

In silico Lung Deposition Profiles of Three Single-Inhaler Triple Therapies in Patients with COPD Using Functional Respiratory Imaging [Letter]

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Dear editor

We read with interest the publication by Singh et al on the In silico Lung Deposition Profiles of Three Single-Inhaler Triple Therapies in Patients with COPD Using Functional Respiratory Imaging (FRI), as published in the International Journal of COPD.¹ While the study provides potential insights into the deposition characteristics of three single-inhaler triple therapies, we would like to request clarification on some of the modelling assumptions and experimental methods used within this study.

Firstly, as the study is carried out in silico using FRI, estimated lung deposition outcomes are reliant on the imputation of several key variables, one of which is plume velocity. However, important information on plume velocity is missing within Singh et al. In particular, only one plume velocity of 21m/s at a 10mm distance from the actuator is reported for beclomethasone/glycopyrronium/formoterol (BDP/G/F) pMDI, whereas the study refers to plume velocities of 16.2, 8.2 and 7.1m/s at 25mm, 75mm and 100mm distances from the actuator being modelled for budesonide/glycopyrronium/formoterol (BGF) pMDI but does not report whether the comparison between BGF and BDP/G/F was conducted using equivalent methodological assumptions, considering that when measured and compared with the same methods the two products show similar plume velocity.² Plume velocity has the potential to significantly affect lung deposition outcomes, with a high aerosol velocity known to be associated with increased oropharyngeal deposition,² and therefore a reduced total lung deposition.

Secondly, the lung deposition observed for BGF in this study is inconsistent with previous studies. The Singh et al study reports a peripheral deposition of 31.9% compared to 16.9–23.6% (dependent on inhalation profile) reported in another BGF FRI study carried out by some of the same authors.³ In contrast, results for the other two triple therapies included in the study demonstrate consistency in lung deposition between studies.^{3,4}

Finally, what is deemed as small airway deposition is not representative of how particles are transported and deposited in the functional airways (between generations 12 and 14). Whilst models for airway deposition can be valuable, they do not account for the effect of breath-holding and/or exhalation manoeuvres which are important factors for the deposition of fine particles in the peripheral airways. The translation of such models into clinical practice must not therefore be over emphasised and any differences in modelled small airways deposition should be viewed as mechanistic hypotheses, not as proof of clinical superiority.

For transparency, we respectfully request the authors publish an addendum to clarify the modelling assumptions in terms of plume velocity and other spray parameters used in this study and whether these were implemented in an equivalent manner across therapies, to ensure a fair and scientifically robust comparison. Additionally, we ask the authors to explain why BGF small airway estimates appear higher than those reported in earlier FRI studies.

Disclosure

All authors are employees of Chiesi. The authors report no other conflicts of interest in this communication.

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