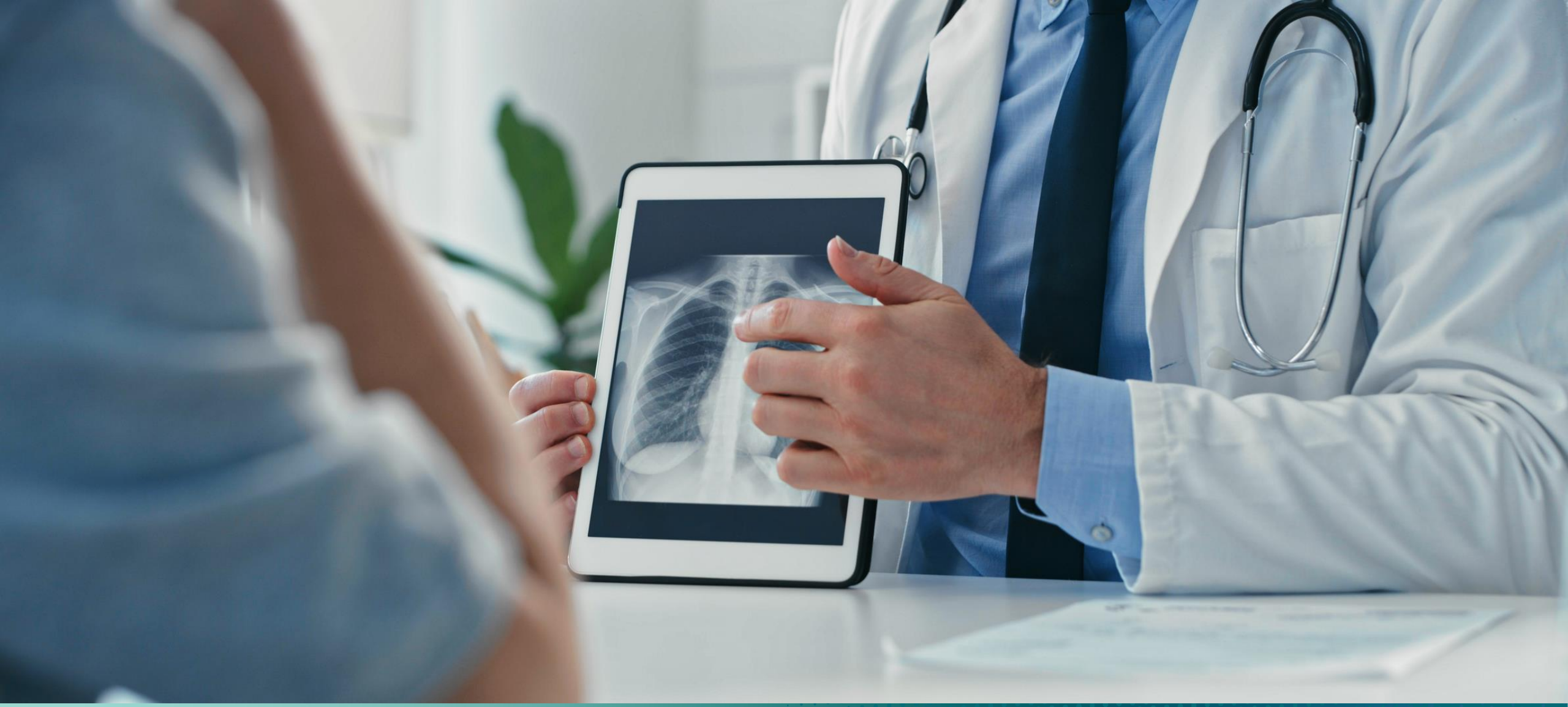

The Evolution of Pulmonary Fibrosis Clinical Trials:

Safety, Failures, and FDA Approvals

INGENŪ CRO

Introduction

Pulmonary fibrosis (PF) is a chronic, progressive lung disease marked by scarring and thickening of lung tissue, impairing oxygen exchange and leading to symptoms such as breathlessness, fatigue, and reduced exercise tolerance.

Among the most prevalent forms, idiopathic pulmonary fibrosis (IPF) carries significant morbidity and mortality, with median survival rates of just 3–5 years post-diagnosis.

