Pirfenidone in IPF

Katerina Samara MD, PhD
Respiratory Physician

Medical Head Hematology/ Specialty Care
Roche Hellas

Thessaloniki 11 May 2019

1. Pirfenidone

2. Randomized Clinical Trials

3. Real world data

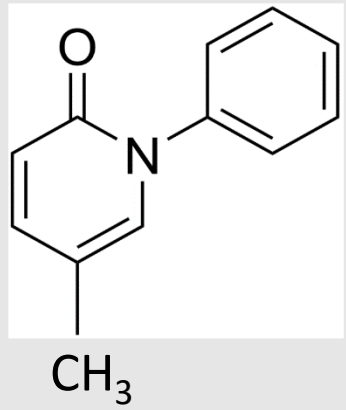
Pirfenidone: An overview

Pirfenidone is an antifibrotic, anti-inflammatory and antioxidant agent that slows functional decline and disease progression in patients with IPF[1]

Pirfenidone (5-methyl-1-phenyl-2-[1H]-pyridone)

- Orally bioavailable[2]
- A synthetic non-peptide molecule[2]
- Of low molecular weight (FW = 185.22 g/mol)[2]
- A pyridone that contains a pyridine ring bearing a ketone[2]

Pirfenidone = $C_{12}H_{11}NO$



Pirfenidone was the first treatment to be approved to treat IPF in Europe and Japan

Pirfenidone is licensed for use in Europe, North America, Asia and Latin America[1]

1. King TE, et al. N Engl J Med 2014;370:2083–2092; 2. National Center for Biotechnology Information. PubChem Compound Database; CID=40632, https://pubchem.ncbi.nlm.nih.gov/compound/40632. Accessed Aug 2017.

Annu. Rev. Med. 2016. 67:25.1–25.9

Pirfenidone Initiates a New Era in the Treatment of Idiopathic Pulmonary Fibrosis

Anna S. Selvaggio and Paul W. Noble

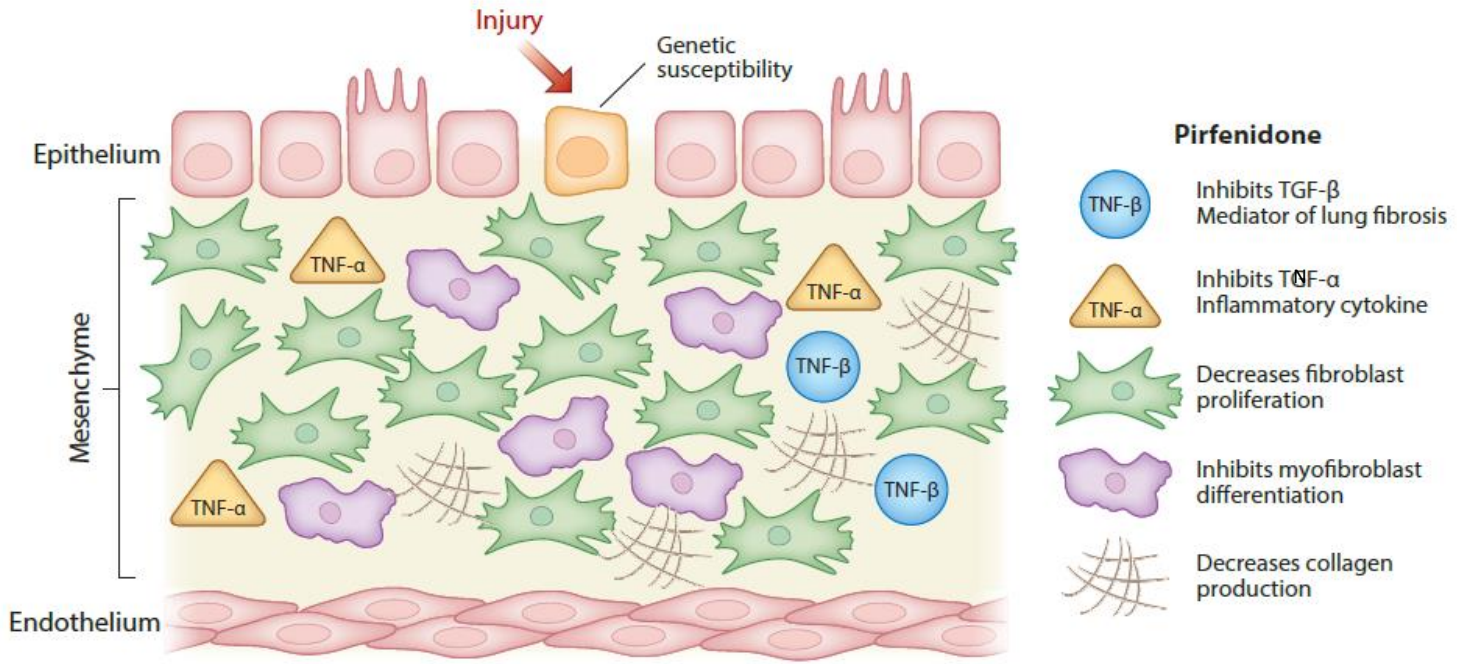
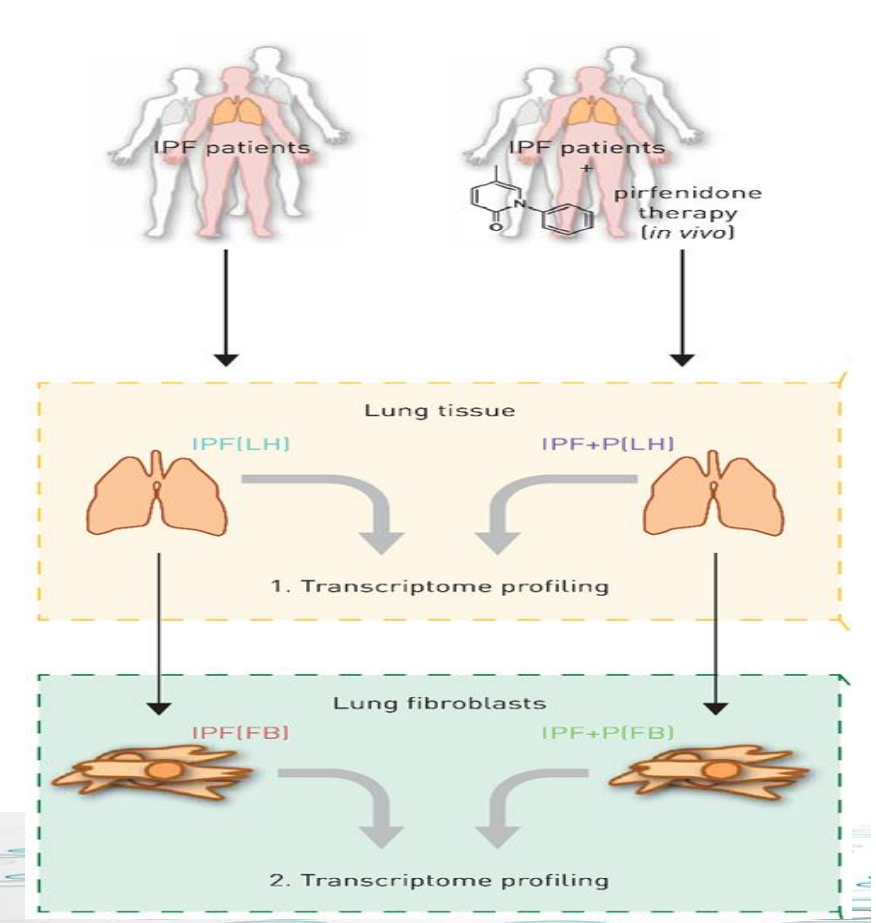
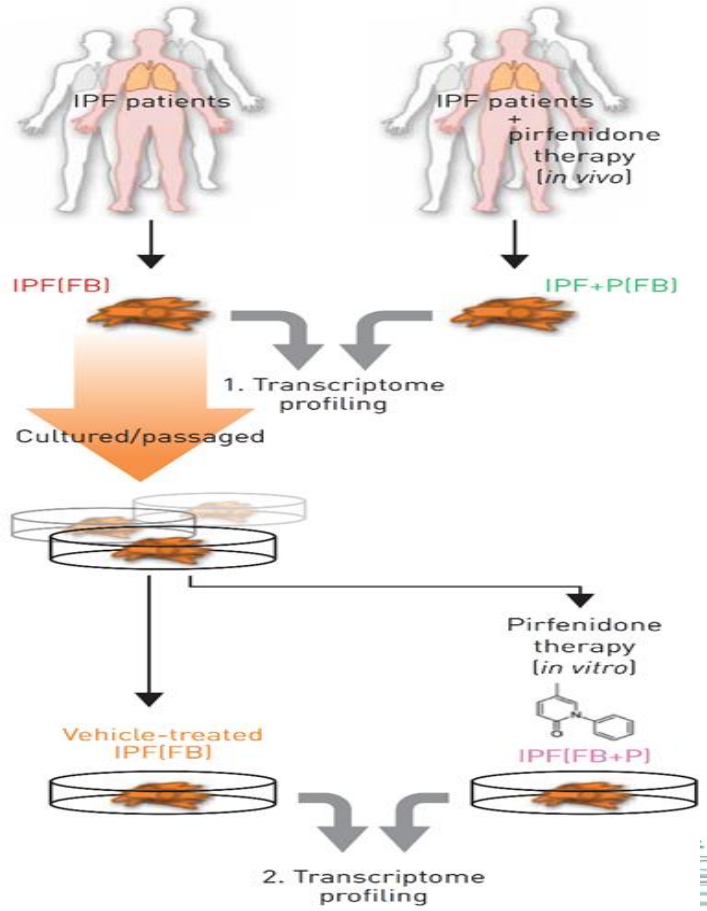


Figure 1

Pirfenidone's proposed mechanism of action is illustrated in a schematic representation of an alveolar septal wall and the extracellular matrix as they appear in idiopathic pulmonary fibrosis.

Transcriptome profiling reveals the complexity of pirfenidone effects in idiopathic pulmonary fibrosis





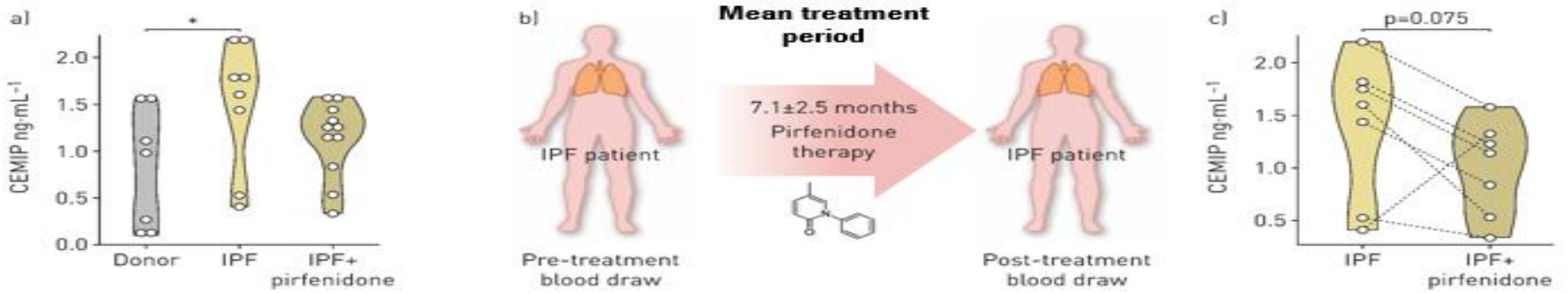
Objective

To ascertain the mechanism of action of pirfenidone by using a comparative transcriptomic approach and analysing lung homogenates (LH) and fibroblasts (FB) from patients with IPF treated with or without pirfenidone

Kwapiszewska et al, Eur Respir J. 2018;52:1800564.

