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Convegno di presentazione della versione italiana delle linee guida per la diagnosi di fibrosi polmonare idiopatica

1 Febbraio 2020

Hotel Enterprise Milano

Linee guida ufficiali ATS/ ERS/JRS/ALAT per la pratica clinica

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La realtà italiana

Antonella Caminati

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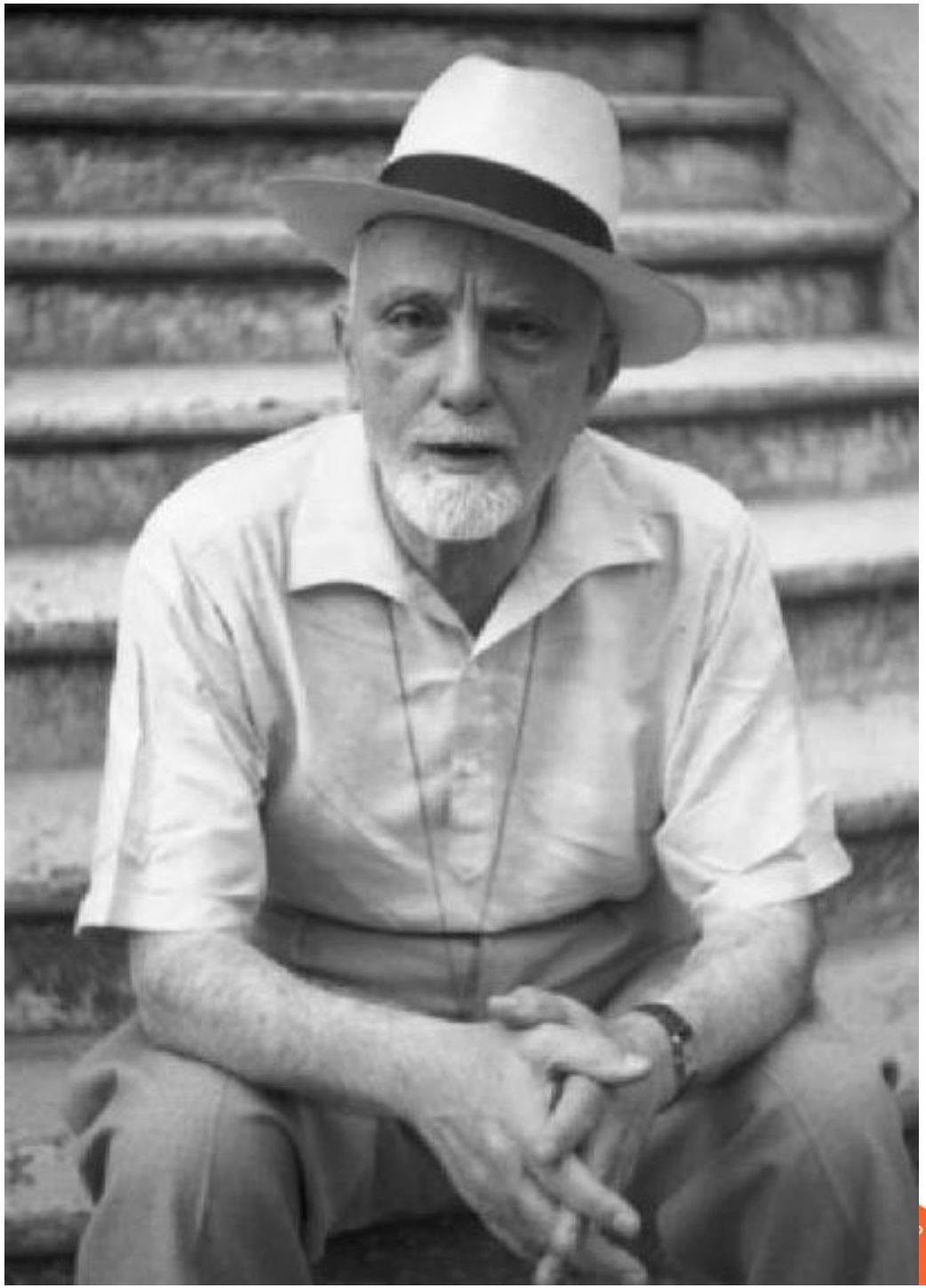


The prevalence of IPF increases with age

Estimates of the mean annual standardized IPF incidence rates (for 100000 person/years) in Lombardy during 2005 -2010 by age and NCD

Age classes	
<55	0.39 (0.33–0.46)
55–59	2.22 (1.75–2.70)
60–64	4.13 (3.45–4.80)
65–69	5.59 (4.78–6.39)
70–74	7.53 (6.52–8.53)
75–79	10.40 (9.08–11.72)
80–84	11.45 (9.81–13.10)
85+	8.29 (6.69–9.88)

Harari S et al. PLoS ONE 2016; 11 (2): e0147072.

Idiopathic pulmonary fibrosis (IPF) incidence and prevalence in Italy

Agabiti N, Porretta MA, Bauleo L, Coppola A, Sergiacomi G, Fusco A, Cavalli F, Zappa MC, Vignarola R, Carlone S, Facchini G, Mariotta S, Palange P, Valente S, Pasciuto G, Pezzuto G, Orlandi A, Fusco D, Davoli M, Saltini C, Puxeddu E.

Sarcoidosis Vasc Diffuse Lung Dis 2014 ; 20 (3): 191-7

RESULTS: Annual prevalence and incidence of IPF were estimated at 25.6 per 100,000 and 7.5 per 100,000 using the ICD9-CM code 516.3 without chart audit while they were estimated at 31.6 per 100,000 and at 9,3 per 100,000 for the IPF "confident" definition after hospital chart audit.

PLOS ONE

RESEARCH ARTICLE

Epidemiology of Idiopathic Pulmonary Fibrosis in Northern Italy

Sergio Harari[1]*, Fabiana Madotto[2], Antonella Caminati[1], Sara Conti[2], Giancarlo Cesana[2]

- The mean annual incidence rate was estimated at 2.3 and 5.3 per 100,000 person-years. Trend remained stable over the years.
- The estimated annual prevalence rate was 35.5, 22.4, and 12.6 per 100,000 person-years using GCD, BCD and NCD, respectively,

Harari S et al. PLoS ONE 2016; 11 (2): e0147072.

Internal and Emergency Medicine
https://doi.org/10.1007/s11739-019-02195-0

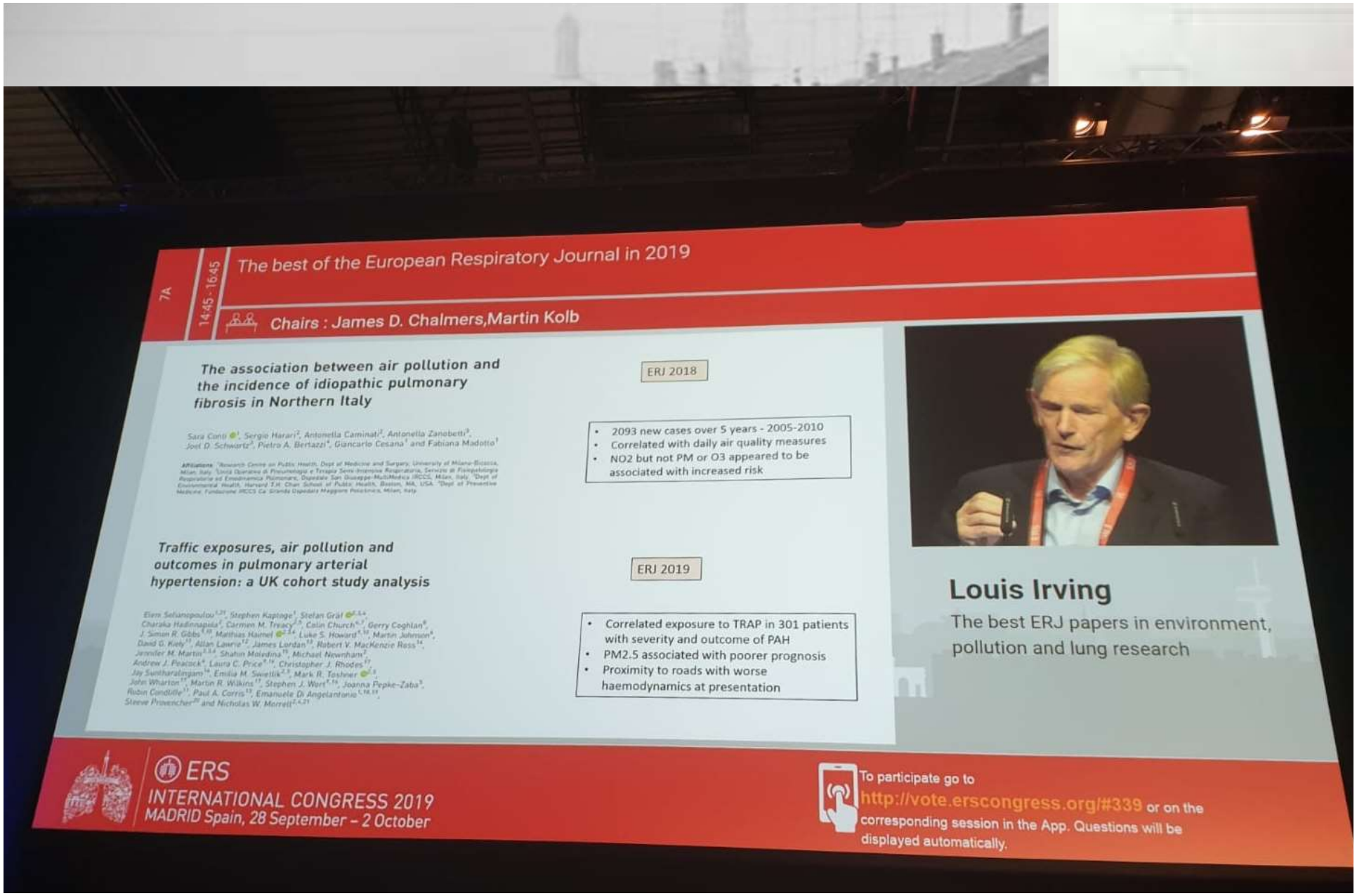
IM - ORIGINAL

Check for updates

Epidemiology of idiopathic pulmonary fibrosis: a population-based study in primary care

Sergio Harari[1] · Michele Davì[2] · Alice Biffi[1] · Antonella Caminati[1] · Alessandra Ghirardini[2] · Valeria Lovato[2] · Claudio Cricelli[3] · Francesco Lapi[4]

The increase of the incidence rates is likely due to a growing awareness for IPF among General Practitioners, while the increase of prevalence rates may be due to an increase of survival, a result of recent advances in the diagnosis, management and therapies for the disease.



