P10 EFFECT OF PIRFENIDONE ON GAS TRANSFER IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Background Idiopathic pulmonary fibrosis (IPF) is a severe and progressive interstitial lung disease (ILD). Treatment with the anti-fibrotic agent Pirfenidone slows decline in forced vital capacity (FVC). Pulmonary vasculopathy is a relatively common and life-limiting complication of IPF and is frequently associated with a reduction in the diffusing capacity of the lung for carbon monoxide (DLco). However, it is not known what effect Pirfenidone may have on DLco.

Methods We performed a retrospective analysis of patients with diagnoses of IPF on long term Pirfenidone treatment. Lung function data were collected at treatment initiation and then at 12 months, (6–18 months). To assess for a treatment effect, similar data were also collected from an untreated control cohort of biopsy proven IPF patients from the pre-Pirfenidone era managed at the same centre. Data were analysed using Stata.

Results 138 patients were studied; n = 66 patients in the untreated control group and n = 72 patients in the Pirfenidone treated group. The control group had a higher baseline predicted FVC (74.8% v 67.5%) ($p < 0.05$) but baseline predicted DLco measurements were similar (44% v 40%) ($p = 0.19$). 12 month relative FVC change was greater in the untreated group; 9.9% (273 mL) (±11.4%) versus 3.9% (123 mL) (±11.9%) ($p < 0.005$). 12 month relative DLco decline was also greater in the untreated group; 16.4% (±20.5%) versus 7.5% (±17.6%) ($p < 0.01$). In multivariate analyses, the effect of Pirfenidone treatment had a 6.7% impact on FVC change (2.7–10.6) ($p < 0.001$) and a 9.0% impact on DLco change (2.5–15.5) ($p < 0.01$). Right ventricular systolic pressure correlated with baseline predicted DLco ($p < 0.005$, $r^2 = -0.14$).

Discussion In this study we have demonstrated that over 12 months, Pirfenidone confers a reduction in gas transfer decline paralleling that seen for FVC. This treatment effect on DLco may be due to a combination of deceleration in ILD progression as well as attendant effects at the level of the pulmonary vasculature. This may have particularly relevance given the correlation between DLco and echocardiographic parameters of pulmonary vascular disease.

Conclusion Treatment of IPF with Pirfenidone markedly attenuates declines in gas transfer. This is of interest as it may provide insights into mechanisms underpinning disease stabilisation.

P11 PIRFENIDONE TREATMENT IS ONLY AVAILABLE IN THE UK FOR A MINORITY OF PATIENTS WITH USUAL INTERSTITIAL PNEUMONITIS

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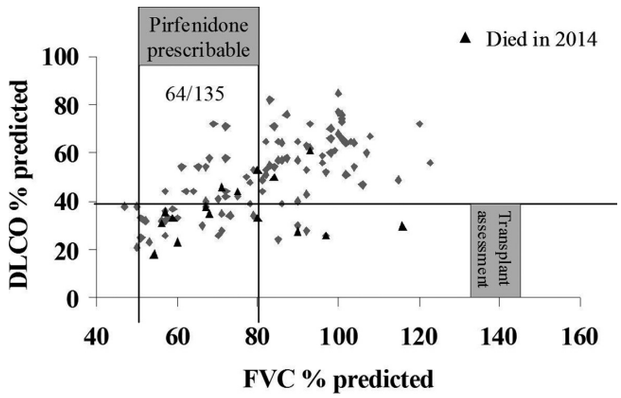
Introduction Usual Interstitial Pneumonitis (UIP) may be caused by asbestos exposure (asbestosis), collagen vascular diseases (CVD) or agents causing hypersensitivity pneumonitis (HP), or may be idiopathic (IPF). Referrals to our ILD MDT have increased since the limited availability of pirfenidone which is only prescribable for IPF with a FVC 50–80% predicted. We have reviewed presentation in 2014 to identify patients suitable for Pirfenidone prescription.

Methods Our hospital provides a regional service for Pirfenidone prescription. All patients with a MDT diagnosis of definite UIP were included. A standard proforma requested information on exposures, CVD and antibodies relevant to CVD and HP. If there were no relevant exposures and CVD was excluded, a diagnosis of IPF was made. Asbestosis, HP and CVD associated UIP were diagnosed when the relevant information supported this, unspecified UIP was diagnosed in the absence of specific information.

Results 202/546 referrals in 2014 were judged to have definite UIP after consideration by a fully constituted ILD MDT including histopathologists, radiologists, clinicians and CNS'. After exclusion of 22 with asbestosis, 11 with CVD associated UIP, 17 with CPFE and 17 with HP associated UIP, 51 with IPF and 84 with unspecified UIP remained for consideration of Pirfenidone treatment. Only 64/135 suitable patients had a FVC 50–80% predicted (Figure 1).



Abstract P11 Figure 1

Conclusions The decisions of an ILD MDT are limited by the completeness of investigation. We found causes for 50/200 patients with UIP. Pirfenidone was not prescribable for 53% of otherwise suitable patients. If the FVC limit was raised to 90% 32% would still be excluded, including 2 who died of their disease within 12 months. The FVC is often preserved even in terminal IPF.