Conclusions

CEMIP levels in the plasma of healthy controls and pirfenidone-treated or -naïve patients with IPF



- Analysis of circulating CEMIP revealed significantly elevated levels in IPF samples compared with age- and sex-matched healthy controls (a)
- In 6 of 7 patients with IPF treated with pirfenidone, treatment was associated with a marked decrease in CEMIP levels (c)

Pirfenidone treatment was associated with major changes in inflammatory processes and cell-cell contacts in LHs, while the most significantly perturbed pathways in FBs were related to metabolic reprogramming, growth and cell division. Genes regulated in both groups were primarily related to the ECM

This study is the first to demonstrate the pro-fibrotic role of CEMIP (cell migration-inducing and hyaluronan-binding protein) in the pathogenesis of IPF, which could serve as a potential pharmacodynamic marker of pirfenidone

Pirfenidone exerts beneficial effects via its action on multiple pathways in both FBs and other pulmonary cells

Kwapiszewska et al, Eur Respir J. 2018;52:1800564.

CEMIP, cell migration-inducing and hyaluronan-binding protein; ECM; extracellular matrix; FB, fibroblast; LH, lung homogenate.

Pirfenidone has antifibrotic, anti-inflammatory and antioxidant actions

Antifibrotic

- Inhibits the synthesis and activity of **TGF-β**, a potent mediator of fibrogenesis[1,2,3]
- Inhibits **fibroblast proliferation**[1,2]
- Attenuates **collagen secretion**[1,2,3,4]
- Attenuates expression of **pro-fibrotic genes** in response to fibrotic stimuli[1,3]

Anti-inflammatory

- **↓ TNF-α** secretion in endotoxin-stimulated cells[5,6,7]
- Prophylactic pirfenidone protects mice from endotoxic shock
  - **↓ Pro-inflammatory** cytokine levels[6]
  - **↑ Anti-inflammatory** cytokine levels[6]

Antioxidant

- Potent **antioxidant** and antifibrotic activity in experimental cirrhosis[8]

Although the exact mechanism of action is unclear, evidence from *in vitro* and *in vivo* studies suggests that pirfenidone has multiple biological effects

TGF-β, transforming growth factor-β; TNF-α, tumour necrosis factor-α.

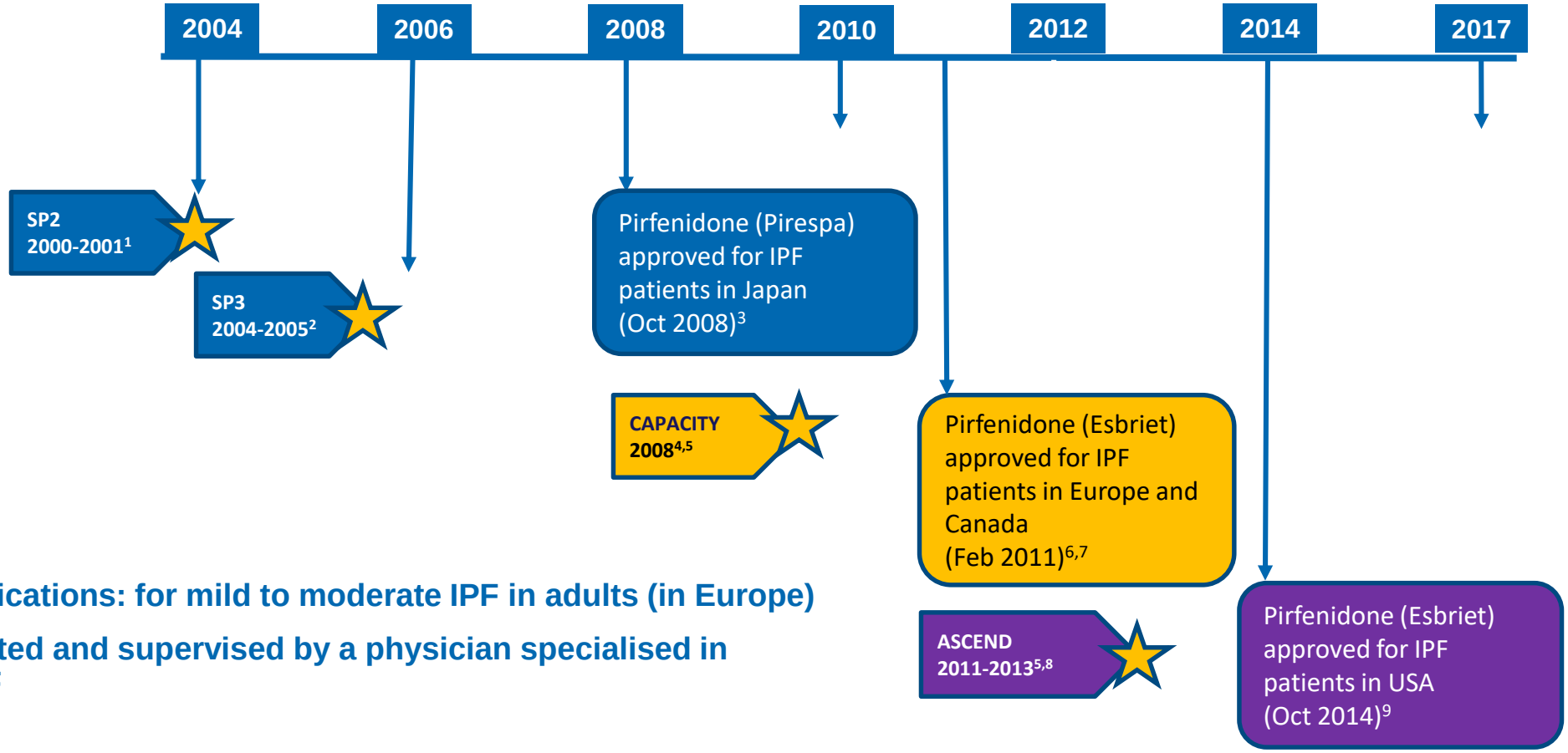
1. Di Sario A, et al. J Hepatol 2002;37:584–591; 2. Schaefer CJ, et al. Eur Respir Rev 2011;20:85–97; 3. Nakayama S, et al. Life Sci 2008;82:210–217; 4. Iyer SN et al. J Pharmacol Exp Ther 1999;289:211–218; 5. Oku H, et al. Eur J Pharmacol 2008;590:400–408; 6. Oku H, et al. Eur J Pharmacol 2002;446:167–176; 7. Grattendick KJ, et al. Int Immunopharmacol 2008;8:679–687; 8. Salazar-Montes A, et al. Eur J Pharmacol 2008;595:69–77.

1. Pirfenidone overview

2. Randomized Clinical Trials

3. Real world data

Pirfenidone: the first approved IPF drug



Therapeutic indications: for mild to moderate IPF in adults (in Europe)

Should be initiated and supervised by a physician specialised in treatment of IPF

1. Azuma A et al. Am J Respir Crit Care Med 2005;171:1040-1047; 2. Tanaguchi H et al. Eur Respir J 2010;35:821-829;
3. Japanese approval. Available at: https://www.pmda.go.jp/files/000153687.pdf;
4. Noble PW et al. Lancet 2011;377:1760-1769; 5. Noble PW et al. Eur Respir J 2016;47:243-253;
6. Esbriet SmPC. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002154/human_med_001417.jsp&mid=WC0b01ac058001d124;
7. Esbriet Product Monograph (Canada). Available at: http://www.rochecanada.com/en/products/pharmaceuticals/consumer_information/esbriet.html;
8. King TE Jr et al. N Engl J Med 2014;370:2083-2092; 9. Esbriet PI. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022535s001lbl.pdf

Pirfenidone: Overview of key clinical trials (1718 pts)

Study (geographical region)	Treatment protocol	N	Duration	Primary efficacy analysis
InterMune-sponsored multinational Phase III studies				
CAPACITY Study 004 (Europe/US/Australia)[1]	Pirfenidone 2403 mg/d vs placebo vs pirfenidone 1197 mg/d	435	72 weeks	Change in % predicted FVC from baseline to Week 72
CAPACITY Study 006 (Europe/US/Australia)[1]	Pirfenidone 2403 mg/d vs placebo	344	72 weeks	Change in % predicted FVC from baseline to Week 72
ASCEND Study 016 (Europe/US/Australia/Asia/ South America)[2]	Pirfenidone 2403 mg/d vs placebo	555	52 weeks	Change from baseline at Week 52 in % predicted FVC
Shionogi-sponsored studies				
SP2 Phase II[3] (Japan)	Pirfenidone 1800 mg/d vs placebo	109	52 weeks	Change in 6MWT Sp_{O_2} from baseline to 48 weeks
SP3 Phase III[4] (Japan)	Pirfenidone 1800 mg/d vs placebo vs 1200 mg/d	275	325 days	Change in VC from baseline to 52 weeks

6MWT: 6-minute walk test; FVC: forced vital capacity; ITT: intention to treat; Sp_{O_2}: oxygen saturation measured by pulse oximetry; VC: vital capacity.

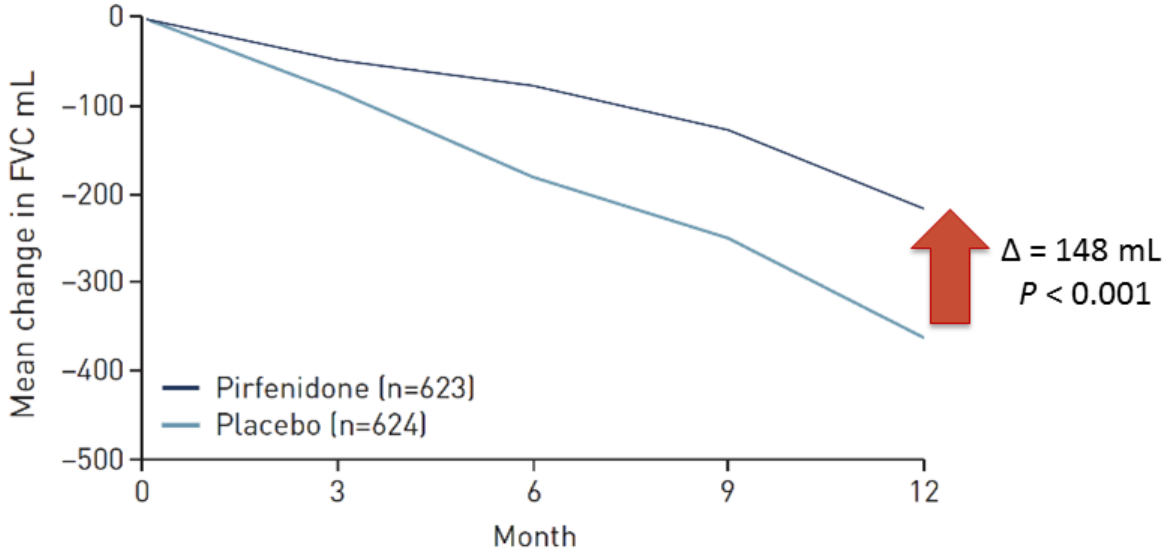
1. Noble PW et al. *Lancet* 2011;377:1760–1769;
2. King TE et al. *N Engl J Med* 2014; 370:2083–2092;
3. Azuma A et al. *Am J Respir Crit Care Med* 2005;171:1040–1047;
4. Taniguchi H et al. *Eur Respir J* 2010;35:821–829.