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..but real life is not a clinical trial…

Respiratory Medicine 159 (2019) 105803

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: http://www.elsevier.com/locate/rmed

Real-life comparison of pirfenidone and nintedanib in patients with idiopathic pulmonary fibrosis: A 24-month assessment

Stefan
Martir
Maria

[a] Pneumolo
[b] Alma Ma
Bologna, B
[c] Respirato
[d] Departme
[e] Cardio-Tl
[f] Alma Mat
[g] Clinical a

Pulmonol. 2019;25(3):149–153

PULMONOLOGY

www.journalpulmonology.org

ORIGINAL ARTICLE

Pirfenidone and Nintedanib in idiopathic pulmonary fibrosis: Real-life experience in an Italian referral centre

E. Bargagli[a,*], C. Piccioli[a], E. Rosi[a], E. Torricelli[a], L. Turi[a], E. Piccioli[a], M. Pistolesi[a], K. Ferrari[a], L. Voltolini[b]

Convegno di
versione itali
diagnosi di fi

Pirfenidone in real life: a retrospective observational multicentre study in Italian patients with idiopathic pulmonary fibrosis

Vancheri C, Sebastiani A, Tomassetti S, Pesci A, Rogliani P, Tavanti L, Luppi F, Harari S, Rottoli P, Ghirardini A, Kirchgaessler K-U, Albera C.

Respir Med 2019

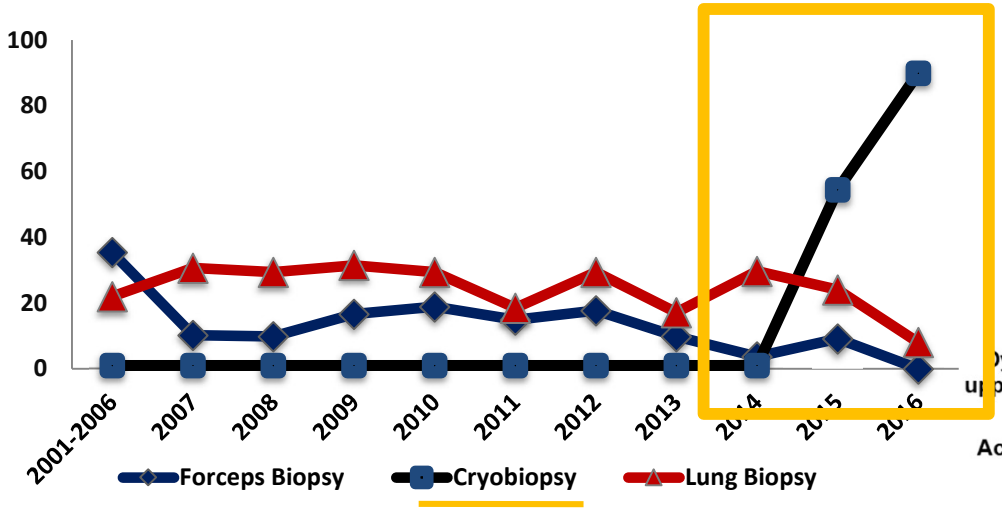
IRENE was a multicentre, retrospective, observational study of Italian patients with IPF treated with pirfenidone in ***real-world clinical practice***.

Characteristic[a]	All patients (N = 379)
Age, years	67.6 (7.1)
Male, n (%)	296 (78.1)
BMI, kg/m^2[b]	28.9 (4.1)
Smoking status, n (%)	
Former smoker	261 (68.9)
Nonsmoker	91 (24.0)
Time since first symptom onset, months	28.1 (30.3)
Time since diagnosis of IPF, months	5.9 (19.1)
HRCT pattern at diagnosis, n (%)[c]	
Definite UIP	259 (71.9)
Possible UIP	99 (27.5)
Inconsistent with UIP	2 (0.6)
Biopsy type, n (%)[d]	
Transbronchial cryobiopsy	29 (43.9)
Surgical lung biopsy	37 (56.1)
Bronchoalveolar lavage, n (%)[e]	143 (38.1)
FVC, % predicted	80.1 (16.4)
DLco, % predicted	53.5 (13.9)
FEV_1/FVC ratio, %	89.6 (13.0)
6MWD, m[f]	411.3 (114.2)

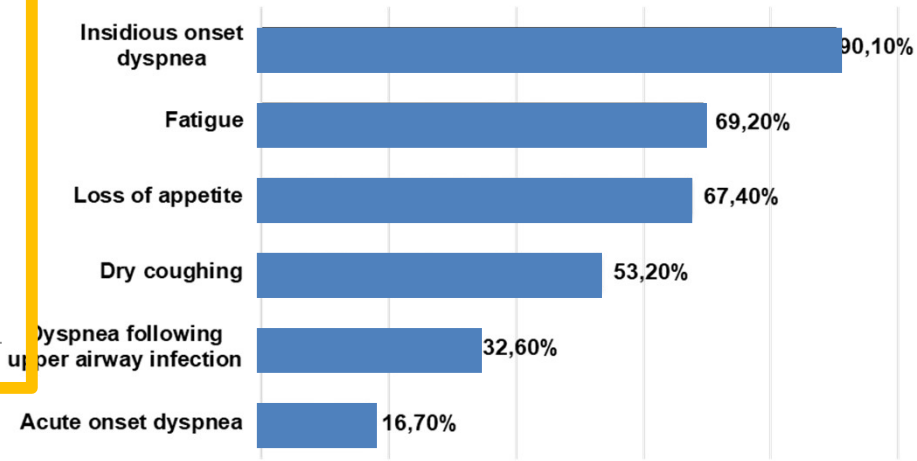
17%

The European IPF Registry

525 IPF subjects recruited between 11/2009 and 10/2016.



Change in biopsy procedures in IPF over time.
Data are given as percentage of the respective procedure undertaken in IPF subjects in the year of first diagnosis.



Distribution of self-reported symptoms of IPF patients.
Data are presented as percentage of all patients with reported symptom.

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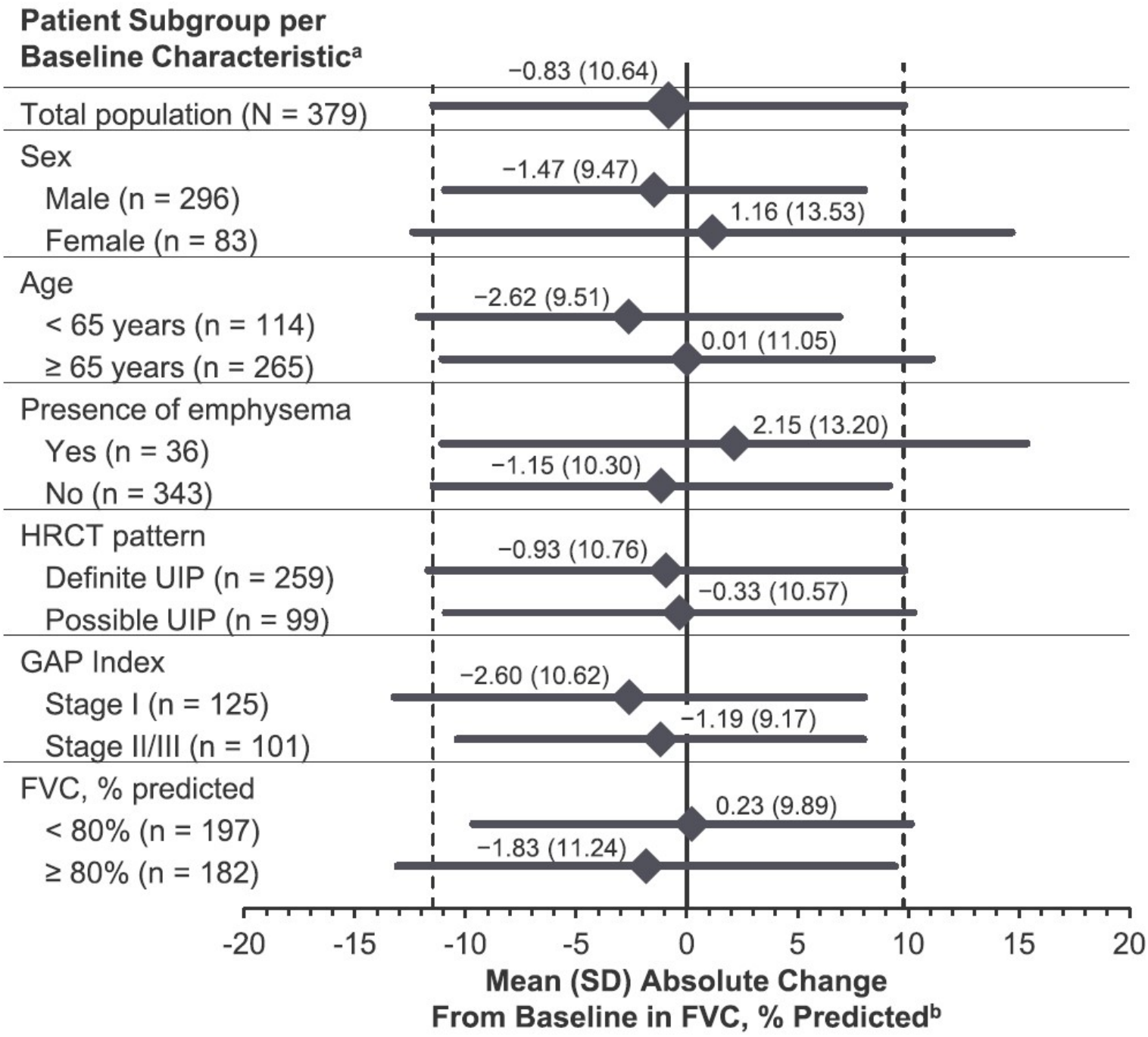
Effectiveness outcomes in the total population

