Reply to: Nebulised liposomal amphotericin-B: a promising strategy for preventing ABPA relapse

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Reply to Yang Liu and co-workers:

We wish to thank Yang Liu and co-workers 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 our randomised trial, we decided to include a well-defined population and to explore without "a priori" 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 computed tomography (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 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 hospitalisation, development of bronchiectasis, permanent obstructive ventilation defect and fibrotic lung lesions [4, 5]. 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 ABPA 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 randomised controlled trials are urgently needed to evaluate the efficacy of nebulised liposomal amphotericin-B in ABPA patients with the "frequent exacerbator" phenotype, which will address the question of the benefit of this treatment.

Shareable abstract (@ERSpublications)
Is nebulised liposomal amphotericin-B a promising strategy for preventing allergic bronchopulmonary aspergillosis relapse? https://bit.ly/3qTDMCA

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Cendrine Godet[1], Jacques Cadranel[2], Jean-Pierre Frat[3,4], Stéphanie Ragot[5,6] and Francis Couturaud[7]

[1]Assistance Publique – Hôpitaux de Paris, Hôpital Bichat, Service de Pneumologie, Paris, France. [2]Assistance Publique – Hôpitaux de Paris, Hôpital Tenon, Service de Pneumologie et Oncologie thoracique, Centre constitutif Maladies pulmonaires rares and Sorbonne Université, Paris, France.

[3]CHU Poitiers, Médecine Intensive Réanimation, Poitiers, France. [4]INSERM, CIC-1402, IS-ALIVE, Université de Poitiers, Poitiers, France. [5]INSERM, CIC-1402, Biostatistics, Poitiers, France. [6]Université de Poitiers, Faculté de Médecine et de Pharmacie de Poitiers, Poitiers, France. [7]Centre Hospitalo-Universitaire de Brest, Université de Bretagne Occidentale, Département de Médecine Interne et Pneumologie, INSERM U1304, CIC INSERM 1412, FCRIN INNOVTE, Brest, France.

Corresponding author: Cendrine Godet (cendrine.godet@aphp.fr)

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