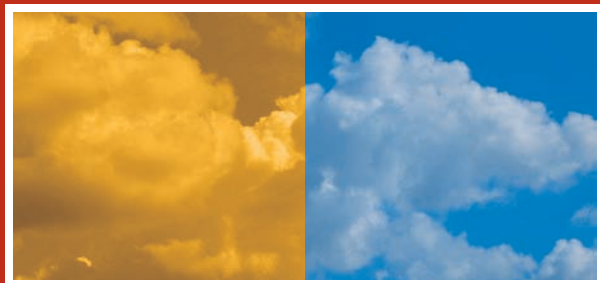


PILOT™ 2008

Pulmonary Fibrosis Identification: Lessons for Optimizing Treatment

Two separate CME activities enclosed.
IPF EXPERT ROUNDTABLE SUMMARY
IPF EXPERT ROUNDTABLE DISCUSSION (CD)



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IPF EXPERT ROUNDTABLE SUMMARY

CME INFORMATION

EDUCATIONAL NEEDS STATEMENT

Idiopathic Pulmonary Fibrosis (IPF) is a debilitating and almost uniformly fatal disease. Despite recent progress, the diagnosis and management of IPF remain distinct clinical challenges. In addition, emergence of scientific evidence has prompted a reexamination of clinical approaches. The aim of the PILOT™ initiative is to provide a forum for the open exchange of scientific ideas that results in the timely dissemination of emerging knowledge, facilitates clinical decision making, and improves patient outcomes.

TARGET AUDIENCE

This educational activity is intended for pulmonologists, pathologists, radiologists, and primary care physicians treating patients with IPF.

EDUCATIONAL ACTIVITY OBJECTIVES

Upon completion of this activity, the participants should be able to:

- Describe recent progress in diagnosing IPF comorbid conditions, including pulmonary arterial hypertension (PAH)
- Describe recent clinical trial results on IPF therapies and incorporate this information into the management of IPF patients
- Incorporate expert recommendations into the management of IPF, including participation in clinical trials, pulmonary rehabilitation, evaluation for lung transplantation, management of comorbidities, and management of sleep disorders

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CREDIT STATEMENT

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PILOT™ IPF EXPERT ROUNDTABLE SUMMARY

OBJECTIVE

The purpose of this roundtable meeting on idiopathic pulmonary fibrosis (IPF) was to discuss recent publications, relevant clinical study results, and critical issues.

INTRODUCTION

A PILOT expert roundtable discussion was convened to highlight recent progress in IPF and to solicit expert opinion on the state-of-the-art. There are no FDA-approved treatments for IPF, so practitioners look to experts for guidance on how to deal with the challenging issues. The discussion that is summarized here took place in Chicago on November 14, 2007. The meeting topics have been divided into sections, which were discussed by the group and are presented by participants as noted. Publications of scientific data are cited where possible; consensus and individual opinions are identified as such.

PULMONARY HYPERTENSION

Steven D. Nathan, MD

Maria L. Padilla, MD

One of the hot topics in the past year has been pulmonary hypertension (PH) in IPF. This condition is a comorbidity of IPF and can adversely affect symptoms, functional capacity, and survival.¹ At one transplant center the prevalence of PH in IPF patients is 30% at the time of evaluation for lung transplant, and increases to 85% at the time of transplantation. A significant unanswered question is whether PH treatment impacts the outcomes of the disease.

Some centers are now using estimated right ventricular systolic pressures (RVSP) obtained by echocardiogram to assess for PH. This is a good screening test if patients have moderate to severe PH. However, most PH in the context of IPF tends to be mild to moderate, and therefore traditional echocardiography does not suffice as a screening tool in the majority of cases. Recently developed (but unpublished) echocardiography protocols are much better at estimating RV function and RVSP and may offer greater sensitivity.

Roundtable participants agreed that current echocardiography methodology is not optimal to diagnose pulmonary hypertension. This method overestimates pulmonary arterial (PA) pressures in about 30% of the cases, and underestimates PA pressures in another 10% or 12%. Both echocardiographic measurement of pulmonary pressure and tricuspid regurgitation (TR) jet are technique and operator-dependent.

