**Objectives**:

Severe asthma (SA) is a multifactorial disease that seriously affects patients’ quality of life. In last years, new biologics treatments targeting specifically T2 inflammation, greatly improved SA control. However, these biologics are limited to T2-high SA patients and clinical remission varies from 30 to 50%. We hypothesized that the fungal exposome, in connection with the lung mycobiome, could be one of the factors explaining this response heterogeneity. Indeed, the fungal exposome has been shown to be directly involved in the onset and evolution of immune-allergic diseases, including SA. Moreover, the inhalation of fungal spores from the environment drives the lung mycobiome composition, which dysbiosis is also associated with SA evolution.

**Materials & Methods:**

To evaluate these connections, we conducted a 1-year bicentric prospective longitudinal study, including T2-high SA patients treated by biologics for at least one year before inclusion (n=76). We deployed electrostatic dust collectors in patients’ bedroom for 10 weeks during each season and we collected sputum samples. Then, we analyzed their fungal composition using an ITS2-based targeted metagenomics approach (NextSeq 2000, Illumina). We also assessed SA clinical remission and fungal sensitization at the inclusion and at the end of the follow-up.

**Results**:

Preliminary results revealed that the intra-domiciliary fungal exposome composition depends significantly on the seasons (PERMANOVA, p=0.01), but not the lung mycobiome, suggesting the importance of a “core” exposome. Indeed, beta-diversity analyses showed that the 1-year fungal core exposome was significantly associated with clinical remission at the end of the follow-up (PERMANOVA, p=0.01). Notably, responders’ exposome was chronically enriched with *Alternaria* and *Cladosporium* species, which surprisingly are rather known to be involved in asthma exacerbations.

**Conclusions**:

Mechanistic pathways, including fungal sensitization are still under investigation, but these preliminary results suggest the intra-domiciliary fungal exposome could be a predictive remission marker to biologics and/or an interventional leverage in SA management.