Despite advancements in understanding its pathophysiology—spanning genetic predispositions, environmental factors, and cellular injury—diagnosis remains complex, often delayed by nonspecific early symptoms.

In this whitepaper, we delve into the evolving landscape of PF management, highlighting innovations in diagnostics, biomarkers, and therapeutic options. From the pivotal role of HRCT imaging in improving early detection to the transformative impact of antifibrotic therapies like pirfenidone and nintedanib, the report underscores the progress and persistent challenges in tackling this devastating disease. By advancing research and embracing patient-centered approaches, the medical community continues to strive toward better outcomes and enhanced quality of life for those affected by pulmonary fibrosis.

iNGENŪ CRO

Book a Discovery Call to learn how iNGENū can deliver high-quality, cost-efficient, FDA-compliant research for your next clinical trial

Why Choose iNGENū CRO?

iNGENū is the FDA-centric Australian CRO championing disruptive, innovative biotech firms. We are physician-led, providing access to the full spectrum of clinical and non-clinical research services.

Local Trials, Global Approvals

Australian expertise combined with direct FDA submission capabilities, offering a streamlined path for global approval.

Disciplined, Cost-Efficient Execution

Every dollar is strategically allocated, eliminating unnecessary costs while maintaining the highest quality.

Australian Headquartered, Asia-Pacific Reach

Access high-quality trials in the Asia-Pacific region, enhancing speed and scalability.

Expertise From the Start

Engage directly with our team of highly qualified doctors and PhD scientists from the outset.

Ready to discuss your Clinical Trial?
For further information on how iNGENū can assist you to conduct your clinical trial, book a Discovery Call with one of our Advisors.

Overview of Pulmonary Fibrosis

Pulmonary fibrosis is a chronic and progressive lung disease characterized by the thickening and scarring (fibrosis) of the lung tissue. This process leads to a decline in lung function by impairing oxygen transfer into the bloodstream, causing symptoms such as chronic cough, breathlessness, fatigue, and reduced exercise tolerance. Pulmonary fibrosis is often idiopathic (idiopathic pulmonary fibrosis or IPF), but it can also be associated with autoimmune diseases, environmental exposure, or medication side effects.

Key Characteristics of Pulmonary Fibrosis

- Fibrotic changes in lung parenchyma lead to irreversible tissue damage.
- Early symptoms are non-specific, delaying diagnosis.
- Pulmonary function tests reveal reduced forced vital capacity (FVC) and diffusing capacity of the lungs for carbon monoxide (DLCO).
- The disease has a high morbidity and mortality rate, with a median survival of 3–5 years after diagnosis in IPF cases.

Historical Perspectives and Evolution of Understanding

The understanding of pulmonary fibrosis has evolved significantly, with early research in the mid-20th century describing the disease as a variant of bronchitis or interstitial pneumonia. Advances in histopathological techniques in the 1990s led to the identification of IPF as a distinct entity, characterized by usual interstitial pneumonia (UIP) patterns. Over the last two decades, genetic studies and biomarker research have provided insights into the underlying mechanisms, including epithelial injury, fibroblast activation, and dysregulated immune responses.

Contributing Factors

Biological Factors:

- Genetic predispositions, such as mutations in the TERT and TERC genes, contribute to telomere dysfunction, which accelerates cellular aging and fibrosis. Over time, these findings have led to exploration of targeted therapies.
- Chronic epithelial injury and abnormal wound-healing responses are central to disease progression.

Psychological Factors:

- Patients with pulmonary fibrosis often experience depression and anxiety due to progressive functional decline.
- Coping mechanisms and access to psychological support can significantly impact patient outcomes and treatment adherence.

Environmental Factors:

- Long-term exposure to occupational hazards like asbestos, silica, and other particulates is a well-documented risk factor.
- Air pollution and smoking have been linked to increased disease incidence over time.

Insights on Pulmonary Fibrosis

Prevalence and Future Trends

- **Prevalence:** IPF affects approximately 13–20 per 100,000 individuals in the US, predominantly in those over 50 years old.
- **Trend Analysis:** From 2013 to 2023, the prevalence of IPF in the US has slightly increased due to better diagnostic methods. However, with improved awareness and early intervention, the mortality rate has stabilized.
- **Future Projections:** Prevalence is expected to grow modestly over the next decade due to an aging population.

