Late-breaking abstract: VX-770, an investigational CFTR potentiator, in subjects with CF and the G551D mutation

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Introduction: Preschool and school aged children with CF have been reported to show an elevated lung clearance index (LCI), which further increases in the presence of Pseudomonas aeruginosa infection. In contrast, increased LCI is less prevalent in infants with CF. The aim of this study was to assess the impact of pulmonary infection and the presence of free neutrophil elastase (NE) as a marker for airway inflammation, on ventilation distribution in infants and children ≤ 2 years with CF.

Methods: Multiple breath washout (MBW) using 5% SF6 and an ultrasonic flowmeter (Ecomedics, Switzerland) was performed 1-3 days prior to bronchoalveolar lavage (BAL) in 85 children. LCI and the 1st and 2nd moment ratio (M1/M0 and M2/M0) were determined from the washout. Generalised estimating equations with exchangeable working correlation structure were used to estimate linear regression coefficients. Adjustments were made for sex, height and functional residual capacity.

Results: The presence of a pulmonary infection (n=13; ≥105 cfu.ml−1) had no impact on LCI (p=0.355), but did result in increased M1/M0 (p=0.027) and M2/M0 (p=0.052) when compared to un-infected infants (n=36). Children with P. aeruginosa (n=4) colonisation showed no altered MBW outcomes when compared to the un-infected group. Similarly, the presence of NE (n=14) was not associated with altered MBW outcomes

Conclusion: LCI in this group of children was not a sensitive measure of CF lung disease as indicated by free NE or endobronchial infection. Moment ratios appear to be more sensitive to lung disease associated with infection than LCI.

Comparison of cystic fibrosis structural lung disease detected by inspiratory and expiratory chest CT scans in infants and preschool children

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Introduction: Chest computed tomography (CT) reveals early cystic fibrosis (CF) structural lung disease. Typically, bronchiectasis (Bx) is assessed on inspiration and gas trapping on expiration, but in older children inspiratory scans reliably detect both, reducing radiation exposure.

Objective: To compare the presence and extent of CF structural lung disease detected on volumetric inspiratory and expiratory scans in young children.

Methods: 38 children with CF age 1-5 years underwent inspiratory and expiratory volumetric chest CT. De-identified scans were assessed in random order by 2 observers using the Brody II score. Intra-class correlation coefficients (ICC) and Bland-Altman plots using mean scores determined agreement between expiratory and inspiratory scans.

Results: There was substantial agreement between mean Brody II component scores from inspiratory and expiratory scans (ICC range 0.637 to 0.866). For Bx, the ICC was 0.864, however, there was a systematic bias evident on Bland-Altman plot as shown, with consistently higher scores on inspiration. Further, analysis of binary outcomes (presence/absence of Bx) indicated that Bx was not demonstrated...
What is the significance of *Aspergillus fumigatus* in BAL in children with disease. Supported by Mukoviszidose e.V.

Little is known about the onset and spontaneous progression and routine lung function testing is not available for monitoring of early CF lung disease. The aim of the present study was to validate pulmonary MRI to study the onset and progression of lung disease in infants and young children with CF.

In 34 CF patients (age: 2.5±0.4; 17m) MRI (1.5T) was performed in free breathing. For morphological imaging a T2w (HASTE PACE) and a T1w T1-TSE sequences pre and post contrast media in coronal and transversal orientation were used. Functional imaging was performed using a 3D-FLASH-sequence with a temporal resolution of 1.5s after iv injection of Gadolinium-DTPA. Two independent radiologists analyzed the images with a dedicated MRI score (range 0-72).

Morphological and functional abnormalities in the CF lung were detected by MRI in the first year of life (MRI score 6.3±1.1; n=6) and the score increased significantly to 16.2±1.7 (p<0.05; n=5) at the age of 4 years. Perfusion defects were reversible in follow up scans in a substantial number of patients. Further, MRI scores were reduced after antibiotic therapy for pulmonary exacerbations (pre treatment: 20.2±2.7vs post treatment: 13.0±4.9; p<0.05).

