

# PIRFENIDONE (ESBRIET)

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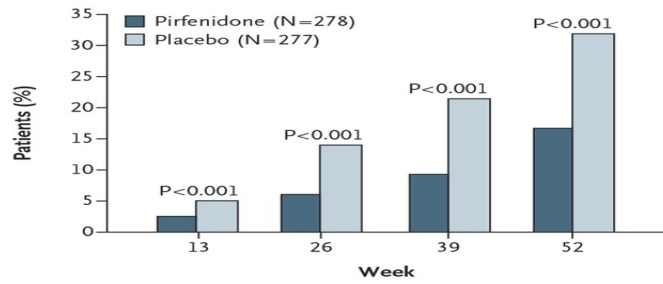
- ▶ First recognized as an anti-fibrotic agent in 1994 by SB Margolin
- ▶ Initial data supporting a role for pirfenidone in IPF
  - ▶ Raghu et al, 1999 – 54 patients with severe IPF
    - ▶ Study design suboptimal
    - ▶ Many dropouts
    - ▶ Possible signal suggesting stabilization/equivalence with more toxic therapies
- ▶ Development rights purchased by Intermune in 2007
  - ▶ First American Phase III Trials completed in 2009
  - ▶ “Tie Breaker “ Trial reported in May 2014
- ▶ Approval for clinical use by FDA – 1 year ago

## HISTORY

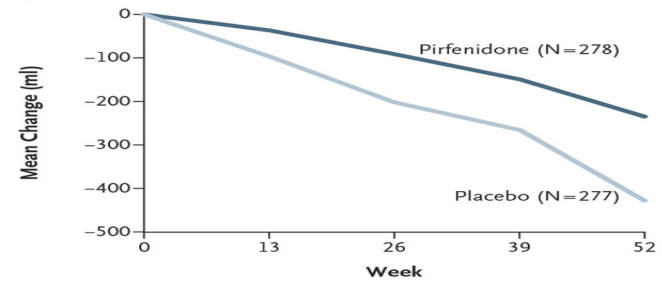


15 YEARS FROM CONCEPT TO  
APPROVAL

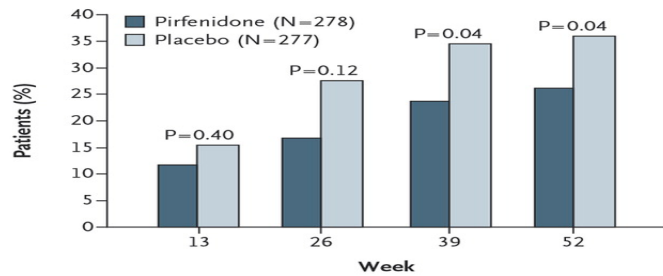
**A Decreased FVC or Death**



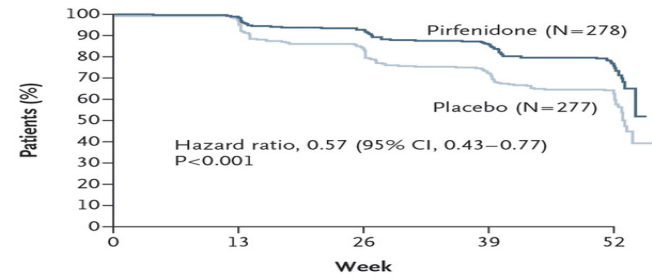
**B Change in FVC**



**C Decreased Walk Distance or Death**



**D Progression-free Survival**



No. at Risk	0	13	26	39	52
Pirfenidone	276	269	243	219	144
Placebo	273	262	225	192	113

DOES IT WORK?

- ▶ After 52 weeks, only half as many patients receiving pirfenidone had a significant decline in FVC ( $\geq 10\%$  predicted) as did placebo patients (46 vs. 88 respectively). More than twice as many subjects taking pirfenidone lost no lung function (63 vs. 27), and slightly fewer patients taking pirfenidone had a decline in 6 minute walk distance by  $\geq 50$  meters.
- ▶ Pirfenidone did not reduce mortality compared to placebo in the ASCEND trial. However, when ASCEND's results were pooled with those from CAPACITY and the Japan trial, **patients taking pirfenidone had half the risk of death from all causes, and one-third the risk of death from idiopathic pulmonary fibrosis** (0.52 and 0.32 hazard ratios respectively, compared to placebo). The pooled numbers (n=1,247) showed:
  - ▶ 22 deaths of any cause on pirfenidone, vs. 42 on placebo
  - ▶ 7 deaths attributable to IPF (pirfenidone) vs. 22 (placebo)

## DOES IT WORK?

- ▶ All patients had IPF
- ▶ Mild to Moderate Disease
- ▶ No data for severe patients
- ▶ Ascend Criteria
  - ▶ FEV1/FVC ratio > 80%
  - ▶ FVC > 50%

WHO SHOULD TAKE IT?

- ▶ How do I know if it is working for me?
  - ▶ We rely on study data
- ▶ How long will I have to take it?
  - ▶ RECAP lasted 7 years !

DOES IT WORK?



SIDE EFFECTS



- ▶ Photosensitivity

- ▶ Use SPF 50 > whenever you go outside
- ▶ Wide brim hat
- ▶ Can possibly occur on exposure to strong artificial light

## SIDE EFFECTS

- ▶ GI toxicity
  - ▶ Nausea, vomiting, diarrhea
    - ▶ Must take with food
    - ▶ Divide pills at meals
    - ▶ Improves over time
  - ▶ Liver function abnormalities
- ▶ Dose adjustment and re-titration

## SIDE EFFECTS

- ▶ Why do I have to take 9 pills a day?
- ▶ Can I take a lower dose?
- ▶ Can I take this drug if I have a disease related to IPF
  - ▶ Rheumatoid Arthritis?
- ▶ Can I take it with other drugs for IPF

QUESTIONS I'VE BEEN ASKED



THANKS

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THANKS