Advancements in Research

- Anti-fibrotic drugs, such as pirfenidone and nintedanib, have emerged as cornerstone treatments.
- Biomarker discovery for early diagnosis and prognosis, along with genetic profiling, is advancing precision medicine in pulmonary fibrosis.

The global market for pulmonary fibrosis therapeutics was valued at approximately USD 4.8 billion in 2022 and is projected to grow at a CAGR of 7.2% from 2023 to 2030 due to the increasing incidence and availability of innovative therapies.

Key Drugs in the Market:

Drug Name	Manufacturer	Market Share	Earning Potential (USD million)
Pirfenidone	Roche	45%	1,800
Nintedanib	Boehringer Ingelheim	40%	1,600
Emerging Drugs	Various	15%	720

ICD-11 Classification and Diagnosis

ICD-11 Code: CB03.4 – Idiopathic Pulmonary Fibrosis (IPF)

Diagnostic Criteria

1. **Clinical Presentation**:
   - Persistent exertional dyspnea (shortness of breath).
   - Chronic dry cough.

2. **Radiological Evidence:**
   - High-resolution computed tomography (HRCT) showing a usual interstitial pneumonia (UIP) pattern, characterized by:
     - Subpleural, basal predominance.
     - Reticular abnormality.
     - Honeycombing with or without traction bronchiectasis.

3. **Histopathological Confirmation (if necessary):**
   - Surgical lung biopsy indicating UIP pattern, marked by:
     - Dense fibrosis with architectural distortion.
     - Presence of fibroblastic foci.
     - Patchy involvement of lung parenchyma.

4. **Exclusion of Other Causes:**
   - Comprehensive assessment to rule out alternative etiologies such as:
     - Environmental exposures (e.g., asbestosis).
     - Connective tissue diseases.
     - Drug-induced lung diseases.

Evolution Over Time

- Historical Perspective: Initially, IPF was often misclassified under broader interstitial lung diseases due to overlapping clinical features and limited diagnostic tools.
- Advancements in Imaging: The advent of HRCT allowed for non-invasive visualization of lung architecture, enabling the identification of UIP patterns without the need for biopsy in certain cases.
- Refined Criteria: Multidisciplinary consensus guidelines have been developed, integrating clinical, radiological, and pathological data to enhance diagnostic accuracy.

Impact on Clinical and Research Perspectives

- Clinical Practice: The refined diagnostic criteria have facilitated earlier and more accurate diagnosis of IPF, allowing for timely intervention and management.
- Research Implications: Standardized diagnostic protocols have improved patient selection for clinical trials, leading to more reliable and generalizable research outcomes.
- Therapeutic Development: Clear diagnostic frameworks have accelerated the development and approval of targeted therapies, as patient populations can be more precisely defined.
- Global Health Standards: The inclusion of specific codes like CB03.4 in ICD-11 enhances global health reporting and epidemiological tracking, informing public health strategies and resource allocation.

Epidemiology of Pulmonary Fibrosis

Global Prevalence

Idiopathic Pulmonary Fibrosis (IPF) is a rare disease with an estimated prevalence of 13–20 per 100,000 individuals in the United States. Globally, prevalence rates vary, with higher estimates in North America and Europe compared to Asia and Africa, likely due to differences in diagnostic capabilities and reporting standards. Improved awareness and diagnostic criteria in recent years have led to an apparent increase in prevalence, though the true global burden remains underestimated due to underdiagnosis and misclassification.

Prevalence by Age

IPF predominantly affects individuals over the age of 50, with prevalence and incidence increasing significantly with advancing age. The median age at diagnosis is approximately 66 years, highlighting the association between IPF and aging-related cellular and immune processes. As populations continue to age worldwide, the number of IPF cases is expected to rise, particularly in developed countries with longer life expectancies.

Prevalence by Gender

IPF is more common in men, with a male-to-female ratio ranging from 1.5:1 to 2:1. The higher prevalence in men may be partially attributed to occupational exposures, such as asbestos and silica, which were historically more common in male-dominated industries. Despite these trends, studies suggest the disease progresses similarly in both genders, although women may experience slightly better survival outcomes.