Outcome	All patients (N = 379)[a]	
	Month 6	Month 12
Absolute change from baseline in FVC	(n = 359)	(n = 268)
Mean (SD), mL	−98.6 (484.3)	−81.8 (419.6)
P value (paired *t*-test)	< 0.001	0.002
Absolute change from baseline in % predicted FVC	(n = 372)	(n = 274)
Mean (SD)	0.20 (8.98)	−0.83 (10.64)
P value (paired *t*-test)	0.661	0.199
Patients with ≥ 10% absolute decline in % predicted FVC	(n = 372)	(n = 274)
Percentage (95% CI)	10.5 (7.8, 14.0)	16.0 (12.2, 20.9)


Patient Subgroup per Baseline Characteristic[a]
Total population (N = 379)
−0.83 (10.64)
Sex
Male (n = 296)
−1.47 (9.47)
Female (n = 83)
1.16 (13.53)
Age
< 65 years (n = 114)
−2.62 (9.51)
≥ 65 years (n = 265)
0.01 (11.05)
Presence of emphysema
Yes (n = 36)
2.15 (13.20)
No (n = 343)
−1.15 (10.30)
HRCT pattern
Definite UIP (n = 259)
−0.93 (10.76)
Possible UIP (n = 99)
−0.33 (10.57)
GAP Index
Stage I (n = 125)
−2.60 (10.62)
Stage II/III (n = 101)
−1.19 (9.17)
FVC, % predicted
< 80% (n = 197)
0.23 (9.89)
≥ 80% (n = 182)
−1.83 (11.24)
-20
-15
-10
-5
0
5
10
15
20
Mean (SD) Absolute Change From Baseline in FVC, % Predicted[b]

Summary of adverse events over 12 months

Patients with ≥ 1 event, n (%)	All patients (N = 379)
≥ 1 AE	149 (39.3)
≥ 1 AE of mild intensity	107 (28.2)
≥ 1 AE of moderate intensity	32 (8.4)
≥ 1 AE of severe intensity	24 (6.3)
≥ 1 SAE	31 (8.2)
≥ 1 AE related to pirfenidone[a]	95 (25.1)
≥ 1 SAE related to pirfenidone[a]	9 (2.4)
AE leading to discontinuation of pirfenidone	9 (2.4)
AE leading to death	15 (4.0)

AE, adverse event; SAE, serious adverse event.

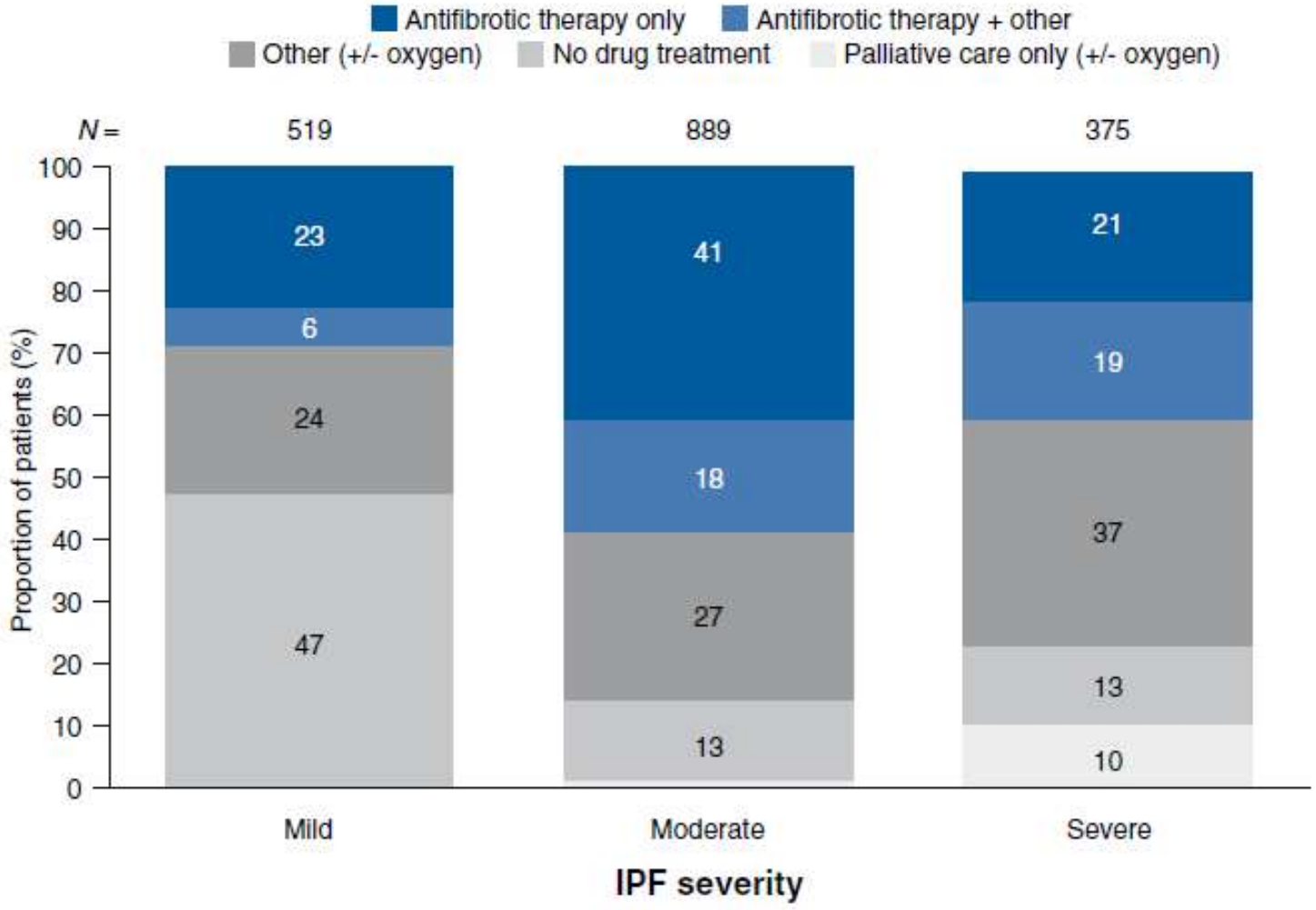
[a] Investigator judgment.

The real-world nature of this study may capture a more complete picture of pirfenidone effectiveness than controlled clinical trials.

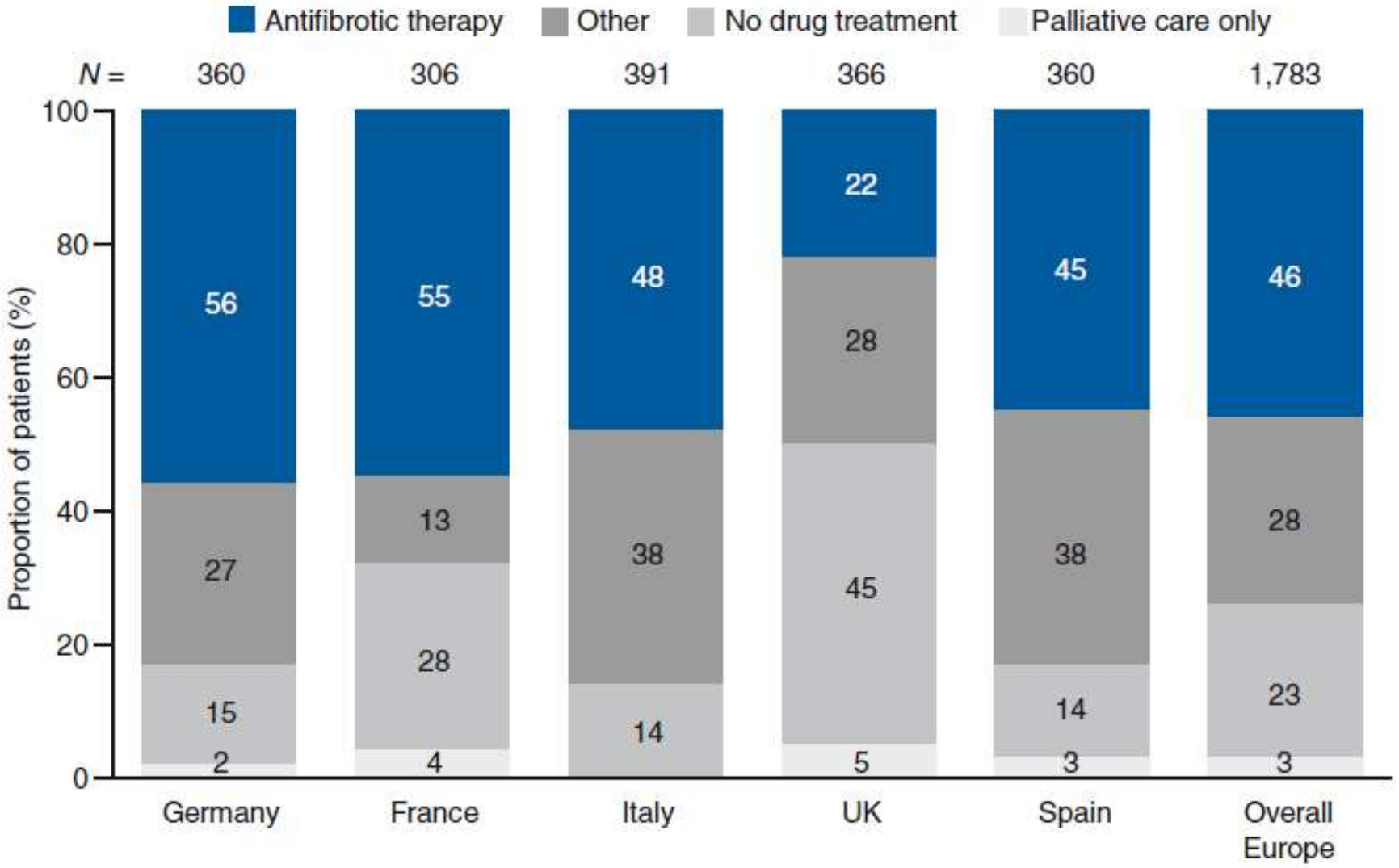
No data were captured in patients who discontinued pirfenidone at or before month 6, and the number of excluded patients was not recorded.

