Clinician - PACT
New Clinical Trial and Research

Study title	A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study of Safety, Tolerability and Efficacy of Pirfenidone in Patients with Rheumatoid Arthritis Interstitial Lung Disease(RAILD)
Trial synopsis	This is a phase 2, randomized, double blind, placebo controlled trial of pirfenidone for the treatment of RA associated interstitial lung disease. Participants will be randomized to receive Pirfenidone 2403 mg per day or placebo in a 1:1 ratio. The primary outcome of this study is to assess the efficacy of pirfenidone 2403 mg/day versus placebo in patients with RA associated interstitial lung disease, as defined by progression free survival over the 52 weeks of treatment. Patients will receive blinded study treatment from the time of randomization until the Week 52 Visit.
Investigational medicinal product	Pirfenidone(oral)/Placebo(oral)
Disease target	Patients with Rheumatoid Arthritis Interstitial Lung Disease (RAILD)
Sponsor	Brigham and Women's Hospital USA
Duration	Up to 60 weeks
Comparator and randomisation	Pirfenidone three times daily (2403 mg) for 52 weeks Placebo three times daily for 52 weeks
Trial Status	Recruiting
Trial phase	2
Key inclusion criteria	1. Age 18 through 85 years, inclusive, at Screening 2. Probable or definite diagnosis of RA according to revised 2010 ACR/EULAR criteria, without evidence or suspicion of an alternative diagnosis that may contribute to their interstitial lung disease. 3. Diagnosis of ILD a. supported by clinically indicated HRCT, and when available surgical lung biopsy (SLB), prior to Screening, and b. defined as the first instance in which a patient was informed of having ILD, at least 6 months before Screening, and c. presence of fibrotic abnormality affecting more than 10% of the lung parenchyma, with or without traction

	bronchiectasis or honeycombing, on Screening and confirmed by adjudicated HRCT prior to Baseline 4. Clinical symptoms consistent with ILD (i.e., cough, dyspnea), at least 6 months before Screening 5. No features supporting an alternative diagnosis on transbronchial biopsy, or SLB, if performed prior to Screening 6. Attainment of the following centralized spirometry criteria (based on local spirometry on standardized equipment and centralized quality controlled): a. percent predicted FVC ≥ 40% and ≤ 80% at Screening b. change in pre-bronchodilator FVC (measured in liters) between Screening (Visit 1) and Baseline (Visit 2) must be a <10% relative difference, calculated as: 100% * [absolute value (Screening FVC – Baseline FVC) / Screening FVC] c. percent predicted DLCO ≥30% and ≤80% at Screening 7. Stable dose (at least three months at the time of Screening) of corticosteroids or any cytotoxic, immunosuppressive or cytokine-modulating, or receptor-antagonist agent prescribed for rheumatoid arthritis, including but not limited to azathioprine, cyclophosphamide, cyclosporine, etanercept, iloprost, infliximab, leukotriene antagonists, methotrexate, mycophenolate mofetil, tacrolimus, montelukast, tetrathiomolybdate, TNF-a inhibitors, rituximab, abatacept, tofacitintib, tociluzimab. 8. Able to understand and sign a written informed consent form
Key exclusion criteria	1. Not a suitable candidate for enrollment or unlikely to comply with the requirements of this study, in the opinion of the investigator 2. Cigarette smoking within 3 months of Screening or unwilling to avoid tobacco products throughout the study 3. History of clinically significant environmental exposure known to cause pulmonary fibrosis (PF), including but not limited to drugs (such as amiodarone), asbestos, beryllium, radiation, and domestic birds 4. Concurrent presence of other interstitial lung disease, including but not limited to radiation, drug toxicity, sarcoidosis, hypersensitivity pneumonitis, bronchiolitis obliterans organizing pneumonia, human immunodeficiency virus (HIV), viral hepatitis, and cancer 5. Concurrent presence of other pleuropulmonary manifestations of RA, including but not limited to rheumatoid nodular disease of the lung, pleuritis/pleural thickening, and obliterative bronchiolitis 6. Post-bronchodilator FEV1/FVC < 0.7 at Screening 7. Presence of pleural effusion occupying more than 20% of the hemithorax on Screening HRCT

	8. Clinical diagnosis of a second connective tissue disease or overlap syndrome (including but not limited to scleroderma, polymyositis/dermatomyositis, systemic lupus erythematosus) 9. Coexistent clinically significant COPD/emphysema or asthma in the opinion of the site principle investigator 10. Clinical evidence of active infection, including but not limited to bronchitis, pneumonia, sinusitis, urinary tract infection, or cellulitis 11. Any history of malignancy diagnosed within 5 years of screening, other than basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or low grade cervical carcinoma in situ. 12. History of severe hepatic impairment or end-stage liver disease 13. History of end-stage renal disease requiring dialysis 14. History of unstable or deteriorating cardiac or disease, myocardial infarction within the previous year, heart failure within the last 3 years, or cardiac arrhythmia requiring drug therapy 15. Any condition that, in the opinion of the investigator, might be significantly exacerbated by the known side effects associated with the administration of pirfenidone 16. For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use two adequate methods of contraception, including at least one method with a failure rate of <1% per year, during the 52 weeks of treatment. a. A woman is considered to be of childbearing potential if she is postmenarcheal, has not reached a postmenopausal state (≥ 12 continuous months of amenorrhea with no identified cause other than menopause), and has not undergone surgical sterilization (removal of ovaries and/or uterus). b. Examples of contraceptive methods with a failure rate of <1% per year include bilateral tubal ligation, male sterilization, established and proper use of hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine devices, and copper intrauterine devices. c. The reliability of sexual abstinence should be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not acceptable methods of contraception. 17. For men who are not surgically sterile: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures, and agreement to refrain from donating sperm, as defined below:

	a. With female partners of childbearing potential, men must remain abstinent or use a condom plus an additional contraceptive method that together result in a failure rate of < 1% per year during the treatment period and for at least 118 days after the last dose of pirfenidone. b. Men must refrain from donating sperm during this same period. 18. Investigational therapy, defined as any drug that has not been approved for marketing for any indication in the country of the participating site, at the time of Screening 19. History of alcohol or substance abuse in the past 2 years, at the time of Screening 20. Family or personal history of long QT syndrome 21. Any of the following liver function test criteria above specified limits: a. Total bilirubin above the upper limit of normal (ULN), excluding patients with Gilbert's syndrome; aspartate or alanine aminotransferase (AST/SGOT or ALT/SGPT) >3 × ULN; alkaline phosphatase >2.5 × ULN b. Creatinine clearance (CrCl <30) mL/min, calculated using the Cockcroft-Gault formula c. Electrocardiogram (ECG) with a QTcB interval >500 msec at Screening 22. Prior use of pirfenidone or known hypersensitivity to any of the components of study treatment 23. Use of any of the following therapies within 28 days before Screening: a. Investigational therapy, defined as any drug that has not been approved for marketing for any indication in the country of the participating site b. Fluvoxamine c. Sildenafil (daily use). Note: intermittent use for erectile dysfunction is allowed
Primary endpoint	Incidence of the composite endpoint of decline from baseline in percent predicted FVC of 10% or greater or death during the 52-week treatment period
Number of participants sought	270
Lead site	The Prince Charles Hospital QLD
Additional sites	Royal Prince Alfred Hospital NSW, The Alfred Hospital VIC
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