Title: Preventive effect of carbocysteine on exacerbation of asthma, GAIA randomised, placebo-controlled multi-centre study

Body: Background: Management of exacerbation is clinically very important in asthma control. Carbocysteine, which improves airway mucus clearance and has anti-inflammatory effects, including antioxidant effect, is expected to prevent asthma exacerbation in addition to COPD exacerbation. Objective: To evaluate the preventive effect of carbocysteine (C) on exacerbation in asthma patients using placebo (P) as a control. Methods: A total of 286 patients with mild to moderate asthma were randomly assigned to receive either C (1500mg/day) or P for 48 weeks. Patients were allowed to use long-term asthma control medications. The primary endpoint was annual frequency of exacerbations, and the secondary endpoints were pulmonary function and asthma control by ACQ. Results: At the time of enrollment, the disease type (atopic or non-atopic asthma) was significantly different (p = 0.02) between the two groups (C, n = 140; P, n = 140), but no statistically significant differences were observed in any other baseline characteristics of patients. The frequency of asthma exacerbations, the primary endpoint, was 5.40/year in the C group and 8.04/year in the P group, showing a significant decrease in the C group compared with the P group. The risk ratio of exacerbation was 0.658 (95% CI, 0.595-0.727; p < 0.001). No significant differences were observed in the pulmonary function or in the asthma control between the two groups. Conclusion: C significantly reduced the frequency of asthma exacerbations and thus provides a new therapeutic concept for long-term asthma management.