We step back

Patients with mild IPF are least likely to receive treatment

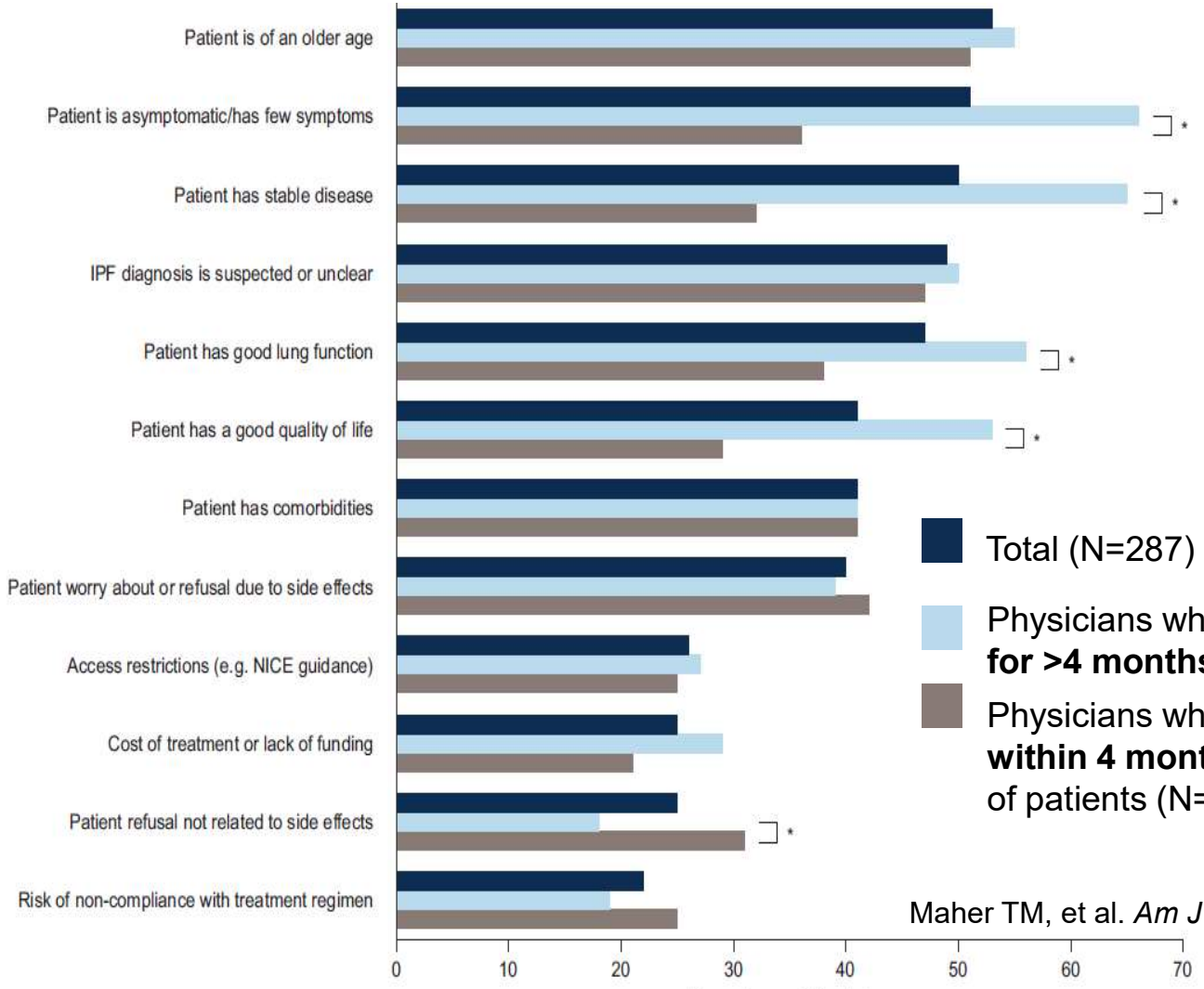


Maher et al. BMC Pulmonary Medicine (2017) 17:124



Maher et al. BMC Pulmonary Medicine (2017) 17:124

Reasons cited by physicians for not treating patients with mild IPF



Maher TM, et al. *Am J Respir Crit Care Med* 2017;195:A1123

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Approximately 40% of European patients with confirmed IPF do not receive antifibrotic treatment despite the regulatory approval of two antifibrotic therapies and the recommendation in international guidelines

Maher et al. BMC Pulmonary Medicine (2017) 17:124

New Italian results

Clinical course of IPF in Italian patients during 12 months of observation: results from the FIBRONET observational study

Poletti V, Vancheri C, Albera C, Harari S, Pesci A, Refini RM, Campolo B, Rizzoli S, on behalf of FIBRONET study group, ERS Congress 2019

Convegno di presentazione della versione italiana delle linee guida per la diagnosi di fibrosi polmonare idiopatica
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Study design

IPF diagnosis

- Diagnosed within last 3 months based on 2011 ATS/ERS/JRS/ALAT guidelines[1]

20 Italian pulmonary centres

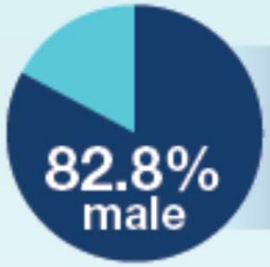
- 36 patients withdrew
  - 13 died

- 12-month, observational, prospective, cohort study
- Three intermediate evaluations at 3, 6 and 9 months

AIM: To describe the baseline characteristics of patients with IPF and the clinical course of the disease during 12 months of observation in term of changes in lung function (FVC% predicted)

Clinical course of IPF Italian patients during 12-month of observation: results from the FIBRONET observational study.
Poletti V. et Al.: Thematic poster Session: Interstitial lung disease registries, ERS Congress 2019

Patients characteristics



- 173 men
- 36 women
- 100% Caucasian/white

- 138 patients (**66.0%**) former smokers
- Nine patients (**4.3%**) current smokers

Mean age (SD):
69.54 years (±7.43)

- 70 patients (34.0%) exposed to environmental risk factors (e.g. metal dust, asbestos)
- Two patients (1.0%) exposed to amiodarone

81.8% (n=171)
with comorbidities

- 25 patients (12.0%) with a family history of IPF

FVC% PREDICTED AT BASELINE:
80.01% (±19.23)

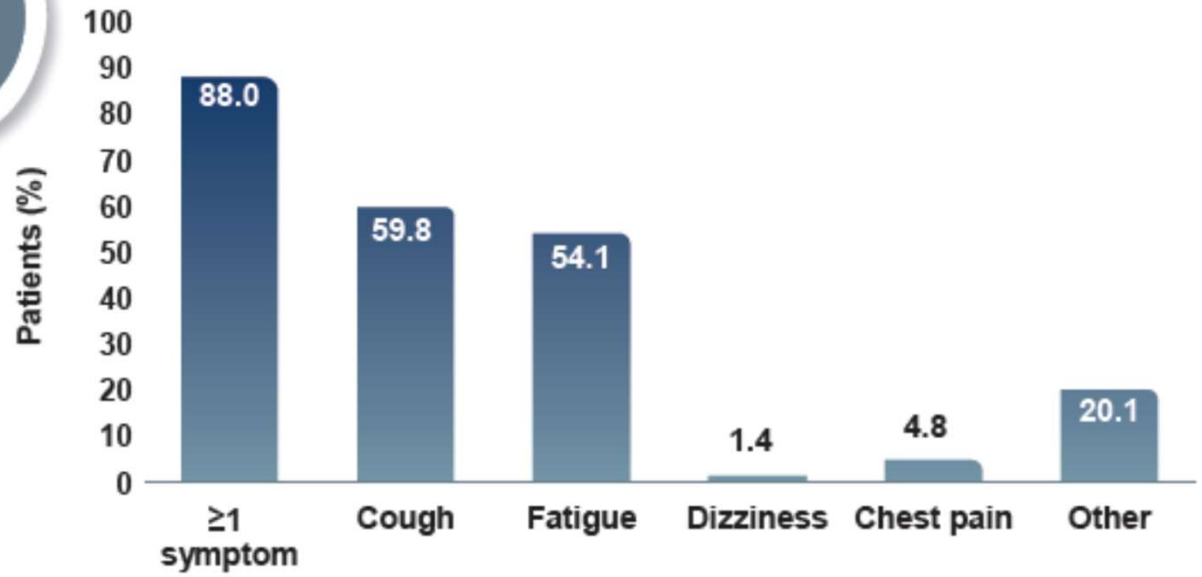
Clinical course of IPF Italian patients during 12-month of observation: results from the FIBRONET observational study.
Poletti V. et Al.: Thematic poster Session: Interstitial lung disease registries, ERS Congress 2019