Our study indicates that MRI of the lung is sensitive to detect abnormal morphology, function and response to therapy in early CF lung disease. These results add to the growing evidence that *AF* in the airways of children with CF is associated with a worse clinical state, whether identified on direct smear or culture.

Conclusions: In early CF Bxs, the presence and extent of Bxs is underestimated with inspiratory scans alone compared with inspiratory scans.
We use PET since 2006 and EBUS since October 2008. 75% of patients didn’t need hospitalization. The mean days, when needed, was 3.1 (IQR). Patients required surgical treatment in 22.8%, oncologic in 68.5% and Palliative Care as first choice in 8.7%. Average delay from PC* to treatment was 37.4 days (5-103) and from RDPfv to treatment was 31.4 days (0-90).

**Conclusions:** With our RDP we have achieved a lower time delay to diagnosis and treatment (no difference between kind of treatment) of LC comparing with most of the existing recommendations.

We haven’t need hospitalization in most cases and the mean of days was low.

**Table 1**

| PC*—RDPfv | 70 | 6 |
| RDPfv—CTC | 70 | 6.8 |
| RDPfv—Bronch. | 51 | 9.7 |
| RDPfv—TFFNA | 20 | 19.4 |
| RDPfv—TFFNA | 4 | 22.2 |
| RDPfv—FNA | 1 | 21 |
| RDPfv—PET | 33 | 17.4 |
| RDPfv—EBUS | 9 | 19.7 |

**4671 Self reporting of symptoms and delays in patients presenting to a rapid access lung cancer clinic (RALCC)**

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**Introduction:** The RALCC at our hospital is aimed at expediting the diagnosis of suspected thoracic malignancies.

**Methods:** A self-reported questionnaire to consecutive patients on their first visit. Patients perception of why they were attending, symptoms, duration before seeking medical attention, time to referral and risks for lung cancer recorded.

**Results:** 154 patients, 81 male, 73 female, mean age 63 years (21-86). GP’s made most referrals 87% and 68% perceived abnormal radiology as reason for attendance. Majority were symptomatic 86.6% with 57% reporting ≥ 3 symptoms. Cough was most common presenting symptom 61%, fatigue 52%, dyspnoea 45%, chest pain 45%, weight loss 32% and haemoptysis 25%. Average delay in seeking medical attention and referral to RALLC was 14 weeks. 22% current or ex-smokers and 21% reported at least one first degree relative with lung cancer.

**Conclusions:** significant delays exist between symptom onset and presentation to a health care provider and depends on symptom type. The bulk of the delay was before patients sought medical attention but there was still a sizeable delay between presentation and referral to RALCC. One in 5 patients had a first degree relative with lung cancer indicating that this may have been a factor in the decision to refer. Our study highlights the need for increased public awareness regarding the presenting symptoms of lung cancer and there exists the opportunity to reduce delays in diagnosis resulting in better outcomes.

**4672 Managing patient pathways to achieve lung cancer waiting time targets:**

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**Background:** England’s NHS introduced a 62-day target, from referral to treatment, to make lung cancer patient pathways more efficient. This study aims to understand pathway delays that lead to breaches of the target when patients need care in both secondary and tertiary setting so more than one institution is involved.

**Methods:** Mixed method cross case analysis. Qualitative methods include pathway mapping and semi-structured interviews. Quantitative analysis of patient pathway times from cancer services records.

**Setting:** Two tertiary referral hospitals in London

**Participants:** Database records of 53 patients were analysed. 19 sets of patient notes were used for pathway mapping. 17 doctors, 4 nurses, 8 managers and administrators were interviewed.

**Results:** The majority of the patient pathway (68.4%) is spent in secondary centres. There is more variability in the processes of secondary centres but tertiary centres do not have perfect processes either. Three themes emerged from discussions: information flows, pathway performance, and the role of the multidisciplinary approach.

**Conclusions:** The actions of secondary centres have a greater influence on whether a patient breaches the 62-day target, compared to tertiary centres. Nevertheless variability exists in both, with potential for improvement.

