Pirfenidone for idiopathic pulmonary fibrosis: Analysis of pooled data from three multinational phase 3 trials

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Online Data Supplement

On-line Data Supplement

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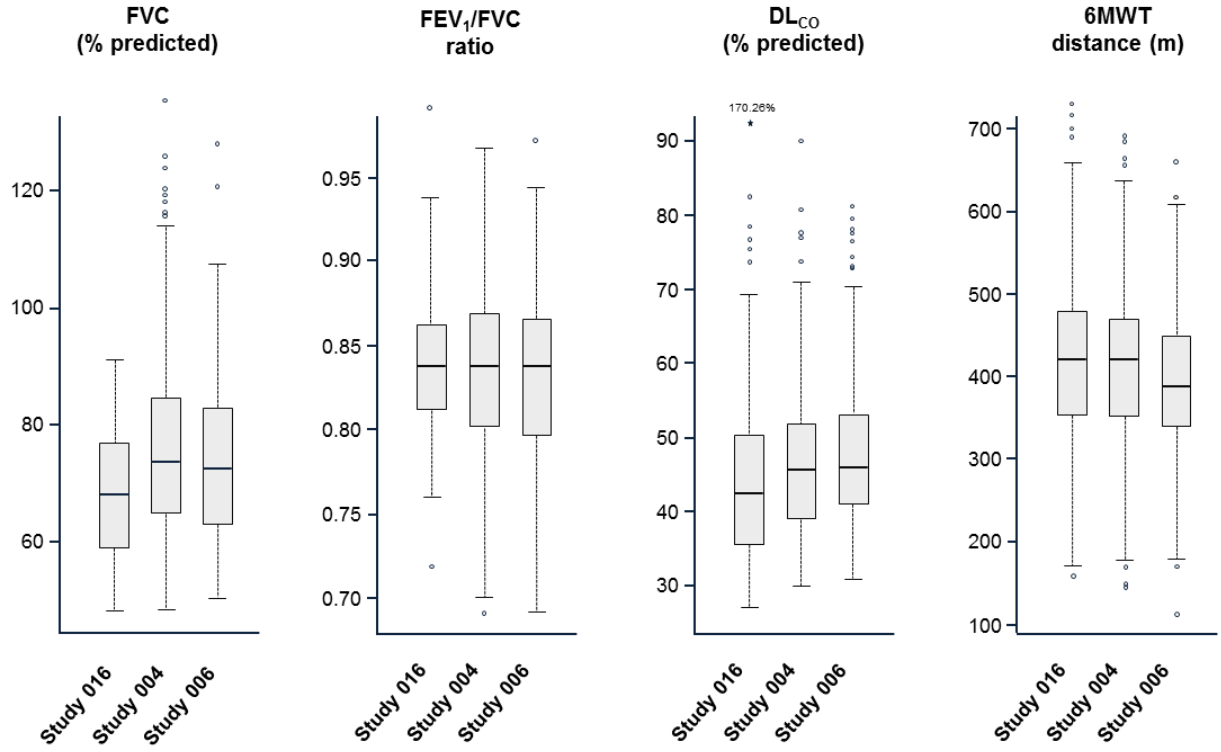
Figure S1 Distribution of baseline physiologic measures of disease status in ASCEND (Study 016) and CAPACITY (Studies 004 and 006)*



6MWT=6 minute walk test; DL_{CO}=carbon monoxide diffusing capacity; FVC=forced vital capacity; FEV_1=forced expiratory volume in 1 second

*Displayed as median, interquartile range (IQR, shaded boxes), and the upper and lower range (whiskers), defined as the third quartile plus 1.5 times the IQR (upper range) and the first quartile minus 1.5 times the IQR (lower range). Values outside the upper and lower range are displayed as circles.

Table S1 Patient disposition at one year in ASCEND (Study 016) and CAPACITY (Studies 004 and 006)

Patients, n (%)	ASCEND (Study 016)		CAPACITY (Study 004)		CAPACITY (Study 006)	
	Pirfenidone (N=278)	Placebo (N=277)	Pirfenidone (N=174)	Placebo (N=174)	Pirfenidone (N=171)	Placebo (N=173)
Completed treatment*	223 (80.2)	238 (85.9)	152 (87.4)	152 (87.4)	151 (88.3)	153 (88.4)
Discontinued study treatment	55 (19.8)	39 (14.1)	22 (12.6)	22 (12.6)	20 (11.7)	20 (11.6)
Primary reason for discontinuing treatment						
Adverse event	35 (12.6)	24 (8.7)	14 (8.0)	11 (6.3)	18 (10.5)	13 (7.5)
Death	4 (1.4)	5 (1.8)	1 (0.6)	6 (3.4)	0	4 (2.3)
Lung transplant	6 (2.2)	1 (0.4)	1 (0.6)	2 (1.1)	0	1 (0.6)
Other	10 (3.6)	9 (3.2)	6 (3.4)	3 (1.7)	2 (1.2)	2 (1.2)
Completed study period†	261 (93.9)	261 (94.2)	168 (96.6)	168 (96.6)	162 (94.7)	167 (96.5)