From a practical standpoint, if an echocardiogram shows no evidence of pulmonary hypertension, is a right heart catheterization warranted? There are no data to guide this clinical decision. Significant desaturation during the course of a six-minute walk test tends to correlate with the presence of pulmonary hypertension, even when echocardiography is negative. Consideration should be given to performing right heart catheterizations in such patients, especially if studies show that PAH medications are effective in the IPF population with PH.

A positive practical outcome of right heart catheterization is that treatable conditions, such as diastolic dysfunction, can be detected. Indeed, approximately 15%–20% of patients with pulmonary hypertension have evidence of diastolic heart failure on right heart catheterization.

Right heart catheterization is an integral component of the work-up for potential lung transplant recipients since pulmonary pressures are routinely included in the calculation of the lung allocation score.

Other markers, such as brain natriuretic peptide (BNP), may increase the diagnostic accuracy. A combination of clinical, biochemical, exercise physiology, and radiological indexes may be useful for choosing the best patients for right heart catheterization. Ideally, such factors could be used for diagnosing PH without the catheterization procedure. Clinical studies suggest that BNP may be useful, but the positive and negative predictive power of the test, its relation to physiological parameters, and the best way to incorporate it into disease management are yet to be defined.

Dr. D. Zisman and colleagues recently examined whether the extent of pulmonary fibrosis or main pulmonary artery diameter (MPAD) correlate with PH in patients with advanced IPF.² They studied 65 cases of advanced IPF with available right heart catheterization and chest HRCT. Chest CT-determined fibrosis score, ground-glass opacity score, honeycombing score, total profusion score, diameter of the main pulmonary artery, and the ratio of the pulmonary artery to aorta diameter did not differ between those with and without PH. There was no significant correlation between mean pulmonary artery pressure and any of the chest CT-determined measures. It was concluded that chest HRCT-determined extent of pulmonary fibrosis and/or MPAD is not useful to screen for PH in patients with advanced IPF.

Therapy of PH in IPF cannot be routinely recommended until appropriate efficacy and safety studies have been done. However, there have been anecdotes of patients being treated with PAH medications as well as a few case reports attesting to the potential utility of this therapeutic approach. It was emphasized that therapeutic strategies must be

substantiated with clinical data. It was pointed out that therapy with epoprostenol³ can be problematic because of the potential to worsen V/Q matching. This might outweigh the benefit of decreased pulmonary pressures and increased cardiac outputs. A small study by Ghofrani⁴ compared the vasodilator sildenafil to prostacyclin and showed similar hemodynamic effects but better preservation of V/Q matching with sildenafil.

A phase 2 study of iloprost in IPF⁵ examined the use of iloprost in subjects with IPF and PH. The primary endpoint of this study was the six-minute walk distance (6MWD). There was no apparent benefit from the inhaled iloprost compared to placebo treatment. This study was somewhat flawed in design since it relied on echocardiography to assess for PH.

CLINICAL TRIAL RESULTS

Paul W. Noble, MD

Glenn D. Rosen, MD

Several important clinical studies were completed last year:

1. Results of the BUILD-1 clinical trial with bosentan were published.⁶
(To be addressed on the PILOTforIPF.org Web site in 2008)
2. Results of the INSPIRE trial with IFN γ -1b were announced.
3. Reports of adult-onset pulmonary fibrosis caused by mutations in telomerase were published.^{7,8}
(To be addressed on the PILOTforIPF.org Web site in 2008)
4. Increased mortality attributed to IPF 1992–2003.⁹
5. Study that showed that the measurement of the PA diameter on chest CT did not correlate with or predict the presence of PH.²
6. Community and specialist center diagnosis of IPF.¹⁰
7. Shionogi & Co announced positive results from a pirfenidone trial.¹¹
8. Sildenafil effect on walk distance was published.¹²

The BUILD-1 trial⁶ was a randomized controlled trial with 158 IPF patients receiving placebo or bosentan. The primary endpoint was 6MWT. There was a greater, but statistically insignificant, loss of 6MWT distance in the bosentan group than in the placebo group, so the primary endpoint was not met. The authors of the BUILD-1 report⁶ suggest that they might not have reached the primary endpoint because the bosentan group had worse pulmonary function at entry than the placebo group. Analysis of patients who received surgical lung biopsy revealed that bosentan had a positive effect on the secondary outcome of time to progression (defined as decline in the FVC of 10% or death). Of the bosentan-treated patients, 68% received lung biopsies compared to 60% of the placebo-treated patients. There were trends in delayed time to death or disease progression, and improvement in QoL with bosentan.

