3 de Gracia J, Vendrell M, Álvarez A, *et al*. Immunoglobulin therapy to control lung damage in patients with common variable immunodeficiency. *Int Immunopharmacol* 2004; 6: 745–753.
4 de Gracia J, Morell F, Bofill JM, Rodrigo MJ, Cosculluela C. Impaired lung function in patients with IgA deficiency and low levels of IgG2 or IgG3. *N Engl J Med* 1986; 314: 925–926.
5 de Gracia J, Miravitlles M, Vendrell M, Rodrigo MJ, Codina R, Morell F. Study of the IgG subclasses in symptomatic patients with IgA deficiency. *Med Clin (Barc)* 1995; 104: 728–731.
6 Rodrigo MJ, Vendrell M, Cruz MJ, *et al*. Utility of the antibody response to a conjugated *H. influenzae* type B vaccine for diagnosis of primary humoral immunodeficiency. *Am J Respir Crit Care Med* 2000; 162: 1462–1465.
7 Rodrigo MJ, Miravitlles M, Cruz MJ, *et al*. Characterization of specific immunoglobulin G (IgG) and its subclasses (IgG1 and IgG2) against the 23-valent pneumococcal vaccine in a healthy adult population: proposal for response criteria. *Clin Diagn Lab Immunol* 1997; 4: 168–172.
8 Vendrell M, de Gracia J, Rodrigo MJ, *et al*. Antibody production deficiency with normal IgG levels in bronchiectasis of unknown etiology. *Chest* 2005; 127: 197–204.
9 Ambrosino DM, Siber GR, Chilmonczyk BA, Jernberg JB, Finberg RW. An immunodeficiency characterized by impaired antibody responses to polysaccharides. *N Engl J Med* 1987; 316: 790–793.
10 de Gracia J, Rodrigo MJ, Morell F, *et al*. IgG subclass deficiencies associated with bronchiectasis. *Am J Respir Crit Care Med* 1996; 153: 650–655.
11 Miravitlles M, de Gracia J, Rodrigo MJ, *et al*. Specific antibody response against the 23-valent pneumococcal vaccine in patients with α_1-antitrypsin deficiency with and without bronchiectasis. *Chest* 1999; 116: 946–952.

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Combination therapy with bosentan and phosphodiesterase-5 inhibitor in pulmonary arterial hypertension

To the Editors:

HOEPER *et al*. [1] have produced an interesting report of their clinical experience of combined therapy with bosentan and sildenafil in patients with idiopathic pulmonary arterial hypertension. Whilst it is true that the relatively scant literature supporting the use of phosphodiesterase-5 inhibitors is centred around sildenafil, its relatively short duration of action requires the use of a thrice-daily regime. This has significant implications for compliance and, since treatment is continual, has large implications in the cost of treatment. It would be more logical to use a long-acting phosphodiesterase-5 inhibitor, and, with the advent of tadalafil, once-daily treatment becomes possible.

Here, we report our experience with a combination of bosentan and tadalafil in a 42-yr-old male with idiopathic pulmonary hypertension who had documented poor compliance with nebulised iloprost. Sildenafil 25 mg *t.d.s.* was added to bosentan, following a clinical deterioration and the finding of an estimated pulmonary artery systolic pressure of 130 mmHg, and this caused a fall in pulmonary artery pressure to 50 mmHg. Treatment with sildenafil was stopped 1 month later at another centre, and the pulmonary artery systolic pressure increased to 100 mmHg. Subsequently, sildenafil was restarted in combination with bosentan, and exercise tolerance doubled. After 3 months of combination treatment, the issue of compliance was raised by the patient and it was decided to substitute tadalafil 20 mg once daily for the sildenafil. The patient has continued on tadalafil for 9 months with an excellent symptomatic response. The last estimated pulmonary artery pressure was 61 mmHg.

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REFERENCE

1 Hoeper MM, Faulenbach C, Golpon H, Winkler J, Welte T, Niedermeyer J. Combination therapy with bosentan and sildenafil in idiopathic pulmonary arterial hypertension. *Eur Respir J* 2004; 24: 1007–1010.

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From the authors:

I am grateful for the comments by A.H. Morice and coworkers, although their case report leaves several questions unanswered. More information than just the systolic pulmonary artery pressure is needed to appraise the haemodynamic response to tadalafil. One wonders whether this patient ever underwent pulmonary vasoreactivity testing. With such a

dramatic fall in pulmonary artery pressure, the patient might fulfil the responder criteria (fall in mean pulmonary artery pressure by >10 mmHg to <40 mmHg in the presence of a cardiac output), and may, therefore, be a candidate for treatment with calcium channel blockers [1].

