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## **Single Triple vs Dual Inhaler Therapy**

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## Single triple versus dual inhaler therapy

To the Editor,

We read with interest the well conducted meta-analysis of triple therapy which comprised of randomised controlled trials evaluating adding long acting muscarinic antagonist (LAMA) to inhaled corticosteroid and long acting beta-agonist (ICS/LABA) in COPD<sup>1</sup>. Their results showed that two long acting bronchodilators (LAMA and LABA) are better than one (LABA) in terms of improving lung function, symptoms and health status as well as reducing exacerbations.

It is important to consider those trials where there was a possible impact of inhaler bias due to different devices being used in comparator arms. This is pivotal to take into account when appraising such trials in order to obviate potential differences in lung deposition, inhaler technique and adherence. Hence we consider the only pertinent trials which meet these stringent criteria are those which compared single triple versus single ICS/LABA via the same inhaler device, namely TRILOGY, IMPACT and KRONOS<sup>2-4</sup>.

We also believe it is also imperative to look at real life studies in patients who have experienced a longer period of follow up. In this regard a real life observational study using health informatics and time dependent analysis showed that adding LAMA to ICS/LABA over 4.65 years in 2853 patients with COPD resulted in significant reductions in a number of key outcomes including hospital admissions by 15% (95%CI 1-27) , exacerbations requiring oral corticosteroids by 29% (95% CI 20-37) , all cause mortality by 35% (95%CI 25-43), respiratory mortality by 30% (95% CI 16-43) and cardiovascular mortality by 51% (95%CI 27-67)<sup>5</sup>.

Hence we would duly suggest using single triple inhaler therapy rather than single ICS/LABA for patients with the frequently exacerbating eosinophilic phenotype of COPD.

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## Conflict of interest

Dr. Lipworth reports grants and personal fees from AZ, personal fees and other from Teva , personal fees from Novartis , personal fees from Sanofi , non-financial support from GSK, grants and personal fees from Chiesi , personal fees from Thorasys , during the conduct of the study; grants and personal fees from Meda , grants from Janssen, grants from Roche, personal fees from Lupin, grants and personal fees from Boehringer Ingelheim , personal fees from Cipla, personal fees from Sandoz , personal fees from Dr Reddys , personal fees and other from Circassia, outside the submitted work. The son of BJL is an employee of AstraZeneca.

Dr. Kuo reports personal fees from Pfizer/ Bristol-Myers Squibb, personal fees from Circassia, personal fees from AstraZeneca, outside the submitted work.