P261 TIOTROPIUM SAFETY AND PERFORMANCE IN RESPIMAT® (TIOSPIR™): SAFETY AND EFFICACY IN PATIENTS NAÏVE TO TREATMENT WITH ANTICHOLINERGICS

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Introduction The TIOSPIR™ trial showed similar safety and exacerbation efficacy profiles for tiotropium Respimat® and HandiHaler® in patients with chronic obstructive pulmonary disease (COPD). We present here the results for patients who were naïve to anticholinergic treatment at baseline.
Methods TIOSPIR™ (n = 17,135), a 2–3 year, randomised, double-blind, parallel-group, event-driven trial, compared safety and efficacy of once-daily tiotropium Respimat® 5 and 2.5 µg with HandiHaler® 18 µg in patients with COPD. Primary endpoints were time to death (noninferiority of Respimat® 5 or 2.5 µg versus HandiHaler®) and time to first COPD exacerbation (superiority of Respimat® 5 µg versus HandiHaler®). Safety, including cardiovascular safety, was assessed.
Results Overall, 6966 patients from TIOSPIR™, naïve to anticholinergic treatment at baseline, were randomised and treated (n = 2345, n = 2312 and n = 2309 for tiotropium Respimat® 2.5 and 5 µg and HandiHaler® 18 µg). There was similar risk of death (vital status follow up) (measured as time to death) for the Respimat® groups versus HandiHaler® (Respimat® 5 µg: hazard ratio [HR], 0.93; 95% confidence interval [CI], 0.75–1.17; Respimat® 2.5 µg: HR, 1.05; 95% CI, 0.84–1.30) with similar results for the on-treatment sensitivity analysis (Respimat® 5 µg: HR, 0.91; 95% CI, 0.71–1.17; Respimat® 2.5 µg: HR, 1.11; 95% CI, 0.87–1.40). Risk of exacerbation was also similar for the Respimat® groups versus HandiHaler® (measured as time to first exacerbation) (Respimat® 5 µg: HR, 0.99; 95% CI, 0.90–1.08; Respimat® 2.5 µg: HR, 1.04; 95% CI, 0.95–1.14). Risk of major adverse cardiovascular event (MACE) or fatal MACE were similar for the Respimat® groups versus HandiHaler® (MACE: Respimat® 5 µg: HR, 1.20; 95% CI, 0.88–1.63; Respimat® 2.5 µg: HR, 1.11; 95% CI, 0.81–1.51; fatal MACE: Respimat® 5 µg: HR, 1.14; 95% CI, 0.75–1.71, Respimat® 2.5 µg: HR, 1.12; 95% CI, 0.75–1.69).
Conclusions Analogous to the global analysis, patients naïve to anticholinergic treatment and treated with tiotropium Respimat® 2.5 or 5 µg or HandiHaler® in the TIOSPIR™ trial exhibited similar safety and exacerbation efficacy profiles.

P262 TIOTROPIUM SAFETY AND PERFORMANCE IN RESPIMAT® (TIOSPIR™): SAFETY AND EFFICACY IN PATIENTS WITH TIOTROPIUM HANDIHALER® USE AT BASELINE