**4673 Lung cancer multi-disciplinary team (MDT) decisions audit**

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**Background:** Lung cancer resection and survival rates in the UK vary; the reasons for this are unclear.

**Aims:** To compare lung cancer MDT decision outcomes in 4 hospitals in one cancer network.

**Methods:** Each lung cancer MDT randomly selected 5 of their MDT cases and submitted them to the other MDTs for assessment. MDT decision outcomes for each case, including each MDT’s own previously discussed MDT cases were collated. Mean percentage agreement of MDT outcomes was calculated for TNM staging and referrals for PET scan, curative surgery, radical radiotherapy and palliative chemotherapy.

**Results:** 3 hospital MDTs discussed 15 cases as well as having previously discussed their own 5 cases. 1 hospital submitted their 5 previously discussed cases but failed to discuss the other cases submitted to them. There were 17 non-small cell lung cancer cases, 2 indeterminate cases and 1 small cell lung cancer case. The number of cases referred for curative surgery varied between 6 to 7 cases per MDT. Percentage agreement was 83% for T staging, 91% for N staging, 98% for M Staging, 87% for referral for PET scan, 98% for curative surgery referral, 95% for radical radiotherapy referral and 93% for palliative chemotherapy referral.

**Discussion:** There was good agreement for staging and very high agreement for treatment referral. In this pilot study the high agreement for potentially curative treatment does not support the view that some MDTs are not referring patients for potentially curative treatment. As numbers are small we propose this issue be addressed by a national web-based quality assurance programme where each MDT assesses and reports sample cases each month and is given formative feedback.

**4674 Histological typing of lung cancer in biotopically obtained specimens under the aspect of therapeutical approaches – A multi-center study**

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Histological typing of lung cancer as SCCL or NSCLC clinical arose with the approval of the antifolate pemetrexed, which has a lower antitumorous effect in Squamous Cell Carcinoma. Often only biopsy specimens are available to exclude a squamous differentiation before chemotherapy/decision.

The restrictive nature of subtyping lung cancer in biopsies demanded a skilled and experienced pathologist. This interlaboratory comparison should discover the accuracy of subtyping of lung cancer biopsies evaluated in 5 different pathological institutes in Germany. Is it possible to improve the accuracy histological typing by additional immunohistochemistry (IHC) panel?

60 biopsy specimens with Hematoxylin-eosin (HE) stain and immunohistological stained slides of at least C3, CK56, p63, TTF1 were assembled and analysed from the pathologists. An estimation of predominantly-non-squamous yes/no and the histological subtype was done after examination the HE slide and again after the examination of the IHC. These two results were compared.

All 60 cases were analysed by all 5 participants. In average the agreement of...
483. The impact of the organisation of care on costs: the role of the physician in home care

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An evaluation of the safety, efficacy and cost-effectiveness for patients with acute respiratory illness of a community-based intravenous medication service: The first 26 months

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Background: Patients with acute respiratory illnesses such as acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and pneumonia occupy significant proportion of acute hospital beds. There is therefore an increasing focus on intermediate care initiatives to facilitate early supported discharge (ESD) and admission avoidance (AA) in such patients. Since 10.11.08, our hospital in partnership with Community Intervention Team (C.I.T.) provided service for administration of intravenous (IV) medications, facilitating ESD/AA.

Aim: To evaluate the AMNCH/C.I.T. IV service, in terms of safety, readmission rates, adverse events, bed-days saved, patient satisfaction and cost-effectiveness.

Results: Up to 31.11.11, of 285 patients referred to this service, 32% had a primary diagnosis of acute respiratory illness. 44 patients were male, 48 female. Mean age was 58.5 years (range 18-95). ESD and AA was facilitated in 67% and 33% respectively. Respiratory diagnoses were: pneumonia (n = 63), AECOPD (n = 7), exacerbation of asthma (n = 4), exacerbation of bronchiectasis (n = 5) and non-pneumonic respiratory infection (n = 13). IV treatment saved a minimum of 486 bed-days. Average length-of-stay in the service was 5.3 days. Readmission rate was 3.2%. No adverse incidents were reported. Patient satisfaction was 100%.