*Completed 12 months of study treatment
†Completed 12 months of study (includes patients who died or had a lung transplant)

Table S2 Summary of treatment emergent adverse events at one year in the pooled population from ASCEND (Study 016) and CAPACITY (Studies 004 and 006)

Patients (%)	Pirfenidone (N=623)	Placebo (N=624)
Any TEAE	98.7	96.5
Grade 3 TEAE	24.6	24.0
Grade 4 TEAE	3.5	5.4
Any TE SAE	20.5	22.3
Treatment emergent death*	2.2	5.1
Any TEAE leading to treatment discontinuation	11.9	8.7

TEAE=treatment emergent adverse event; TE SAE=treatment emergent serious adverse event
*Death occurring between baseline and 28 days after the last dose of study treatment

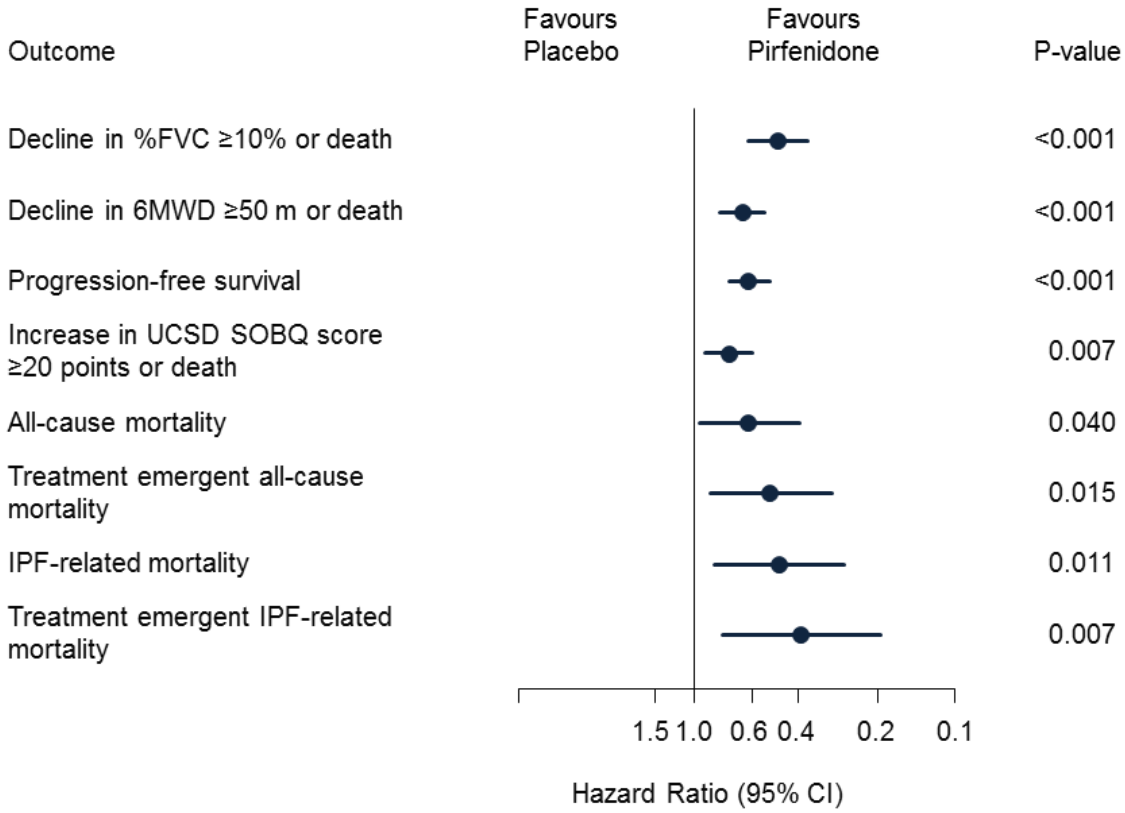
Table S3 Sensitivity analysis: Effect of alternative data imputation strategies on the change in percent predicted FVC from baseline to month 12