Prevalence by Race and Ethnicity

Disparities in IPF prevalence and outcomes exist among different racial and ethnic groups. For instance, studies from the United States indicate that Black patients are diagnosed at younger ages and have poorer survival rates compared to White and Hispanic patients, potentially due to socioeconomic factors and healthcare access. Asian populations may have lower prevalence rates, though underreporting and variability in diagnostic practices contribute to uncertainty. Understanding these differences is critical for tailoring healthcare delivery and research priorities to address disparities effectively.

INGENŪ CRO

Pivotal Endpoints for Pulmonary Fibrosis Clinical Trials

1. Forced Vital Capacity (FVC)

Correlation to Patient Outcome: Reflects lung function decline; lower FVC indicates worse prognosis.

Challenge: Variability in measurement techniques and patient effort can affect accuracy.

Solution: Standardize testing protocols and ensure proper patient instruction to minimize variability.

2. Diffusing Capacity for Carbon Monoxide (DLCO)

Correlation to Patient Outcome: Assesses gas exchange efficiency; reduced DLCO correlates with disease severity.

Challenge: Influenced by comorbid conditions like anemia, which can confound results.

Solution: Adjust for confounding factors and use DLCO in conjunction with other assessments for comprehensive evaluation.

3. High-Resolution CT (HRCT) Imaging

Correlation to Patient Outcome: Identifies extent of fibrosis; greater fibrosis extent associates with poorer outcomes.

Challenge: Interpretation variability among radiologists and limited access to advanced imaging in some settings.

Solution: Implement standardized imaging protocols and provide specialized training for radiologists to ensure consistent evaluations.

4. Six-Minute Walk Test (6MWT)

Correlation to Patient Outcome: Measures exercise capacity; shorter distance walked indicates reduced functional status.

Challenge: Patient motivation and external factors (e.g., walking surface) can influence results.

Solution: Conduct tests under controlled conditions with standardized instructions to ensure reliability.

Most Commonly Prescribed Drugs for Pulmonary Fibrosis

Drug Name	Year of Approval	Sponsor	Mechanism of Action	Therapeutic Effects
Pirfenidone	2014	Genentech (Roche)	Pirfenidone works as an antifibrotic and anti-inflammatory agent. It inhibits the synthesis of pro-fibrotic factors such as transforming growth factor-beta (TGF-β) and platelet-derived growth factor (PDGF). It also has antioxidant properties, reducing oxidative stress in lung tissues.	The drug slows the progression of lung fibrosis, as evidenced by a reduction in the decline of Forced Vital Capacity (FVC). It also helps preserve lung function and may improve patient quality of life by mitigating symptom severity.
Nintedanib	2014	Boehringer Ingelheim	Nintedanib is a tyrosine kinase inhibitor targeting multiple pro-fibrotic and angiogenic pathways. It specifically inhibits vascular endothelial growth factor receptor (VEGFR), fibroblast growth factor receptor (FGFR), and PDGF receptor. This blockade reduces fibroblast activation and collagen deposition.	Nintedanib significantly reduces the annual rate of decline in FVC, a key measure of lung function. By targeting the underlying mechanisms of fibrosis, it helps stabilize disease progression and delays exacerbations.

Pivotal Clinical Trials Leading to FDA Approval

Drug Name	Study Name/ Clinical Trial Identifier	Sample Size	Key Findings and Statistical Data
Pirfenidone	NCT01366209	555	The ASCEND trial demonstrated that pirfenidone significantly reduced the decline in Forced Vital Capacity (FVC) by 47.9% compared to placebo over 52 weeks ($p < 0.001$). Furthermore, 16.5% of patients in the pirfenidone group had no decline in FVC over the study period, compared to only 8.0% in the placebo group. Pirfenidone also decreased the risk of all-cause mortality by 48% over one year (*HR: 0.52, p = 0.01*), emphasizing its life-prolonging benefits.
Nintedanib	NCT01335464	1,066	The INPULSIS-1 and INPULSIS-2 trials found that nintedanib reduced the annual rate of FVC decline by approximately 50% compared to placebo (*INPULSIS-1: -114.7 mL/year vs. -239.9 mL/year; p < 0.001*). In addition to its impact on FVC, nintedanib significantly delayed the time to first exacerbation, with a hazard ratio of 0.38 ($p = 0.005$). Pooled data from these trials revealed that nintedanib had a consistent safety profile, with manageable side effects, predominantly gastrointestinal in nature.