I agree with A.H. Morice and coworkers that the relatively short half-life of sildenafil (3–4 h) may be a drawback of this drug. Patients' compliance may rarely be an issue. However, the fluctuations in sildenafil plasma concentrations are poorly tolerated by some patients. A drug with a much longer half-life, such as tadalafil (~18 h), might be advantageous, but caution is necessary. GHOFRANI *et al*. [2] have demonstrated substantial variability in the haemodynamic effects of several phosphodiesterase-5 inhibitors. For the time being, there is a strong body of evidence for the safety and efficacy of sildenafil in pulmonary arterial hypertension, but there is a lack of comparable data for other phosphodiesterase-5 inhibitors, such as tadalafil.

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REFERENCES

1 Galie N, Torbicki A, Barst R, *et al.* Guidelines on diagnosis and treatment of pulmonary arterial hypertension. The Task Force on Diagnosis and Treatment of Pulmonary Arterial Hypertension of the European Society of Cardiology. *Eur Heart J* 2004; 25: 2243–2278.
2 Ghofrani HA, Voswinckel R, Reichenberger F, *et al.* Differences in hemodynamic and oxygenation responses to three different phosphodiesterase-5 inhibitors in patients with pulmonary arterial hypertension: a randomized prospective study. *J Am Coll Cardiol* 2004; 44: 1488–1496.

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Efficacy of fluticasone on cough

To the Editors:

In the original article by PONSIOEN *et al*. [1], there is no mention of the predictive value of the type of airway inflammation that is associated with cough, or whether there was any benefit from inhaled corticosteroid treatment.

There is increasing evidence that eosinophilic airway inflammation, *i.e.* an eosinophilic bronchitis, which can be identified from spontaneous or induced sputum cell counts, predicts the benefit from corticosteroid treatment in chronic cough, asthma and chronic obstructive pulmonary disease and that a lack of eosinophilia indicates an absence of any benefit [2–6].

An eosinophilic bronchitis occurs in only 10–30% of patients referred to a specialist with an isolated chronic cough [7–9]. Hence, in an unselected population of patients with cough, the majority of whom will not have eosinophilic bronchitis, the benefit from inhaled steroid treatment is likely to be small, as indicated in the study by PONSIOEN *et al*. [1], or absent. Measurement of airway inflammation is necessary to interpret the results of treatment with anti-inflammatory medications.

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REFERENCES

1 Ponsioen BP, Hop WCJ, Vermue NA, Dekhuijzen PNR, Bohnen AM. Efficacy of fluiticasone on cough: a randomised controlled trial. *Eur Respir J* 2005; 145: 147–152.
2 Gibson PG, Dolovich J, Denburg J, Ramsdale EH, Hargreave FE. Chronic cough: eosinophilic bronchitis without asthma. *Lancet* 1989; 17: 1346–1348.
3 Pavord ID, Brightling CE, Wolkman G, Wardlaw AJ. Non-eosinophilic corticosteroid unresponsive asthma. *Lancet* 1999; 353: 2213–2214.
4 Pizzichini E, Pizzichini MM, Gibson P, *et al.* Sputum eosinophilia predicts benefit from prednisone in smokers with chronic obstructive bronchitis. *Am J Respir Crit Care Med* 1998; 158: 1511–1517.
5 Brightling CE, Monteiro W, Ward R, *et al.* Sputum eosinophilia and short-term response to prednisolone in chronic obstructive pulmonary disease: a randomized controlled trial. *Lancet* 2000; 365: 1480–1485.
6 Pizzichini MM, Pizzichini E, Parameswaran K, *et al.* Non-asthmatic chronic cough: no effect of treatment with an inhaled corticosteroid in patients without sputum eosinophilia. *Can Respir J* 1999; 6: 323–330.
7 Brightling CE, Ward R, Goh KL, Wardlaw AJ, Pavord ID. Eosinophilic bronchitis is an important cause of cough. *Am J Respir Crit Care Med* 1999; 160: 406–410.
8 Carney IK, Gibson PG, Murnee-Allen K, Saltos N, Olson LG, Hensley MJ. A systematic evaluation of mechanisms in chronic cough. *Am J Respir Crit Care Med* 1997; 156: 211–216.
9 Ayik SO, Basoglu OK, Erdinc M, Bor S, Veral A, Bilgen A. Eosinophilic bronchitis as a cause of chronic cough. *Respir Med* 2003; 97: 695–701.

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From the authors:

We would like to thank F. Hargreave and K. Parameswaran for their suggestion that sputum eosinophils and the provocative dose causing a 20% fall in forced expiratory volume in one