Conclusion: We estimate that home treatment of these patients saved €457,300 for AMNCH compared to equivalent treatment in hospital.

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Potential economic savings of administration of home intravenous antibiotic therapy to patients with acute respiratory infections in Ireland

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Introduction: Acute respiratory infections (ARI) account for a significant proportion of prolonged hospital stays. Intermediate care initiatives supporting home intravenous antibiotics (HIVAs) aim to facilitate early discharge and avoid unnecessary hospital admissions. Numerous studies have demonstrated the efficacy of HIVA for acute infections. International studies have shown increased patient satisfaction, improved quality of life, fewer investigations, decreased social disruptions and increased cost-effectiveness.

Objective: The purpose of this study was to analyse the potential cost-effectiveness of HIVA in patients with ARI in Ireland.

Methods: Using the Health Service Executive (HSE) Casemix and assuming a 60% uptake of ARI patients satisfying HIVA criteria with a length of stay (LOS) of 1-3 days, cost-estimates relating to cost/bed and LOS were used to calculate cost/bed-day savings if HIVA is introduced.

Results: The approx. annual admission rate for ARI conditions such as pneumonia, COPD, asthma, CF and bronchiectasis is 26,700 patients/yr with an average cost per admission of €70,600. Based on an average LOS of 9.2 days at a cost/bed day of €1,920, the cost/ARI admission is €17,664. This equates to €473m. An LOS of 1-3 days would result in cost-estimates of €51.4-154.2m, a gross difference of €318.8m. Accounting for expenses such as capacity, staff, training, equipment, travel and others, we estimate bed-day savings of €200-220/yr.

Conclusion: HIVA administration is a safe, cost-effective alternative in suitable patients with ARI, potentially providing significant savings to the health service in Ireland.

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A prospective re-audit of admissions and discharge delays occurring in patients admitted to a district general hospital’s respiratory ward in the United Kingdom

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Introduction: The National Confidential Inquiry into Patient Outcome and Death recommends that following initial assessment and treatment, patients should be transferred to a ward which is appropriate for their clinical condition.

Objective: To assess delays prior to discharge for patients (respiratory vs non-respiratory) whom are medically fit for discharge, following a reduction in respiratory beds from 62 to 46 as recommended by Sarkar et al 2010.

Methods: A prospective 2-week audit was conducted on respiratory wards and in-
cluded patients admitted under three respiratory consultants. Information collated: date of admission and of discharge, age, primary medical diagnosis and reason for delay.

Results: Conclusions: A reduction in respiratory beds lead to a reduction in patients with delayed discharge regardless of the underlying medical diagnosis. All delays were still attributable to social reasons. Efficient triage and transfer to appropriate wards on admission will further reduce the number of delayed discharges.

4680 The attitude of physicians for asthma treatment and results in the inhaler market between 2004-2009 in Turkey Sedat Atli1, 2, H. Volkan Kara1. 1Department of Chest Diseases, Yedikule Education Hospital for Chest Diseases and Thoracic Surgery, Istanbul, Turkey; 2Department of Thoracic Surgery, Gumushane State Hospital, Gumushane, Turkey

We evaluated the effects Turkey Conversion Programme in Health in 2004 on drug market used for treatment of asthma.

We analyzed the data from IMS the programme following the drug market and the data from the Social Security Institution (SSI) for comparative studies. In 2004 SSI paid nearly 4.0 billion Euro for drugs which increased to 8.5 billion (119%) Inhaler dust asthma drugs was 88.9 million and increased to 280.6 million (316 fold). Drug prescribed was 6.037.172 and increased to 20.848.085 boxes (3.45 fold).In the market of subgroup for inhaler dust asthma drugs distribution was; the rescue drugs 31.5%, combined drugs 17.7%, nebul 10.5%. The rates in 2009 were 20.2%, 29.6% and 18% respectively. Economically distribution was; 48.4% for combined drugs, 63.5% for nebul and 6.3% for rescue drugs. Rates for 2009 were 58.4%, 9.2% and 4.1%. The number of rescue drugs increased from 1.901.938 boxes to 4.220.664 (2.22 folds). The financial increase was 4.62 fold from 5.570.177 to 25.739.326. The number for nebul was 631.184 and increased to 3.762.806 (5.6 fold) the cost for them was 5.570.177 increased to 25.739.326 (4.62 fold). The combined drug subgroup the number of prescriptions were 1.066.486 increased to 6.178.315 (5.79 fold). The cost was 43.006.559 and increased to 163.814.343.