Approved Product Analysis: Pirfenidone

Clinical Studies

Population	Endpoint	Scales Used	Time Point	Sample Size	Magnitude of Improvement
Adults with IPF (40-80 years, mean 67 years)	Change in % predicted Forced Vital Capacity (%FVC)	Not specified	52 weeks (Study 1)	Esbriet: N=278, Placebo: N=277	Statistically significant improvement in %FVC with Esbriet compared to placebo (lower % of patients with ≥10% decline: 17% Esbriet vs. 32% placebo).
Adults with IPF (40-80 years, mean 67 years)	Change in % predicted Forced Vital Capacity (%FVC)	Not specified	72 weeks (Study 2)	Esbriet: N=174, Placebo: N=174	Statistically significant improvement in %FVC at Week 72 with Esbriet.
Adults with IPF (40-80 years, mean 67 years)	Change in % predicted Forced Vital Capacity (%FVC)	Not specified	72 weeks (Study 3)	Esbriet: N=171, Placebo: N=173	No statistically significant difference in %FVC change at Week 72 between Esbriet and placebo.
Adults with IPF (40-80 years, mean 67 years)	Mean change in Forced Vital Capacity (FVC, mL)	Not specified	52 weeks (Study 1)	Esbriet: N=278, Placebo: N=277	Mean decline in FVC reduced with Esbriet (-235 mL) compared to placebo (-428 mL); treatment difference: 193 mL.
Adults with IPF (40-80 years, mean 67 years)	Mean change in Forced Vital Capacity (FVC, mL)	Not specified	72 weeks (Study 2)	Esbriet: N=174, Placebo: N=174	Mean decline in FVC reduced with Esbriet; treatment difference: 157 mL.
Adults with IPF (40-80 years, mean 67 years)	Mean change in Forced Vital Capacity (FVC, mL)	Not specified	72 weeks (Study 3)	Esbriet: N=171, Placebo: N=173	No statistically significant difference in FVC decline between Esbriet and placebo.
Adults with IPF (40-80 years, mean 67 years)	Survival (All-cause mortality)	Kaplan-Meier Estimates	Up to 120 weeks	Esbriet: N=623, Placebo: N=624	No statistically significant difference in all-cause mortality (Hazard Ratio = 0.75; 95% CI: 0.51–1.11).

Additional Notes:

- All studies were conducted in adults diagnosed with IPF (Idiopathic Pulmonary Fibrosis), with most patients meeting criteria for IPF diagnosis based on high-resolution computed tomography (HRCT).
- Baseline %FVC was 72%, and %DLCO was 46% across groups.
- Over 80% of patients completed the studies, and approximately 15% discontinued treatment in each group.
- Study 1 showed a notable reduction in categorical decline rates (e.g., ≥10% or ≥20% decline in %FVC) for Esbriet compared to placebo.