EXERCISE TOLERANCE

6-Minute Walk Test

Mean (SD) 395.70 metres (±121.70) at baseline

IPF SYMPTOMS

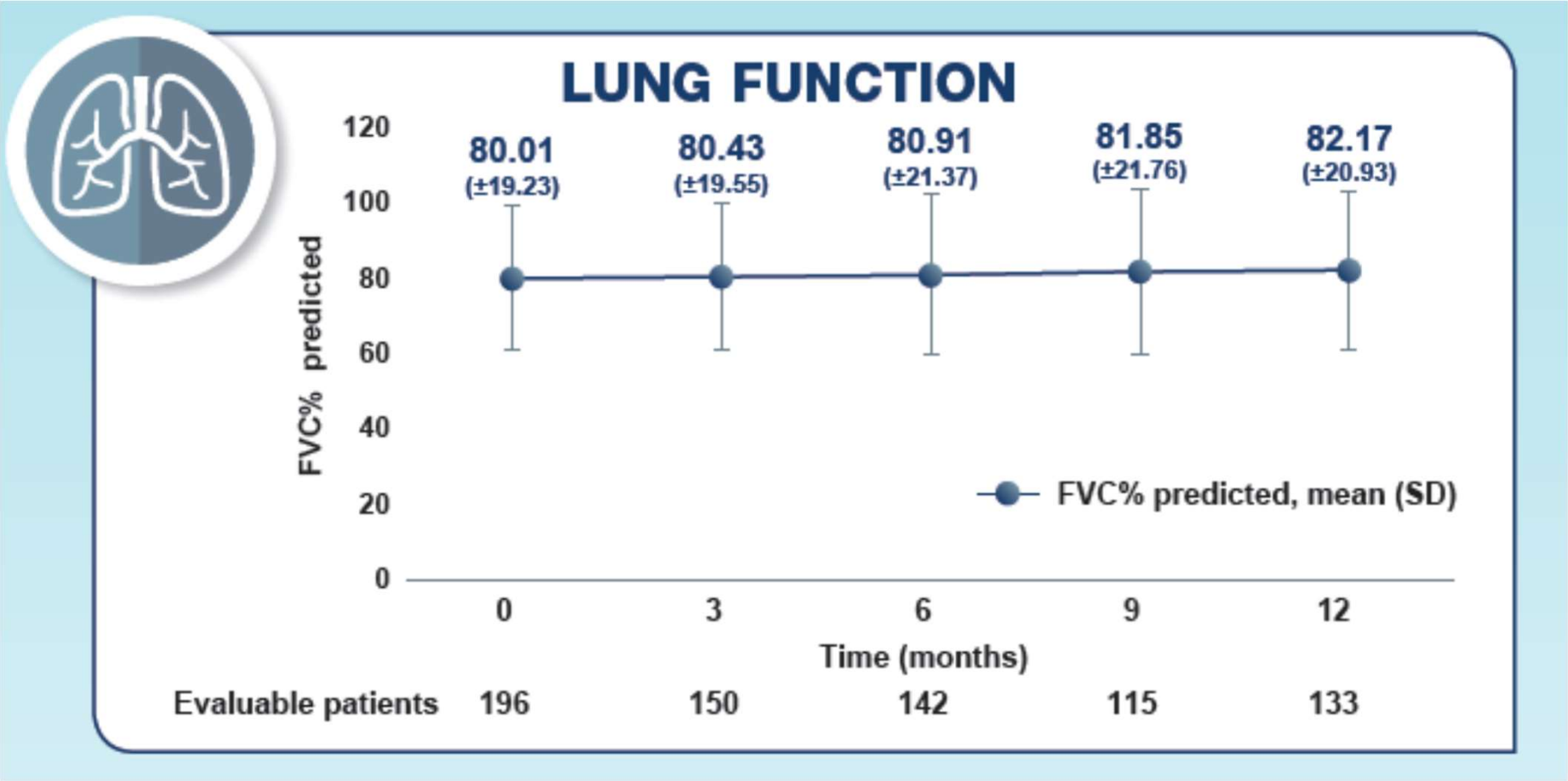


88% of patients had ≥1 symptom at baseline

Antifibrotic treatment

- Percentage of patients receiving antifibrotic therapy increased during the 12 months:
  - baseline: **15.8%** (n=33)
  - 3 months: 72.3% (n=138)
  - 6 months: 80.8% (n=139)
  - 12 months: **83.9%** (n=146)

Clinical course of IPF Italian patients during 12-month of observation: results from the FIBRONET observational study.
Poletti V. et Al.: Thematic poster Session: Interstitial lung disease registries, ERS Congress 2019



Clinical course of IPF Italian patients during 12-month of observation: results from the FIBRONET observational study.
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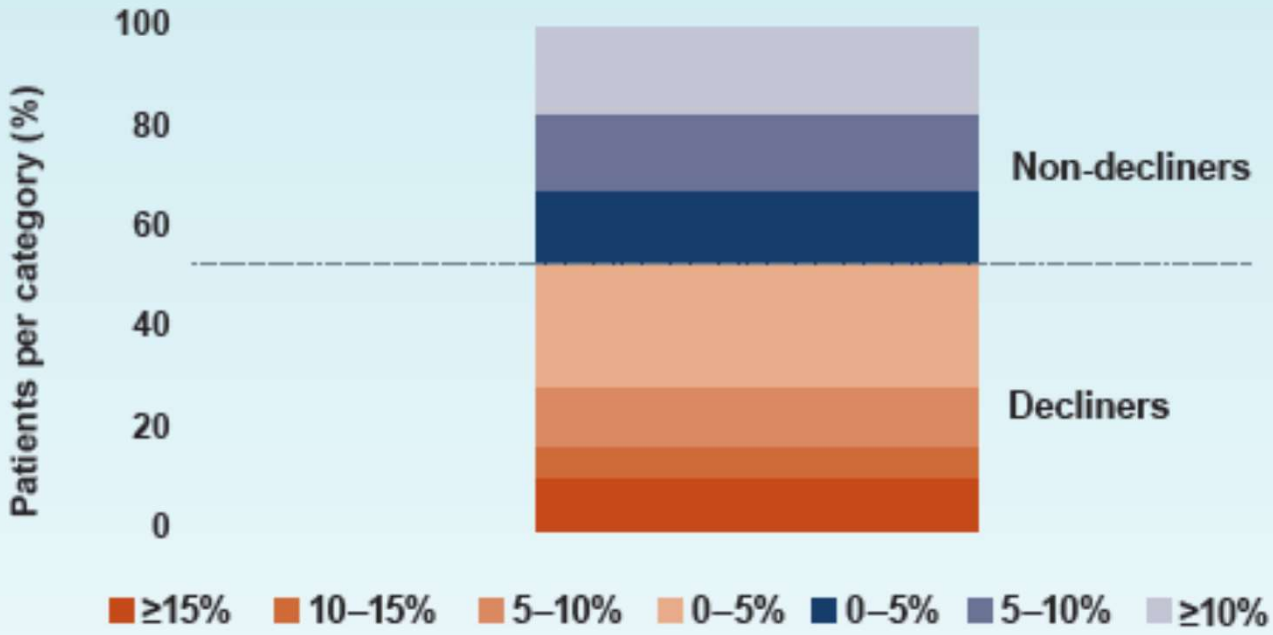

FVC% predicted: relative change (12-month follow-up)

- Considering the relative change in FVC% predicted at 12 months versus baseline:

47.4%
patients had no decline in FVC% predicted after 12 months

52.6%
patients had a decline in FVC% predicted after 12 months

Discussion

- Socio-demographic and clinical characteristics of FIBRONET patients are consistent with those described in the literature for patients with IPF
- Mean FVC is relatively preserved and consistent with other Italian data, suggesting that, in Italy, **patients are diagnosed early**
- In FIBRONET **the average time between diagnosis and start of antifibrotic therapy was short** – only 6.38 weeks
- We speculate that this **early therapeutic intervention** resulted in the high proportion of patients with no decline in FVC

Clinical course of IPF Italian patients during 12-month of observation: results from the FIBRONET observational study.
Poletti V. et Al.: Thematic poster Session: Interstitial lung disease registries, ERS Congress 2019

Key Finding

After 12 months of real-world observation, 84% of patients newly diagnosed with IPF were receiving antifibrotic therapy, and 47% of patients had no decline in FVC% predicted

Clinical course of IPF Italian patients during 12-month of observation: results from the FIBRONET observational study.
Poletti V. et Al.: Thematic poster Session: Interstitial lung disease registries, ERS Congress 2019

Conclusion

Early diagnosis of IPF might enable early initiation of antifibrotic therapy, which may improve patient outcomes (average 6 weeks between diagnosis and therapy initiation, with an average FVC of 80.01% predicted at baseline)

Clinical course of IPF Italian patients during 12-month of observation: results from the FIBRONET observational study.
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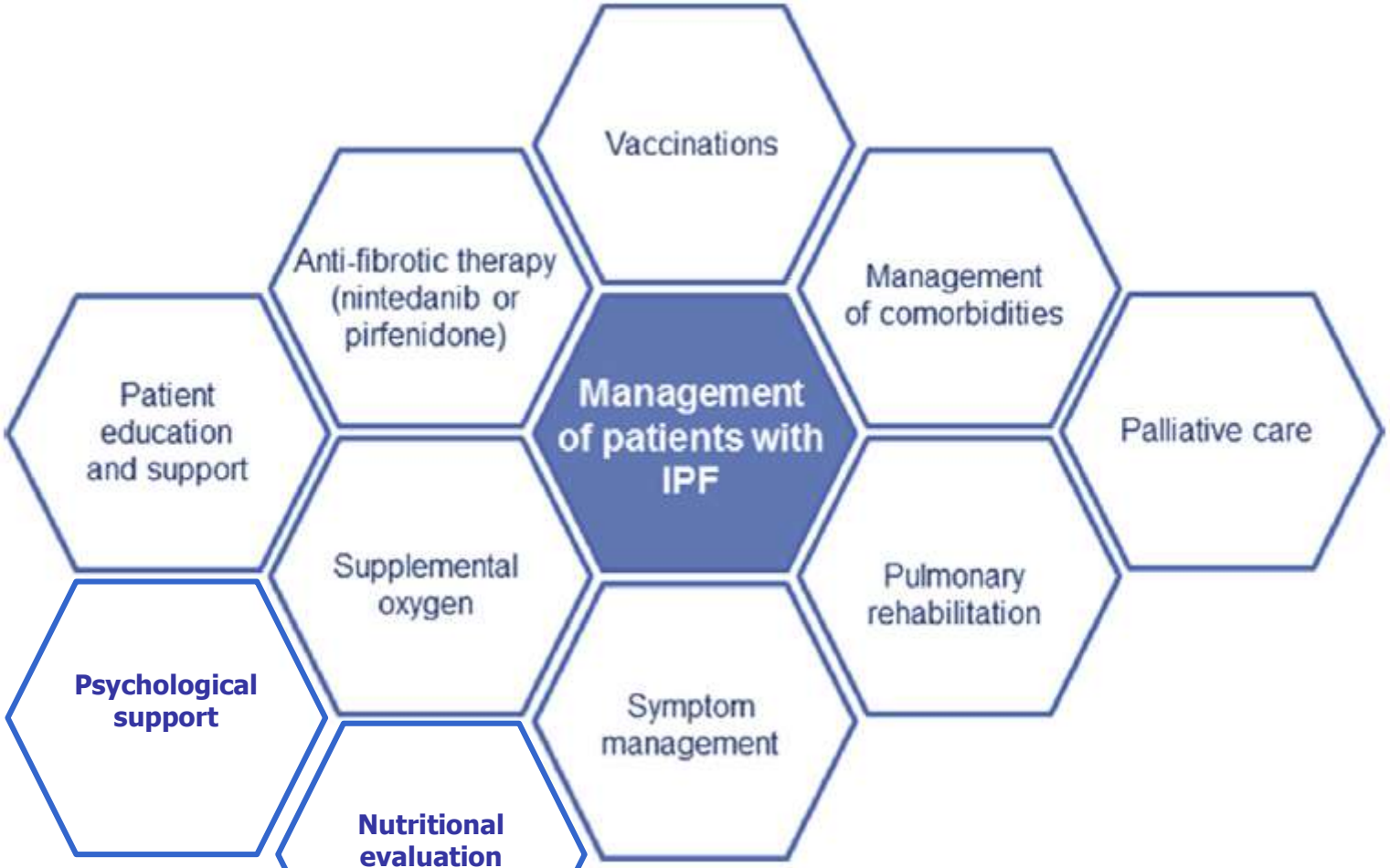
Optimal clinical management of patients with IPF is multifaceted