10

Pirfenidone reduces annual rate of FVC decline in pooled population from three phase III RCT

Update on Pirfenidone Efficacy: Change in FVC

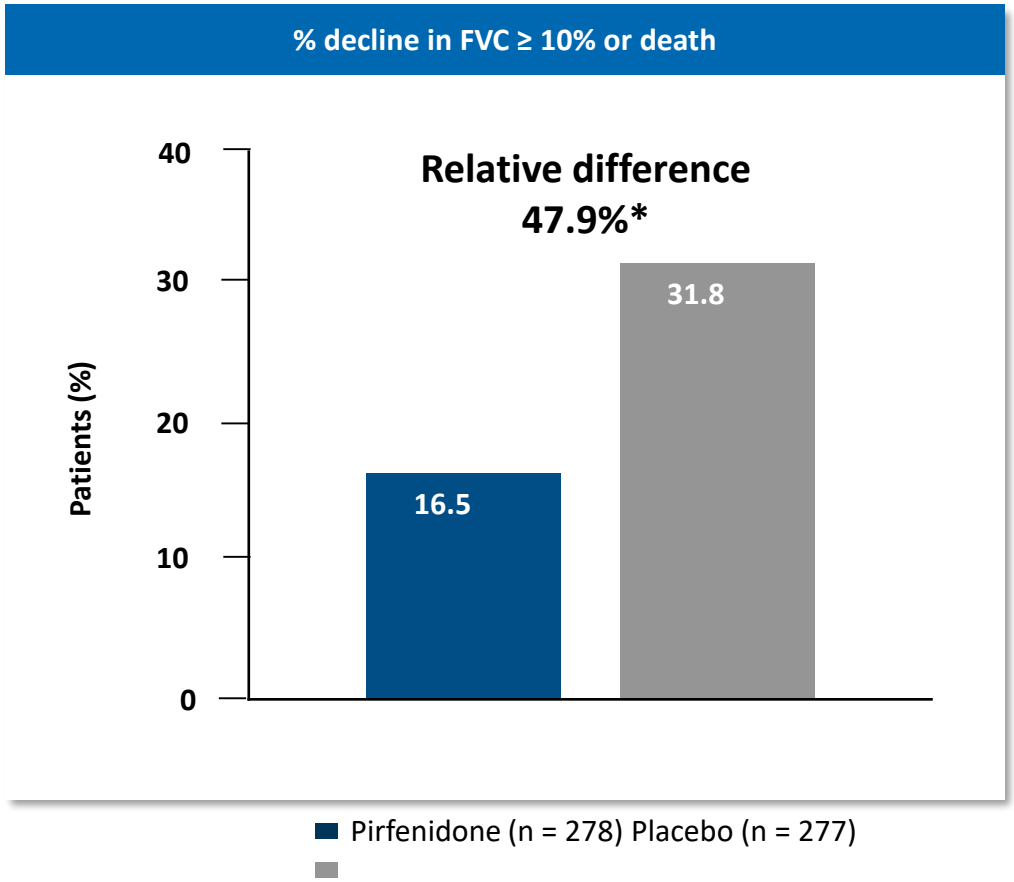
ASCEND + CAPACITY 1 + CAPACITY 2

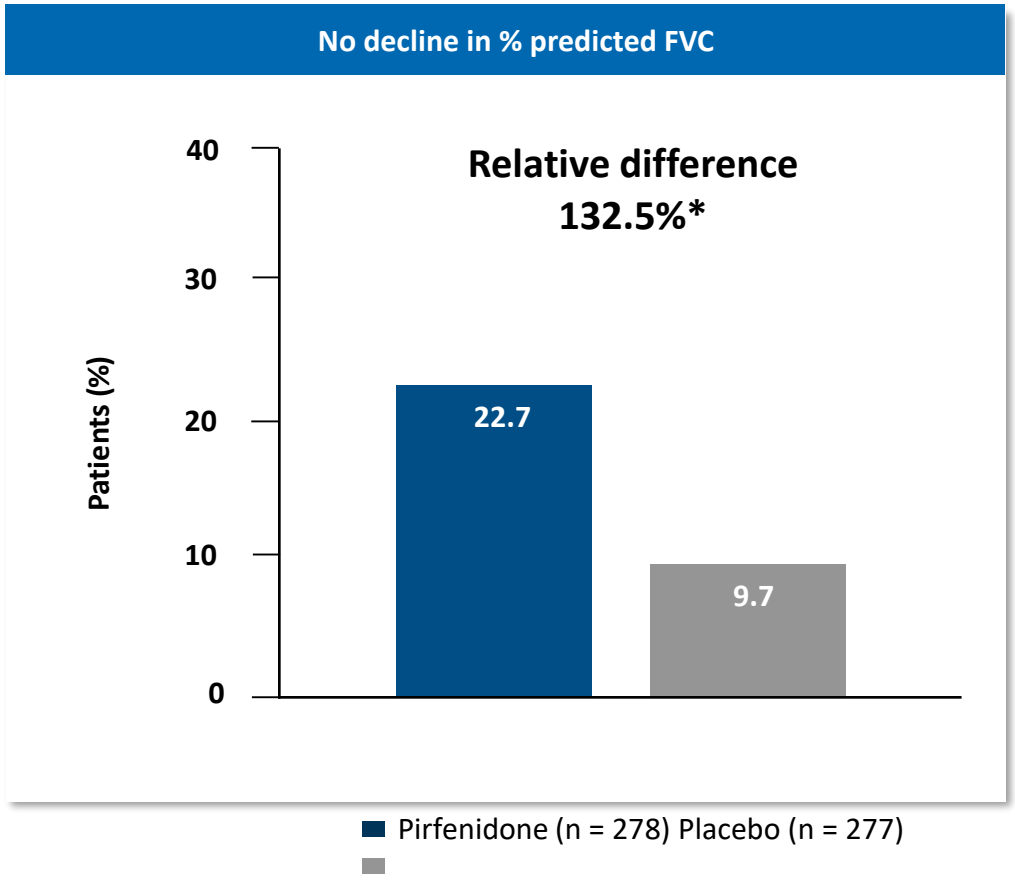


Absolute difference mL	36	104	123	148
Relative difference %	43.5	57.3	49.1	40.7
Rank ANCOVA p-value	<0.001	<0.001	<0.001	<0.001

Noble et al. Eur Respir J. May 2016

ASCEND: Effect of pirfenidone on FVC at Week 52

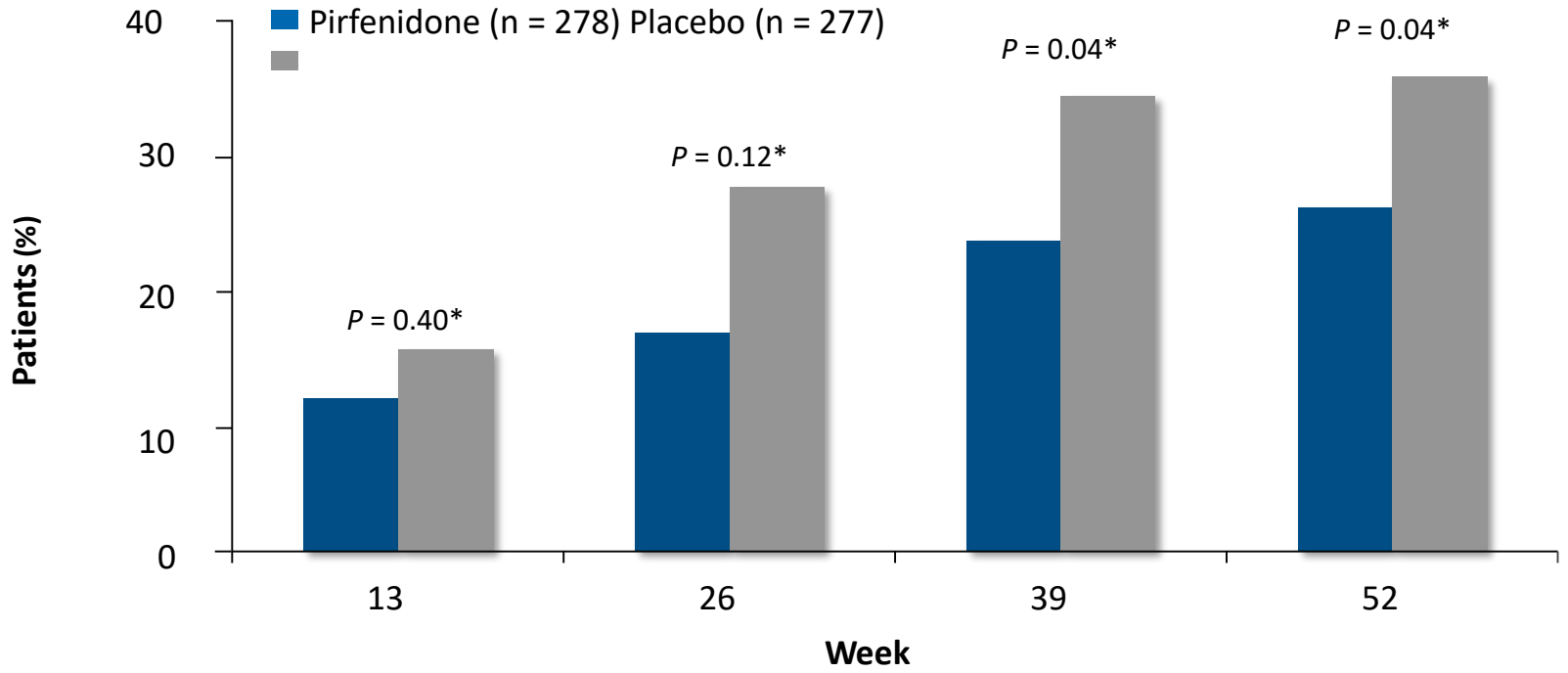




* Rank ANCOVA (pirfenidone vs placebo) *P*-value < 0.000001. FVC: forced vital capacity.

King TE et al. N Engl J Med 2014;370:2083–2092.

