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Idiopathic Pulmonary Fibrosis Update: Reconciliation with Hypersensitivity Pneumonitis Guidelines Required?

To the Editor:

Clinicians welcome the updated idiopathic pulmonary fibrosis (IPF) clinical practice guidelines recently published in the *Journal* (1). Raghu and a multidisciplinary group of experts did a great job at providing evidence-based recommendations and suggestions to guide clinicians in the diagnosis and management of IPF and progressive pulmonary fibrosis. However, the updated IPF guidelines do not emphasize the role of ruling out known causes of usual interstitial pneumonia (UIP) or probable UIP patterns on high-resolution computed tomography (HRCT) of the chest, as previous guidelines did (2). In particular, they do not address the role of BAL in the diagnosis of hypersensitivity pneumonitis (HP), arguably the most important differential diagnosis of IPF. Furthermore, in the diagnostic algorithm proposed in the guidelines in Figure 10, the authors do not recommend or suggest any additional testing in patients with UIP or probable UIP pattern on HRCT to rule out HP (1).

Hence, how do current guidelines reconcile with recent HP guidelines (3, 4), which suggest that, in patients with UIP or probable UIP pattern on HRCT (called indeterminate for HP pattern in the HP guidelines), BAL is required to define the diagnosis? It would have been very helpful if the current guidelines had provided further clarification on this matter. ■

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Progressive Pulmonary Fibrosis: Should the Timelines Be Taken Out of the Definition?

To the Editor:

The new ATS/ERS/JRS/ALAT (American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Asociacion Latinoamericana del Torax) guideline on pulmonary fibrosis (1) includes an important section proposing a definition and criteria for the diagnosis of progressive pulmonary fibrosis (PPF) other than idiopathic pulmonary fibrosis. Multiple definitions of disease progression have been used in clinical studies assessing the efficacy and tolerability of antifibrotic therapy in PPF despite management (2–4) (also known as interstitial lung disease with a progressive fibrotic phenotype [5]). The guideline authors propose the term PPF (first proposed in a review article [6]) and defining criteria that, if widely adopted, will help to standardize research in the field.

As noted by the authors, satisfying one or more of the proposed criteria (especially decline in pulmonary function tests over 6–12 mo) has been associated with an adverse prognosis, with less evidence that they also identify patients best suited for antifibrotic therapy. A key element of this definition is that changes in respiratory symptoms, physiology, and/or radiologic features should be assessed over the preceding year. However, the benefit:risk assessment guiding management decisions often depends on the kinetics of disease progression. Progression recognized as occurring over 6 months is often considered more worrisome than progression occurring over 2 years. In specifying that progression should occur over a 1-year period, the authors may have intended to discourage clinicians from waiting for 2 years to

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assess progression, as the enrolment criteria in the INBUILD trial (progression over 6 mo to 2 y) (2) have occasionally been misunderstood to require.

However, it may be challenging to ascertain progression over 12 months. Travel distance, logistics, or even a pandemic may conspire to delay and/or prevent routine measures of disease activity. Conversely, there is often no reason to wait, with disease progression clearly occurring over a shorter period of time (e.g., 3–9 mo). In this situation, clinically relevant changes should be identified as early as possible.

We propose that criteria for progression should be dissociated from the timelines during which they occur. In essence, in the absence of another explanation for the measured changes, progression is progression, whether it occurs at 3 months or 3 years. For example, an absolute decline in FVC of more than 5% predicted (a threshold chosen to exceed measurement variability) indicates disease progression, whatever the timelines. Although strict criteria are required to define eligibility criteria in clinical trials, in an individual patient, it is the responsibility of the bedside clinician to make the best management decision. This decision may differ if disease progression is recognized to have occurred over 3, 6, 9, 12, 24, or 36 months. Disease progression, at whatever rate, should lead to a reevaluation of current management, often including the institution of antifibrotic therapy. Rapid progression, as opposed to insidious progression, may reduce the threshold for management change.

So that the criteria may not be inadvertently misinterpreted by clinicians and regulatory bodies, we wish to stress that it is not required that progression occurs over a full 1-year period. We further suggest that, whereas thresholds of physiologic and radiologic disease progression are well-defined by guidelines, the timelines over which progression takes place and their implications should be left to the discretion of the clinicians, taking into account patient preferences and benefit:risk ratio of the management strategy, and to those who design the clinical studies. ■

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Progressive Pulmonary Fibrosis: Putting the Cart Before the Horse

To the Editors:

We congratulate Raghu and colleagues for publication of the updated idiopathic pulmonary fibrosis (IPF) clinical practice guidelines (1). This update incorporates advancements in IPF understanding and the evidence-informed recommendations should benefit patient care. We applaud the committee for giving the newly conceptualized entity of progressive pulmonary fibrosis the exposure it requires to generate further research and evidence. However, we find its inclusion within this clinical practice guideline to be both premature and a missed opportunity.

Clinical practice guidelines exist to provide evidence-informed diagnostic and treatment recommendations to guide decision-making in specific clinical scenarios. While no firm rules determine which clinical conundrums warrant a guideline, most clinical practice guidelines address the diagnosis and management of specific diseases. In interstitial lung disease (ILD), these are typically clinical-radiologic–pathologic entities for which diagnostic and treatment data exist that require synthesis to inform patient care. To date, these have included IPF, hypersensitivity pneumonitis, and sarcoidosis (2–4). Alternative document options include research statements, clinical statements, workshop reports, and perspective pieces. These

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