Idiopathic Pulmonary Fibrosis: Treatment

Joseph P. Lynch, III, MD

Holt and Jo Hickman Endowed Chair of Advanced Lung Diseases and Lung Transplantation

Professor of Clinical Medicine, Step VIII

Division of Pulmonary & Critical Care Medicine, Clinical Immunology and Allergy

The David Geffen School of Medicine at UCLA
Survival: UIP, NSIP, other ILDs

Survival %

Years

UIP

NSIP

Other ILD

Mayo Clinic

Bjoraker, AJRCCM, 1998:157;199
Survival in UIP, NSIP and RBILD

Flaherty, *Eur Respir J* 2002;19;275
Survival in UIP and NSIP

Nicholson, AJRCCM 2000; 162: 2213
Idiopathic Pulmonary Fibrosis (IPF)

- Mortality > 50% at 3-5 years
- Medical therapy marginally effective
- Lung transplant (selected)
Therapy for IPF/UIP

- Early referral for lung transplant
- May lose “window for transplant”
IPF: Histology

- Usual Interstitial Pneumonia (UIP pattern)
Usual Interstitial Pneumonia (UIP)

- Heterogeneity
- Fibroblastic foci
- Honeycombing
Nonspecific interstitial pneumonia

Histological criteria for NSIP:

- Temporal homogeneity
  (lesions of same age)
- Lacks features of other IIPs
  (UIP, AIP, DIP/RBILD)
• Distinguishing IPF and NSIP important since prognosis and treatment differ
IPF and NSIP

Discriminatory features

- Age
- HRCT (GGO vs HC)
Idiopathic Pulmonary Fibrosis

- Primarily a disease of the elderly
- Not seen in children
Prevalence IPF according to age

New Mexico

Coul tas, AJRCCM 1994:150;967
Prevalence IPF according to age

USA (1996-2000)

prevalence per 100,000

227

Age (years)

Raghu, AJRCCM 2006:174;810
Deaths due to IPF according to age


<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Deaths/100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>1.8</td>
</tr>
<tr>
<td>55-64</td>
<td>7.1</td>
</tr>
<tr>
<td>65-74</td>
<td>30.6</td>
</tr>
<tr>
<td>75-84</td>
<td>82.7</td>
</tr>
<tr>
<td>85+</td>
<td>138</td>
</tr>
</tbody>
</table>

Olson, AJRCCM 2007:176;277
IPF: Prevalence > 65 years

Medicare (5%), USA (2001-2011)

Median age newly diagnosed IPF was 79.4 years

Raghu, Lancet Respir Med 2014:2;566
IPF Primarily Affects Older Adults (UK)

Mean age IPF 71 y

Gribbin, *Thorax* 2006;61;980
IPF and NSIP

Discriminatory features

- Older age favors IPF
- Honeycombing (IPF)
Discriminating IPF from other ILDs

UIP (n=97); other ILD (n=38) (1995-2006)

- No honeycombing on HRCT
- No connective tissue disease
- All had surgical lung biopsy

Fell, *AJRCCM* 2010:181;832
Discriminating IPF from other ILDs

- Age and extent CT interstitial score most predictive of UIP
- Gender, desaturation, distance walked on 6MWT, PFTs did not discriminate IPF from other ILD

Fell, AJRCCM 2010:181;832
Discriminating IPF from other ILDs

Risk of IPF:

- Age  HR 1.09 per year
- CT int score  HR 10.4 per unit

Fell, AJRCCM 2010:181;832
Age Powerful Predictor of IPF

- Age $\geq 70$ yrs, $> 95\%$ had IPF
- Age $\geq 75$ yrs, $100\%$ had IPF

Fell, *AJRCCM* 2010:181;832
Can CT distinguish UIP from NSIP?
UIP: HRCT Features

- Patchy, heterogeneous
- Lower lobes, subpleural
- Reticular (linear) lines
- Honeycomb cysts
- Ground glass minimal or absent
CT criteria (UIP vs NSIP)

Key discriminatory elements:

- Honeycombing
- Ground glass opacities
### HRCT scan: NSIP vs UIP

<table>
<thead>
<tr>
<th></th>
<th>UIP</th>
<th>NSIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Honeycombing</td>
<td>+++</td>
<td>+/-</td>
</tr>
<tr>
<td>Ground glass</td>
<td>+/-</td>
<td>+++</td>
</tr>
</tbody>
</table>
CT features of NSIP and UIP overlap

NSIP (n=21) or UIP (n=32)

MacDonald *Radiology* 2001:221:600
Diagnosis of UIP or NSIP by HRCT

IPF (n=32); NSIP (n=21) (Brompton, 1990-2000)

- *Predominantly* ground glass attenuation cardinal feature NSIP
- Other patterns (mixed; reticular) did not discriminate NSIP from UIP

MacDonald, Radiology, 2001:221:600
HRCT features of NSIP

76%
GGO

30%
Honeycomb

50 pts NSIP

CT features of NSIP

- Ground glass: 100%
- Tract bronch: 91%
- Honeycombing: 87%
- Distortion: 95%
- Intralob retic: 55 pts NSIP

Johkoh Radiology 2002:225;199
Diagnosis of UIP or NSIP by HRCT

96 CTs (all UIP or NSIP) graded as:

- Definite UIP
- Probable UIP
- Indeterminate
- Definite NSIP
- Probable NSIP

Flaherty, *Thorax*, 2003:58;143
HRCT highly specific for UIP

<table>
<thead>
<tr>
<th>Lung biopsy</th>
<th>UIP</th>
<th>NSIP</th>
<th>% correct CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definite UIP</td>
<td>16</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Probable UIP</td>
<td>11</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>20</td>
<td>5</td>
<td>NA</td>
</tr>
<tr>
<td>Probable NSIP</td>
<td>9</td>
<td>10</td>
<td>53%</td>
</tr>
<tr>
<td>Definite NSIP</td>
<td>17</td>
<td>8</td>
<td>32%</td>
</tr>
</tbody>
</table>
“Typical” CT is specific for UIP and eliminates need for surgical lung biopsy
CT with “atypical” patterns are non-specific; could represent UIP or NSIP or other ILDs

- Need surgical lung biopsy
“Classical” CT features for UIP likely reflect more advanced disease
HRCT appearance vs survival

Daniil, *AJRCCM* 1999;160:899

CT “atypical” of CFA

CT “typical” of CFA

Time from presentation (years)
Honeycomb change in *any lobe* (CT-fib \( \geq 2 \)) associated with higher mortality

Flaherty, *Eur Resp J* 2002:19;276

168 cases IIP (U Mich)
CT fib $\geq 2$ worse survival

- 168 cases IIP (U Mich)
- All lobes $< 2$
- No honeycombing
- Honeycombing
- At least one lobe $\geq 2$

Flaherty *Eur Respir J* 2002:19;275
HRCT in IIPs

Surgical lung Bx and HRCT in 96 patients with IIPs

- UIP (n=73); NSIP (n=23)

Flaherty, *Thorax* 2003:58;143
Survival by HRCT Diagnosis

Flaherty, *Thorax* 2003:58;143

UIP (n=73); NSIP (n=23)
UIP predicts worse prognosis

Flaherty, Thorax, 2003
CT in IPF: Prognostic Significance

- Extent of fibrosis (reticulation, HC) on CT correlates with mortality
  - Shin, *Radiology* 2008:249;328
  - Sumikawa, *AJRCCM* 2008:177:433
IIP: HRCT and Prognosis

Seoul (1996-2008) Fibrotic IIP (n=154)

- UIP (n=101); fibrotic NSIP (n=53)
- < 5% honeycombing on CT
- Cellular NSIP, CTD excluded

Lee, AJR 2012:199;982
UIP and NSIP: Prognosis

Predictor of mortality:

- Global extent of disease on initial CT predicted mortality

- Initial PFT did not predict

Lee, AJR 2012:199;982
Survival: initial extent HRCT abnormalities

<table>
<thead>
<tr>
<th>Overall extent</th>
<th>Median Survival</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 35%</td>
<td>3.9 y</td>
<td>2.9–4.9</td>
</tr>
<tr>
<td>&gt; 35%</td>
<td>0.8 y</td>
<td>0–2.2</td>
</tr>
</tbody>
</table>