ASCEND: Proportion of patients with decline ≥ 50 m in 6-minute walk distance or death over time



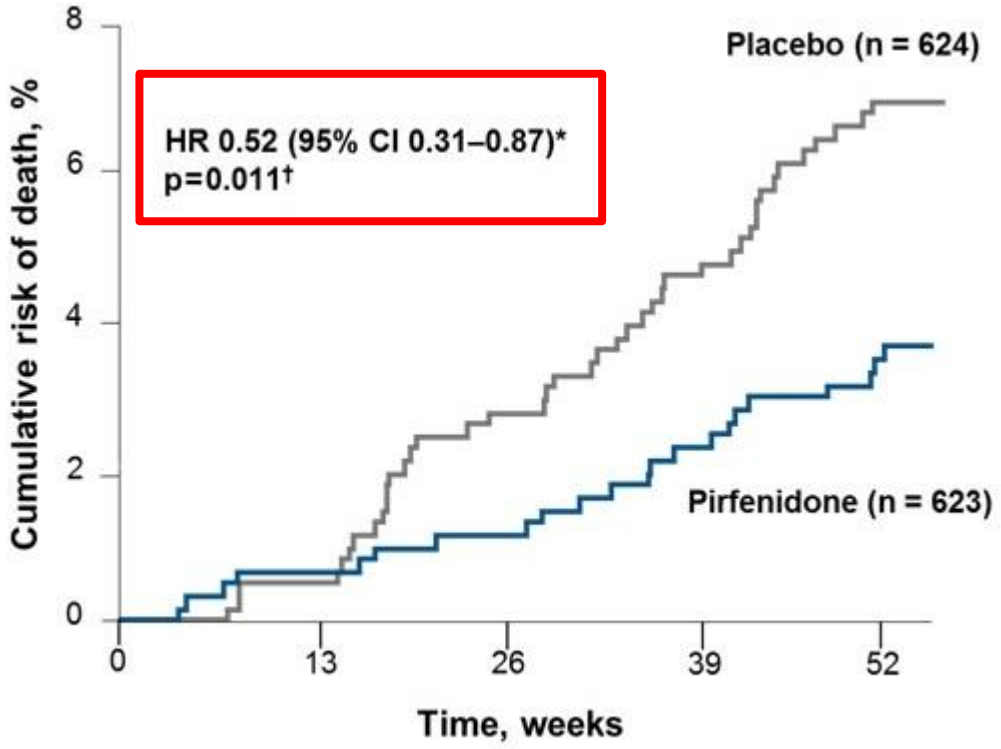
Pirfenidone led to a 27.5% relative reduction in the proportion of patients who had a decrease of 50 m or more in 6MWD or death at Week 52

* Ranked analysis of covariance. 6MWD: 6-minute walk test distance.

King TE et al. N Engl J Med 2014;370:2083–2092.

13

Pirfenidone has been associated with a significant reduction in mortality



All-cause mortality: pooled analysis of ASCEND and CAPACITY

Patients at risk, n

Week	Pirfenidone	Placebo
0	623	624
13	618	619
26	609	603
39	596	586
52	509	490

*Cox proportional hazards model; †Log-rank test

Pirfenidone reduced the risk of mortality by 48% at Week 52 compared with placebo (HR, 0.52; 95% CI, 0.31, 0.87; p=0.011)

Nathan SD et al. Lancet Respir Med 2017;5:33–41

CI, confidence interval; HR, hazard ratio

Pirfenidone reduced the risk of All Cause Mortality over 120 weeks

		Pooled Analysis (004, 006, 016)		Random-Effects Meta-Analyses (004, 006, 016, SP2, SP3)			
				Frequentist Approach (DerSimonian and Laird)		Bayesian Approach	
		PFD n = 623	PBO n = 624	PFD n = 806	PBO n = 769	PFD n = 806	PBO n = 769
ACM Week 52	Deaths, n (%)	22 (3.5)	42 (6.7)	25 (3.1)	50 (6.5)	25 (3.1)	50 (6.5)
	Relative RR	48%		50%		50%	
	HR (95% CI)	0.52 (0.31–0.87)		0.50 (0.31–0.80)		0.50 (0.29–0.83)	
	P-value	0.0107		0.0042		–	
ACM Week 72	Deaths, n (%)	32 (5.1)	50 (8.0)	35 (4.3)	58 (7.5)	35 (4.3)	58 (7.5)
	Relative RR	37%		40%		41%	
	HR (95% CI)	0.63 (0.41–0.98)		0.60 (0.39–0.91)		0.59 (0.37–0.93)	
	P-value	0.0404		0.0166		–	
ACM Week 120	Deaths, n (%)	38 (6.1)	54 (8.7)	41 (5.1)	62 (8.1)	41 (5.1)	62 (8.1)
	Relative RR	31%		35%		35%	
	HR (95% CI)	0.69 (0.46–1.05)		0.65 (0.44–0.97)		0.65 (0.41–1.00)	
	P-value	0.0789		0.0346		–	

The magnitude of pirfenidone's treatment benefit on ACM was generally consistent across individual studies, with a lower risk of death versus placebo at Weeks 52, 72 and 120

Similar results were observed using the FDA approach to censoring. ACM, all-cause-mortality; CI, confidence interval; FDA, U.S. Food and Drug Administration; HR, hazard ration; PBO, placebo, PFD, pirfenidone

Nathan SD, et al. Lancet Respir Med 2017;5:33–41.

Pirfenidone has a significant effect on IPF-related mortality over 120 weeks

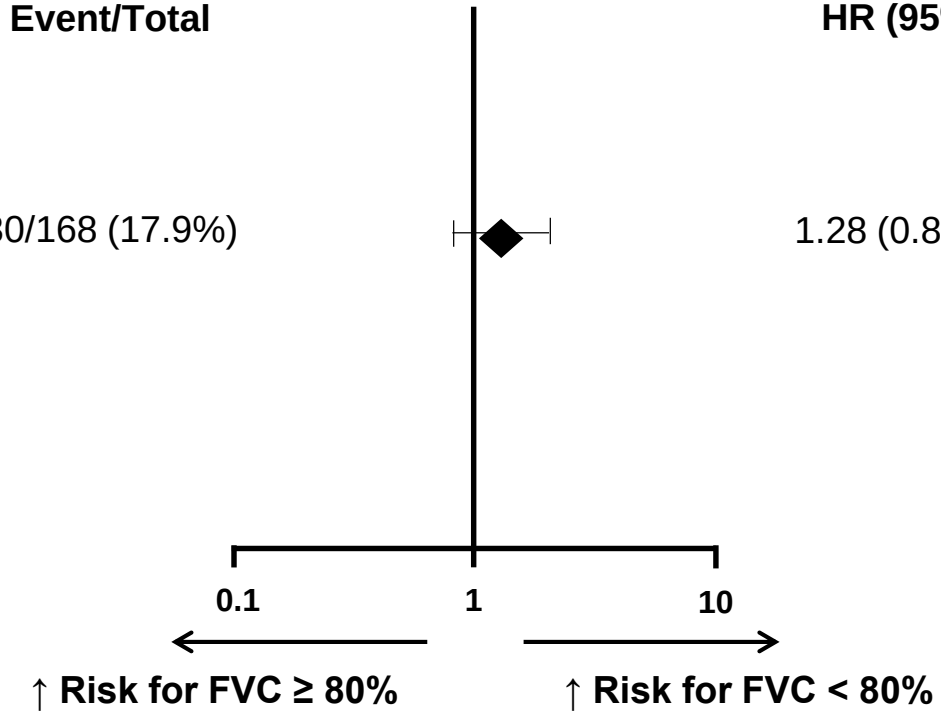
		Pooled analysis (ASCEND & CAPACITY)		Random-effects meta-analyses (ASCEND, CAPACITY, SP2, SP3)			
				Frequentist approach (DerSimonian and Laird)		Bayesian approach	
		PFD n=623	PBO n=624	PFD n=806	PBO n=769	PFD n=806	PBO n=769
IPF-related mortality Week 52	Deaths, n (%)	10 (1.6)	28 (4.5)	13 (1.6)	35 (4.4)	13 (1.6)	35 (4.4)
	Relative RR	65%		62%		62%	
	HR (95% CI)	0.35 (0.17, 0.72)		0.38 (0.20, 0.72)		0.38 (0.20, 0.73)	
	P-value	0.0029		0.0030		–	
IPF-related mortality Week 72	Deaths, n (%)	17 (2.7)	35 (5.6)	20 (2.5)	42 (5.5)	20 (2.5)	42 (5.5)
	Relative RR	52%		52%		53%	
	HR (95% CI)	0.48 (0.27, 0.85)		0.48 (0.28, 0.81)		0.47 (0.27, 0.83)	
	P-value	0.0107		0.0065		–	
IPF-related mortality End of study	Deaths, n (%)	22 (3.5)	39 (6.3)	25 (3.1)	46 (6.0)	25 (3.1)	46 (6.0)
	Relative RR	45%		46%		47%	
	HR (95% CI)	0.55 (0.33, 0.93)		0.54 (0.33, 0.88)		0.53 (0.31, 0.90)	
	P-value	0.0237		0.0137		–	

Pirfenidone significantly reduced the relative risk of IPF-related mortality versus placebo in the pooled analysis and a meta-analysis

Should patients be treated as soon as they are diagnosed?

Pooled placebo population

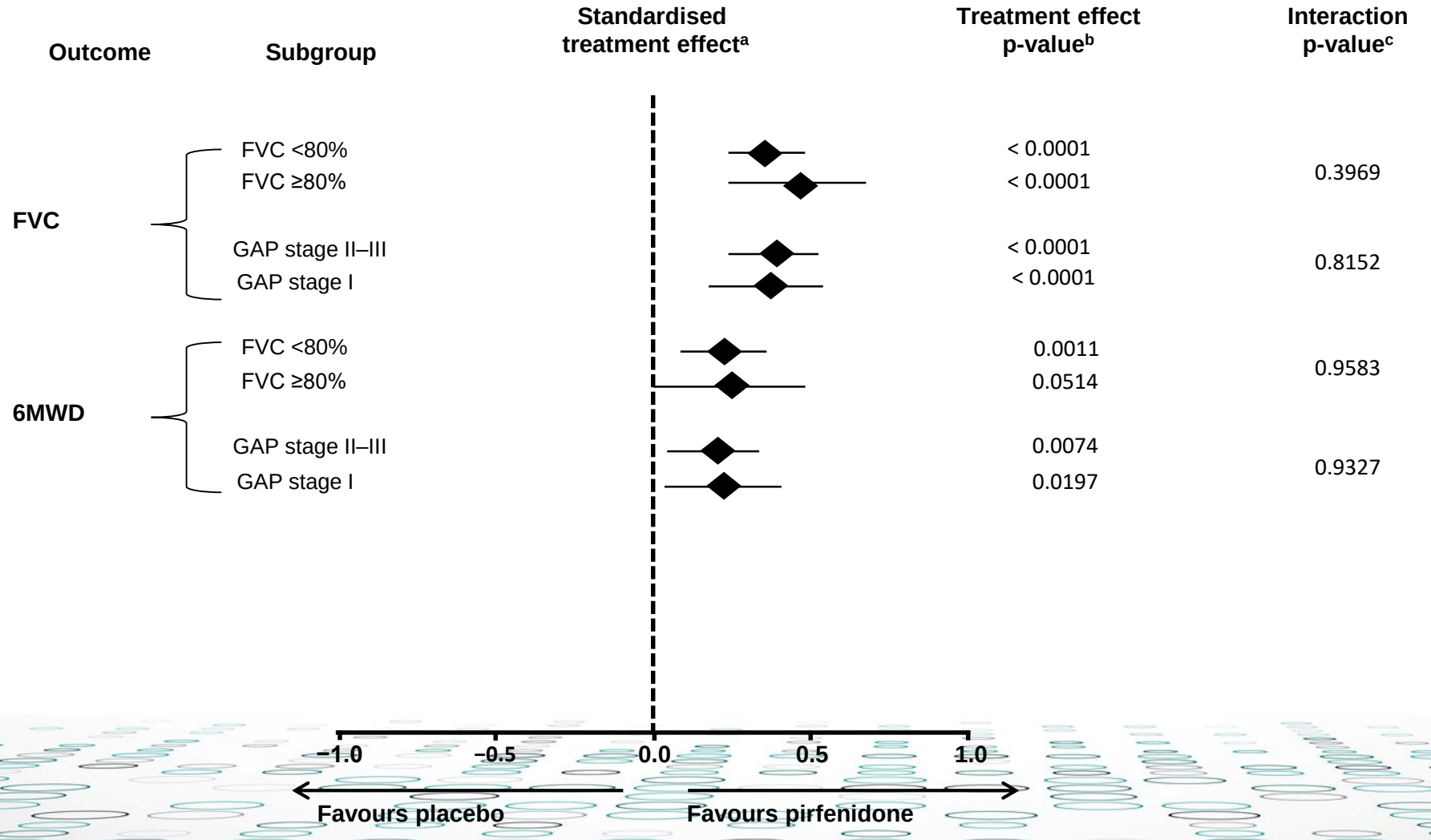
	FVC < 80% Event/Total	FVC ≥ 80% Event/Total	HR (95% CI)	Between-Subgroup *P* Value
FVC decline ≥ 10% or death	99/450 (22.0%)	30/168 (17.9%)	1.28 (0.85-1.92)	0.2403