Modified from Raghu G and Richeldi L. Respir Med 2017, 129: 24-30



Nutrition in patients with idiopathic pulmonary fibrosis: critical issues analysis and future research directions

Faverio P, Bocchino ML, Caminati A, Fumagalli A, Gasbarra M, Iovino P, Petruzzi A, Scalfi L, Sebastiani A, Stanziola A, Sanduzzi A

submitted

NutrIPF: Nutritional assessment in IPF
Multicenter pilot study

Monza, CasateNovo, Milano, Garbagnate, Novara, Brescia, …

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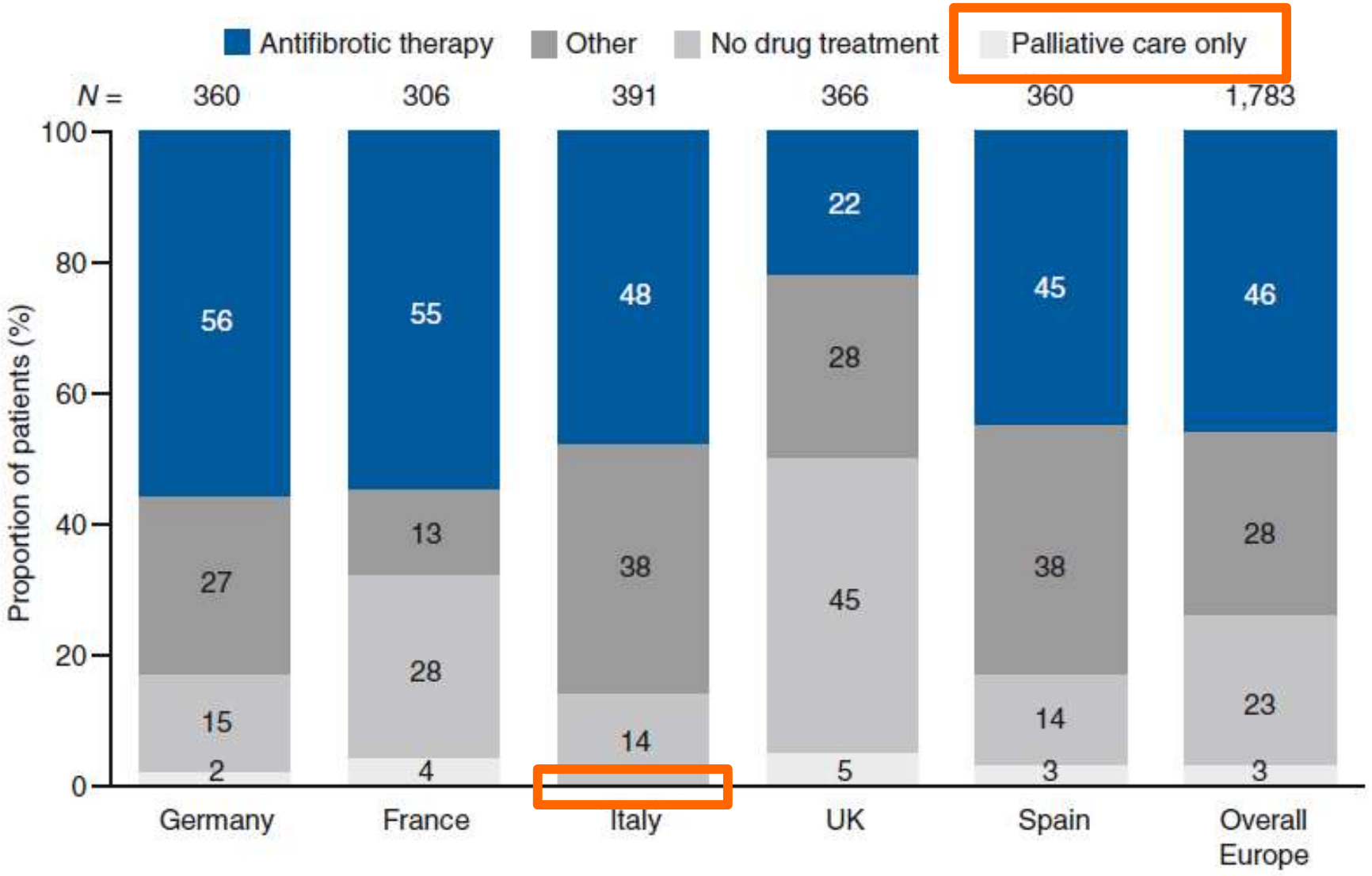


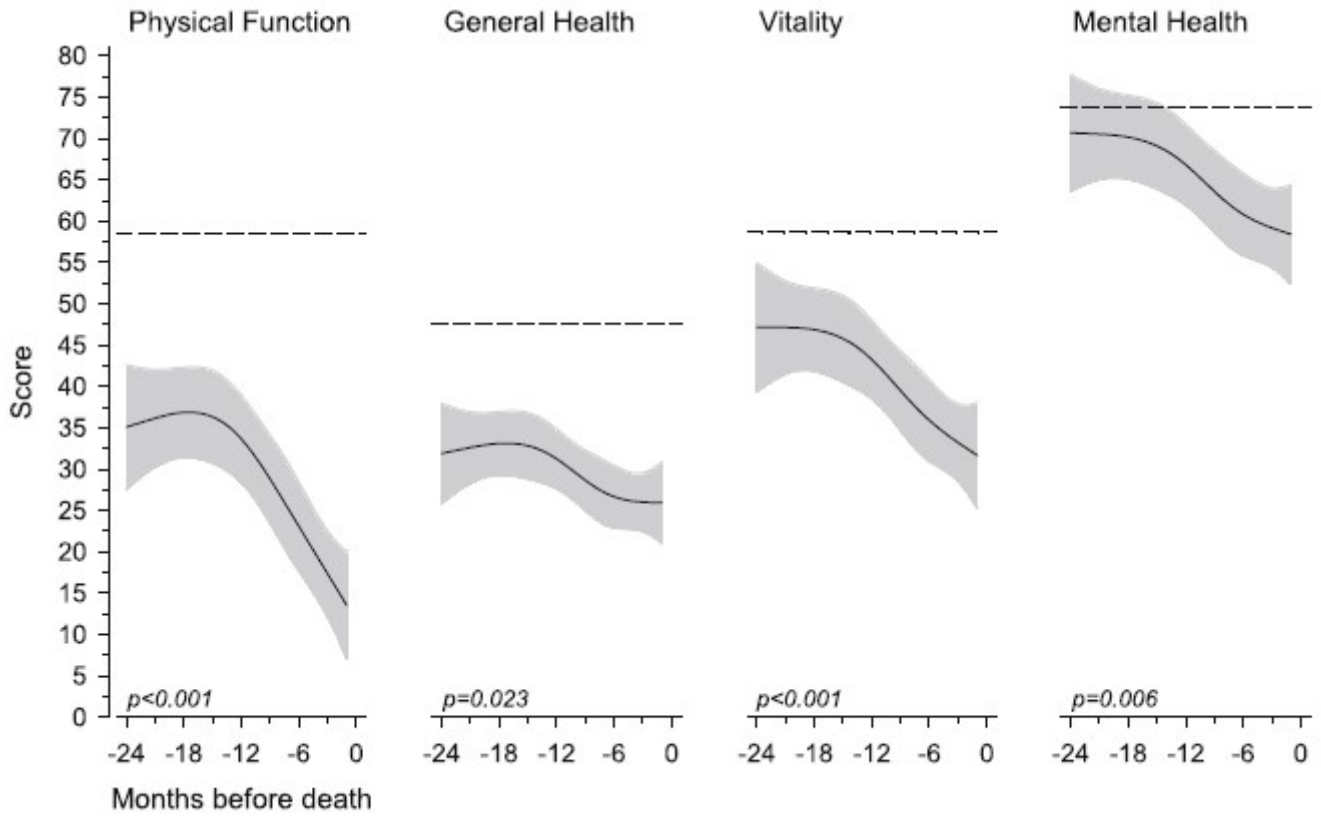
Maher et al. BMC Pulmonary Medicine (2017) 17:124

Many patients appeared to receive inadequate additional symptom management measures. Oxygen therapy and supportive treatments, such as anti-cough treatments, vaccines, etc., were used in only half of patients overall and in approximately a quarter of patients in the treated population