Bosentan significantly slowed disease progression in patients who obtained a surgical lung biopsy (SLB). The participants warned against the temptation to perform subgroup analysis. The hypotheses generated are frequently not substantiated when tested rigorously. How are patients who receive a surgical lung biopsy different from other IPF patients? Typically, patients who have less honeycombing on HRCT receive biopsies. They may have milder disease and thus fare better, so the results should not be generalized to all IPF patients. Another problem is that honeycombing, a critical diagnostic feature of IPF, is not well-defined. Disease heterogeneity may also be an issue both for clinical progression and for responsiveness to therapy.

One concern about studies that utilize the 6MWT as an endpoint is that they frequently do not control for pulmonary rehabilitation. It is known that the timing of entry into rehabilitation has an impact on the 6MWT distance. Another uncertainty is the appropriate definition of the endpoint; should IPF clinical trials focus on distance or saturation? Perhaps a combination of time to desaturation and the amount of desaturation that has been used by some Japanese researchers may be most appropriate. In using the 6MWT to assess dyspnea in the elderly, it is important to ascertain that the patients are not limited by other factors, such as fatigue or cardiac output.

The interferon gamma-1b (IFN γ -1b) INSPIRE trial was terminated recently due to lack of efficacy at a predefined interim analysis. Although the report has not been published, the results were presented at the ERS meeting in Stockholm (September 2007). Despite prior subgroup analyses, the recommendation from the participants based on the total available clinical evidence is that physicians should not be offering this drug for treatment of IPF. The detailed records from the placebo group in the INSPIRE trial should yield valuable information about the natural course of IPF.

The roundtable participants described a different attitude toward IPF therapy in Europe. IFN γ -1b is more accepted in Europe, where there is interest in using the drug for some subgroups. On the other hand, European investigators are generally more skeptical about the prospects of positive results from the *N*-acetylcysteine (NAC) PANTHER trial.

Another publication of high interest was Dr. K. Flaherty's paper on diagnosis of IPF in community and central hospitals.¹⁰ This study concluded that significant disagreement exists in the diagnosis of diffuse parenchymal lung disease (DPLD) between physicians based in communities and those in academic centers. The authors recommend that patients should be referred to centers with expertise in DPLD to help clarify the diagnosis and provide suggestions regarding treatment options.



A notable finding in the paper was that the community doctors diagnose IPF more frequently than other interstitial lung diseases. After the first evaluation at the tertiary medical center, the IPF diagnosis rate decreases. On subsequent iterations, the frequency of IPF diagnosis increases.

There are multiple reasons why patients should go to a referral center: 1) to receive a second opinion; 2) to participate in clinical trials; and 3) to receive expert evaluation as a lung transplant candidate. Because the regional centers see far more patients with IPF, they are more familiar with the subtle differences between IPF and other interstitial lung diseases. The regional center radiologists are more specialized and often give better interpretation of the high resolution CT scans. Typically, participants in a clinical trial are followed closely and therefore may receive better care, irrespective of which test group they are in.

CURRENT CLINICAL TRIALS AND DISEASE MANAGEMENT

Harold Collard, MD
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There are several ongoing phase 3 clinical trials in IPF:

1. CAPACITY^{13,14}

Pirfenidone is an orally active small molecule drug that is thought to work by inhibiting collagen synthesis, down-regulating production of multiple cytokines, and blocking fibroblast proliferation and stimulation in response to cytokines. Pirfenidone has activity in fibrotic conditions affecting multiple organs, including lung, kidney, and liver. Preliminary results from the published literature¹⁵ and a recent press release regarding a phase 3 study of pirfenidone conducted in Japan suggest it may be beneficial in patients with IPF. Two parallel trials of pirfenidone (CAPACITY) have completed enrollment in the United States and should be completed in late 2008-early 2009. The objective of the CAPACITY trials is to assess the safety and efficacy of pirfenidone compared with placebo in patients with IPF. The primary efficacy outcome variable is the absolute change in percent predicted forced vital capacity (FVC) from baseline to week 72.

