LUMACAFTOR/IVACAFTOR (LUM/IVA) THERAPY IN PATIENTS AGED 6 TO 11 YEARS WITH CYSTIC FIBROSIS (CF) HOMOZYGOUS FOR F508DEL-CFTR

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Objective Lumacaftor/ivacaftor (LUM/IVA) was well tolerated and had beneficial effects on lung function, sweat chloride (SwCl), and body mass index (BMI) in a 24 week, open-label study (VX15–809–011B [011B]) in patients aged 6 to 11 years with cystic fibrosis (CF) homozygous for F508del. We report 36 weeks of additional safety and efficacy data in an ongoing 96 week extension (EXT) study (VX15–809–110; NCT02544451).

Methods Eligible patients from 011B received LUM 200 mg/IVA 250 mg every 12 hours (q12h; 6–11 years) or LUM 400 mg/IVA 250 mg q12h (>12 years). Primary endpoint was safety. Secondary endpoints included changes in SwCl and lung clearance index based on lung volume turnover required to reach 2.5% of starting N2 concentration (LCI2.5) through week 24, and BMI and percent predicted FEV1 (ppFEV1) through week 36.

Results Of the 49 enrolled patients (mean age [SD], 9.2 [1.48] years), 47 completed 36 weeks of the EXT study. Adverse events (AEs) were reported in 91.8% of patients (34.7% mild; 49.0% moderate). Common AEs (cough, n=18; infective pulmonary exacerbation, n=18) were consistent with expected CF manifestations. Eight (16.3%) patients had serious AEs. Four (8.2%) patients had ≥1 respiratory AE (2 wheezing; 1 bronchial hyper-reactivity; 1 dyspnea; 1 respiration abnormal). Six (12.2%) patients had elevated alanine aminotransferase or aspartate aminotransferase (>3 to 5×upper limit of normal [ULN], n=3; ≥5 to 8×ULN, n=1; ≤8×ULN, n=2). No drug discontinuations were due to AEs. Changes from 011B baseline (BL) in ppFEV1, and SwCl were similar to those at 011B week 24 (Table). BMI continued to improve. LCI2.5 improvements were stable through EXT week 4 (n=18); values at EXT week 24 in a reduced sample size (n=12) were similar to those at 011B BL.

Conclusion LUM/IVA was well tolerated for up to 60 weeks in patients aged 6 to 11 years, with no new safety concerns compared with previous LUM/IVA studies conducted in this patient population. LUM/IVA was associated with improved BMI and maintenance of lung function.

Please refer to page A257 for declarations of interest in relation to abstract S96.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study 011B baseline, mean (SD)</th>
<th>Absolute change from 011B baseline with LUM/IVA, mean (SD)</th>
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<tr>
<td></td>
<td>Study 011B wk 24</td>
<td>EXT wk 4</td>
</tr>
<tr>
<td>ppFEV1% predicted at time of diagnosis</td>
<td>91.4 (13.7) n=57</td>
<td>2.4 (10.2)</td>
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<td>BMI, kg/m²</td>
<td>16.89 (1.93) n=58</td>
<td>0.65 (0.69)</td>
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<td>SwCl, mmol/L</td>
<td>105.9 (10.2) n=58</td>
<td>−25.6</td>
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<tr>
<td>LCI2.5</td>
<td>9.99 (2.67) n=25</td>
<td>−0.95</td>
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</tbody>
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Improvements in lung cancer treatment

MANAGEMENT OF EARLY STAGE LUNG CANCER IN THE ELDERLY: AN OBSERVATIONAL STUDY

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Introduction  Elderly patients are less likely to receive radical treatment for lung cancer. Palma et al (2010) demonstrated an increase in radical treatment rates for patients aged ≥75 years in Holland following the introduction of Stereotactic Ablative Radiotherapy (SABR), without reduction in surgical resections. This was associated with improved overall survival. There are international differences in radical treatment rates and outcomes in lung cancer. We aim to evaluate the changes in lung cancer treatment and outcomes following the introduction of SABR in the UK.

Methods This is a retrospective observational study at a large UK teaching hospital. Data for patients diagnosed over seven years (2008–2014) were analysed from a local dataset maintained for the National Lung Cancer Audit. SABR was introduced for lung cancer in Leeds in 2010. Statistical analyses were performed using Chi-square, t-test and Kaplan Meier survival analysis.

Results There were 1874 new diagnoses of lung cancer in patients aged ≥75 years, accounting for 45.3% of all new diagnoses. Comparing patients ≥75 years pre-SABR (2008–2009) and post-SABR (2011–2014), there was an increase in the proportion of early stage disease (stage I-IIA 22.5% to 29.2%, p=0.0054). Of the 502 patients with early stage disease, there was no change in performance status (PS 0%–2 68.4% to 63.3%, p=0.2468) or age at diagnosis (median (IQR) 81.1 (78.0–84.3) to 80.9 (77.7–85.1) years, p=0.7422).

Rates of radical radiotherapy/SABR (12.2% to 39.2%, p<0.001) have increased, while surgical resections (28.9% to 28.5%, p=1.000) have remained stable and the proportion of patients receiving palliative treatment/best supportive care (BSC) has decreased (58.8% to 32.3%, p<0.001) (figure 1). Median overall survival has increased (518 to 687 days, p=0.0016).

Discussion The proportion of elderly patients being diagnosed with early stage lung cancer is increasing. There has been no significant change in the demographics of those with early stage disease. Following the introduction of SABR in 2010, there has been an increase in radical radiotherapy treatment for elderly patients with early stage disease, with no sustained change in surgical resection rates and increase in overall rates of radical treatment. This was associated with a significant improvement in overall survival.

Abstract S97 Figure 1 Treatment of stage I-IIA lung cancer in patients ≥75 years.