The risk of disease progression (especially FVC decline ≥ 10% or death) is comparable in patients with FVC above versus below 80%

Albera C et al, ERJ 2016

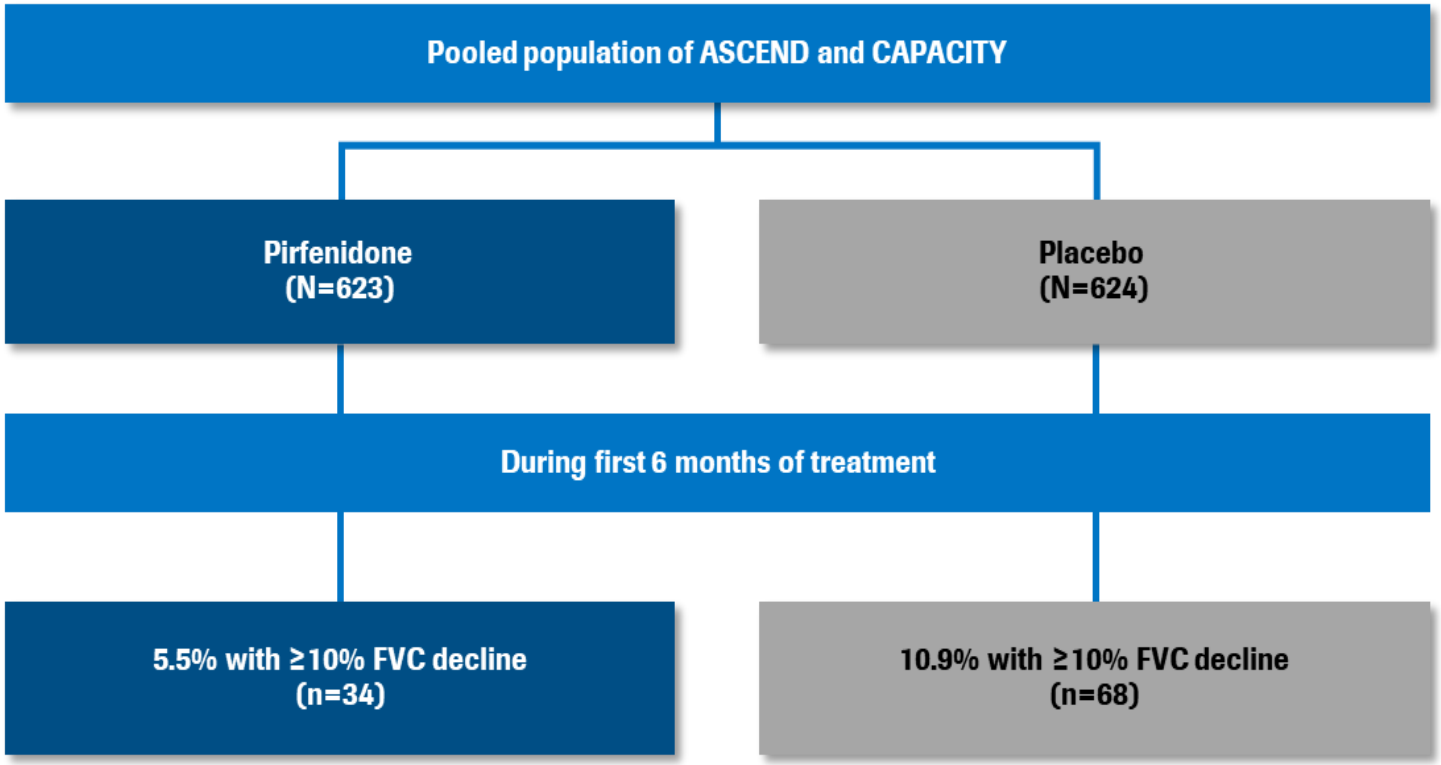
Treatment effect of pirfenidone by baseline disease severity



Albera C et al. ERJ 2016

The treatment benefit of pirfenidone: preventing a first progressive event (FVC decline)

A post-hoc exploratory analysis was performed of outcomes following 6 months of continued treatment with pirfenidone or placebo in patients who experienced a ≥10% decline in FVC during the first 6 months of treatment in ASCEND or CAPACITY



Nathan SD et al. Thorax 2016;71:429–435

Continued treatment with pirfenidone may confer a benefit to patients with IPF following disease progression

- In patients with a ≥10% decline in FVC during the first 6 months of treatment:

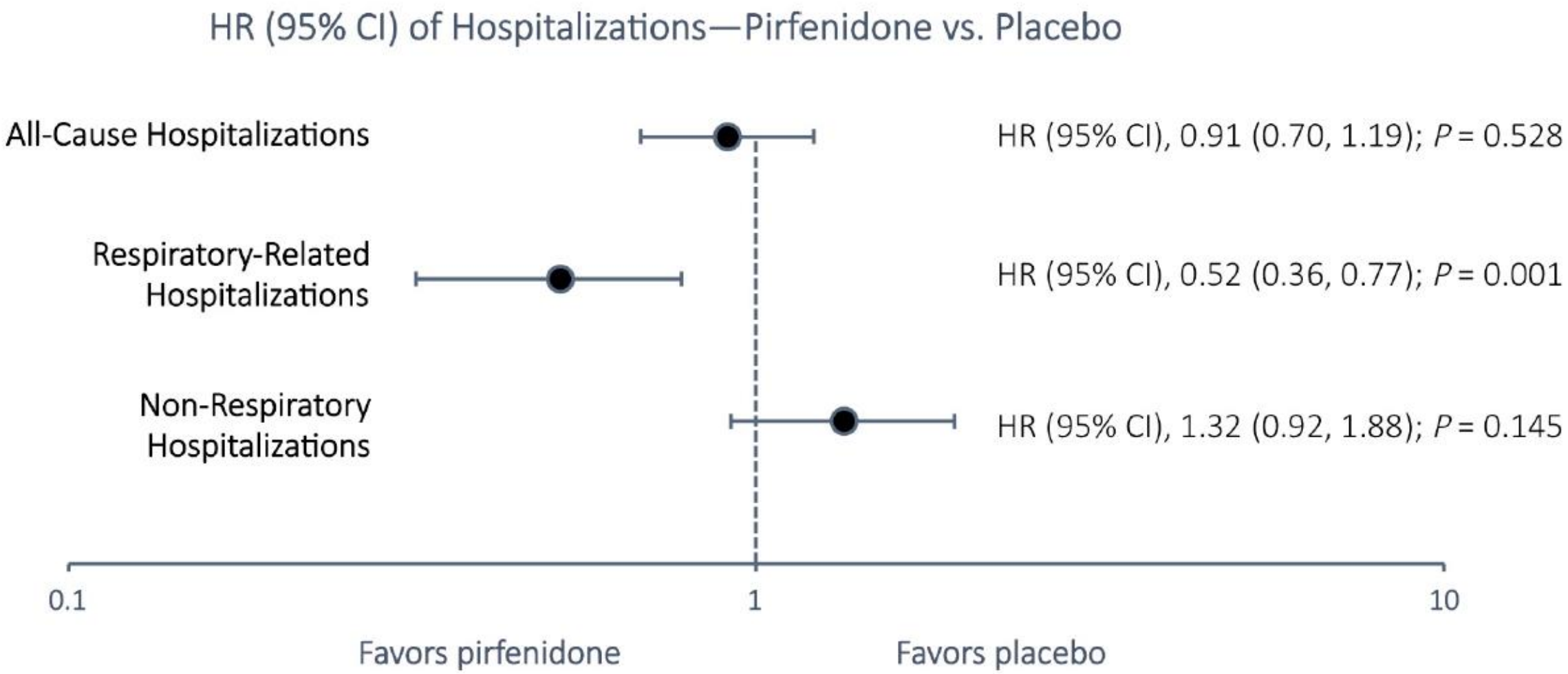
Outcomes during second 6 months of treatment				
	Pirfenidone (N=34)	Placebo (N=68)	Relative difference	P-value[a]
≥10% decline in FVC or death	2 (5.9%)	19 (27.9%)	–78.9%	0.009
No further decline in FVC[b]	20 (58.8%)	26 (38.2%)	–53.8%	0.059
Death	1 (2.9%)	14 (20.6%)	–85.7%	0.018

Significantly fewer patients in the pirfenidone group experienced a second ≥10% decline in %FVC or death during the subsequent 6-month period compared with placebo

Nathan SD et al. Thorax 2016;71:429–435

[a]Fisher's exact test; [b]Either no decline or increase in FVC
%FVC, percent predicted forced vital capacity

Pirfenidone reduces all-cause hospitalizations in 1247 patients from three phase III RCTs



Collard et al. Am J Respir Crit Care Med. May 2017

1. Pirfenidone

2. Randomized Clinical Trials

3. Real world data

An Open-Label Study of the Long-Term Safety of Pirfenidone in Patients with Idiopathic Pulmonary Fibrosis (RECAP)

Ulrich Costabel[a] Carlo Albera[b] Lisa H. Lancaster[c] Chin-Yu Lin[d]
Philip Hormel[d] Henry N. Hulter[d] Paul W. Noble[e]

