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Early View

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Nebulised liposomal amphotericin-B: A promising strategy for preventing ABPA relapse

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To the Editor.

The authors reply to Yang Liu:

Nebulised liposomal amphotericin-B: A promising strategy for preventing ABPA relapse

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To the Editor:

We wish to thank Yang Liu and colleagues for their thoughtful remarks on the NEBULAMB study [1].

Regarding their first comment on the study population, we acknowledge that a maintenance treatment might be more warranted and even more effective in patients with previous recurrent exacerbations than in patients without previous exacerbation. In our study, this hypothesis was supported by our analysis, which was restricted to patients with previous exacerbations (i.e., in the past years). During the 24-month follow-up period, we found that in patients with at least one previous severe exacerbation before inclusion, the proportion with at least two or more severe exacerbations was 27% in the active treatment group as compared to 53% in the placebo group (p=0.03) [1]. However, in the setting of this first randomised trial, we decided to include a well-defined population and to explore without "a priori" but according to some predefined subgroups the impact of a maintenance treatment following a homogeneous attack treatment. In fact, the presence or absence of previous exacerbations might not be the only factor influencing the effect of maintenance therapy. For example, according to the CT-scan phenotype at inclusion [2], it could be interesting to evaluate the benefit of a maintenance strategy and its influence on future relapse or complete remission. Another interesting issue could be the impact of predictive factors such as high-attenuation mucus impactions on future relapses or complete remission.

Regarding the comment on the primary outcome, we decided to consider all episodes of exacerbations, whether related or d unrelated to allergic bronchopulmonary aspergillosis (ABPA), because even if a definition of relapse has been proposed in the literature, this definition evolves over time. Furthermore, we also have to admit that the notion of a clinical or a radiological worsening is lacking in precise definition [3, 4]. Moreover, it seems interesting to consider the impact of such a strategy on all-cause relapses to better assess the patient's overall quality of life.

We fully agree that the concept of maintenance treatment is based on the objective of limiting the recurrence of exacerbations, which, when left untreated, increase the risk of hospitalization, development of bronchiectasis, permanent obstructive ventilation defect and fibrotic lung lesions [5, 6]. Thereby, although during the 24-month follow-up period the experimental strategy did not result in a reduction of the overall cumulative incidence of a first severe exacerbation in allergic bronchopulmonary aspergillosis patients, it was associated with delayed occurrence of a first severe exacerbation and a reduction of the number of exacerbation episodes per patient in the "frequent exacerbator" phenotype (exploratory outcomes). These are clinical elements of major importance regarding patient comfort and ABPA stability. We do agree that relevant RCTs are urgently needed to evaluate the efficacy of nebulised liposomal amphotericin-B in ABPA patients with "frequent exacerbator" phenotype, which will address the question of the benefit of this treatment.

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Conflict of interest

Dr Godet reports having received speaker fees, travel support from Pfizer, MSD; fees for board memberships from SOS Oxygène and Pulmatrix; grant support from Ohre Pharma, Pfizer, MSD, SOS Oxygène, ISIS Medical, and AstraZeneca.

Dr Cadranel reports having received speaker fees from MSD and Pfizer on pulmonary aspergillosis and for participating on experts grants on cancer drugs. Gants from Pfizer and SOS oxygen for study outside the submitted work.

Dr Frat reports having received grants from the French Ministry of Health, outside the submitted work; grants, personal fees and non-financial support from Fisher & Paykel HeathCare, outside the submitted work; personal fees and non-financial support from SOS Oxygène, outside the submitted work.

Dr Ragot: no disclosure was reported.

Dr Couturaud reports having received research grant support from Bristol-Myers Squibb/Pfizer and fees for board memberships or symposia from Bayer, Bristol-Myers Squibb/Pfizer, Merck Sharp & Dohme and AstraZeneca and having received travel support from Bayer, Bristol-Myers Squibb/Pfizer, Leo Pharma, Merck Sharp & Dohme and Actelion.