There was a discussion about the pros and cons of the FVC endpoint. FVC is recognized as a useful surrogate marker for death in IPF, but it is not as robust an outcome measure as dyspnea or death. The ideal endpoint for IPF trials was thought to be a combination of event-driven variables such as death, change in a physiological parameter such as FVC or DL_{CO}, worsening dyspnea, and acute exacerbation. There was support for an event-driven design whenever possible. Another challenging issue is how to account for patient deaths in a study where FVC is the primary endpoint. Neither assigning a value of zero nor imputing an FVC value is a complete solution. It is also unclear how large a difference in FVC between groups is clinically significant. It was pointed out that small but statistically significant differences may be relevant on a population basis but may not be clinically meaningful for an individual patient. This is well known in hypertension, where lowering blood pressure by 2 millimeters of mercury has a statistically significant effect on mortality, but may not be clinically important for an individual patient.

2. STEP-IPF¹⁶

Sildenafil is a phosphodiesterase-5 inhibitor that has been approved for the treatment of pulmonary arterial hypertension. Its role in secondary pulmonary hypertension is unclear, but there are small studies that suggest a benefit. STEP-IPF is enrolling advanced IPF patients with a DL_{CO} of less than 35%, based on evidence that patients with advanced disease have a high incidence of pulmonary hypertension. The objective of the STEP-IPF trial is to assess the efficacy of sildenafil compared with placebo in patients with IPF. The primary endpoint is six-minute walk distance. This trial is currently enrolling patients.

3. BUILD-3¹⁷

Bosentan is an endothelin receptor antagonist that has been studied in IPF previously with mixed results. A recently published report⁶ found no difference between bosentan and placebo groups in six-minute walk distance (primary endpoint) but suggested a potential survival benefit in patients who had undergone surgical lung biopsy. It is unknown why patients who received surgical lung biopsy appeared more responsive. Based on these results, a larger study of bosentan in IPF (BUILD-3) has been developed and is currently enrolling patients. BUILD-3 is an ongoing multicenter, double-blind, randomized, placebo-controlled, event-driven, phase 3 study of bosentan in patients with IPF. The primary outcome measure is time to disease worsening or death. The secondary outcome measure is the proportion of patients who experience either disease worsening or death at 1 year. The enrollment will be 390 patients and the expected completion date is June 2009. BUILD-3 is nearly half-enrolled at multiple worldwide sites.

4. PANTHER (IN DEVELOPMENT)

The PANTHER study is a 3-arm placebo-controlled study comparing the IFIGENIA NAC combination therapy with NAC alone or placebo. This 1-year study is designed to address whether NAC is effective alone or in combination with the “conventional” drug cocktail of prednisone and azathioprine. This trial is part of the NIH IPF clinical research network (IPFNet).

A common concern for current clinical trials concerns subgroup responses, particularly in an elderly population with extensive comorbidities. One practical model that might be adopted is from cancer clinical practice, in which many oncologists give a drug and wait for a response. One distinguishing feature of IPF is that the disease course is relatively long and unpredictable. Treatment is an exercise in intervention when patients deteriorate rapidly, and few clinical trials are available for advanced patients. The staging system describing lung cancer progression is well-defined and a similar staging system could be developed for IPF. This would allow clinical trials to include patients with both mild and late stage disease.

DISEASE MANAGEMENT

IPF poses a difficult challenge for patients and physicians. At the present time there is no medication that is approved by the FDA for treating the disease. With these challenges in mind, the participants next addressed the question, “What’s the best way to manage the patients?” There was consensus that recommending any pharmacological therapy is not advisable. However, discussion of recent clinical results with patients is appropriate.

