Supplemental material

Unfavourable effects of medically indicated oral anticoagulants on survival in IPF

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SUPPLEMENTARY TABLE S1. Summary of anticoagulant use and indication

Parameter	AC baseline users (N=32)	AC ever-users (N=54)
Indication, n (%)		
Atrial fibrillation	11 (34.4)	18 (33.3)
Prophylaxis	8 (25.0)	12 (22.2)
Deep vein thrombosis	6 (18.8)	11 (20.4)
Other[a]	4 (12.5)	8 (14.8)
Pulmonary embolism	2 (6.3)	3 (5.6)
Cardiovascular disease	1 (3.1)	2 (3.7)
Anticoagulant, n (%)		
Warfarin	29 (90.6)	44 (81.5)
Dabigatran	2 (6.3)	4 (7.4)
Fondaparinux	0	4 (7.4)
Acenocoumarol	1 (3.1)	1 (1.9)
Bivalirudin	0	1 (1.9)

[a]Carotid artery disease, cerebrovascular accident, hepatocancer, mitral valve replacement, pulmonary arterial hypertension, aortic valve replacement, worsening osteoarthritis, acute blood clot

AC: anticoagulant

SUPPLEMENTARY TABLE S2. Summary of baseline demographics: anticoagulant ever-users versus non-users

Parameter	AC ever-users (N=54)	AC non-users (N=570)	p-value
Mean age, years (SD)	70.7 (6.4)	66.8 (7.5)	0.0002
Sex, n (%)			
Male	40 (74.1)	425 (74.6)	0.9374
Mean % predicted FVC (SD)	69.3 (13.0)	72.2 (13.7)	0.1349
Mean % predicted DLco (SD)	42.6 (8.2)	45.9 (11.3)	0.0091
Mean 6MWD, m (SD)	374.2 (109.7)	415.4 (91.9)	0.0023
Mean UCSD SOBQ score (SD)	39.0 (23.0)	34.5 (21.4)	0.1436
Medical history, n (%)			
Cardiovascular disease	22 (40.7)	145 (25.4)	0.0152
Chronic renal failure	5 (9.3)	15 (2.6)	0.0082
Chronic obstructive pulmonary disease	2 (3.7)	20 (3.5)	0.9408
Pulmonary embolism	5 (9.3)	1 (0.2)	<0.0001
Pulmonary hypertension	4 (7.4)	15 (2.6)	0.0509
Atrial fibrillation	19 (35.2)	10 (1.8)	<0.0001
Deep vein thrombosis	11 (20.4)	6 (1.1)	<0.0001
Cardiovascular risk factors			
Hypertension	33 (61.1)	307 (53.9)	0.3064
Smoker (current/former)	35 (64.8)	349 (61.2)	0.6046
Diabetes	11 (20.4)	123 (21.6)	0.8362
Hypercholesterolemia	29 (53.7)	266 (46.7)	0.3222
Obesity (BMI >30 kg/m^2)	25 (46.3)	240 (42.1)	0.5515

6MWD: 6-minute walk distance; AC: anticoagulant; BMI: body mass index; DLco: carbon monoxide diffusing capacity; FVC: forced vital capacity; SD: standard deviation; UCSD SOBQ, The University of California in San Diego Shortness of Breath Questionnaire

SUPPLEMENTARY TABLE S3. Unadjusted 1-year risk of study outcomes for anticoagulant ever-users and non-users

Outcome	AC ever-users (N=54)	AC non-users (N=570)	p-value
Disease progression composite outcome,[a] n (%)	29 (57.4)	216 (37.9)	0.0230
All-cause mortality	9 (16.7)	23 (4.0)	<0.0001
FVC decrease ≥10%	8 (14.8)	56 (9.8)	0.2480
6MWD decrease ≥150 m	12 (22.2)	137 (24.0)	0.7652
Mortality, n (%)			
All-cause mortality	11 (20.4)	31 (5.4)	<0.0001
IPF-related mortality	10 (18.5)	18 (3.2)	<0.0001
FVC change, n (%)			
Absolute decrease ≥10%	9 (27.8)	102 (17.2)	0.0536
Relative decrease ≥10%	12 (38.9)	170 (28.8)	0.1198
Mean FVC change observed, % predicted (SD)	−6.9 (7.5)	−5.1 (6.8)	0.0997
6MWD decrease ≥50 m, n (%)	9 (27.8)	157 (26.5)	0.8380
All-cause hospitalisation, n (%)	12 (38.9)	102 (17.2)	0.0001

[a]Only the first disease progression event was counted for each patient

6MWD: 6-minute walk distance; AC: anticoagulant; FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; SD: standard deviation

SUPPLEMENTARY TABLE S4. Multivariate analyses: anticoagulant ever-users versus non-users

Parameter	HR	95% CI	p-value
Disease progression[a]	2.5	1.4, 4.3	0.001
Mortality			
All-cause mortality	4.8	1.9, 11.7	<0.001
IPF-related mortality	8.1	2.9–22.9	<0.001
FVC			
Absolute decrease ≥5%	2.3	1.3, 3.9	0.002
Relative decrease ≥5%	1.7	1.0, 2.7	0.034
Absolute decrease ≥10%	4.2	2.1, 8.4	<0.001
Relative decrease ≥10%	2.5	1.3, 4.8	0.005
Death or FVC (absolute) ≥10% decrease	3.5	2.0, 6.1	<0.001
Death or 6MWD decrease ≥50 m	2.5	1.5, 4.4	<0.001
All-cause hospitalisation	3.7	2.1, 6.7	<0.001

[a]Defined as ≥10% decrease in % predicted FVC, ≥50 m decline in 6MWD or death

6MWD: 6-minute walk distance; CI: confidence interval; FVC: forced vital capacity; HR: hazard ratio; IPF: idiopathic pulmonary fibrosis