Outcome	Imputation Methodology		Pirfenidone (N=623)	Placebo (N=624)	Relative Reduction
	Missing other than death	Missing due to death			
Percent predicted FVC (categorical analysis)*	SSD	Worst Category	14.8%	26.3%	43.8%
	SSD	SSD	11.9%	22.8%	47.8%
	LOCF	Worst Category	14.8%	25.8%	42.8%
	LOCF	LOCF	11.7%	22.1%	47.0%
	No imputation	No imputation	10.7%	20.4%	47.4%

LOCF=last observation carried forward; SSD=sum of squared differences

*Proportion of patients with a ≥10% decline in percent predicted FVC

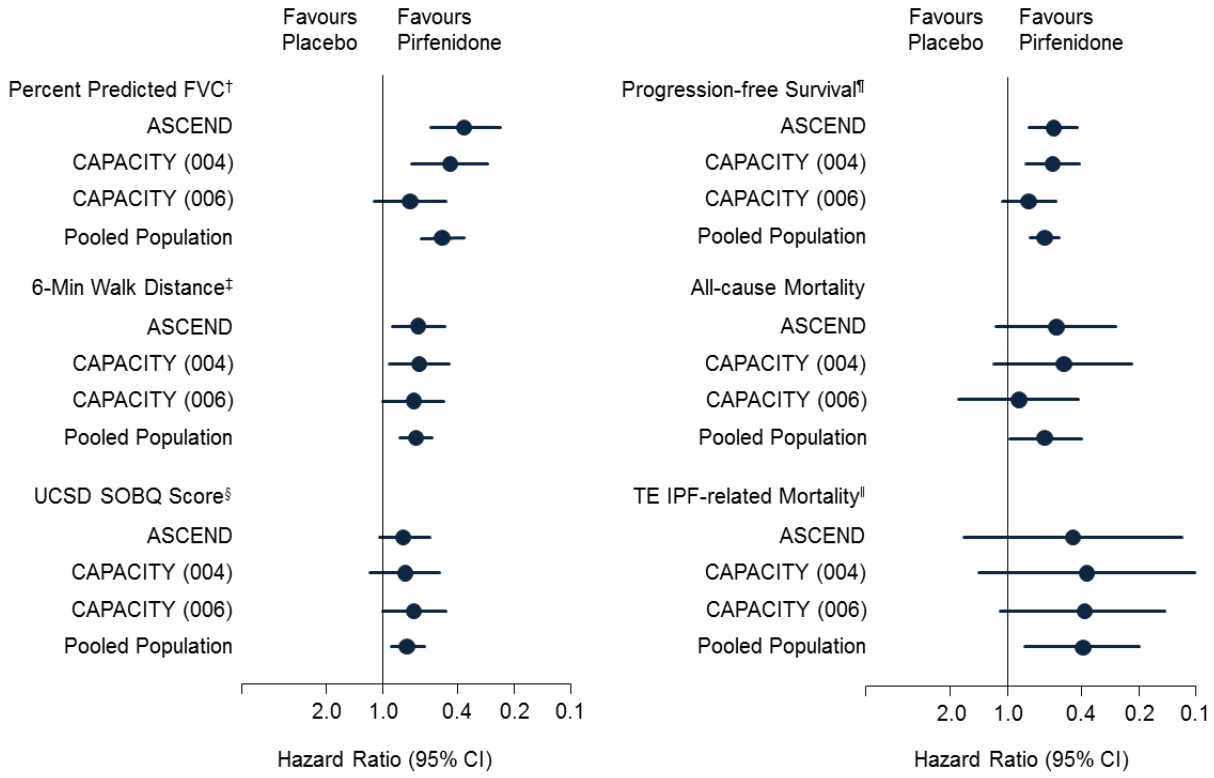
Figure S2 Summary of clinical efficacy outcomes at study primary endpoint in the pooled population from ASCEND and CAPACITY (N=1247)*



Definition of abbreviations: 6MWD=6-minute walk distance; FVC=forced vital capacity; UCSD SOBQ= University of California San Diego Shortness of Breath Questionnaire

*Week 52 in ASCEND and week 72 in CAPACITY

Figure S3 Summary of clinical efficacy outcomes at study primary endpoint in the individual studies*



Definition of abbreviations: FVC=forced vital capacity; TE=treatment emergent; UCSD SOBQ=University of California San Diego Shortness of Breath Questionnaire

*Assessed at week 52 in ASCEND and week 72 in CAPACITY
†Time to decline in percent predicted FVC ≥10% or death
‡Time to decline in 6-min walk distance ≥50 m or death
§Time to increase in UCSD SOBQ score ≥20 points or death
¶Time to death or disease progression (confirmed ≥10% decline in percent predicted FVC or ≥50 m decline in 6MWD)
‖Deaths adjudicated by mortality assessment committee in ASCEND and assessed by blinded investigators in CAPACITY