P12 PIRFENIDONE POST-AUTHORISATION SAFETY REGISTRY (PASSPORT) – UPDATE AND CONCOMITANT USE OF N-ACETYLCYSTEINE AND/OR CORTICOSTEROIDS

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Background PASSPORT is a post-authorisation safety registry for pirfenidone to collect real-world data in EU patients with idiopathic pulmonary fibrosis (IPF). This analysis assessed the safety of pirfenidone as monotherapy and in combination with N-acetylcysteine (NAC) and/or corticosteroids (CS).

Methods 109 EU sites dosed 1006 patients. Safety data were recorded at routine clinic visits for up to 2 years. Pirfenidone-associated adverse drug reactions (ADR) were collected.

Results At baseline, mean±SD age was 70 ± 8.5 years and mean ±SD time since IPF diagnosis was 1.6 ± 2.5 years; 80% of patients were male; supplemental oxygen was used by 27% of patients; mean±SD FVC was 2.56 ± 0.78 L; mean±SD% predicted FVC was 66 ± 16% (14% had <50% predicted FVC). The most common comorbidities (>10%) were hypertension, gastroesophageal reflux disease, hypercholesterolemia and coronary artery disease.

At this interim analysis, median time on pirfenidone was 7.6 months and total exposure was 803 patient-years. Overall, 67% of patients had ≥1 ADR, most commonly: nausea, 17%; fatigue, 15%; decreased appetite, 13%; decreased weight, 12%; rash, 10%; and diarrhoea, 9%. Of patients who had an ADR, 55% experienced their first ADR within the first 30 days' treatment. Around 5% of patients completed 2 years' treatment, 55% are ongoing, 9% died and 21% discontinued due to pirfenidone-related ADRs (most commonly nausea, rash and decreased weight). 11% discontinued for other reasons.

Patients with FVC <50% had a higher discontinuation rate than other patients (48% vs 39%, respectively). The imbalance was mainly driven by higher rates of death and lung transplantation. The discontinuation rate due to pirfenidone ADRs was similar among patients with FVC <50% and ≥50% (20.3% vs 20.9%, respectively).

62% of patients received pirfenidone alone; 11%, 8% and 8% received pirfenidone plus NAC, CS, or NAC+CS, respectively. The remaining 11% had partial use of NAC and/or steroids. ADR incidence was generally consistent for these subgroups except weight decrease and ALT increase, which occurred more often in the pirfenidone+CS group.

Conclusions In this real-world setting, pirfenidone was generally safe and well tolerated as monotherapy or combined with NAC and/or CS. The rate of discontinuation due to pirfenidone-related ADRs was similar regardless of disease severity.

P13 SAFETY OF PIRFENIDONE IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (IPF): INTEGRATED ANALYSIS OF CUMULATIVE DATA FROM 5 CLINICAL TRIALS

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Introduction and objectives IPF is a chronic, progressive and irreversible disease that requires long-term clinical management. To further evaluate the clinical safety of pirfenidone in patients with IPF, we performed a comprehensive integrated analysis of safety data from 5 clinical trials.

Methods All patients assigned to receive pirfenidone (2403 mg/d) in the Phase 3 ASCEND (016) and CAPACITY (004/006) studies and all patients receiving ≥1 dose of pirfenidone in either of two ongoing open-label studies (studies 002 and 012) comprised the integrated population. EAP (002) is a compassionate use study in the U.S.; RECAP (012) is evaluating pirfenidone in patients who completed one of the Phase 3 studies. Analyses were based on the January 15, 2014 interim data cut.

Results 1299 patients were included in the integrated population. The cumulative total exposure to pirfenidone was 3160 person exposure years (PEY). The median duration of exposure was 1.7 years (range, 1 week–9.9 years); 545 (42%) patients received pirfenidone for ≥2 years and 325 (25%) patients received pirfenidone for ≥4 years. The majority of patients (75.8%) received a mean daily dose of ≥1800 mg. Consistent with prior observations, gastrointestinal and skin-related events were among the most common treatment emergent adverse events (Table 1); these were almost always mild to moderate in severity, reversible with dose modification and rarely led to treatment discontinuation. Cough, dyspnoea and IPF were the most common respiratory adverse events in the integrated population—a finding that is consistent with expectations in patients with a chronic progressive respiratory disease followed over a long period of observation. Aminotransferase (ALT or AST) elevations (>3 × ULN) occurred in 40/1299 (3.0%) patients in the integrated population.

Abstract P13 Table 1 Treatment emergent adverse events in the integrated population compared with the pooled pirfenidone 2403 mg/d and placebo groups in the Phase 3 trials*

	Integrated population (N = 1299)† OE = treatment emergent adverse event ment emergent adverse events d sun exposure during treatment with pirfenidone. the skin du
Median (range) duration of exposure, yr	1.7 (>0, 9.9)
Treatment emergent adverse event,%	
Nausea	37.6
Cough	35.1
Dyspnea	30.9
Upper respiratory tract infection	30.6
Idiopathic pulmonary fibrosis	29.3
Fatigue	28.2
Diarrhoea	28.1
Rash	25.0
Bronchitis	23.8
Headache	21.6
Nasopharyngitis	21.3
Dizziness	21.2
Dyspepsia	18.4
Vomiting	15.9
Weight decreased	15.6
Back pain	15.4
Anorexia	15.2

*Occurring in ≥15% of patients in the cumulative clinical database.
†Includes 2 patients in Study 002 with a diagnosis of "pulmonary fibrosis."