When faced with the question, “What would you recommend for a member of your family?” one expert answered, “Take NAC.” Although the evidence for using NAC alone from the IFIGENIA study is indirect, many patients elect this course. Clinical experience has shown that NAC is very low-risk as well as inexpensive. It was emphasized that no therapeutic approach is proven and there is no consensus on how to approach therapy. There are many experts who believe that treatment with triple combination therapy (prednisone, azathioprine, and *N*-acetylcysteine) is the more appropriate approach. Clearly, more research is needed.

Patients who have been receiving experimental or off-label medications and whose IPF is stable present an interesting quandary. Some experts would not recommend altering the medications of a stable patient unless those medications have clearly been proven to have no efficacy. Emerging clinical results are expected to affect insurance reimbursement for various therapies.

The other expert recommendations for IPF disease management are:

1. Participation in clinical trials
2. Pulmonary rehabilitation
3. Oxygen therapy if indicated
4. Evaluation for lung transplantation
5. Evaluation for comorbidities
6. Management of sleep disorders
7. Appropriate vaccinations
8. Advanced directives

The unpredictable natural history of IPF makes prognosis difficult. Stable patients can experience acute clinical worsening (acute exacerbation) that is unpredictable and highly morbid. This possibility mandates early discussion of end-of-life issues¹⁸ and early evaluation for lung transplantation.¹⁹ Some patients suffer from pulmonary embolism that can be detected by a CT angiogram when they have acute decompensation. Acute decompensation must be distinguished from acute exacerbation. Some conditions for these patients are treatable and physicians should be alert to different possibilities.

LUNG TRANSPLANTATION

Steven D. Nathan, MD

Jeffrey A. Golden, MD

Survival rates have improved for lung transplantation. The 5-year survival for lung transplantation remains around 50%. As many as 75% of transplants are now double lung, with single lung transplants constituting just 25%. The improved survival benefit for the 2 operations is similar until about 5 years, after which the double lung transplant has a higher survival rate.

An important consideration is that a donated lung can go to 1 double lung transplant recipient or 2 single lung recipients. Since patients are still dying while waiting for a donated lung, it is difficult to decide between single and double lung transplant strategies. The trend at some institutions is to transplant single lungs into patients in their 60s but double lungs into younger patients. However, in IPF patients there are no conclusive data that show that bilateral lung transplantation is the better procedure. Indeed in 2005, Whelan et al²⁰ suggested that bilateral lung transplants for IPF were actually a risk factor for mortality.



There have been more lung transplants into IPF patients since the new allotment system was put into place, which has ironically led to a drop in survival in some centers because more ill patients are being transplanted.

Lung cancer is an interesting issue in the context of IPF. In the non-transplant IPF population, lung cancer is thought to occur in as many as 10% of patients. The question was raised whether the incidence might be higher in people who get transplants and survive longer, especially the single lung recipients with one native lung which might be at higher risk of developing cancer. One faculty member reported that the rate of lung cancer as a cause of mortality in COPD and IPF patients after transplant is low, in the 1% to 2% range. Histology shows that the lung cancers that occur in patients with IPF are heterogeneous, but are most commonly squamous cell carcinoma or adenocarcinoma.

DISEASE MECHANISM

William D. Travis, MD

A question arose about the importance of fibroblastic foci in IPF. Although fibroblastic foci are the histologic hallmark of UIP, they can occasionally be found in other idiopathic interstitial pneumonias and by themselves are not pathognomonic for IPF. One panelist suspects that fibroblastic foci observed in these different conditions might reflect different disease processes. It is noteworthy that a classic UIP pattern, including honeycombing, is sometimes observed with hypersensitivity pneumonitis.

One paper was cited where pathologists analyzed serial sections of IPF lung tissue for fibroblastic foci.²¹ Three-dimensional reconstruction indicated that foci are part of a continuous fibrotic reticulum that extends from the pleural surface into the lung parenchyma. In addition, clonality analysis revealed that the foci are polyclonal, rather than monoclonal. This supports the longstanding impression that UIP/IPF is not a malignant but a reactive process.

