INPLASY

Efficacy and safety of pirfenidone in interstitial lung disease: a systematic review and meta-analysis of randomized clinical trials

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ADMINISTRATIVE INFORMATION

Support - National Natural Science Foundation of China(82274453).

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202470066

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 July 2024 and was last updated on 16 July 2024.

INTRODUCTION

Review question / Objective To assess the effect and safety of pirfenidone in interstitial lung disease.

Rationale Interstitial lung disease (ILD) is a large group of diseases that cause fibrosis of the lungs. Pirfenidone has been shown to slow disease progression in patients with idiopathic pulmonary fibrosis (IPF). In view of the pathomechanistic and clinical similarities between IPF and other progressive fibrotic ILDs, we aimed to assess the efficacy and safety of pirfenidone in patients with ILDs, providing support for clinical application across a wide spectrum of patients.

Condition being studied Interstitial lung disease (ILD) is a large group of diseases that cause fibrosis of the lungs. There is significant geographic heterogeneity of ILD, the incidence of ILD ranged from 1 to 31.5 per 100,000 person-years and prevalence ranged from 6.3 to 71 per 100,000 people. The 5-year survival among patients with ILD has been estimated to be 56%. The Global Burden of Disease Study noted that ILDs contributed to 0.26% of all-cause mortality and that there had been an 86% increase in ILD-related years of life lost over the past two decades. The fibrosis causes stiffness in the lungs which makes it difficult to breathe and get oxygen to the bloodstream. Lung damage from ILDs is often irreversible and gets worse over time. ILD describes a heterogenous group of disorders that are subclassified based on similar radiographic or pathologic manifestations. Pirfenidone has been shown to slow disease progression in patients with idiopathic pulmonary fibrosis (IPF). However, there are few treatment options for progressive fibrotic interstitial lung diseases. In view of the pathomechanistic and clinical similarities between IPF and other progressive fibrotic ILDs, we aimed to assess the efficacy and safety of pirfenidone in patients with ILDs, providing support for clinical application across a wide spectrum of patients.

METHODS

Search strategy Terms: #1 pirfenidone OR esbrit OR dmnpirfenidone OR deokar

#2 Lung Diseases, Interstitial OR Diffuse Parenchymal Lung Disease OR Interstitial Lung Diseases OR Diffuse Parenchymal Lung Diseases OR Interstitial Lung Disease OR Lung Disease, Interstitial OR Pneumonia, Interstitial OR Interstitial Pneumonia OR Interstitial Pneumonias OR Pneumonias, Interstitial OR Pneumonitis, Interstitial OR Interstitial Pneumonitides OR Interstitial Pneumonitis OR Pneumonitides, Interstitial OR Interstitial lung disease
#3 Pulmonary Fibrosis OR Idiopathic Pulmonary Fibrosis OR Alveolitis, Extrinsic Allergic OR Bird Fancier's Lung OR Farmer's Lung OR Silo Filler's Disease OR Trichosporonosis OR Anti-Glomerular Basement Membrane Disease OR Granulomatosis with Polyangiitis OR Histiocytosis, Langerhans-Cell OR Eosinophilic Granuloma OR Pneumoconiosis OR Anthracosis OR Asbestosis OR Berylliosis OR Byssinosis OR Caplan Syndrome OR Siderosis OR Silicosis OR Radiation Pneumonitis OR Sarcoidosis, Pulmonary
#4 randomized controlled trial OR controlled clinical trial OR randomized OR placebo OR drug therapy OR randomly OR trial OR groups
Electronic databases: PubMed; Embase; Cochrane Library; Clinicaltrials.gov; China National Knowledge Infrastructure (CNKI); Wanfang Data; Chinese Biomedical Literature Database (SinoMed) and China Science and Technology Journal database (VIP). Hand searching of references of included articles, any relevant systematic reviews and pre-published articles, and contacting experts will be also performed to find additional relevant articles.

Participant or population Patients were adults (≥18 years old) with interstitial lung disease, regardless of race, gender or economic status will be included.

Intervention Experimental intervention is pirfenidone, administered orally.

Comparator Control intervention is placebo.

Study designs to be included Randomized clinical trials (RCTs).

Eligibility criteria Randomized clinical trials (RCTs) comparing pirfenidone with placebo will be included, regardless of language and publication status.

Information sources PubMed; Embase; Cochrane Library; Clinicaltrials.gov; China National Knowledge Infrastructure (CNKI); Wanfang Data; Chinese Biomedical Literature Database (SinoMed) and China Science and Technology Journal database (VIP). Hand searching of references of included articles, any relevant systematic reviews and pre-published articles, and contacting experts will be also performed to find additional relevant articles.

Main outcome(s) Patients with >10% decline in FVC or greater, Change in FVC (mL) from baseline, Change in FVC % predicted from baseline, Change from baseline of ≥50 m in 6 min walk distance, Change in 6MWD from baseline, Change in worst SpO2 during 6MWT (%), Change in DLCO % predicted from baseline, All-cause mortality, Serious adverse event (SAE).

Quality assessment / Risk of bias analysis We will use the Cochrane “Risk of bias”tool of Cochrane Handbook for Systematic Reviews of Interventions to evaluate each trial’s methodological quality, and then recorded in the table. The key components in the tool were: sequence generation, allocation concealment, blinding of participants, personnel and outcomes assessors, incomplete outcome data, selective outcome reporting and other possible sources of bias. Any disagreements will resolve through discussion with a third author.

Strategy of data synthesis Data entry and analysis will be conducted using Excel and ReviewManager (RevMan). Mean difference (MD) with 95% confidence interval (CI) of the outcomes and risk ratio (RR) will be calculated as the effect measure. The I2 statistic for heterogeneity will be calculated as a measure of the proportion of the overall variation attributable to between-study heterogeneity. A fixed-effects model will be chosen if I210 comparative studies were included for analysis.

Subgroup analysis Subgroup analysis will be performed based on the ILD classifications.

Sensitivity analysis Undetermined.

Country(ies) involved China.

Keywords Pirfenidone; Interstitial lung diseases; meta-analysis; randomized clinical trials.

Contributions of each author
Author 1 - Xiaoming Xing.
Author 2 - Mingzhu Zhang.
Author 3 - Jing Wang.
Author 4 - Shiqun Song.
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Author 6 - Lishan Zhang.