There has been an increase in the costs for inhaler drugs used for asthma treatment. Our analyses showed that this increase mostly caused by increase in the number of prescribed combined drugs. This increase we believe decreased the need for rescue drugs but had no effect on the nebul that has been used.

4681 Stepping up the controller medication in asthma patients: Impact of various treatment options on costs Mohsen Sadatsafavi1, Pierrick Bedouch1, Mark FitzGerald2, Carlo Narra3, Larry Lynd.1, 2Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada; 3Department of Medicine, University of British Columbia, Vancouver, BC, Canada

Introduction: To compare asthma-related costs among adults who step-up their controller medication.

Methods: A population-based study was conducted using the administrative health data of British Columbia, Canada (1997 to 2007). Hospitalization, physician visits, and prescription records were used to identify asthma patients (age 14-65) and calculate direct costs. Four cohorts were constructed as those who: increased the dose of inhaled corticosteroids (ICS+ group), switched to ICS/long-acting beta-agonist (LABA) in a single formulation (ICS/LABA group), added LABA in separate formulations (ICS+LABA group), or added leukotriene receptor antagonist (ICS+LRA group). The outcome was the direct cost of asthma (2008 CAD) in the year after the step-up, adjusted for multiple demographic, resource use, and comorbidity variables from the previous year.

Results: 52,640 patients (average age 42.3, 60.3% female) were included (7,115 ICS+, 19,457 ICS/LABA, 4,086 ICS+LABA, and 1,982 ICS/LRA). The average costs of asthma for the year after the index date for the ICS+ group was $509. Compared to ICS+, all other groups had significantly positive incremental costs: +$358.0 for ICS/LABA, +$504.3 for ICS+LABA, and +$541.6 for ICS/LRA (all P-values <0.01). Higher age, higher resource use, and higher cumulative dose of rescue medication in the year prior to the step-up date were predictors of higher costs after the step-up date (all p<0.01).

Conclusions: Based on relatively large sample and adjusted for several potential confounders, increasing ICS dose as a step-up approach was associated with the lower costs compared to addition of a second class of controller medication.


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Purpose: To evaluate the cost and diagnostic efficacy of microbiological studies of pleural fluids.

Method: Hospitalized patients with exudative pleural effusion were prospectively evaluated. The fluid samples were examined for Gram stain, acid-fast bacilli smear together with specific bacterial, fungal and mycobacterial cultures.

Results: Bacteriologic and EZN stains of the pleural fluids were negative in 89 cases included whereas fluid cultures were positive in 9 (10.1%) cases (3 (12.5%) of the 24 with tuberculous pleurisy and 6 (28.5%) of the 21 with empyema or other parapneumonic pleural effusion). The cultures of the malignant, non-specific and paramalignant fluids were negative. In cases with empyema or other parapneumonic pleural effusion and tuberculous pleurisy, no significant difference was determined between culture-positive and culture-negative cases regarding age, gender, fever or fluid LDH and glucose levels; positive cultures were more frequent in the presence of fluid purulence (55.6% versus 8.3%, p=0.046). In 5 (83.3%) of the 6 culture-positive and in 6 (40%) of the 15 culture-negative cases with empyema or other parapneumonic effusion, change in antibiotic treatment was necessary. The costs of the microbiological studies was 39.4 Euro for each case and 1735 Euro and 1419 Euro for cases with noninfectious and infectious fluids, respectively.

Conclusion: Diagnostic yield of the routine microbiological studies of pleural fluids was determined low. It was concluded that requesting microbiological studies of pleural fluids in cases strongly considered to have infection on clinical basis and/or in cases with purulent fluid would be more beneficial regarding diagnostic yield and cost.