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Introduction The TIOSPIR™ trial showed that tiotropium Respimat® and HandiHaler® have similar safety and exacerbation efficacy profiles in patients with chronic obstructive pulmonary disease (COPD). We present here results for patients from the United States (US) using tiotropium HandiHaler® at baseline.
Methods TIOSPIR™ (n = 17,135), a 2–3 year, randomised, double-blind, parallel-group, event-driven trial, compared safety and efficacy of once-daily tiotropium Respimat® 5 and 2.5 µg with once-daily HandiHaler® 18 µg in patients with COPD. Primary endpoints were time to death and time to first COPD exacerbation. Safety, including cardiovascular safety, was assessed. Tiotropium Respimat® was unavailable in the US (baseline tiotropium HandiHaler® use only), therefore this subgroup was analysed.
Results Overall, 1779 patients from TIOSPIR™ treated with tiotropium HandiHaler® 18 µg at baseline in the US were randomised and treated (n = 572, n = 602 and n = 605 for tiotropium Respimat® 2.5 and 5 µg and HandiHaler® 18 µg). A numerically lower time to death was observed for patients within the Respimat® groups versus HandiHaler® (vital status follow up: Respimat® 5 µg: hazard ratio [HR], 0.77; 95% confidence interval [CI], 0.53–1.12; Respimat® 2.5 µg: HR, 0.76; 95% CI, 0.52–1.12). Risk of major adverse cardiovascular event (MACE) and fatal MACE was numerically lower for the Respimat® groups versus HandiHaler® (MACE: Respimat® 5 µg: HR, 0.69; 95% CI, 0.41–1.18; Respimat® 2.5 µg: HR, 0.83; 95% CI, 0.50–1.39; fatal MACE: HR, 0.60; 95% CI, 0.26–1.37; Respimat® 2.5 µg: HR, 0.42; 95% CI, 0.16–1.09). Overall incidence of a fatal event (on-treatment) was lower in the Respimat® groups versus HandiHaler® (Respimat® 5 µg: HR, 0.60; 95% CI, 0.39–0.92; Respimat® 2.5 µg: HR, 0.67; 95% CI, 0.44–1.02). Time to first exacerbation was similar across groups (Respimat® 5 µg versus HandiHaler®: HR, 0.94; 95% CI, 0.82–1.08).
Conclusions Patients treated with tiotropium HandiHaler® 18 µg at baseline, and who were randomised and subsequently received tiotropium Respimat® 2.5 or 5 µg, had a similar risk of exacerbation as patients who continued to be treated with tiotropium HandiHaler® 18 µg. In this subgroup of patients, all-cause mortality was similar between tiotropium Respimat® and HandiHaler® 18 µg.

Abstracts M263 to M272 are found on page A218–A223.

ILD: diagnosis, co-morbidities and treatment

P273 ASSESSMENT OF LUNG MICROSTRUCTURE IN INTERSTITIAL LUNG DISEASE WITH HYPERPOLARISED GAS MRI

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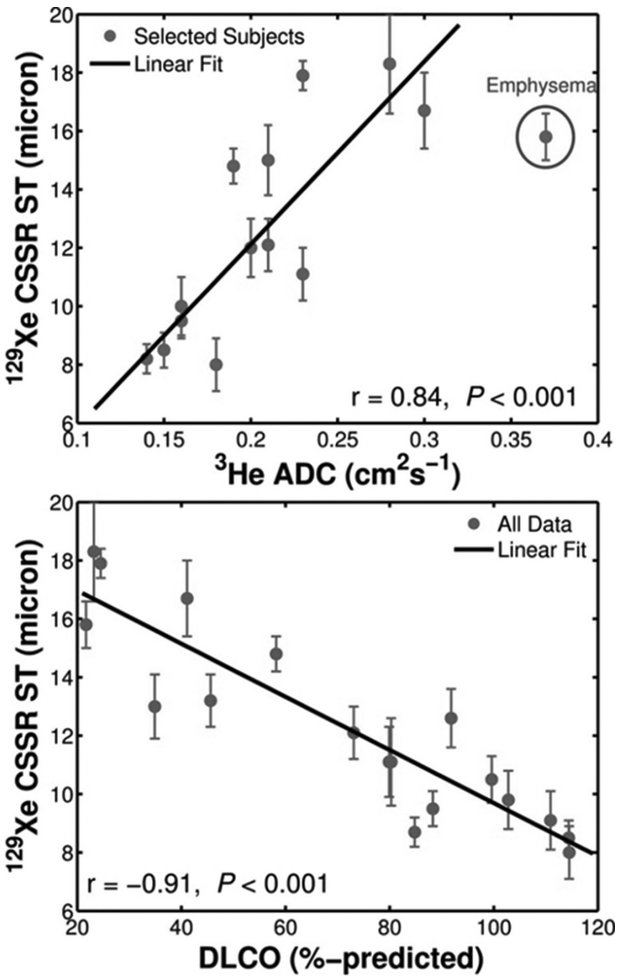
Introduction and objectives Magnetic resonance (MR) imaging of the hyperpolarised noble gases ^{3}He and ^{129}Xe provides



Abstract P273 Figure 1 Top panel – statistically significant correlation between ^{129}Xe CSSR-derived alveolar septal thickness (ST) and ^{3}He diffusion-weighted MRI-derived apparent diffusion coefficient (ADC) of helium in the alveolar airspace. Bottom panel – corroboration of the ^{129}Xe CSSR method as a probe of gas-exchange using the whole-lung transfer factor, DLCO

exquisite depiction of pulmonary ventilation. In addition, MR measurement of the apparent diffusion coefficient (ADC) of ^{3}He gas has proven clinical utility in assessment of emphysema. Furthermore, xenon is soluble and is a promising marker of pulmonary gas-exchange. The motivation of this work was to demonstrate non-invasive quantification of whole-lung septal thickness (ST) and helium ADC in subjects with idiopathic pulmonary fibrosis (IPF) and systemic sclerosis (SSc) using ^{129}Xe and ^{3}He MR.