Lee, *AJR* Nov 2012:199;982
UIP and NSIP Patterns

- Both patterns may be present in individual patients (e.g., CTD, idiopathic)
Surgical lung biopsies

Multiple biopsies (≥ 2 lobes)

- Concordant (all lobes same)
- Discordant (UIP + NSIP)

UIP or NSIP (n=109) U Michigan, 1989-2000

Flaherty, AJRCCM 2001:64:1722
### Multiple lobe biopsies

<table>
<thead>
<tr>
<th>Histology</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concordant UIP</td>
<td>51 (47%)</td>
</tr>
<tr>
<td>Both UIP and NSIP</td>
<td>28 (26%)</td>
</tr>
<tr>
<td>Concordant NSIP</td>
<td>30 (28%)</td>
</tr>
</tbody>
</table>

UIP or NSIP (n=109)

Flaherty, *AJRCCM* 2001:64;1722
### Multiple lobe biopsies

64 pts, UIP or NSIP Brompton, 1984-2001

<table>
<thead>
<tr>
<th>Histology</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concordant UIP</td>
<td>25</td>
<td>(39%)</td>
</tr>
<tr>
<td>Both UIP and NSIP</td>
<td>8</td>
<td>(13%)</td>
</tr>
<tr>
<td>Concordant NSIP</td>
<td>31</td>
<td>(48%)</td>
</tr>
</tbody>
</table>

Monaghan, *Chest* 2004:125;522
Survival best with NSIP

5-year survival

UIP

UIP + NSIP

NSIP

Monaghan, *Chest* 2004
Nonspecific Intersitial Pneumonia

- Distinguishing fibrotic NSIP from UIP is difficult
- Does NSIP evolve to UIP?
• IPF: course highly variable and unpredictable
Increased Mortality if:

- Older age
- Severe impairment PFTs
- Hypoxemia
- Honeycombing on CT
- Pulmonary hypertension
Not surprisingly, severe impairment or decline in FVC, DL$_{CO}$, oxygenation, or 6MWD predicts worse mortality.
Changes in FVC at 6 months

UIP (n=80); NSIP (n=29) (U Mich)

> 10% decline FVC at 6 months independent predictor mortality (HR 2.47)

Flaherty, *AJRCCM* 2003:168;543
Serial PFTs Predict Prognosis

IPF (n=81) (Denver)

> 10% decline FVC at 6 or 12 mo assoc with higher mortality

Collard, AJRCCM 2003:168;538
Serial PFTs Predict Prognosis

IPF (n=131); NSIP (n=48) (Korea)

> 10% decline FVC at 6 mo
best predictor of mortality

Jegal, *AJRCCM* 2005:171;169
• Declining FVC warrants consideration for lung transplant

• However, fatalities can occur even with prolonged stability
Predicting Mortality in IPF

3 centers (n=228 UCSF; Mayo Clinic (n=330); Italy (n=208))

- GAP* index to predict mortality
  (*gender, age, physiology)

Predicting Mortality in IPF

Risk factors for death:

- Gender (G)
- Age (A)
- Physiology (P)
  - FVC and DLCO

Ley, Ann Intern Med 2012:156;684
Predicting Mortality in IPF

GAP Score (0-8 points)

Gender (G)  Score

- Male  1
- Female  0
## Predicting Mortality in IPF

### GAP Score

<table>
<thead>
<tr>
<th>Age (A)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60 y</td>
<td>0</td>
</tr>
<tr>
<td>60-65 y</td>
<td>1</td>
</tr>
<tr>
<td>&gt; 65 y</td>
<td>2</td>
</tr>
</tbody>
</table>
# GAP Score: IPF

<table>
<thead>
<tr>
<th>FVC</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 75%</td>
<td>0</td>
</tr>
<tr>
<td>50% - 75%</td>
<td>1</td>
</tr>
<tr>
<td>&lt; 50%</td>
<td>2</td>
</tr>
</tbody>
</table>
### GAP Score: IPF

