Il Buono, Il Brutto, Il Cattivo

We appreciate the constructive commentary by Dr Paul Corris and colleagues[1] that highlights the merits and limitations of our manuscript. A recent editorial from Dr Vincent Cottin requested that clinical trials, in the setting of pulmonary fibrosis (PF)-associated pulmonary hypertension (PH), 'should first be conducted in subjects with disproportionate elevation of pulmonary vascular resistance as compared to the severity of pulmonary fibrosis…in whom PH likely contributes the most to exercise limitation and morbidity'.[2]

In this spirit, the purpose of our study is to emphasise the inclusion of a specific, although less common PF-PH phenotype (excluding sarcoidosis and scleroderma) with *advanced pulmonary haemodynamics and right heart dysfunction*. Indeed, the severity of our cohort's baseline haemodynamics (mean mPA 47 mm Hg) represents only 5% of the PF-PH population.[3] Importantly, the treatment variable in this study was the addition of parenteral treprostinil to either naive patients or those on stable background PH-targeted therapy. As such, we chose to focus on the complexities of this therapy in the setting of this advanced PF-PH phenotype and attempt to physiologically explain the positive effects (haemodynamic and echocardiographic markers of RV dysfunction) seen, and those negative (systemic oxygenation) not seen.[4]

The Newcastle group correctly emphasises the lack of treatment benefit of bosentan (BUILD-3) and ambrisentan (ARTEMIS-IPF) in the treatment of idiopathic pulmonary fibrosis.[5 6] However, these studies specifically excluded PH. Moreover, the BUILD-3 and ARTEMIS-IPF studies were completed while our study was actively enrolling. Finally, until recently, there have been no studies evaluating the treatment effect of PH-targeted therapy in patients with PF associated with *advanced pulmonary haemodynamics and right heart dysfunction*.[4 7]

The limitations of this manuscript were addressed and included the use of variable background PH-targeted therapy.[4] The posthoc analysis conducted by our colleagues, albeit small numbers and inherently problematic, highlights this limitation. However, and most critically, the central premise of this manuscript remains simply that the advanced PF-PH phenotype may be particularly receptive to PH-targeted therapy, and this PF-PH subset ought to be considered in future clinical studies. As importantly, any analysis into the specific PH-targeted therapies employed (ie, specific combinations or prostanoid-based regimens), while perhaps hypothesis-generating, appears premature, and was deliberately de-emphasised in this manuscript.

The good, the bad, and the ugly (il buono, il brutto, il cattivo) was a 1966 Italian spaghetti Western film that revolutionised cinematography. Similarly, we hope the results (good, bad and ugly) of this small, but important study in 2014, will set the stage for the design of a future clinical trial that hopefully revolutionises the management of patients with PF-PH.

Rajeev Saggar,[1] Dinesh Khanna,[2] Paul R Forfia,[3] Rajan Saggar[4]

[1]Thoracic Transplantation, Heart-Lung Institute, St Joseph Hospital and Medical Center, Phoenix, Arizona, USA
[2]Division of Rheumatology, Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA
[3]Cardiovascular Division, Temple University School of Medicine, Philadephia, Pennsylvania, USA
[4]David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, USA

Correspondence to Dr Rajan Saggar, David Geffen School of Medicine, University of California Los Angeles, 10833 Le Conte Ave. CHS 37-131, Los Angeles, CA 90095, USA; rsaggar@mednet.ucla.edu

Contributors RS: conceptual design; writing of manuscript; editing of manuscript; agreement to be accountable for all aspects of the work. DK: conceptual design; writing of manuscript; editing of manuscript; agreement to be accountable for all aspects of the work. PRF: conceptual design; writing of manuscript; editing of manuscript; agreement to be accountable for all aspects of the work. RS: conceptual design; writing of manuscript; editing of manuscript; agreement to be accountable for all aspects of the work.

Competing interests None.

Provenance and peer review Not commissioned; internally peer reviewed.

To cite Saggar R, Khanna D, Forfia PR, *et al*. *Thorax* 2014;**69**:871–872.

Accepted 2 April 2014
Published Online First 1 May 2014

▶ http://dx.doi.org/10.1136/thoraxjnl-2014-205337

Thorax 2014;**69**:871–872.
doi:10.1136/thoraxjnl-2014-205511

REFERENCES

1 Corris PA, Sithamparanathan S, Thirugnanasothy L. The good the bad and the ugly. *Thorax* 2014;69:870–1.
2 Cottin V. Treatment of pulmonary hypertension in interstitial lung disease: do not throw out the baby with the bath water. *Eur Respir J* 2013;41:781–3.
3 Kimura M, Taniguchi H, Kondoh Y, *et al*. Pulmonary hypertension as a prognostic indicator at the initial evaluation in idiopathic pulmonary fibrosis. *Respiration* 2013;85:456–63.
4 Saggar R, Khanna D, Vaidya A, *et al*. Changes in right heart haemodynamics and echocardiographic function in an advanced phenotype of pulmonary hypertension and right heart dysfunction associated with pulmonary fibrosis. *Thorax* 2014;69:123–9.
5 King TE Jr., Brown KK, Raghu G, *et al*. BUILD-3: a randomized, controlled trial of bosentan in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2011;184:92–9.
6 Raghu G, Behr J, Brown KK, *et al*. Treatment of idiopathic pulmonary fibrosis with ambrisentan: a parallel, randomized trial. *Ann Intern Med* 2013;158:641–9.
7 Hoeper MM, Halank M, Wilkens H, *et al*. Riociguat for interstitial lung disease and pulmonary hypertension: a pilot trial. *Eur Respir J* 2013;41:853–60.