Respiration 2017

Editorial Comment

Respiration

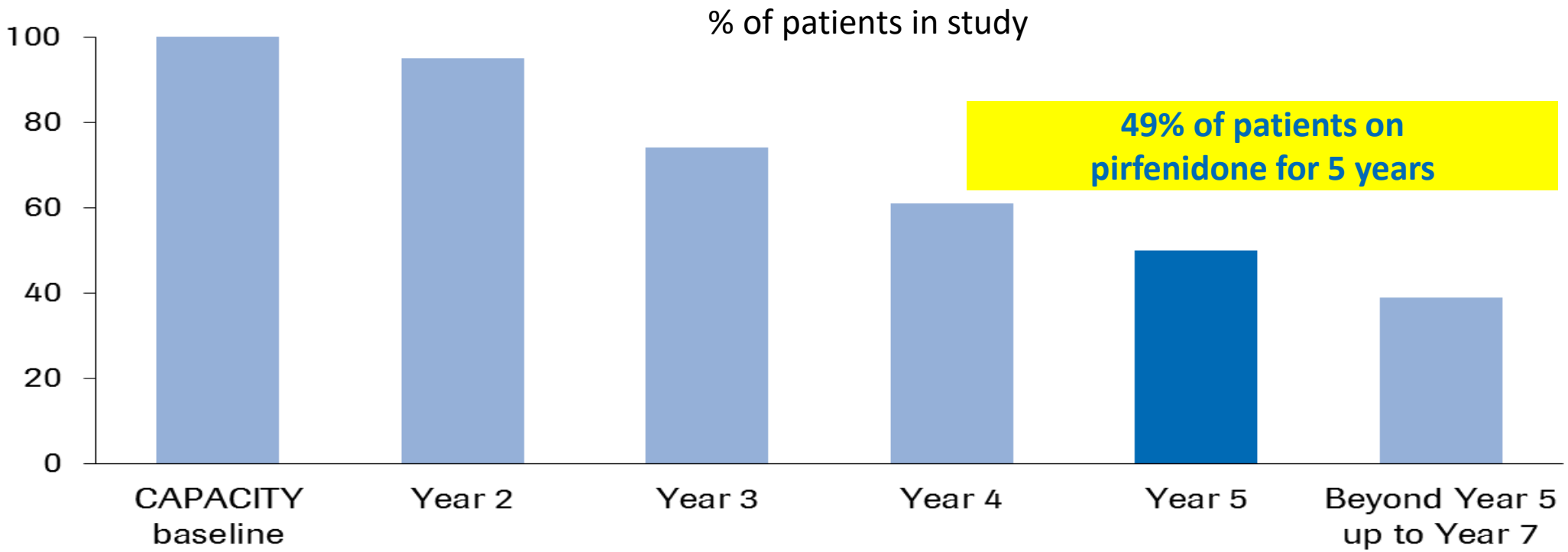
Published online: September 5, 2017

Pirfenidone in Idiopathic Pulmonary Fibrosis "RECAP-itulating Safety into the Real World"

Argyris Tzouvelekis[a, b] Evangelos Bouros[a] Vasilios Tzilas[a]
Demosthenes Bouros[a]

Prospective observational studies in the context of registries that collect well-defined supporting data over time can provide a real-world view of pirfenidone in clinical practice and answer residual questions on safety and efficacy of the drug in a broad spectrum of patients with IPF irrespective of disease severity, race, and gender. The RECAP study represents the first step in this direction.

RECAP study: duration of study follow-up for patients randomised to pirfenidone in CAPACITY



Patients discontinuing treatment also terminated the study after a follow-up period of at least 4 weeks after the last dose

Cottin V & Maher T. Eur Resp Rev 2015;24:58-64

RECAP study: treatment-emergent adverse events*

Adjusted incidence rates (number of events per 100 person-exposure-years)	RECAP (N=603)	CAPACITY PFD 2403 mg/day (N=345)	CAPACITY Placebo (N=347)
Median exposure (range), weeks	163 (1-257)	73 (2-118)	72.7 (>0-120)
PEY	1726	483	487
Bronchitis	21.8	14.3	17.3
Upper respiratory tract infection	21.6	32.3	33.3
Idiopathic pulmonary fibrosis	19.7	31.5	40.7
Dyspnoea	17.3	14.7	20.7
Nausea	16.8	40.4	15.8
Nasopharyngitis	16.8	21.7	24
Cough	16.5	26.7	27.3
Diarrhoea	14.7	31.7	17.5
Headache	11.5	19	17.9
Fatigue	10.5	26.7	17.9
Dizziness	9.7	16.2	8.2
Sinusitis	9.4	16.2	13.1
Vomiting	8.3	12.8	3.5
Rash	8.2	32.9	10.7
Back pain	7.2	8.9	8.6

*Occurring at a crude rate of ≥20% in the RECAP group
PEY, patient exposure years; PFD, pirfenidone

Costabel U et al. Eur Resp J 2014:1903.

Key safety aspects of Pirfenidone

Number of patients treated in clinical trials at approval

- N=1650 (EU SmPC)

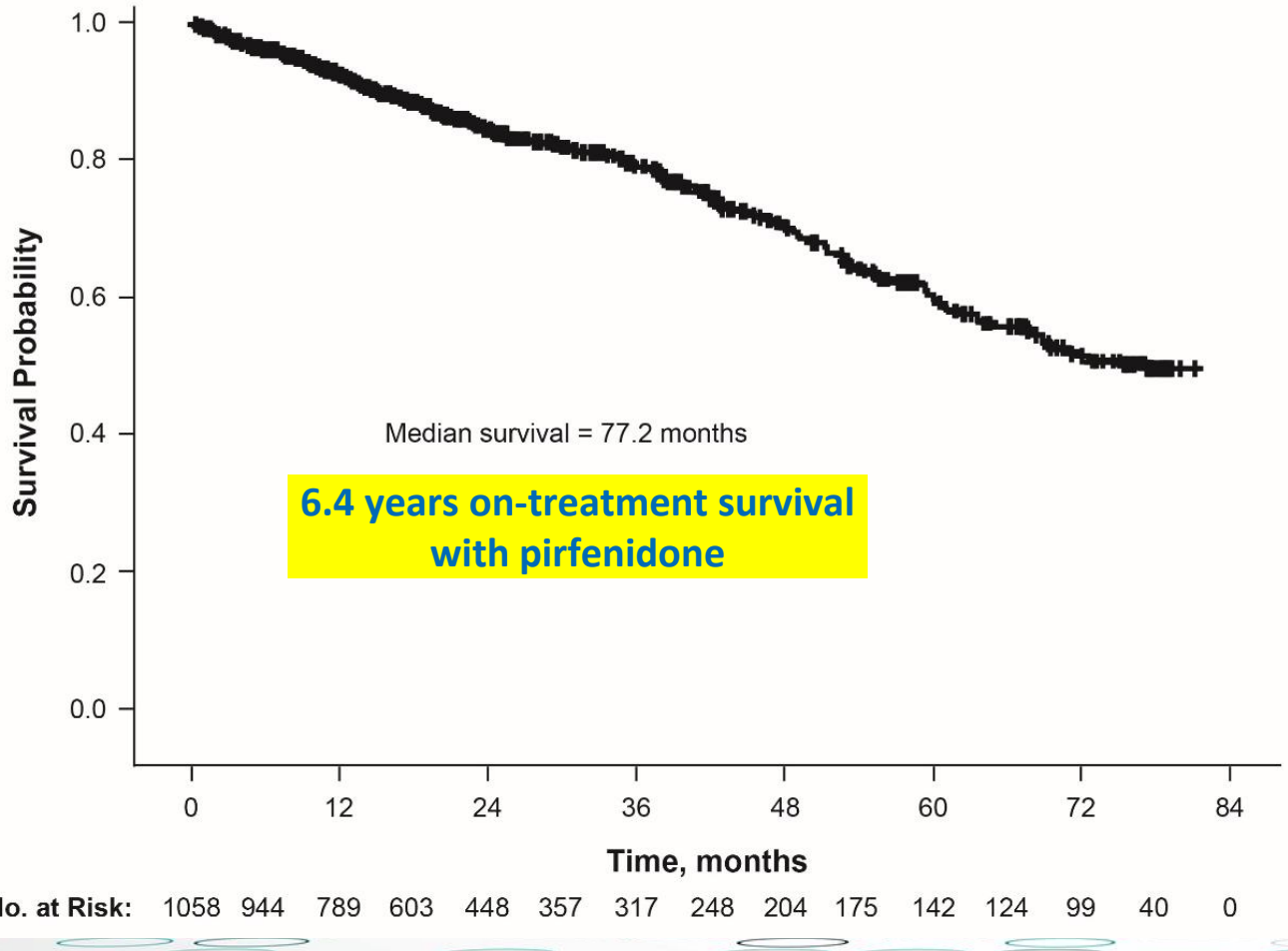
Duration and extent of exposure

- Up to 11 years
- More than 63,000 patient-years post-marketing

Major risks identified

- GI-related events (Nausea, diarrhea, vomiting, dyspepsia)
- Skin-related events (rash, photosensitivity)
- Fatigue
- Weight loss
- Anorexia
- LFT elevations

Clinical outcomes – Data on Survival from RECAP



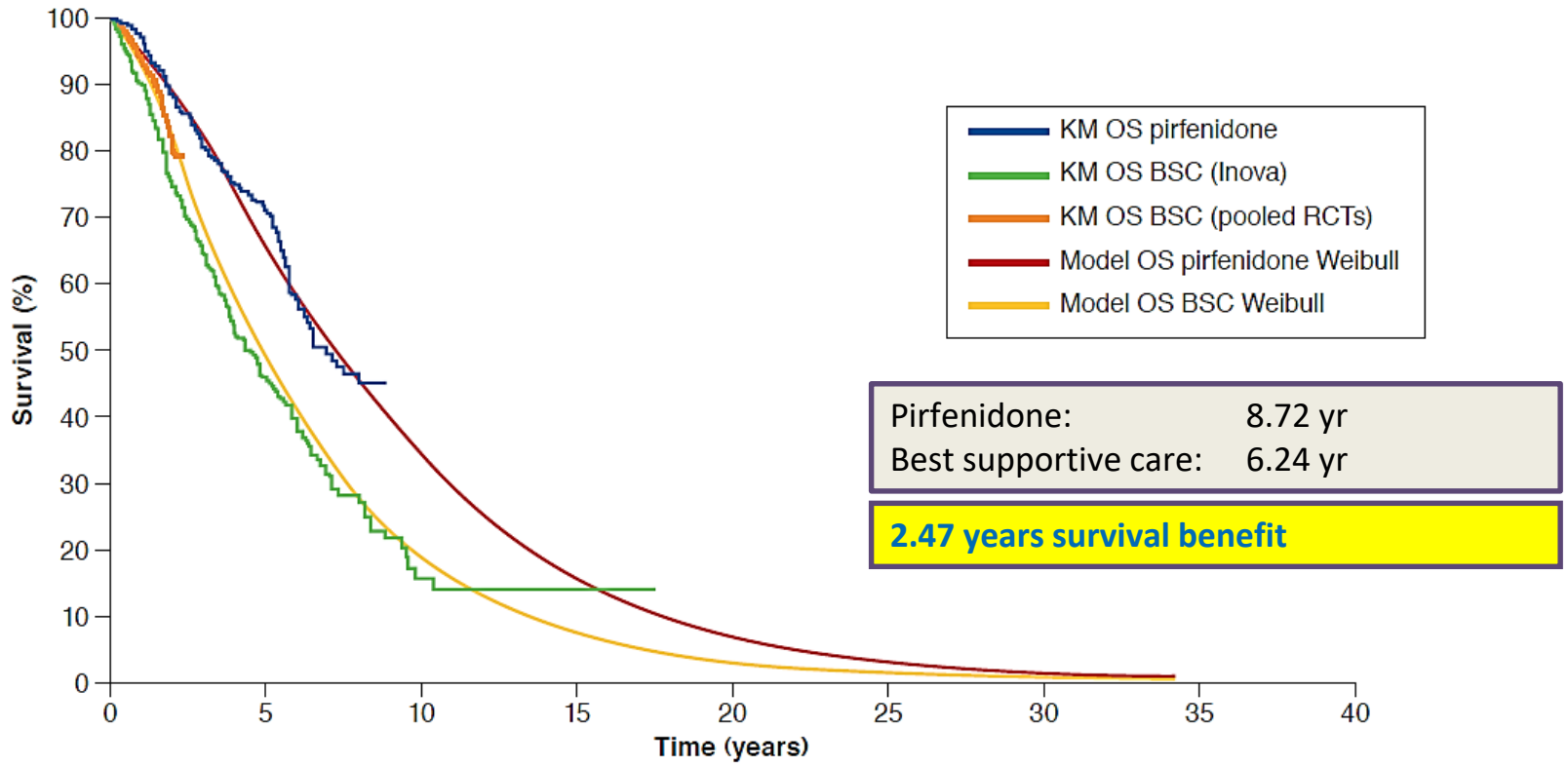
The **median on-treatment survival** from the first dose of 2403 mg/day pirfenidone* in the RECAP study was **77.2 months**

*Assume 1 month = 30.4375 days.