3% of overall patients and 10% with severe disease received palliative care

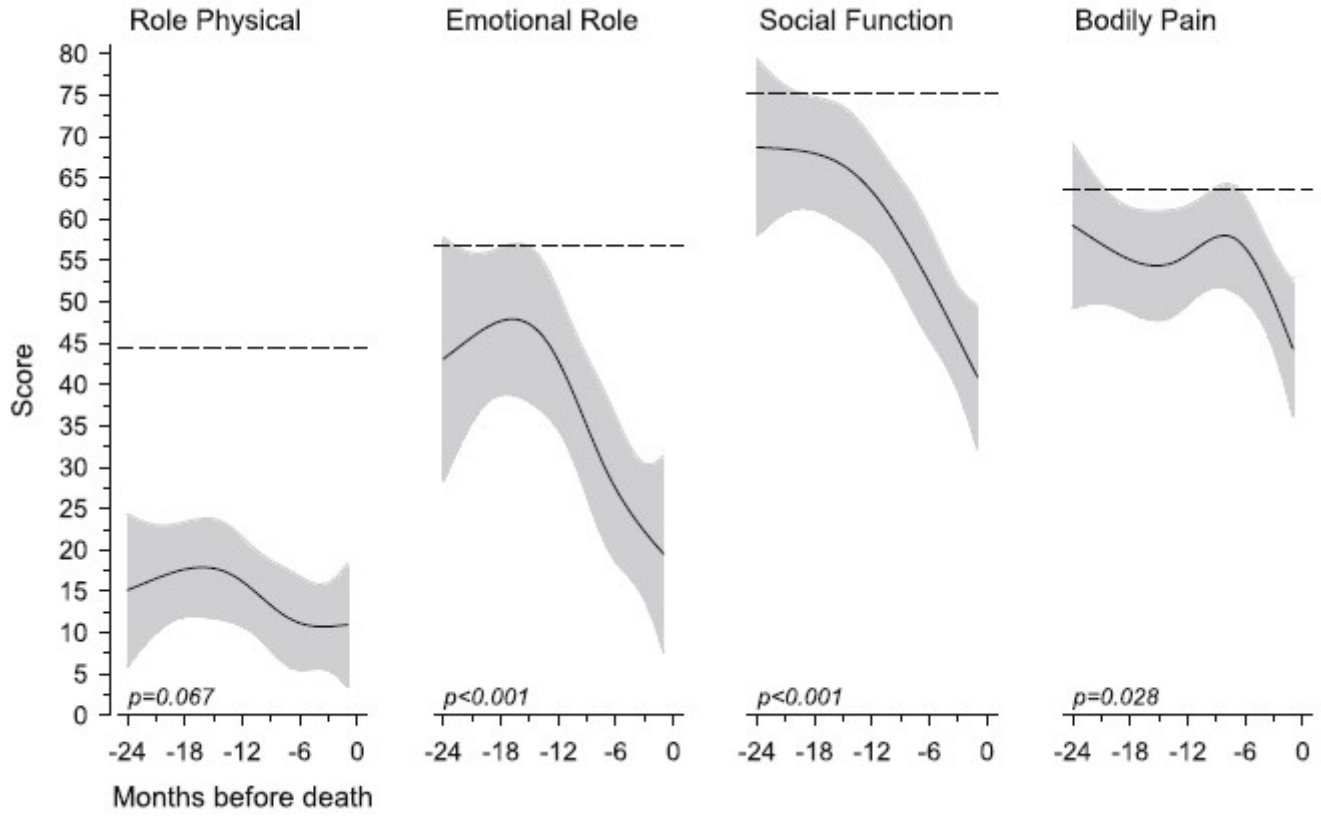
Maher et al. BMC Pulmonary Medicine (2017) 17:124

Marked deterioration in the quality of life of patients with idiopathic pulmonary fibrosis during the last two years of life

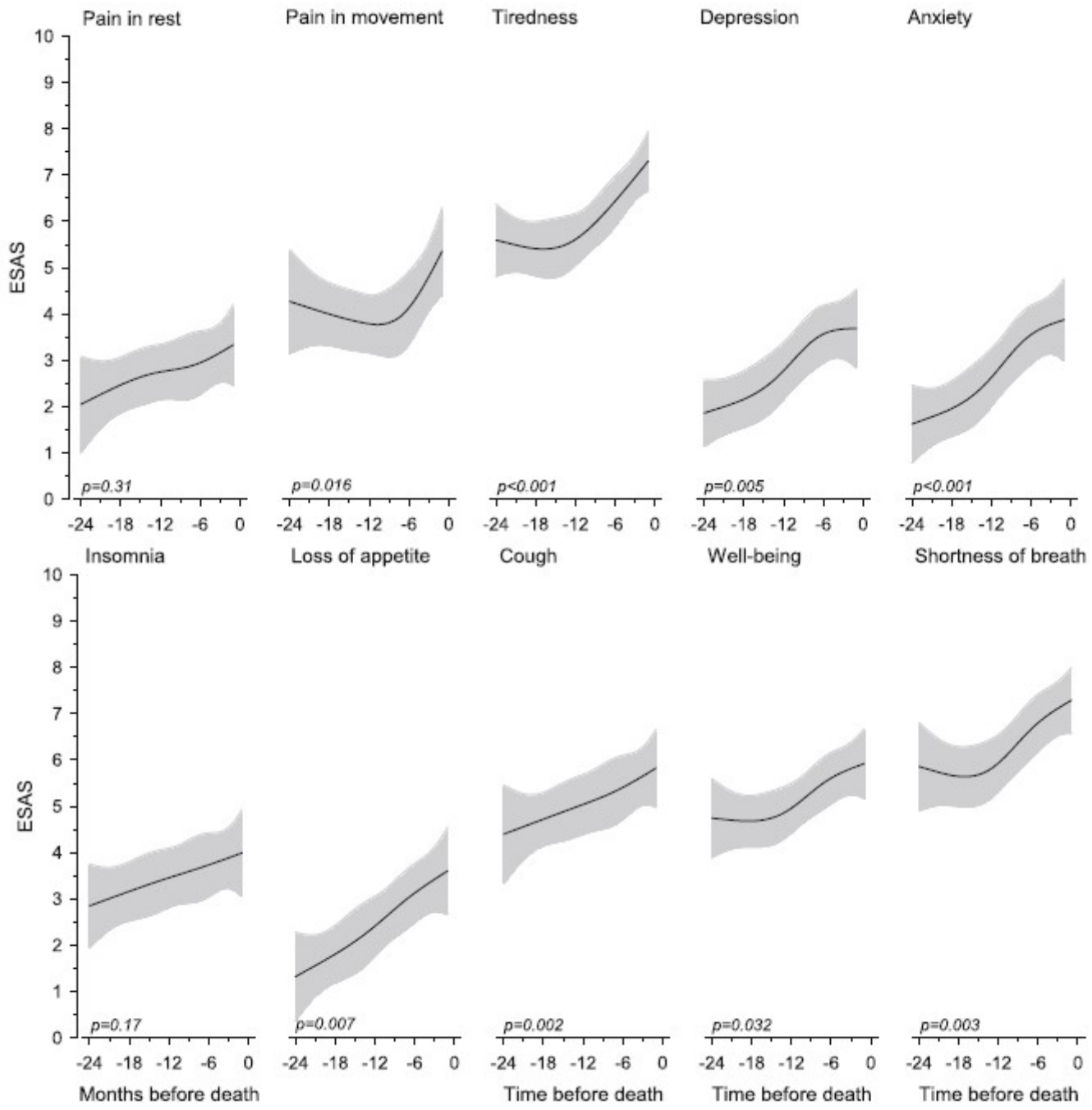


Rajala K et al. BMC Pulmonay Medicine 2018; 18 : 172

Marked deterioration in the quality of life of patients with idiopathic pulmonary fibrosis during the last two years of life



Rajala K et al. BMC Pulmonay Medicine 2018; 18 : 172


Pain in rest
Pain in movement
Tiredness
Depression
Anxiety
ESAS
p=0.31
p=0.016
p<0.001
p=0.005
p<0.001
Insomnia
Loss of appetite
Cough
Well-being
Shortness of breath
p=0.17
p=0.007
p=0.002
p=0.032
p=0.003
-24 -18 -12 -6 0
Months before death
Time before death
Time before death
Time before death

Low HRQOL was actually an independent prognostic factor

The relief of activity-limiting symptoms together with psychosocial support may improve HRQOL in advanced IPF

Early integrated palliative care for patients with lung cancer has shown substantial benefits, such as lower depression scores, higher HRQOL, better communication of end-of-life care preferences, less aggressive care at the end-of-life, and longer overall survival

Structured measurements of HRQOL and symptoms are necessary to guide high-quality early-integrated palliative care and end-of-life planning in IPF patients.

Early referral to palliative care services in patients with IPF: a tool to take a step forward

Proposed criteria for the referral of patients with IPF to specialist palliative care service

IPF (presence of *two or more* of the following criteria)

- GAP index stage III.
- Baseline DLCO <40% of predicted.
- Disease progression, despite optimal medical management, defined as FVC decline ≥10% and/or DLCO decline ≥15% over 6 months.
- 6MWT desaturation (SpO_2 <88%) and/or 6MWT distance <250 m and/or decrease in 6MWD over 50 m at 6 months.
- Need for long-term oxygen therapy 24 hours/day and/or high oxygen requirements.
- Extent of fibrosis and honeycombing on HRCT and its progression during the follow-up, despite optimal medical management.
- At least one hospitalisation for acute exacerbation of IPF.
- Presence or development of pulmonary hypertension.

Faverio P, et al. BMJ Supportive & Palliative Care 2019

A timely and personalized communication

However, it is important to start explaining to the patient about the disease course and management so that they know what to expect.

The exact content of the discussion should be sensitively tailored to the individual, and is a process which will evolve over time.

Raising awareness on physician-patient communication in IPF: an Italian multicenter study exploring the pneumologist's perspective

Tomassetti S , Sebastiani A, Caminati A, Oggionni T, Davì M, Ghirardini A, Martinoli M.