Investigators have been developing techniques to examine gene expression patterns of different interstitial disorders. For example, Selman et al evaluated clinical and molecular features of “rapid” and “slow” IPF progression.²² They found that a subgroup of IPF patients, predominantly smoking males, displays an accelerated clinical course and has a gene expression pattern that is different from those with slower progression and longer survival. These findings highlight the variability in the progression of IPF, and may partially explain the heterogeneous therapeutic responses in IPF clinical studies. Similar gene expression profiling studies are being extended to examine differences between HP and IPF.²³

Other areas for continuing investigation are epithelial²⁴ and vascular injury.²⁵ There clearly are big differences between epithelium associated with fibroblastic foci compared to those in other areas of the lung. Significant secondary vascular changes can be observed in patients with IPF, apparently resulting from intimal fibrosis and/or medial hypertrophy of arterioles and narrowing of venular lumens by loose and edematous intimal fibrosis. A recent study showed occlusion of venules and small pulmonary veins in 65% of cases in areas of lung tissue that were architecturally preserved.²⁵ They also found a significant positive correlation between the mean pulmonary artery pressure and macroscopic extent of lung fibrosis, but not venous/venular lesions in non-fibrotic areas.

CONCLUSIONS

Paul W. Noble, MD

Several important clinical trials were reported in 2007. The INSPIRE trial was terminated when a predefined interim analysis showed no benefit of IFN γ -1b compared to placebo.

The BUILD-1 trial of bosentan did not meet its primary endpoint, but the BUILD-3 trial assessing bosentan’s effect on time to death or disease progression is currently recruiting.

PH is a critical issue for IPF, although the best course for management of the comorbid condition is not well defined. Right heart catheterization is still the gold standard for diagnosis of PH, although investigation of surrogate markers such as PFTs, DL $_{CO}$, desaturation with activity, and echocardiography are under active investigation. The usefulness of PH therapies such as bosentan and sildenafil is unproven in IPF, and recommending these agents is not warranted at the present time.

No treatment has been shown to positively affect the course of acute exacerbations, and the condition remains unpredictable.

Lung transplantation is the only treatment that has been shown to enhance survival of IPF patients, and the new lung allocation system has increased the number of lungs available to IPF patients.

It is important to manage the comorbidities of IPF, which include PH, gastroesophageal reflux disease (GERD), cough, dyspnea, and depression. Expert opinion supports incorporating preparation for end-of-life issues and pulmonary rehabilitation²⁶ into the disease management plan.

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IPF EXPERT ROUNDTABLE SUMMARY 2008 CME ACTIVITY ATTESTATION/EVALUATION FORM

<p>PARTICIPANT INFORMATION</p> <p>First Name: _____</p> <p>Last Name: _____ Degree: _____</p> <p>Address: _____</p> <p>City: _____ State: _____ ZIP Code: _____</p> <p>Telephone: _____</p> <p>Email: _____</p> <p style="text-align: center;"><i>(Your CME certificate will be sent to this email address)</i></p> <p style="text-align: center;"><small>This is for internal use only and will not be given or sold to other companies for use.</small></p>	<p>If CME credit and a certificate are desired, please fax or mail the completed CME Activity Attestation/Evaluation Form with your Posttest answers to:</p> <p>The France Foundation Attn: PILOT™ Secretariat 230 Shore Road, Suite 202 Old Lyme, Connecticut 06371 Toll free: 1-866-227-6414 Fax: 1-866-227-6415</p>
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Clinician type:

Pulmonology Pathology Radiology Primary Care Physician

Other _____

Number of years in practice: ≤ 5 6–10 11–15 16–20 21–25 > 25

Percent of patients with IPF in your practice: _____

May we contact you in the future with a brief survey to assess how you have used the information presented in this activity or to assess other educational needs? Yes No

Indicate the number of *AMA PRA Category 1 Credits™* you are claiming _____ **May not exceed 1

Signature: _____ Date: _____

I certify that I have completed this CME activity as designated.