Costabel et al. Respiration 2017, DOI: 10.1159/000479976.

Clinical outcomes – Additional Data on Survival

Comparison of ASCEND, CAPACITY and RECAP outcome with Inova registry: Kaplan-Meier overall survival curves



Pirfenidone:	8.72 yr
Best supportive care:	6.24 yr

2.47 years survival benefit

These conclusions are consistent with expectations for a therapy that has been shown to **significantly reduce disease progression and mortality**

BSC = best supportive care; KM = Kaplan-Meier; OS = overall survival; RCTs = randomized controlled trials.

Fisher et al. J Manag Care Spec Pharm. 2017;23(3-b):S17-S24.

Summary

The RECAP study provides long-term safety follow-up data for pirfenidone, with a cumulative total exposure of 2483 PEY

33.8% of patients discontinued RECAP due to AEs over ≥ 5 years of the study; most discontinuations were due to AEs that were unrelated to IPF progression

AE, adverse event; PEY, patient-exposure years.

Longitudinal "Real-World" Outcomes of Pirfenidone in Idiopathic Pulmonary Fibrosis in Greece

ORIGINAL RESEARCH
published: 29 November 2017
doi: 10.3389/fmed.2017.00213

Argyrios Tzouvelekis[1,2†‡], Theodoros Karampitsakos[3†], Paschalis Ntolios[4], Vasilios Tzilas[1], Evangelos Bouros[1], Evangelos Markozannes[1], Ioanna Malliou[1], Aris Anagnostopoulos[1], Andreas Granitsas[1], Paschalis Steiropoulos[2], Katerina Dimakou[3], Serafeim Chrysikos[4], Nikolaos Koulouris[1] and Demosthenes Bouros[1‡]*

frontiers in Medicine

Margaritopoulos *et al. BMC Pulmonary Medicine* (2018) 18:177
https://doi.org/10.1186/s12890-018-0736-z

BMC Pulmonary Medicine

RESEARCH ARTICLE Open Access

Pirfenidone improves survival in IPF: results from a real-life study

George A. Margaritopoulos[1,2†], Athina Trachalaki[1†], Athol U. Wells[2], Eirini Vasarmidi[1], Eleni Bibaki[1], George Papastratigakis[1], Stathis Detorakis[3], Nikos Tzanakis[1†] and Katerina M. Antoniou[1*†]

Real-world Pirfenidone use in 162 patients in Greece

CHARACTERISTICS	BASELINE DATA
Total patients enrolled	80
Male/Female	70/10
Age (years ± SD)	68.1±7.5
Never smokers	4
Current smokers	17
Ex-smokers	59
VATS	11
Prior treatment	0
CPFE (n,%)	24
GERD (n,%)	39
AH (n, %)	39
Hypercholesterolemia (n,%)	14
PH (Echo-RVSP>35mmHg) (n, %)	19
FVC %pred	74.9±17.2
DLco %pred	48.1 ± 16.9
GAP score (median)	3

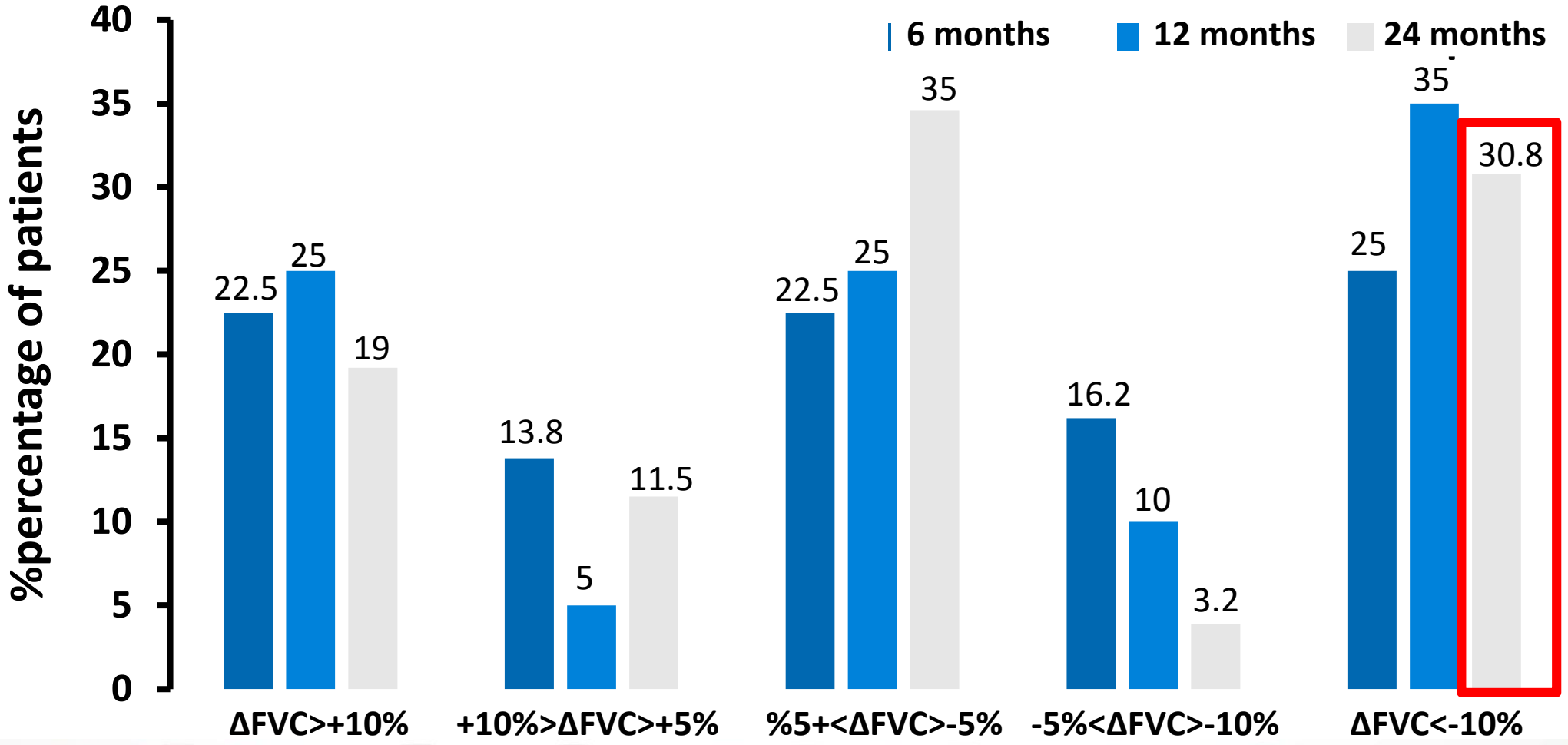
Tzouvelekis et al. Frontiers In Med 2017

Table 1 Demographic characteristics of the UHH cohort ($n = 82$)

Age	74.9 ± 11[a]
Never smokers	29 (35.3%)
Smokers	53 (64.7%)
Pack Years	43.5 ± 32.1[a]
Radiological pattern (Definite UIP/Possible UIP)	47(57.3%)/35(42.7%)
Advanced disease (DLco< 30%)	7(8.5%)
Surgical lung biopsy	13 (15.9%)
FEV_1%	87.4 ± 22.7[a]
FVC %	81.5 ± 19.5[a]
DLco %	54.4 ± 17.9[a]
Median follow-up time (IQR)	17.4 months (9.5–30.9).
Deaths	15 (18.3%)

Antoniou et al. BMC Pulm Med 2018

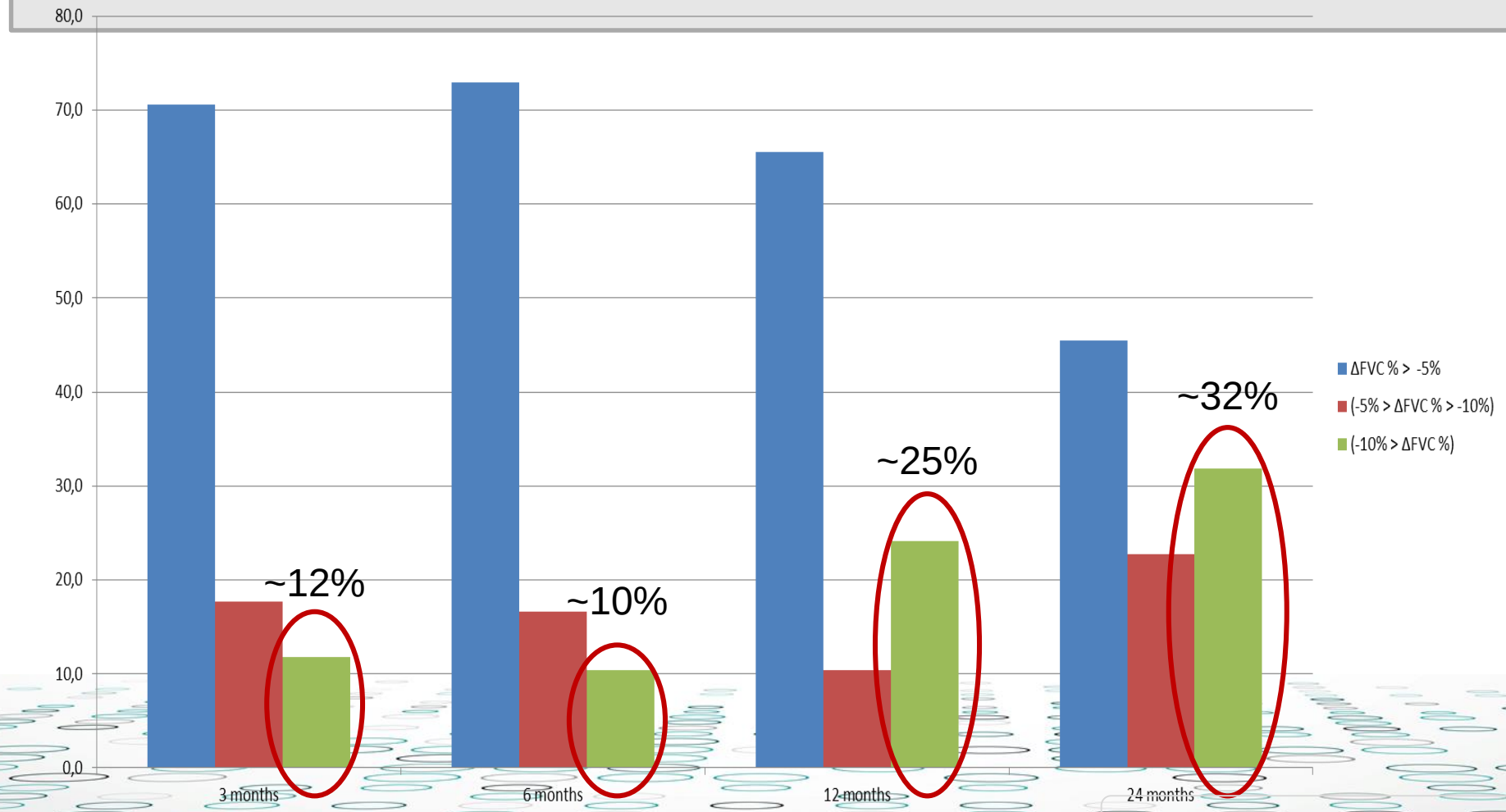
70% of patients exhibited disease stability at 24 months