Conclusions: An adequate training may ameliorate communication and drive towards patient-centeredness. Raising awareness on these topics is crucial to ensure IPF patients optimal care. The pulmonologists' needs emerged may help planning interventions.

submitted

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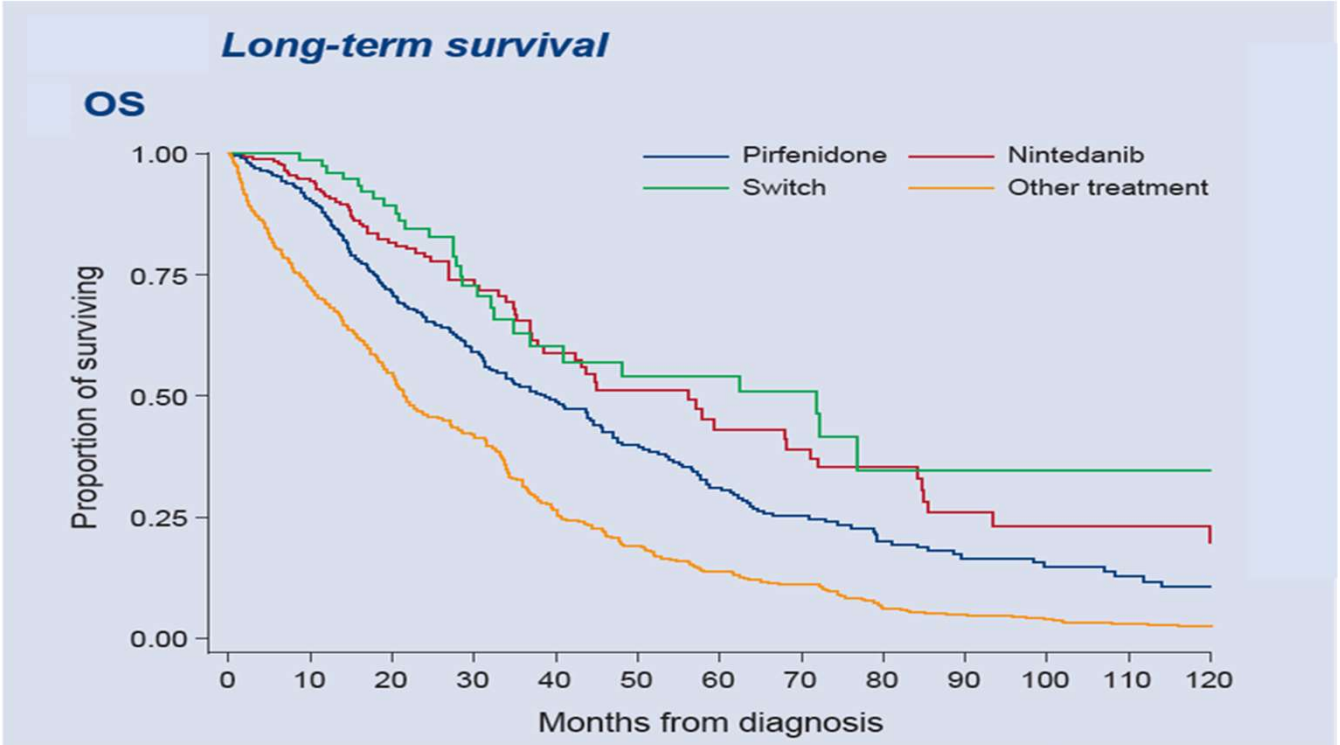
Long-term overall survival in IPF treated by Pirfenidone or Nintedanib or their switch: real-world data from the EMPIRE registry

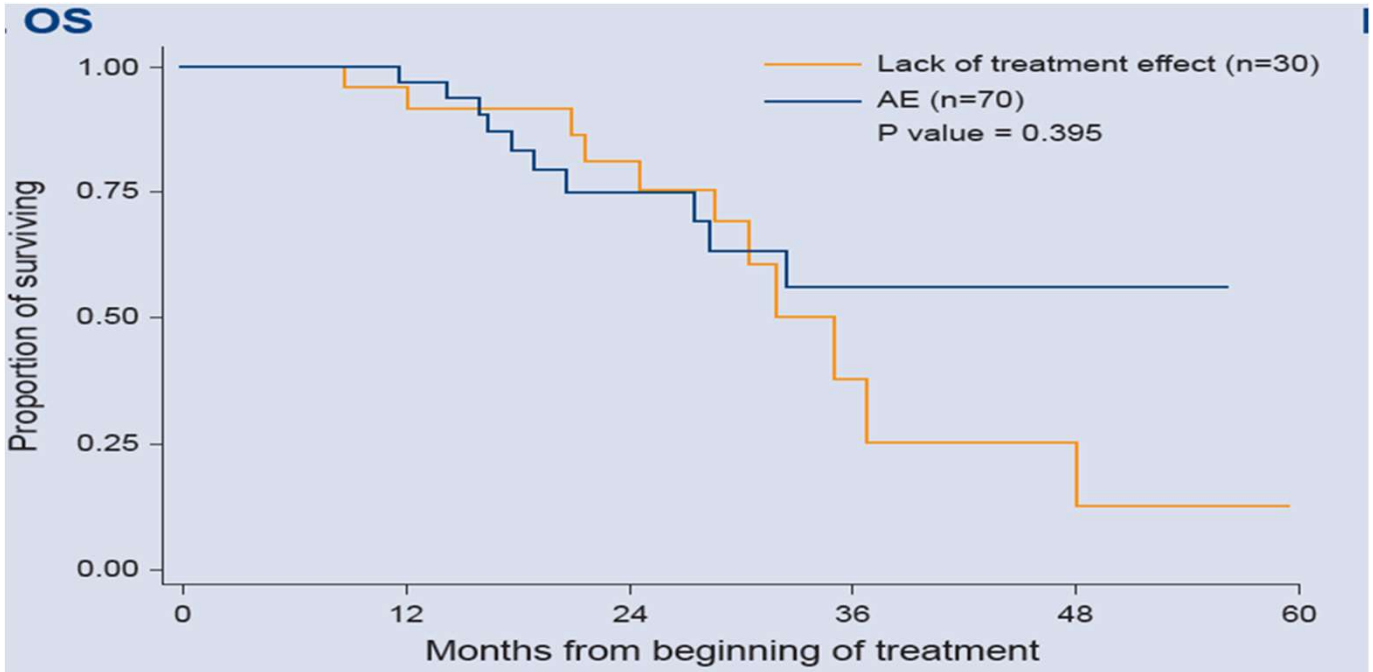


	Median survival (months)	1-year survival (95% CI)	5-year survival (95% CI)	10-year survival (95% CI)
Pirfenidone	38.7	0.872 (0.831–0.904)	0.311 (0.251–0.372)	0.105 (0.060–0.163)
Nintedanib	56.3	0.912 (0.867–0.943)	0.430 (0.314–0.540)	0.197 (0.097–0.323)
Switch	71.9	0.961 (0.884–0.987)	0.540 (0.382–0.674)	0.347 (0.171–0.530)
Other treatment	21.4	0.688 (0.633–0.737)	0.138 (0.101–0.180)	0.023 (0.011–0.042)

Vašáková, M. Poster presented at the ERS Congress 2019

Convegno di presentazione della versione italiana delle linee guida per la diagnosi di fibrosi polmonare idiopatica
Linee guida ufficiali ATS/ERS/JRS/ALAT per la pratica clinica
1 Febbraio 2020
Hotel Enterprise Milano

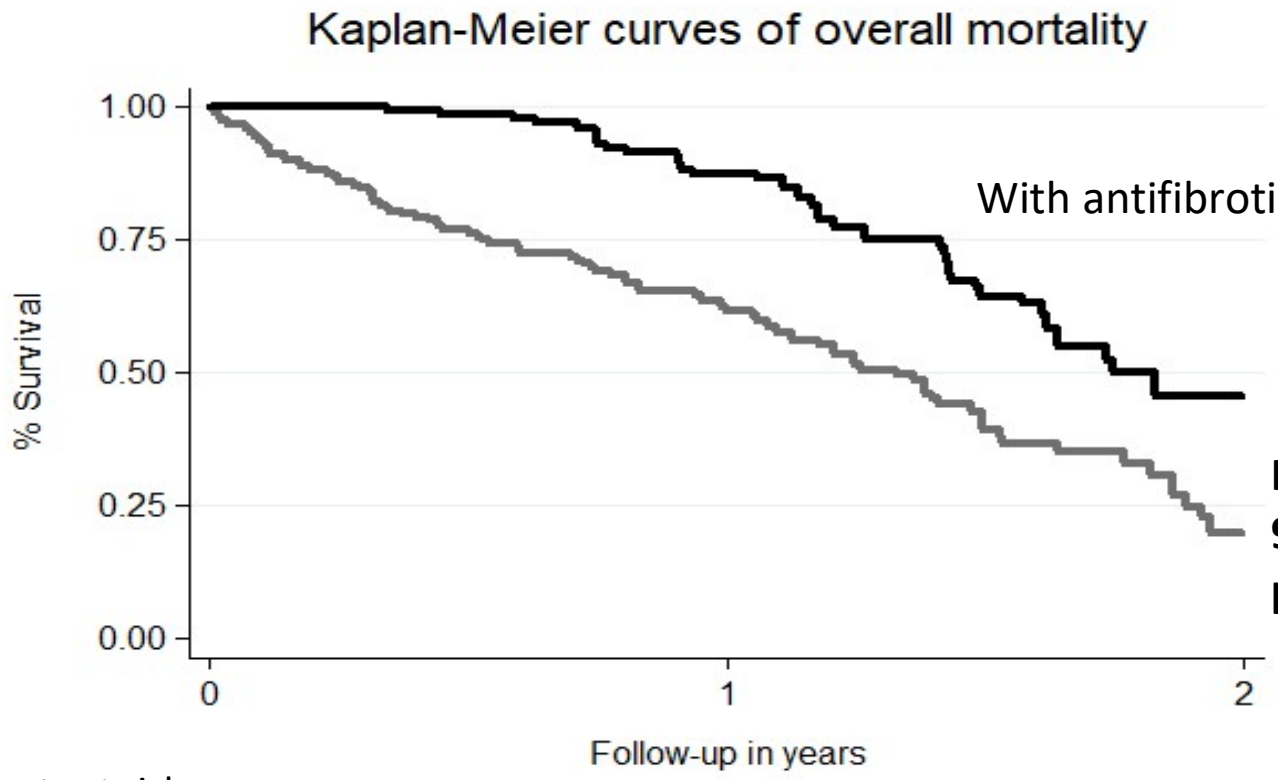
Survival in patients who switched treatment due to AEs or lack of treatment effect



	Median survival (months)	1-year survival (95% CI)	2-year survival (95% CI)	5-year survival (95% CI)
AE	76.9	0.969 (0.798–0.996)	0.752 (0.546–0.874)	0.561 (0.316–0.748)
Lack of treatment effect	34.9	0.915 (0.700–0.978)	0.810 (0.566–0.925)	0.126 (0.008–0.417)

Vašáková, M. Poster presented at the ERS Congress 2019

INSIGHTS-IPF registry, ERS 2019



HR = 0.63
95% CI: 0.45-0.87
p=0.005

Number of patients at risk			
With antifibrotic therapy	281	129	57
No antifibrotic therapy	252	139	93

Grazie per l'attenzione