The good the bad and the ugly

We were, of course, very interested to read the manuscript by Saggar *et al*,[1] and the accompanying editorial by Nathan[2] relating to the use of parenteral treprostinil therapy in patients referred for lung transplantation with pulmonary hypertension (PH) in association with pulmonary fibrosis (PF).

It is good that there is continued interest in finding a clinical phenotype of patient with PF who may benefit on both symptomatic and prognostic grounds from targeted PH therapy. It is also good because there is a great clinical need to help this group of desperate patients awaiting lung transplantation over and above oxygen therapy.

Less good and probably bad was our observation that 9 of the 15 patients entered into this study were already receiving targeted therapy, presumably outside a registered clinical trial? The World PH meeting in Nice (2013), advised that given the lack of evidence of efficacy, such patients should be treated within a clinical trial.[3] Moreover, five patients were receiving an endothelin receptor antagonist (ERA) (Bosentan) either as monotherapy or in combination despite the evidence that another ERA, Ambrisentan, in a randomised clinical trial led to a worse outcome than placebo in patients with idiopathic PF.[4]

Finally, and hopefully, all authors recognise that the ugly connotation is to satisfy our letter's title in response to the accompanying editorial, ugly relates to the lack of appropriate discussion in either the primary paper or the editorial that patients were receiving combination therapy. Indeed the key messages and abstract sections (sometimes the only parts of a paper that are read, dare we say) only mention parenteral treprostinil therapy as

the targeted PH therapy. In idiopathic PH, there is clear evidence of benefit in combining parenteral epoprostenol with an oral phosphodiesterase inhibitor[5] and 7 of the 15 patients in the study were on this combination.

Moreover, careful analysis of the supplementary online data reveals that the greatest benefits in exercise and haemodynamics were seen in patients receiving combination therapy and not treprostinil alone. Although treatment subgroup patient numbers were small and SDs large, there were strong trends towards combinations of targeted therapies being superior to treprostinil alone, and comparison of change in pulmonary vascular resistance achieved a p value of 0.06.

Ugly may be too critical, but correct scientific observation must make use of all factual evidence available, or incorrect conclusions can be drawn and the casual reader of manuscripts potentially led astray.

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