MET LEARNING OBJECTIVES: 4 = strongly agree; 3 = agree; 2 = disagree; 1 = strongly disagree

Upon completion of this activity, I will be able to:

- | | | | | | | | | | | | | | |
|---|--|---|---|---|---|---|---|---|---|---|---|---|---|
| <ul style="list-style-type: none"> • Describe recent progress in diagnosing IPF comorbid conditions, including pulmonary arterial hypertension (PAH) • Describe recent clinical trial results on IPF therapies and incorporate this information into the management of IPF patients • Incorporate expert recommendations into the management of IPF, including participation in clinical trials, pulmonary rehabilitation, evaluation for lung transplantation, management of comorbidities, and management of sleep disorders | <table border="0"> <tr> <td>④</td> <td>③</td> <td>②</td> <td>①</td> </tr> <tr> <td>④</td> <td>③</td> <td>②</td> <td>①</td> </tr> <tr> <td>④</td> <td>③</td> <td>②</td> <td>①</td> </tr> </table> | ④ | ③ | ② | ① | ④ | ③ | ② | ① | ④ | ③ | ② | ① |
| ④ | ③ | ② | ① | | | | | | | | | | |
| ④ | ③ | ② | ① | | | | | | | | | | |
| ④ | ③ | ② | ① | | | | | | | | | | |

ENDURING MATERIAL:

Please rate the overall content presented in this activity: Too basic Appropriate Too complex

BIAS:

Was this activity fair, balanced, objective, and free from commercial bias? Yes No

If no, please state reason(s) _____

PRACTICAL APPLICATION: 4 = strongly agree; 3 = agree; 2 = disagree; 1 = strongly disagree

I felt that the format used in this activity was a beneficial method of learning (4) (3) (2) (1)

What I learned in this activity will improve my ability to care for my patients with IPF (4) (3) (2) (1)

List one thing you will do differently or incorporate into your clinical practice as a consequence of this educational activity: _____

BARRIERS:

What are the top 3 barriers you feel might inhibit your ability to incorporate any of the above changes into your clinical practice? _____

ONGOING UNMET EDUCATIONAL NEEDS:

Recommendations for future CME topics in this disease area: _____

PARTICIPATION:

How did you come to participate in this CME activity?

Direct mail Colleague Web search Conference display E-mail advertisement

Have you participated in a PILOT CME activity in the past? Yes No

If yes, what is the approximate number of activities that you have participated in this calendar year?

1-3 4-6 7-9 > 10

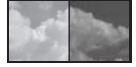
If no, after participating in this activity, how likely would you be to participate in a future PILOT CME activity?

Very likely Likely Unlikely Unsure

POSTTEST ANSWERS

Use the blank boxes below to indicate your answers to the posttest questions on page 11:

- 1. a b c d e
- 2. a b
- 3. a b c d
- 4. a b c d
- 5. a b
- 6. a b c d



SUMMARY POSTTEST

Record your posttest answers by filling in the blank boxes on the previous page with the correct letter from the corresponding question:

1. Pulmonary hypertension is best assessed by
 - a. Right heart catheterization
 - b. Echocardiography
 - c. Echocardiography plus BNP
 - d. HRCT
 - e. No method is dependable
2. Bosentan treatment was associated with an increase in 6MWT distance. This result is being verified in the BUILD-3 trial.
 - a. True
 - b. False
3. Why should IPF patients seek care at a central referral center?
 - a. To receive a second opinion
 - b. To participate in clinical trials
 - c. To receive expert evaluation as a lung transplant candidate
 - d. All of the above
4. Experts recommend offering which of the following to patients with IPF?
 - a. Pulmonary rehabilitation
 - b. Oxygen therapy if indicated
 - c. Evaluation for lung transplantation
 - d. All of the above
5. The survival curves for patients receiving single and double lung transplants are superimposable, so the decision which procedure to recommend depends primarily on surgical considerations.
 - a. True
 - b. False
6. Which statement about fibroblastic foci is supported by evidence?
 - a. Foci are part of a continuous fibrotic reticulum that extends from the pleural surface into the lung parenchyma
 - b. Foci are monoclonal rather than polyclonal
 - c. Foci are pathognomonic for IPF
 - d. All of the above