<table>
<thead>
<tr>
<th>$DL_{CO}$</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 55%</td>
<td>0</td>
</tr>
<tr>
<td>36%-55%</td>
<td>1</td>
</tr>
<tr>
<td>≤ 35%</td>
<td>2</td>
</tr>
<tr>
<td>Can’t do</td>
<td>3</td>
</tr>
</tbody>
</table>
GAP index predicts mortality

IPF GAP Score: Mortality

3 hospitals, 2001-10

1-yr 2-yr 3-yr
I (0-3) 6 11 16
II (4-5) 16 30 42
III (6-8) 39 62 77

Ley, Ann Intern Med 2012:156;684
Predicting Survival in IPF

Key determinants of mortality:

- Advanced disease at presentation
- Rapid progression
- Acute exacerbation (AE)

Mura, *Eur Respir J* 2012:40;101
Complications of IPF

- Acute exacerbations (AE)
- Pulmonary hypertension
Acute Exacerbations of IPF

Definition (arbitrary):
- Unexplained worsening dyspnea < 30 d
- HRCT: new GGO or consolidation superimposed on UIP
- No pulmonary infection (EA or BAL)
- No other cause

Collard, AJRCCM 2007:176;636
Acute Exacerbations of IPF

- Incidence 19-35% < 2 years
- Resembles ARDS
- Diffuse lung damage (DAD)
- Ground glass opacities (CT)
Incidence of AE-IPF

IPF patients, Korea (n=461); Japan (n=74)

1-y
2-y

Incidence AE (%)

Song, ERJ 2011
Kondo, 2010
Acute Exacerbations of IPF

461 pts IPF (Korea)

- AE in 163 (35.4%)
- AE mortality high: HR 2.59, \( p < 0.001 \)

Song, *Eur Respir J* 2011:39;357
Acute Exacerbations (AE) IPF

AE-IPF, Korea (n=163)

Song, ERJ 2011:39;357
AE- IPF: Treatment

- Value of steroid or IS therapy *not* clear

Song, *Eur Respir J* 2011:39;357
Predicting Survival in IPF

Newly diagnosed IPF, Rome (n=70)

AE of IPF in 13 (18.6%)

- 11 of 13 within first 18 months
- Following AE, 69% died within 3-months

*Mura, Eur Respir J 2012:40;101*
Acute Exacerbations of IPF

STEP-IPF (sildenafil trial (n=188))

18 AE (definite n=4; suspected n=14)

- AE more common Nov-May than Jun-Nov (HR 8.06, p= 0.007)
- Prednisone risk factor

Collard, *Respir Res* July 2013:14;73
Infection (viral)
Risk Factors for AE-IPF

- ? Infection
- ? More severe disease
- Prednisone or IS therapy
- Pulmonary hypertension
Thoracic Surgery: ? Risk for AE

Lung biopsies (VATS)

Surgical resection for lung ca
Acute Exacerbations of IPF

- Prognosis poor if require MV
- Unless clearly reversible issue, palliative/comfort care recommended
Pulmonary Hypertension

- PAH in 28-84% of patients with advanced IPF
- PAH markedly worsens survival
Pulmonary hypertension and IPF

88 pts IPF and 2-D echo (Mayo Clinic)

Estimated systolic PAP

- $\leq 35$ mm Hg
- 36-50 mm Hg
- $> 50$ mm Hg

Nadrous, *Chest* 2005:128;2393
PAH and IPF: survival

Median survival

SPAP < 35: 4.8 years
SPAP 36-50: 4.1 years
SPAP > 50: 0.7 years

Nadrous, Chest, 2005:128;2393
Pulmonary hypertension in IPF

PAH increases mortality

• 2-D echo to assess sPAP

• ? If treatment of PAH affects outcome
Treatment of PAH

• Phosphodiesterase inhibitors
• Endothelin-1 receptor antagonists
• Prostenoids
PAH complicating IPF

- Anecdotal responses to PAH-specific agents but RCT lacking
- Impact of therapy uncertain
PH due to lung disease

• “The use of targeted PAH therapy in patients with COPD or ILD and $P_{pa} < 40$ mm Hg is … discouraged”

Galie, *Eur Respir J* (Dec 2009)
PAH due to lung disease

- PAH-specific therapy may have role in patients with severe PAH as a bridge to lung transplantation