Methods Hyperpolarised ^{129}Xe spectroscopy was performed on ten healthy volunteers (23–74 yrs), four subjects with SSc and four with IPF at 1.5 T. A chemical shift saturation recovery (CSSR) method was used to assess the dynamics of xenon uptake into parenchymal tissues and blood and to derive quantitative information about lung microstructure. From the subject cohort, six volunteers and seven patients were also scanned at 1.5 T with a diffusion-weighted sequence to determine ^{3}He ADC values. For comparison with MR experiments, standard pulmonary function tests including the diffusing capacity of carbon monoxide (DL_{CO}) were performed.

Results Pulmonary function was significantly worse in both SSc and IPF subjects than healthy volunteers (DL_{CO} < 45% in IPF patients). Both ^{129}Xe CSSR ST and ^{3}He ADC values were elevated in subjects with SSc, and to a larger degree in those with IPF, compared with healthy volunteers (Figure 1, top). These two MR metrics correlated significantly, suggesting that fibrotic remodelling of tissue both degrades gas-exchange efficiency and induces alveolar widening causing less-restricted gas diffusion (although emphysema was reported for only one subject on CT). The ^{129}Xe CSSR-derived ST values correlated well with whole-lung DL_{CO} (Figure 1, bottom) and in healthy volunteers, ST increased with age ($p < 0.05$).

Conclusions Hyperpolarised ^{129}Xe and ^{3}He MR techniques are sensitive to small changes in gas-exchange efficiency and alveolar surface geometry, respectively. These two factors appear to have an intrinsic link, identified in the presence of fibrotic lung disease without obvious emphysema. Further application of these MR techniques may prove useful in the diagnosis/assessment of different forms of ILD.

P274 ANTI-SYNTHETASE SYNDROME: VALIDITY OF ANA AS A SCREENING TOOL – THE OXFORD ILD SERVICE EXPERIENCE

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Background Anti-synthetase syndrome (ASS) is characterised by interstitial lung disease (ILD), myositis, arthropathy, fever, Raynaud's, and mechanics hands associated with antisynthetase antibodies (including Jo-1, PL-7 and PL-12). ILD is the major determinant of mortality in ASS.

ANA is commonly used to screen for autoimmune diseases. If negative, in many centres extractable nuclear antigens (ENAs) are not tested. This study aims to highlight the inadequacy of this approach.

Method We retrospectively examined consecutive patients in the Oxford ILD and Rheumatology services with ASS-ILD between 2009–2014. CT scans were reviewed to identify the pattern of ILD. Immunology, lung function and medication were identified from patient records.

Results 24 patients were identified with ASS-ILD: age 33–78 years (mean 54); 9 male, 15 female. Disease severity was assessed by lung function at presentation: FVC 42–118% (mean 77.9%) predicted, TLco 10–99% (mean 56%) predicted.

Only 1 of 24 (4.2%) were ANA positive (titre 1:80). 18 of 24 (75%) had a positive ENA screen (ELISA): 13 Jo-1; 4 Jo-1 and Ro-52; and 1 Ro. 6 (25%) patients had a negative ENA screen. 5 of these had a positive myositis blot (1 Jo-1, 3 PL-7, 1 PL-12) and 1 was negative for all 3 autoantibodies. Of 7 patients who were Jo-1 positive on ENA screen, 4 had a negative Jo-1 myositis blot.

CT patterns of disease: organising pneumonia (OP; n = 7), non-specific interstitial pneumonia (NSIP; n = 7), OP/NSIP overlap (n = 9), acute interstitial pneumonia (AIP; n = 1). There was no relationship between anti-synthetase antibody and CT pattern.

The identification of an ASS antibody significantly changed management in most patients; 17 were treated with (iv) cyclophosphamide and rituximab was added to 8 cases.