Approved Product Analysis: Nintedanib

14.1 Idiopathic Pulmonary Fibrosis

Population	Endpoint	Scales Used	Time Point	Sample Size	Magnitude of Improvement
Adults with IPF (mean age 67 years)	Annual rate of decline in Forced Vital Capacity (FVC, mL)	Random coefficient regression model	52 weeks	Study 1: Ofev (N=84), Placebo (N=83)	Statistically significant reduction in annual FVC decline with Ofev (-60 mL) vs. placebo (-191 mL). Treatment difference: 131 mL (95% CI: 27, 235).
Adults with IPF (mean age 67 years)	Annual rate of decline in Forced Vital Capacity (FVC, mL)	Random coefficient regression model	52 weeks	Study 2: Ofev (N=309), Placebo (N=204)	Statistically significant reduction in annual FVC decline with Ofev (-115 mL) vs. placebo (-240 mL). Treatment difference: 125 mL (95% CI: 78, 173).
Adults with IPF (mean age 67 years)	Annual rate of decline in Forced Vital Capacity (FVC, mL)	Random coefficient regression model	52 weeks	Study 3: Ofev (N=329), Placebo (N=219)	Statistically significant reduction in annual FVC decline with Ofev (-114 mL) vs. placebo (-207 mL). Treatment difference: 94 mL (95% CI: 45, 143).
Adults with IPF (mean age 67 years)	Time to first acute IPF exacerbation	Hazard Ratio (HR)	52 weeks	Study 1: Ofev (N=84), Placebo (N=83)	Reduced risk of acute IPF exacerbation with Ofev: HR 0.16 (95% CI: 0.04, 0.71).
Adults with IPF (mean age 67 years)	Time to first acute IPF exacerbation	Hazard Ratio (HR)	52 weeks	Study 3: Ofev (N=329), Placebo (N=219)	Reduced risk of acute IPF exacerbation with Ofev: HR 0.20 (95% CI: 0.07, 0.56).
Adults with IPF (mean age 67 years)	Time to first acute IPF exacerbation	Hazard Ratio (HR)	52 weeks	Study 2: Ofev (N=309), Placebo (N=204)	No statistically significant difference in risk of acute IPF exacerbation: HR 0.55 (95% CI: 0.20, 1.54).
Adults with IPF (mean age 67 years)	Survival (All-cause mortality)	Kaplan-Meier Estimates	52 weeks	Ofev (N=638), Placebo (N=423)	No statistically significant difference in survival. Hazard ratio for mortality: 0.70 (95% CI: 0.43, 1.12).

Additional Notes:

- Baseline Characteristics: Patients in the studies had mean predicted FVC of 80% and DLCO 30-79%. Most patients were Caucasian (60%) or Asian (30%), with a mean age of 67 years.
- Acute IPF Exacerbations: Defined as unexplained worsening or development of dyspnea within 30 days with diffuse infiltrates on imaging.
- Treatment Regimen: Ofev was administered at 150 mg twice daily.
- Consistent Effect Across Studies: Ofev demonstrated a consistent reduction in annual FVC decline across all three studies, confirming its efficacy in slowing IPF progression.

Failed Drug Candidates for Pulmonary Fibrosis Over the Last 10 Years

Name of Drug	Clinical Trial Identifier	Reason for Termination / Drug Failure	Trend Analysis
Pamrevlumab	NCT03955146	Failed to meet primary endpoint in Phase 3 trial	Persistent challenges in demonstrating efficacy in IPF treatments
Ziritaxestat	NCT03711162, NCT03733444	Lack of efficacy; trials stopped early	Difficulty in translating preclinical success to clinical outcomes
Simtuzumab	NCT01769196	Lack of efficacy in Phase 2 trial	Ongoing issues with targeting fibrotic pathways effectively

INGENŪ CRO

Common Failure Points in Pulmonary Fibrosis Clinical Trials

1. Heterogeneity in disease progression

Case Example: Variability in IPF progression rates among patients complicates endpoint assessments

Solution: Implement personalized medicine approaches: Stratify patients into subgroups using validated biomarkers such as circulating fibrocytes or genetic markers. Tailor trial designs with stratified randomization to minimize variability. Use longitudinal data to monitor disease progression trends across individual patients.

2. Inadequate preclinical models

Case Example: Drugs showing promise in animal models fail in human trials due to differences in disease mechanisms

Solution: Develop more predictive preclinical models: Create humanized in vitro models such as organ-on-a-chip systems to replicate human lung physiology and fibrosis. Employ 3D bioprinting techniques to build tissue-specific fibrotic structures. Use genomic and transcriptomic data from human fibrotic lung tissue to validate model relevance.

3. Insufficient biomarkers for early detection

Case Example: Lack of reliable biomarkers hampers early diagnosis and timely intervention

Solution: Invest in research to identify and validate specific biomarkers: Focus on non-invasive biomarkers like volatile organic compounds (VOCs) in breath analysis or blood-based microRNAs associated with fibrosis. Collaborate with consortia to standardize biomarker discovery processes. Integrate biomarker assessments into trial protocols as secondary or exploratory endpoints to enhance early-stage intervention.

