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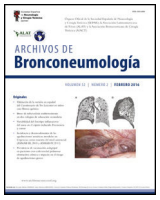

Letter to the Director

Reply to Figueroa-Gonçalves and de Miguel-Díez

To the Director,

We thank Figueroa-Gonçalves and de Miguel-Díez for their interest and comments about our manuscript on a new treatment algorithm for COPD.[1] In our proposal, we restricted the indication of triple therapy with LAMA/LABA/ICS as initial therapy for exacerbators with >300 blood eosinophils (BEC), while they suggest that in case of severe exacerbations triple therapy should be recommended at lower levels of BEC (i.e. >100).[2] They base their recommendation in the fact that severe exacerbations have a high impact on the natural history of COPD, are followed by a high frequency of readmissions, and that it is not uncommon for admitted patients with COPD to be treatment naïve.[2] There is no discussion about this, but there is currently no concrete evidence that triple therapy will be more effective than dual bronchodilation at discharge in naïve patients with 100–300 eosinophils, as suggested by the authors.

To further support their recommendation, Figueroa-Gonçalves and de Miguel-Díez indicate that a post hoc analysis of the IMPACT study demonstrates that the initiation of triple therapy after a severe COPD exacerbation provides a greater benefit in terms of the development of future exacerbations than LAMA/LABA in patients with a level of BEC >100. However, it is of note that patients in IMPACT were by no means treatment naïve; on the contrary, up to 40% were already on triple therapy at screening (therefore, they do not "initiate" triple after admission) and a further 41% were on either LABA/ICS or LAMA/LABA.[3] Moreover, looking at the mortality results, there was no effect whatsoever of triple therapy in reduction of mortality in patients who were not previously on ICS, which are the closer to treatment naïve that we can find in IMPACT.[3] For these reasons, the IMPACT study results cannot be extrapolated to treatment naïve subjects with COPD and cannot be used to justify triple therapy in previously naïve COPD patients after a severe exacerbation in all cases with BEC >100. We do not dispute the indication of triple therapy in discharged patients with BEC >300, since enough evidence exists about the great efficacy of ICS in this population, but naïve patients with BEC between 100 and 300 should try LABA/LAMA first and only escalate to triple in case of a new episode or frequent moderate exacerbations, as indicated in the GESEPOC guidelines.[4]

Figueroa-Gonçalves y de Miguel-Díez also base their recommendation on data from the observational PRIMUS study, which observed lower mortality with the early initiation of triple after an admission compared with delayed initiation, but again patients in PRIMUS were not treatment naïve and the observational design may involve certain bias.[2] There are observational studies suggesting the opposite, for example, Jo et al.[5] observed that patients who discontinued their ICS after being discharged from an exacerbation of COPD had a significant reduction of 35% of the risk of re-hospitalisation or death compared with those who continued using their ICS. Therefore, we need to be very cautious with the recommendation to use triple therapy, even in patients after a hospital admission, because benefits do not always outweigh the risks, particularly in previously naïve patients with less than 300 BEC.

Conflict of Interests

Marc Miravitlles has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Menarini, Kamada, Takeda, Zambon, CSL Behring, Specialty Therapeutics, Janssen, Grifols and Novartis, consulting fees from AstraZeneca, Atriva Therapeutics, Boehringer Ingelheim, BEAM Therapeutics, Chiesi, GlaxoSmithKline, CSL Behring, Inhibrx, Menarini, Mereo Biopharma, Spin Therapeutics, Specialty Therapeutics, ONO Pharma, Palobiofarma SL, Takeda, Novartis, Novo Nordisk, Sanofi, Zambon, Zentiva and Grifols and research grants from Grifols.

Konstantinos Kostikas has received honoraria for presentations and/or consultancy fees from Alector Pharmaceuticals, AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, ELPEN, GILEAD, GSK, Menarini, Novartis, Pfizer, Sanofi, Specialty Therapeutics, WebMD; his department has received funding and/or grants from AstraZeneca, Boehringer Ingelheim, Chiesi, Innovis, ELPEN, GSK, Menarini, Novartis and NuvoAir; he is a member of the GOLD Assembly.

Nikoletta Bizymi has no conflicts of interest related to this paper.

Nikolaos Tzanakis has received speaker and/or consultancy fees from AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, ELPEN, GILEAD, GSK, Innovis, Menarini, Novartis, Pfizer, Sanofi, Specialty Therapeutics, Help and has received research grants from AstraZeneca, Boehringer Ingelheim, Chiesi, Innovis, GSK, Menarini, and Novartis.

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