CORRESPONDENCE

Authors’ response to Walker et al.

The research letter by Walker et al1 questions the generalisability of the results of the 4-year UPLIFT trial comparing tiotropium versus placebo based on potential eligibility for UPLIFT at time of discharge of a COPD patient population in New Zealand hospitalised for an exacerbation. The authors state that 38% of their study population would have been excluded from UPLIFT. The authors’ assertion regarding the limited generalisability of UPLIFT’s findings to clinical practice is not valid for several reasons.

First, patients hospitalised for COPD exacerbations are not representative of the general COPD population. An epidemiological analysis from The Netherlands2 reported that 2.1% and 4.4% of COPD patients (mean age, 68 years) starting treatment with HandiHaler and Respimat, respectively, had a COPD-related hospitalisation in the year preceding the analysis. Analysis of an elderly Canadian COPD population3 showed that 9.8% were recently hospitalised for acute respiratory conditions. These epidemiological data suggest that the COPD population studied by Walker et al is not representative of the general COPD population.

Second, UPLIFT used liberal inclusion/exclusion criteria and allowed all COPD medications except other inhaled anticholinergics. The exclusion from UPLIFT of patients with unstable or life-threatening cardiac arrhythmias, recent acute myocardial infarction (MI) or severe heart failure requiring hospitalisation is consistent with most long-term COPD trials designed to evaluate the benefit/risk of pharmacotherapy, including those evaluating long-acting beta-agonist±inhaled corticosteroid. Furthermore, the Canadian COPD database analysis cited above reported 1.3% of patients hospitalised for acute coronary syndrome, including MI, 0.2% for arrhythmias and 2.2% for heart failure during the 6 months preceding the analysis. The proportion of patients excluded from UPLIFT because of these conditions is therefore very limited and would not limit the generalisability of UPLIFT’s findings.

Third, patients studied in UPLIFT, who therefore did not have these conditions at baseline, could experience such adverse events in a real-world manner as prevalence increases with age (mean age at baseline, 65 years) during the conduct of the 4-year trial. This further supports the generalisability of UPLIFT’s findings to clinical practice. The respective events tended to occur later in the group treated with tiotropium versus placebo. Most patients did not withdraw due to these events, allowing for a robust analysis of serious adverse cardiac events. No findings of concern were detected and a manuscript of the respective analysis is in preparation.

For these reasons, we believe that Walker et al’s assertion regarding the limited generalisability of UPLIFT’s findings is not valid.

D P Tashkin,¹ N Metzdorf,² C Hallmann,² I Leimer,² T Lee,² M Decramer*³

¹David Geffen School of Medicine at University of California Los Angeles, Los Angeles, California, USA
²Clinical Development & Medical Affairs Ingelheim, Boehringer Ingelheim Pharma GmbH & Co KG, Germany
³Pfizer Inc., New York, New York, USA

Correspondence to Dr Norbert Metzdorf, Department of Respiratory Diseases, Boehringer Ingelheim Pharma GmbH & Co KG, Binger Strasse 173, D-55216 Ingelheim am Rhein, Germany; norbert.metzdorf@boehringer-ingelheim.com

Contributors DPT contributed to the analysis and interpretation of a post hoc analysis of ‘patients excluded from UPLIFT at baseline’. DPT also conceived, drafted, read and approved the letter. NM contributed to the analysis and interpretation of a post hoc analysis of ‘patients excluded from UPLIFT at baseline’. NM also, conceived, drafted, read and approved the letter. MD contributed to the analysis and interpretation of a post hoc analysis of ‘patients excluded from UPLIFT at baseline’. MD also, conceived, drafted, read and approved the letter. MJ contributed to the analysis and interpretation of a post hoc analysis of ‘patients excluded from UPLIFT at baseline’. MJ also, conceived, drafted, read and approved the letter. TL contributed to the analysis and interpretation of a post hoc analysis of ‘patients excluded from UPLIFT at baseline’. TL also, conceived, drafted, read and approved the letter.

Funding This work was sponsored and supported by Boehringer Ingelheim Pharma GmbH & Co KG and Pfizer Inc.

Competing interests DPT reports personal fees from Boehringer Ingelheim, personal fees from AstraZeneca, personal fees from Novartis, personal fees from Theravance, personal fees from Dey Laboratories, personal fees from Sunovion, grants from Boehringer Ingelheim, grants from Almirall, grants from AstraZeneca, grants from Dey Laboratories, grants from Merck & Co., grants from Novartis, grants from Pfizer, grants from Sunovion and grants from Forest Laboratories, outside the submitted work. NM reports personal fees from Boehringer Ingelheim as an employee during the conduct of the study; personal fees from Boehringer Ingelheim as an employee, outside the submitted work. CH reports personal fees from Boehringer Ingelheim as an employee during the conduct of the study; personal fees from Boehringer Ingelheim as an employee, outside the submitted work. IL reports personal fees from Boehringer Ingelheim as an employee during the conduct of the study; personal fees from Boehringer Ingelheim as an employee, outside the submitted work. TL reports personal fees from Pfizer Inc. as an employee during the conduct of the study; personal fees from Pfizer Inc. as an employee, outside the submitted work. MD reports personal fees from AstraZeneca, personal fees from Pfizer, personal fees from Dompé, personal fees from GlaxoSmithKline, personal fees from Novartis, personal fees from Nycomed, grants from AstraZeneca, grants from Boehringer Ingelheim/Pfizer, grants from GlaxoSmithKline, outside the submitted work.

Provenance and peer review Not commissioned; internally peer reviewed.

To cite Tashkin DP, Metzdorf N, Hallmann C, et al. Thorax Published Online First: [please include Day Month Year] doi:10.1136/thoraxjnl-2013-204429

Received 30 August 2013
Accepted 26 September 2013

Thorax 2013;0:1. doi:10.1136/thoraxjnl-2013-204429

REFERENCES

Authors' response to Walker et al.

D P Tashkin, N Metzdorf, C Hallmann, I Leimer, T Lee and M Decramer

Thorax  published online October 14, 2013

Updated information and services can be found at:
http://thorax.bmj.com/content/early/2013/10/14/thoraxjnl-2013-204429

These include:

References

This article cites 1 articles, 0 of which you can access for free at:
http://thorax.bmj.com/content/early/2013/10/14/thoraxjnl-2013-204429#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/