CORRESPONDENCE

Author’s response: co-trimoxazole treatment in idiopathic pulmonary fibrosis

We thank Neto et al.1 for their comments on our paper2 and for reiterating the points contained within it. ‘The survival benefit conferred by co-trimoxazole, if real, could be due to its antimicrobial activity as there was a significant reduction in the number of infections in the group receiving active treatment’, and this is likely to occur more frequently in patients receiving immunosuppressive treatment. The proportion of deaths in the intention-to-treat group on immunosuppression was 29 of 37. As stated, ‘this study was not designed to collect microbiological information’ however, the results were adjusted for baseline azathioprine or mycophenylate use, and a subgroup analysis of deaths by immunosuppression treatment at baseline in the per-protocol population was undertaken which could not detect a subgroup effect. Analyses from the intention-to-treat and per-protocol (PP) populations were prespecified, and reporting was appropriate.

As discussed, the results could be ‘due to increased mortality in those withdrawing from the drug because of side effects, or the higher withdrawal rate in the active group could be a marker of the disease severity. However, the reduction in mortality was not due to a disproportionate withdrawal of patients in the treatment arm immediately prior to death, as only four patients (two from each group) withdrew from the study within 1 month of death.’ It would be inappropriate to present the results of the demographic details from the PP population, given the desire not to put emphasis on this type of analysis.

Likewise, the issue regarding patients’ diagnosis has been discussed. The study commenced prior to current diagnostic criteria, however, a sensitivity analysis was undertaken of patients with probable or definite usual interstitial pneumonia (UIP) defined as ‘honeycombing on the high resolution CT scan, a histopathological diagnosis of UIP or predicted to have a histopathological diagnosis of UIP’ according to the criteria of Fell et al.,3 the results of which were similar to the full analysis.

There is a paucity of clinical trials evaluating prophylactic antibiotics with interstitial lung disease, although Enomoto et al.4 showed a benefit with co-trimoxazole prophylaxis against Pneumocystis jiroveci pneumonia in patients with interstitial pneumonia receiving high-dose glucocorticoid therapy. From our study, the odds ratio of having an infection, corrected for azathioprine usage, was 2.17 for patients with more than 10 mg/day prednisolone, compared with those not receiving prednisolone in the control group, and 2.14 in the intervention group. The rate ratio was similar to that found by Greenberg et al.5 (1.30) with reduced rates of infection in the intervention group (70% vs 42%). Interestingly, there were high rates of infection in the control group of patients with idiopathic interstitial pneumonia even in those not receiving prednisolone (62%).

As stated clearly in the manuscript, the study did not detect a beneficial effect in terms of the primary endpoint. However, we believe that the magnitude of effect on survival in the PP analyses means that treatment with co-trimoxazole in patients with idiopathic pulmonary fibrosis warrants further investigation.

Ludmila Shulgina,1 Anthony P Cahn,2 Edwin R Chilvers,3 Helen Parfrey,3 Allan B Clark,1 Edward C F Wilson,1 Orion P Twemey,3 Anthony G Davison,5 John J Curtin,6 Michael B Crawford,4 Andrew M Wilson1

1Norwich Medical School, University of East Anglia, Norwich, UK
2Department of Respiratory Medicine, Bedford Hospital NHS Trust, Bedford, UK
3Respiratory Medicine Division, Department of Medicine, School of Clinical Medicine, University of Cambridge, Addenbrooke’s/CUHNHSFT and Papworth Hospitals, Cambridge, UK
4Department of Respiratory Medicine, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK
5Department of Respiratory Medicine, Southend University Hospital NHS Foundation Trust, Essex, UK

Correspondence to Dr Andrew Wilson, Department of Medicine, Norwich Medical School, University of East Anglia, Norwich NR4 7TJ, UK; a.m.wilson@uea.ac.uk

Competing interests None.

Provenance and peer review Commissioned; internally peer reviewed.

To cite Shulgina L, Cahn A P, Chilvers E R, et al. Thorax Online First: [please include Day Month Year] doi:10.1136/thoraxjnl-2013-203765

Accepted 25 April 2013

http://dx.doi.org/10.1136/thoraxjnl-2013-203395

Thorax 2013;0:1. doi:10.1136/thoraxjnl-2013-203765

REFERENCES

1 Ribeiro Neto ML, Swigris JJ, Culver DAl. Idiopathic pulmonary fibrosis or not: antibiotic prophylaxis for all patients on immunosuppressants. Thorax Published Online First: 5 April 2013. doi:10.1136/thoraxjnl-2013-203395.
Author's response: co-trimoxazole treatment in idiopathic pulmonary fibrosis

Ludmila Shulgina, Anthony P Cahn, Edwin R Chilvers, Helen Parfrey, Allan B Clark, Edward C F Wilson, Orion P Twentyman, Anthony G Davison, John J Curtin, Michael B Crawford and Andrew M Wilson

*Thorax* published online June 21, 2013

Updated information and services can be found at:
http://thorax.bmj.com/content/early/2013/06/20/thoraxjnl-2013-203765

These include:

**References**
This article cites 4 articles, 2 of which you can access for free at:
http://thorax.bmj.com/content/early/2013/06/20/thoraxjnl-2013-203765#BIBL

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/