Shino, *Semin Respir Crit Care Med* (Oct 2013)
Pulmonary Fibrosis: PAH

• ILD and PAH (mPAP > 35) (n=15)

• Trepostinil (s.c. n=14; IV, n=1)

• 12 weeks: hemodynamics, 6MWD, RV parameters improved

Saggar, *Thorax* 2014:69;123
Idiopathic Pulmonary Fibrosis

- Course and “pace” of disease highly variable
- Lung transplant 1\textsuperscript{st} line but only for selected patients
- Who should receive novel agents?
SK #126-99-80 (familial PF)
Interpreting efficacy of treatment difficult since course variable

“Stabilization” cannot be assumed to reflect response to therapy
Treatment of IPF

- High dose prednisone was standard of care for > 40 years *despite no evidence for benefit*
Idiopathic Pulmonary Fibrosis

- Despite lack of randomized, placebo-controlled trials, prednisone + azathioprine used for more than 3 decades
Azathioprine plus prednisone for IPF

Prospective; randomized (n=27)

- Prednisone alone (13)
- Prednisone + azathioprine (14)

- End points: mortality; PFTs

Raghu, ARRD 1991:144;291
Azathioprine + prednisone for IPF

Survival Probability vs. years

Raghu, ARRD 1991;144:291

Aza + predn

Prednisone

years
<table>
<thead>
<tr>
<th></th>
<th>1 yr</th>
<th>Pred</th>
<th>Pred + Aza</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died (1yr)</td>
<td>4 of 13</td>
<td>4 of 14</td>
<td></td>
</tr>
<tr>
<td>FVC, % pred</td>
<td>+ 1.7%</td>
<td>+ 6.5% (NS)</td>
<td></td>
</tr>
<tr>
<td>DL_{CO}, % pred</td>
<td>+ 0.9%</td>
<td>+ 7.3% (NS)</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>77%</td>
<td>43%   (NS)</td>
<td></td>
</tr>
</tbody>
</table>

Raghu, *ARRD* 1991; 144;291
Idiopathic Pulmonary Fibrosis

ATS/ERS Guidelines:

- No proven survival benefit with Rx
- Therapy not always indicated

AJRCCM 2000:161;646
"The committee did not find sufficient evidence to support the use of pharmacologic therapy for patients with IPF"
• PANTHER (Prednisone, Azathioprine, NAC Therapy)
PANTHER-IPF

3 groups (n=390, 1:1:1 ratio)

- NAC 600 mg t.i.d.
- NAC + AZA + pred
- Placebo
Inclusion Criteria:

- Surgical Lung Bx UIP
- HRCT (honeycombing)
PANTHER-IPF

Inclusion Criteria:

- “Mild to moderate” IPF
- $\text{FVC} \geq 50\% \text{ pred}$
- $\text{DL}_{\text{CO}} \geq 30\% \text{ pred}$
Primary End Point:

$\Delta$ FVC at 60 weeks
Azathioprine for IPF

- PANTHER Study (IPFnet) terminated early (Oct 2011) due to higher mortality and morbidity in AZA + prednisone + NAC arm

PANTHER STUDY: IPF

Mortality

Hospitalizations

AE

#

AZ + pred + NAC (n=77)

placebo (n=78)

Other immunosuppressive agents unlikely to be efficacious

- e.g., mycophenolate mofetil
IPF: which target?

- Multiple “targets” (cells, cytokines, inflammation, fibrosis)
- Mechanisms of injury and fibrosis overlap and redundant
Pirfenidone (*Esbriet*)

Nintedanib (*Ofev*)

FDA Approved Oct 15, 2014
Treatment of IPF

- In clinical trials, pirfenidone and nintedanib slow rate of decline but differences small ($\Delta FVC$ 2-4%) at 1 yr
Pirfenidone for IPF

CAPACITY I (006) (n=344)
- pirfenidone (oral) vs placebo

CAPACITY II (004) (n=435)

Noble, Lancet 2011:377:1760
Pirfenidone for IPF

Primary endpoint:

• $\Delta$ FVC at 72 weeks

Pirfenidone for IPF

- No difference survival, $DL_{CO}$, 6MWT, $\Delta O_{2}$ sat
- Less decline FVC at 72 weeks
  [Capacity II (004); not Capacity I (006)]
CAPACITY (004 + 006): $\Delta$FVC 72 wks

CAPACITY (004 + 006): Mortality

Mortality %

<table>
<thead>
<tr>
<th></th>
<th>pirfenidone (n=345)</th>
<th>placebo (n=347)</th>
</tr>
</thead>
<tbody>
<tr>
<td>all causes</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>IPF-related</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

p = 0.117

Noble, *Lancet* 2011;377;1760
CAPACITY I Trial (IPF)

ΔFVC at 72 wks

- Pirfenidone
- Placebo

CAPACITY II Trial (IPF)

ΔFVC at 72 wks

- Pirfenidone
- Placebo

Noble, Lancet 2011:377;1760
Pirfenidone Trials (IPF)

> 10% decline FVC

<table>
<thead>
<tr>
<th>Trial</th>
<th>Pirfenidone</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>pirfen 004 (2403)</td>
<td>20</td>
<td>35</td>
</tr>
<tr>
<td>pirfen 006 (2403)</td>
<td>23</td>
<td>27</td>
</tr>
</tbody>
</table>

Pirfenidone for IPF

- Improvement rare
- < 10% change most common
- No difference mortality
Pirfenidone for IPF

ASCEND Trial (52 wks):

- Primary end-point:
  
  disease progression (Δ FVC > 10%) or death

Pirfenidone for IPF

- Pirfenidone 2403 mg/day (n=278)
- Placebo (n=277)

Pirfenidone (ASCEND) Study

King, *N Engl J Med* 2014;370;2083

![Graph showing decline in FVC and death rates with and without pirfenidone.](image-url)

- **Decline FVC > 10%**
  - Pirfenidone (n=278): 16.5%
  - Placebo (n=277): 31.8%
  - *p* = 0.1

- **Death**
  - Pirfenidone (n=278): 4%
  - Placebo (n=277): 7.2%
  - *p* < 0.001
Pirfenidone for IPF

- Slows rate of progression
- Impact on mortality uncertain
Pirfenidone: Adverse effects

ASCEND Trial

King, *N Engl J Med* 2014;377;2083
• Nintedanib (*Ofev*)
  
  • Tyrosine kinase inhibitor
Nintedanib: Targets Receptors

- Platelet Derived (PDGF)
- Vascular Endothelial (VEGFR)
- Fibroblast Growth (FGFR)
Nintedanib for IPF

Nintedanib 150 mg bid or placebo

52 weeks; change FVC

IMPULSIS-1 (n=511)

IMPULSIS-2 (n=544)

Nintedanib for IPF

Primary endpoint:

- \( \Delta \) FVC at 52 weeks

Nintedanib: ΔFVC 52 wks

<table>
<thead>
<tr>
<th></th>
<th>Impulsis-1</th>
<th>Impulsis-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔFVC (%) at 52 weeks</td>
<td>-2.8</td>
<td>-3.1</td>
</tr>
<tr>
<td>nintedanib</td>
<td>-6</td>
<td>-6.2</td>
</tr>
<tr>
<td>placebo</td>
<td>-7</td>
<td>-6.2</td>
</tr>
</tbody>
</table>

Nintedanib: $\Delta$FVC 52 wks

Nintedanib: Mortality 52 wks

p=0.14

Nintedanib: Adverse effects

Impulsis 1 and 2 trials

Richeldi, N Engl J Med 2014;370;2072
Therapy for IPF/UIP

- Early referral for lung transplant
- May lose “window for transplant”
Lung transplant for IPF

- Survival post-LT lower than other groups

(may reflect age, comorbidities)
ADULT LUNG TRANSPLANTATION
Kaplan-Meier Survival By Diagnosis (Transplants: January 1990 – June 2006)

Survival (%)

CF (N=3,275) COPD (N=7,760) IPF (N=3,931)

Years

0 1 2 3 4 5 6 7 8 9 10

ISHLT 2008
J Heart Lung Transplant 2008;27: 937-983