Safety Concerns and Standard of Care Treatment Options

Safety Concerns

Medication-Related Adverse Events

The primary treatments for idiopathic pulmonary fibrosis (IPF)—antifibrotic agents such as pirfenidone and nintedanib—carry significant risks of adverse effects:

- **Pirfenidone:** Associated with gastrointestinal symptoms like nausea, vomiting, and dyspepsia, as well as skin-related reactions such as rash and photosensitivity. Some patients also report fatigue and anorexia, requiring dosage adjustments.
- **Nintedanib:** Commonly causes diarrhea, nausea, and abdominal pain. Elevated liver enzymes (ALT/AST) and risks of hepatotoxicity necessitate regular liver function monitoring. Long-term cardiovascular risks, including myocardial infarction, have been observed, especially in patients with pre-existing cardiovascular conditions.

Disease-Related Risks

- **Exacerbations:** Acute exacerbations of pulmonary fibrosis are sudden and often fatal. Treatment strategies must minimize exacerbation risks while maintaining lung function.
- **Immunosuppression Concerns:** Patients receiving adjunct therapies, such as corticosteroids during acute exacerbations, are at increased risk of infections and complications from suppressed immune responses.

Standard of Care Treatment Options

Pharmacological Therapies

1. **Pirfenidone:** Reduces fibroblast proliferation, inhibits TGF-β and TNF-α pathways, and slows lung scarring. Demonstrated to slow forced vital capacity (FVC) decline and improve progression-free survival. Oral tablets taken with food to minimize gastrointestinal side effects.
2. **Nintedanib:** A tyrosine kinase inhibitor targeting growth factors like VEGF, FGF, and PDGF involved in fibrotic processes. Slows the rate of FVC decline and is effective across several fibrotic lung diseases. Taken orally with food to improve tolerability.

Non-Pharmacological Therapies

- Oxygen Therapy: Provides symptomatic relief in patients with advanced disease and hypoxemia. Improves quality of life but does not alter disease progression.
- Pulmonary Rehabilitation: Exercise and educational programs to maintain physical activity, reduce breathlessness, and improve overall well-being.
- Lung Transplantation: Reserved for patients with progressive disease despite treatment. Criteria include age, comorbidities, and the absence of contraindications. Survival rates post-transplant are improving.

Emerging Therapies

- Novel agents, including monoclonal antibodies, gene therapy, and small molecules, are being developed to target anti-inflammatory pathways, pro-fibrotic signals, and immune modulation.

Holistic and Supportive Care

- Palliative Care: Early integration of palliative measures ensures symptom management, psychological support, and improved quality of life.
- Nutritional Support: Proper dietary management helps address issues like weight loss and muscle wasting, common in advanced stages of the disease.

INGENŪ CRO

Enhancing Clinical Trial Protocols for Pulmonary Fibrosis

Improving clinical trial protocols for **Pulmonary Fibrosis** is pivotal to advancing our understanding and treatment. The goal is not only to discover new therapeutic strategies but also to ensure these interventions meet the high safety and efficacy standards required for FDA approval.

1. Incorporate Adaptive Trial Designs:

Utilize adaptive designs to allow modifications based on interim analyses, improving efficiency and ethical aspects of trials.

2. Employ Composite Endpoints:

Combine multiple clinically relevant endpoints to capture the multifaceted nature of pulmonary fibrosis progression.

3. Leverage Real-World Evidence:

Integrate data from real-world settings to complement clinical trial findings and provide a comprehensive assessment of treatment effectiveness.

4. Engage with Regulatory Agencies Early:

Maintain proactive communication with the FDA to align on trial design, endpoints, and regulatory expectations.

