ILD Collaborative

Project ECHO

IPF: Natural History and Survival

--"What to tell patients"--

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Disclosures

Clinical Research:

RNAi-investigational drug in patients with IPF; Nitto Denko Corporation

Starscape: Evaluation of Safety and Efficacy of Recombinant Human Pentraxin-2 in IPF; Roche

RECOVER: Researching Covid and Recovery; NIH

IPF- Natural History

A disease of unknown cause characterized by insidious decline in lung function, progressing to hypoxemic respiratory failure and death.

Disease courses range widely from rapid progression, to prolonged durations of stability, to step-wise declines triggered by acute exacerbations.

Upon hearing the diagnosis of IPF

"My doctor said that here is nothing that can be done."

"My doctor said that I have 3 years to live!"

" I looked on the Internet about live expectancy in IPF. Here's what it said: 'In general, the life expectancy with IPF is **about three years**.'

Patient Education-Estimates of Survival

Generated from specialty referral centers biased toward advanced disease, late in its course.

Earlier dx today: ↑ awareness; ↑ use of highly sensitive imaging

Up to 20% of IPF pts die 2º to causes not directly related to pulmonary fibrosis

Patient Education

Estimates of survival reflect the range of life expectancy in a cohort of IPF patients rather than the limit of an individual's life span.

Without a biomarker, no way to predict, for a given patient, whether the course will be the same, better, or worse than average. (? Exception-short telomere)

Report of US Medicare Data Base

Median survival=3.8 years

Survival times ↓ based on age at time of dx

Age 66-69, median survival 8 years

Age 73-79, median survival 4.5 yrs

Age ≥ 80 yrs, median survival 2.5 yrs

Raghu et al, Lancet Respir Med 2014

Factors Influencing Prognosis in IPF

Older age; male gender

Respiratory sx

Pulmonary function (lower FVC, % predicted; DLCO)

O_2 requirement

↑ fibrosis on HRCT

? Weight loss

Gender-Age- Physiology (GAP) Model {Point Score Index}

(Ley et al, Ann Intern Med, 2012)

Predictors of IPF Mortality

↑ Respiratory sx

Decline in FVC > 10% /year

Acute exacerbation (20% chance per year)

Hospitalization for pulmonary disease

Variable rate of progression & co-morbidities

Co-morbidities in IPF

Cardiovascular disease (CAD)

COPD

OSA

Lung cancer

Pulmonary vascular disease: PH; PE

Acute Exacerbation and Decline in FVC Are Associated with Increased Mortality in IPF

Analysis of 1,132 placebo subjects from 6 studies used for drug development of nintedanib and pirfenidone. Followed for mean of 60 weeks.

Death captured as all-cause mortality; compared with FVC % predicted as absolute decline.

Paterniti et al Ann Amer Thorac Soc 2017

Acute Exacerbation and Decline in FVC Are Associated with Increased Mortality in IPF

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Decline in FVC % Predicted	Association with ↑ Risk of Death	Hazard Ratio
<5-10%	Negative	---------
≥10 ≤15%	Positive	2.2
>15%	Positive	6.1

Case#1: 56 yo man with IPF

2003: abd pain→ abd CT; abnl lower lung zones

PMH: Renal stones, obesity, CAD, OSA

Referral: no respiratory sx; Nl PFTs; ILD on ct chest; Neg w/up; R VATS → UIP/IPF

2006: CT chest- subpleural retic chges, architectural distortion, traction bronchiectasis, honey-combing

Case # 1 IPF

Gradual decline over several yrs → Pirfenidone trial (placebo);Open Label Ext.Trial → Improves, stabilizes

After 5 yrs on Pirf., gradual decline again over 2 yrs

2018: Age 71- ↑dyspnea, restrictive defect, on O2 → BLTx

2023: Age 76- Doing well currently

Case #1 Lessons

Early detection and diagnosis

No immunosuppression

Antifibrotic therapy

Importance of clinical trials

Lung Transplantation

20-25% of IPF pts live beyond 10 years from dx

Caveats on Estimates of Survival

Impact of therapy:

Decrease in use of harmful immunosuppression

Increase in use of anti-fibrotic agents

Prednisone, AZA, NAC for IPF

Randomized DBPC trial with 3 groups:

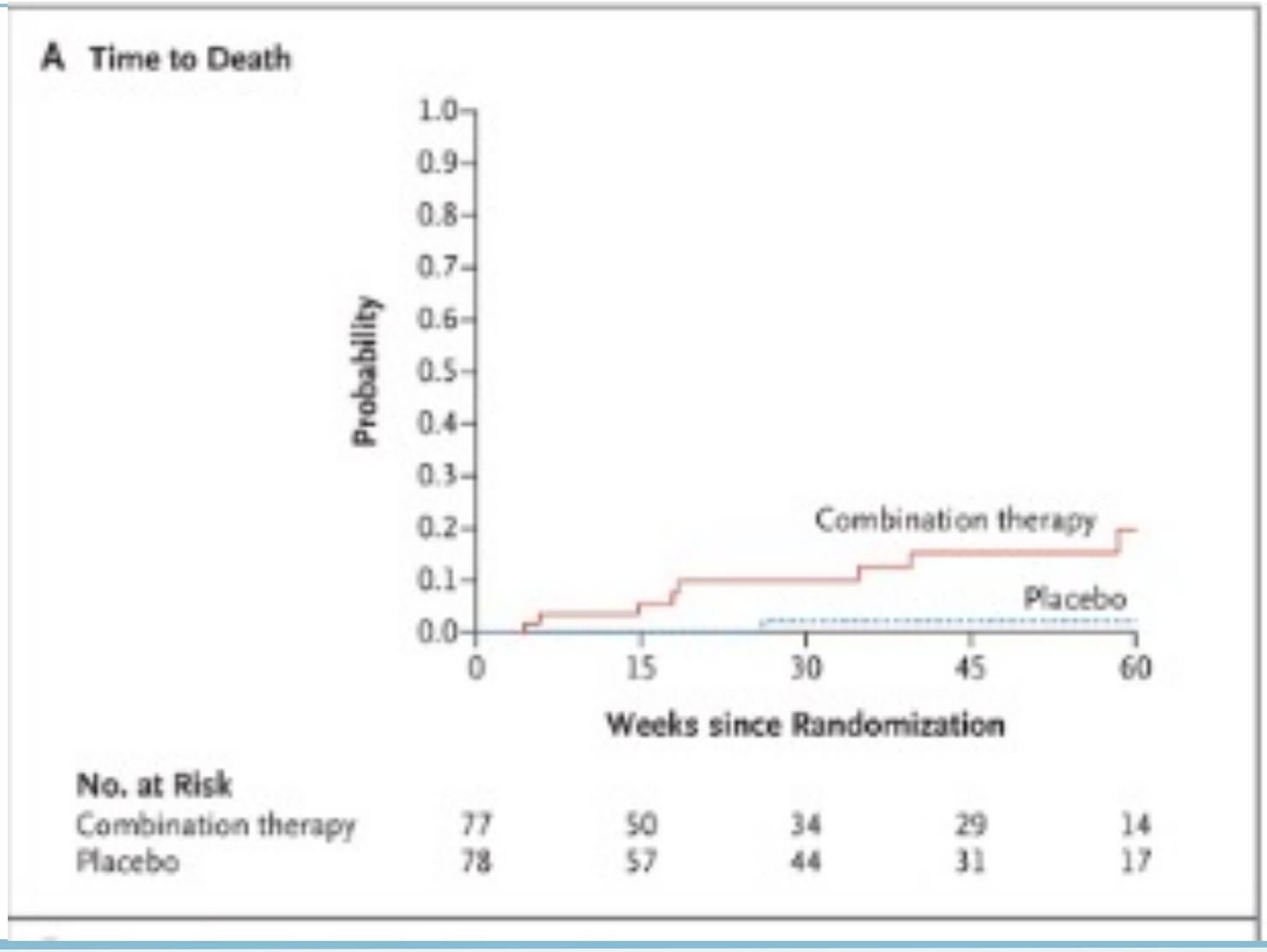
Pred, AZA, NAC

NAC alone

Placebo

NEJM 2012

PANTHER-IPF TRIAL



PANTHER-IPF

When 50% data collected:

Pts in combined group had sig. increase rate of death (8 vs 1) and hospitalization (23 vs 2)

No evidence of physiol. or clinical benefit

DSMB terminated the study

Does Anti-fibrotic Rx Impact Natural History of IPF and Survival?

Meta-Analysis 12,956 pts across 26 studies (8 RCT, 18 Cohort)

Antifibrotics (nintedanib, pirfenidone) assoc with ↓ risk of all cause mortality and ↓ risk of AE

Petnak et al Chest 2021

Rx of PH-Assoc IPF: Inhaled Treprostinil

Modest ↑ in exercise capacity (6 MWD)

Assoc: ↓ risk of clinical worsening, ↓ NT-BNP, fewer AE. Side effect: Headache, cough, SOB, dizziness

? Which patients respond; further studies needed

Waxman et al N Eng J Med 2021

WHAT DO I TELL MY PATIENTS?

MEDICAL TREATMENT IS NOT A CURE FOR IPF, BUT MAY SLOW THE DISEASE PROGRESSION AND PROLONG LIFE EXPECTANCY.

THE PUBLISHED SURVIVAL STATISTICS NEED TO BE CONSIDERED IN CONTEXT

WHAT DO I TELL MY PATIENTS?

IPF remains a serious disease that substantially affects quality of life and life expectancy, but there is room for hope that ongoing therapeutic advances will improve survival..

WHAT DO I TELL MY PATIENTS?

Given the variability in IPF's clinical course, a small proportion of patients may experience prolonged survival and preserved quality of life — a fact at odds with less-nuanced information that a mere internet search about IPF may yield