Tzouvelekis et al. Frontiers In Med 2017

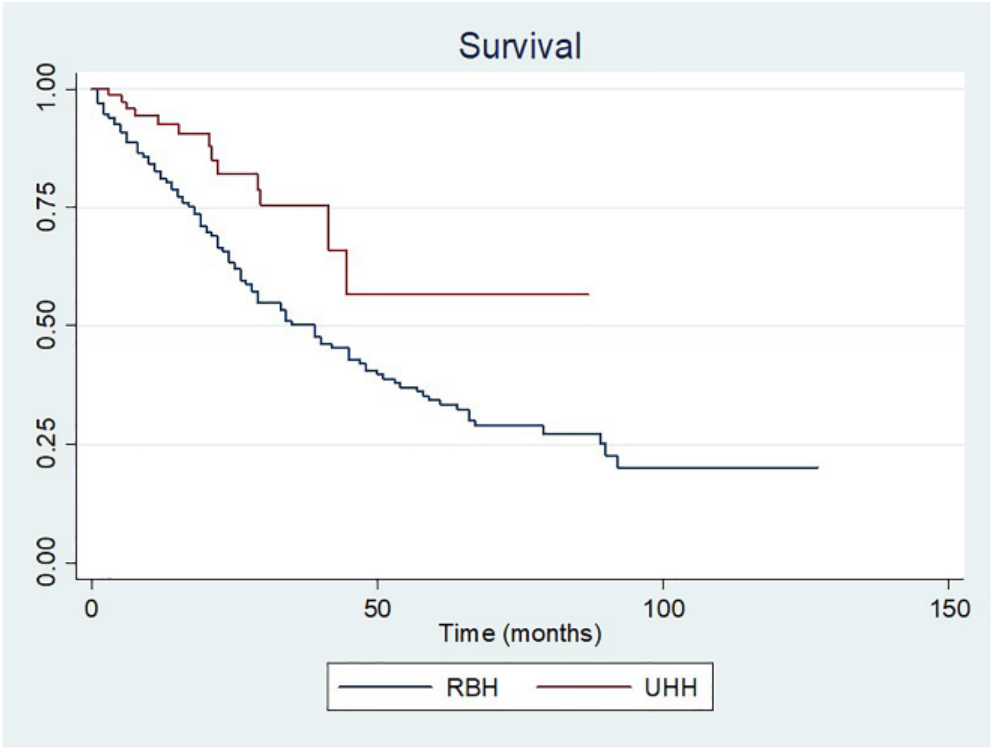
68% of patients exhibited disease stability at 24 months

Percentage of IPF patients on Pirfenidone with significant FVC decline (>10%)



Antoniou et al. BMC Pulm Med 2018

6 years' experience of pirfenidone treatment in patients with IPF in Crete: Pirfenidone improves survival



3-year survival: 73%

The RBH cohort was a historical cohort treated with corticosteroids and/or immunomodulation

RBH, Royal Brompton Hospital; UHH, University Hospital of Heraklion

Margaritopoulos G, Trachalaki A, et al. submitted

Pirfenidone users exhibit similar survival rates in real-world and RCTs

BOUROS COHORT, N=80			POOLED ASCEND+CAPACITY, N=623		
	ABSOLUTE	RELATIVE,%		ABSOLUTE	RELATIVE,%
MORTALITY – 1YR	1	1.25	MORTALITY – 1YR	22	3.5

Fisher exact t-test, p=0.52

BOUROS COHORT, N=80			RECAP, N=1054		
	ABSOLUTE	RELATIVE,%		ABSOLUTE	RELATIVE,%
MORTALITY – 3YRS	26	32.5	MORTALITY – 5YRS	231	21.8

Fisher exact t-test, p=0.11

Tzouvelekis et al. Frontiers In Med 2017

Ανεπιθύμητες Ενέργειες

	Tzouvelekis et al	RECAP	PASSPORT	EAP
		N=1058	N=1009	N=1620
Nausea	6 (7.5%)	242 (23%)	208 (20.6%)	366 (22.6%)
Fatigue	16 (20%)	210 (19%)	187 (18.5%)	317 (19.6%)
Photosensitivity/Rash	20 (25%)	NA	123 (12.2%)	133 (8.2%)
Diarrhea	15 (18.8%)	242 (22.9%)	96 (9.5%)	182 (11.2%)
Discontinuation	18 (22.5%)	178 (16.8%)	282 (28%)	210 (13%)
Dose reduction	13 (16.3%)	202 (19%)	292 (29%)	364 (22.5%)

Tzouvelekis et al. Frontiers In Med 2017.

Esbriet label update in March 2018: Black triangle warning removed

- The Post Authorisation Safety Study (PASSPORT) previously imposed on Esbriet has been completed; as a result Esbriet is no longer under additional monitoring
  - The **black triangle warning** has therefore been **removed** from the EU package leaflet and summary of product characteristics

What is additional monitoring?

- The EU publishes a list of medicines under 'additional monitoring'. These are medicines that are authorised by the EMA but which are being monitored particularly closely by regulatory authorities
- Medicines under additional monitoring have a black inverted triangle displayed in their package leaflet and summary of product characteristics, with a short sentence explaining what the triangle means
- As part of the European marketing authorisation for Esbriet, the EMA requested a Post Authorisation Safety Study (PASSPORT) be conducted; this automatically meant that Esbriet would be subject to additional monitoring until the PASSPORT study was completed

39

Πιρφενιδονη – Καθημερινοί Προβληματισμοί

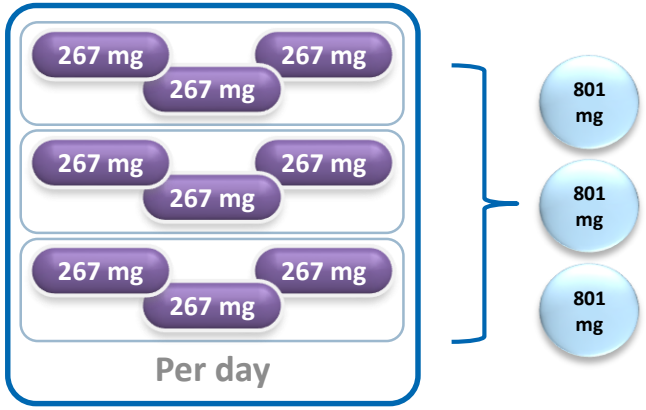
- Pirfenidone – **9 χάπια/day- Γ/Σ διαταραχές**
- Pirfenidone - **φωτοευαισθησία** – (Μεσογειακή χώρα)
- 90% παρενεργειών τις πρώτες 90 ημέρες
- **Συνοσηρότητες? -**Καμία αλληλεπίδραση/τιτλοποίηση δόσης με αντιπηκτικά/καρδιαγγειακό κίνδυνο

Patients with comorbidities

Comorbidities have a significant impact on symptoms and survival associated with IPF. Cardiovascular comorbidities and risk factors are common in IPF [51]. There are no specific warnings or precautions for the use of pirfenidone in patients with cardiovascular comorbidities or in those receiving concomitant anticoagulation therapy, and pharmacodynamics studies have not indicated that pirfenidone prolongs the QTc interval [8]. Of note, the incidence of major cardiac and bleeding AEs was similar over ~14 months between pirfenidone and placebo groups in the pooled phase III population [52].

Costabel et al. Eur Respir Rev 2017. 26:170057

Αντιμετώπιση Προβληματισμών/Παρενεργειών



- Νέο σκεύασμα – **801 mg – 3 χάπια/day** χάπια/day-σκεύασμα

  – **βιοισοδύναμο με 9 χάπια**

- **Καλύτερη συμμόρφωση – μειωμένος γαστρικός φόρτος**
- **Γ/Σ διαταραχές** – **Βραδύτερη κλιμάκωση δόσης** (σε 4 αντί 2 εβδομάδες – LOTUSS study) – ρύθμιση διατροφής (αποφυγή εντερο/γαστροκινητικών τροφών)
- Επιμονή συμπτωμάτων – **ελάττωση δόσης – 1602 mg - αποτελεσματικό**
- **Φωτοευαισθησία** – **Αντι-ηλιακά – αποφυγή έκθεσης σε ήλιο ώρες αιχμής**

Costabel et al. Eur Respir Rev 2017. 26:170057


ΑΡΧΙΚΗ ΣΕΛΙΔΑ
Η ΖΩΗ ΜΕ ΤΗΝ ΙΠΙ
ΑΚΟΥΣΤΕ ΤΟΥΣ ΕΙΔΙΚΟΥΣ
ΚΕΝΤΡΟ ΓΝΩΣΗΣ
ΗΜΕΡΟΛΟΓΙΟ
ΣΗΜΑΝΤΙΚΟΙ ΣΥΝΔΕΣΜΟΙ
AAA
fightipf.gr
ΥΠΟΣΤΗΡΙΞΗ ΑΣΘΕΝΩΝ ΜΕ ΙΔΙΟΠΑΘΗ ΠΝΕΥΜΟΝΙΚΗ ΙΝΩΣΗ
Roche
"Η γνώση, λέγεται ότι, είναι δύναμη – αλλά μόνο μέσω πρωτοβουλιών όπως αυτή η ιστοσελίδα, μπορεί η ακριβής πληροφορία να προσεγγίσει τα άτομα με ΙΠΙ και τους φροντιστές τους. Αυτή η γνώση μπορεί να δώσει τη δυνατότητα στους ανθρώπους που ζουν με την ΙΠΙ να αγωνιστούν για τη φροντίδα, την υποστήριξη και την πρόσβαση σε θεραπείες που χρειάζονται και αξίζουν.
"Είναι πηγή έμπνευσης να βλέπουμε το πάθος και την αποφασιστικότητα των ανθρώπων με ΙΠΙ και των οικογενειών τους να ενώνονται για να καταπολεμήσουν την ΙΠΙ. Οι προσπάθειες αυτού του είδους, παράλληλα με τις εκστρατείες που διοργανώνονται από ομάδες υποστήριξης σε όλο τον κόσμο, ενδυναμώνουν όλη την κοινότητα της ΙΠΙ."
CARLOS LINES MILLÁN
Πρόεδρος, Ευρωπαϊκής Ομοσπονδίας Ιδιοπαθούς Πνευμονικής Ίνωσης και Σχετικών Διαταραχών.
EU-IPFF
EUROPEAN IDIOPATHIC PULMONARY FIBROSIS & RELATED DISORDERS FEDERATION
Η ΖΩΗ ΜΕ ΤΗΝ ΙΠΙ
Μάθετε πώς είναι να ζει κανείς με ΙΠΙ, μέσα από τα βίντεο που ακολουθούν
ΚΑΝΤΕ ΚΛΙΚ ΕΔΩ ΓΙΑ ΠΕΡΙΣΣΟΤΕΡΑ
Η ΕΜΠΕΙΡΙΑ ΜΟΥ ΜΕ ΤΗ ΘΕΡΑΠΕΙΑ
Η ΠΟΡΕΙΑ ΜΟΥ ΠΡΟΣ ΤΗ ΔΙΑΓΝΩΣΗ
ΟΤΑΝ ΜΟΥ ΕΙΠΑΝ ΟΤΙ ΠΑΣΧΩ ΑΠΟ ΙΠΙ