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Pulmonary hypertension in parenchymal lung diseases: any future for new therapies?

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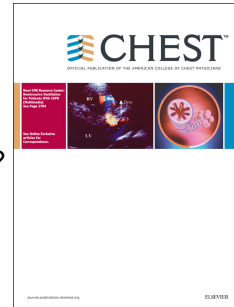
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1 Pulmonary hypertension in parenchymal lung diseases: any future for new therapies?

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11 Conflicts of Interest: SH has relationships with Actelion, Roche, Boehringer Ingelheim and
12 Intermune. In addition to being investigator in trials involving these companies, he is involved in
13 lectures and is a member of scientific advisory boards. DE has nothing to disclose. MH reports
14 personal fees from Actellion, Bayer, GSK, Pfizer and Roche.

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16 ABSTRACT

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18 Pulmonary hypertension (PH) due to chronic lung diseases is associated with a poor prognosis,
19 regardless of the underlying respiratory condition. Updated PH guidelines recommend optimal
20 treatment of the underlying lung disease, including long-term oxygen therapy, in patients with
21 chronic hypoxaemia despite the lack of randomized controlled clinical trials supporting this
22 statement. So far, randomized controlled trials on drugs approved for pulmonary arterial
23 hypertension (PAH) have yielded discouraging results in both interstitial lung diseases (ILD) and
24 chronic obstructive pulmonary diseases (COPD) with PH. In some cases, the trials were terminated
25 because of an increase in death and other major adverse events in the active treatment arm versus
26 placebo. In cases of PH due to idiopathic pulmonary fibrosis (IPF), new investigative therapies use
27 a combination of novel antifibrotic treatments and other treatments approved for PAH. The choice
28 of robust end points as well as a target group of patients with specific haemodynamic criteria may
29 help in the selection of innovative therapeutic strategies. The aim of this review is to discuss recent
30 studies and clinical trials for the treatment of PH due to the main chronic respiratory diseases and
31 discuss possible future scenarios for the evaluation of new therapeutic strategies.

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33 Introduction

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35 Precapillary pulmonary hypertension (PH) is defined by a mean pulmonary artery pressure
36 (mPAP) ≥ 25 mmHg at rest with a normal pulmonary capillary wedge pressure (i.e. ≤ 15 mmHg). A
37 normal mPAP (\pm standard deviation) is equal to 14 ± 3 mmHg. Thus, an mPAP of 21–24 mmHg at
38 rest is above the upper limit of normal but does not qualify for the diagnosis of PH (1). PH due to

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