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Biomarker-defined clusters by level of Type 2 inflammatory involvement in severe asthma

Severe asthma, Biomarkers, Inflammation

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Introduction/Background: Biomarker-defined clusters of severe asthma patients were previously identified via hierarchical cluster analysis; a cluster of older females with low-to-medium Type 2 (T2) biomarkers was characterized (Denton, E. et al. J Allergy Clin Immunol Pract 2021;9:2680-8.e7).

Aims and Objectives: To describe biomarker-defined clusters (blood eosinophil counts [BEC], FeNO, and serum IgE [IgE]) in severe asthma patients, and characterize T2-low asthma using a model-based approach to clustering.

Methods: Patients in the International Severe Asthma Registry (ISAR) with biomarker data were included, regardless of biologic use. A Gaussian finite mixture model was used to perform cluster analyses using BEC, FeNO and IgE standardized by z score. The prespecified thresholds for low biomarkers were BEC <300cells/μL, FeNO <25ppb and IgE <75 IU/mL.

Results: Of 4459 patients, five clusters were identified. Cluster 1 had females with low T2 biomarkers. Cluster 2 had high BEC and FeNO; Cluster 3, triple T2 biomarker high; Cluster 4, high BEC; Cluster 5, high IgE.

Figure: Median (IQR) biomarker levels and characteristics of clusters

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluste
N	747	1038	357	1,503	814
BEC (cells/µL)	200 (200)	850 (752)	1160 (2900)	400 (400)	300 (3
FeNO (ppb)	16 (12)	93 (75)	52 (77)	37 (36)	24 (2
IgE (IU/mL)	28 (40)	304 (362)	1669 (2525)	115 (126)	650 (6
Females	73%	56%	54%	63%	58%
Age	55 (21)	54 (20)	55 (23)	56 (19)	52 (2
BMI	29 (10)	27 (7)	26 (7)	29 (8)	28 (

Conclusions: In line with previous findings, a cluster with females and low biomarkers suggested low T2 involvement. The other 4 clusters varied in biomarker elevations, highlighting the complexity of T2 inflammatory involvement in severe asthma.