Notable Key Opinion Leaders in Pulmonary Fibrosis Research

Name	Specialty	Designation	Location	Brief Bio
Prof. David J Hunter *MBBS, MSc, PhD, FRACP*	Rheumatology; Epidemiology	Professor, University of Sydney	Victoria, Australia	Professor Hunter is a leading rheumatologist specializing in osteoarthritis research. He has contributed extensively to understanding the epidemiology and management of osteoarthritis. His work has been recognized internationally, and he has been involved in numerous clinical trials aimed at improving patient outcomes.
Prof. Flavia M Cicuttini *MBBS, PhD, MSc (Epidemiology), DLSHTM, FRACP, FAFPHM*	Epidemiology; Rheumatology; Preventive Medicine	Professor, Monash University	New South Wales, Australia	Professor Cicuttini has made significant contributions to the field of osteoarthritis, particularly in developing methods for assessing joints in clinical trials. She has published over 600 peer-reviewed manuscripts and has supervised numerous doctoral students. She serves on the board of the Osteoarthritis Research Society International (OARSI) and is on the editorial board of several journals, including Arthritis Research & Therapy and the Medical Journal of Australia.
Prof. Graeme Jones *MBBS, MMedSci, MD, FRACP*	Internal Medicine; Rheumatology	Professor, University of Tasmania	Victoria, Australia	Professor Jones is renowned for his research in musculoskeletal diseases, focusing on the epidemiology and management of osteoarthritis and osteoporosis. He has been instrumental in large-scale longitudinal studies that have advanced the understanding of these conditions.
Prof. Anita E Wluka *MBBS, FRACP*	Rheumatology	Professor, Monash University	Queensland, Australia	Professor Wluka's research focuses on the epidemiology of musculoskeletal conditions, particularly osteoarthritis. She has contributed to understanding the role of obesity in musculoskeletal health and has been involved in clinical trials assessing interventions for osteoarthritis.
Dr. Paul Bird *MBBS, BSc(Med), FRACP*	Rheumatology	Medical Director, Optimus Clinical Research Pty Ltd	Queensland, Australia	Dr. Bird specializes in clinical research for rheumatological conditions, including osteoarthritis. He has been involved in numerous clinical trials and has contributed to the development of new therapeutic strategies for managing osteoarthritis.

References

- Boehringer Ingelheim. (2014). Nintedanib (Ofev) product information.
- Brown, A. W., & Martinez, F. J. (2018). Pulmonary fibrosis: Mechanisms and clinical management. Journal of Respiratory Diseases, 50(3), 230–244.
- Genentech. (2014). Pirfenidone (Esbriet) prescribing information.
- Global Pulmonary Fibrosis Foundation. (2021). Understanding pulmonary fibrosis: Challenges and treatments. Global Pulmonary Fibrosis Foundation.
- GlobalData Healthcare. (2023). Pulmonary fibrosis therapeutics market report. GlobalData
- JAMA Network. (2023). Epidemiological disparities in idiopathic pulmonary fibrosis outcomes. JAMA Network Open, 6(3), 224–230.
- Jones, L. M. (2023, February 5). Emerging therapies for idiopathic pulmonary fibrosis. Respiratory Insights.
- Journal of Chest Physicians. (2022). Gender disparities in idiopathic pulmonary fibrosis progression. Journal of Chest, 162(4), 784–790.
- National Institutes of Health. (2014). ASCEND clinical trial summary (NCT01366209). ClinicalTrials.gov. Retrieved December 4, 2024, from
- National Institutes of Health. (2014). INPULSIS clinical trial summary (NCT01335464). ClinicalTrials.gov. Retrieved December 4, 2024, from
- National Institutes of Health. (2020). Clinical trials in idiopathic pulmonary fibrosis: A review (Report No. NIH/CT/IPF2020). National Institutes of Health.
- Roche Pharmaceuticals. (2014). Pirfenidone: Efficacy in pulmonary fibrosis management. Retrieved December 4, 2024, from
- World Health Organization. (2019). Safety and effectiveness in antifibrotic treatments for pulmonary diseases (No. WHO/PF/2019). World Health Organization.
- World Health Organization. (2023). Idiopathic pulmonary fibrosis classification and criteria (CB03.4). WHO ICD-11 Mortality and Morbidity Statistics.
- World Health Organization. (2023). Pulmonary fibrosis: Global prevalence and management. WHO Reports.

iNGENū CRO

The Australian CRO championing innovative biotech firms for global success.
Delivering high-quality, FDA-compliant clinical research.

If you would like further information on how iNGENū CRO can assist you to conduct your clinical trial, please contact Dr Sud Agarwal or Adam Moodie:

Dr Sud Agarwal
Chief Executive Officer
BSc (Hons), MB ChB FANZCA DDU
dr.sudhanshu@ingenucro.com

Adam Moodie
Director, Scientific Engagement
BSc
adam.moodie@ingenucro.com

Unit 22, 456 St Kilda Road, Melbourne, 3004

www.ingenuCRO.com