|  |
| --- |
| **Distinct clinical asthma phenotypes identified via cluster analysis (ATLANTIS)** |
| Dave Singh1, Pauline Kuks2, Tatiana Karp3, Jorine Hartman2,3, Monica Kraft4, Salman Siddiqui5, Leonardo Fabbri6, Klaus Rabe7, Alberto Papi6, Chris Brightling8, Maxim Kots9, Thys Van Der Molen3, Huib Kerstjens3, Irene Heijink3, Daan Pouwels10, Dirk-Jan Slebos2,3, Maarten Van Den Berge3 |
| *1 Division of Infection, Immunity & Respiratory Medicine, University of Manchester, Manchester University NHS Foundation Trust, United Kingdom;*  *2Department of Pulmonary Diseases, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands;*  *3University of Groningen, University Medical Center Groningen, Groningen Research Institute Asthma and COPD (GRIAC), Groningen, The Netherlands;*  *4Department of Medicine, College of Medicine Tuscon, and Asthma and Airway Diseases; Research Centre, University of Arizona Health Sciences, Tuscon, AZ, United States;*  *5National Heart and Lung Institute, Imperial College London, London, United Kingdom;*  *6Respiratory Medicine, Department of Translational Medicine and for Romagna, University of Ferrara, Ferrara, Italy;*  *7LungenClinic Grosshansdorf and Department of Medicine, Christian Albrechts University, Member of the German Center for Lung Research (DZL), Kiel, Germany;*  *8Institute for Lung Health, NIHR Leicester Biomedical Research Centre, University of Leicester, Leicester, United Kingdom;*  *9Global Medical Affairs, Chiesi Farmaceutici, S.p.A., Parma, Italy;*  *10Department of Medical Biology & Pathology, University Medical Center Groningen, Groningen, The Netherlands.* |
| **Introduction/Aim:**  Better understanding of asthma phenotypes is crucial for understanding, characterising and managing the disease. This post-hoc ATLANTIS study analysis aims to identify clinically distinct clusters including parameters of small airways disease and asthma associated gene-expression based on previous study.  **Methods:**  ATLANTIS included 773 asthma patients (mean age 44 years, 58% female, 76% never-smoker, GINA 1-5). Subjects were characterised using questionnaires, large and small airways disease, nasal brush RNA, blood and sputum samples, and chest computed tomography. Clusters were generated using the Self-Organizing Map-Ward’s method.  **Results:**  We identified four groups: Cluster A (N=277) included predominantly male patients with well controlled symptoms and elevated levels of sputum neutrophils. Cluster B (N=228) characterized by normal lung function, low blood inflammatory cell counts and low sputum eosinophils. Cluster C (N=206) included mostly atopic patients with an early age of asthma onset, more severe bronchial hyperresponsiveness, uncontrolled symptoms and higher nasal epithelial expression of asthma related genes. Cluster D (N=62) was characterized by frequent exacerbations, lower post-bronchodilator FEV1 %predicted and FEFs, small airways disease and hyperinflation. Cluster D patients also had higher sputum and blood eosinophil counts, and exhaled nitric oxide levels.  **Conclusion:**  We identified four clinically distinct patient groups: Neutrophilic, Mild pauci-inflammatory, Atopic, and those with small airways disease, high eosinophil levels in blood and sputum and frequent exacerbations. Future research engaging the biology of these clusters may provide new options for precision medicine.  **Grant Support:**  The ATLANTIS study was funded by Chiesi Farmaceutici SpA.  **Declaration of Interest statement:**  Dave Singh has received personal fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, Epiendo, Genentech, GlaxoSmithKline, Glenmark, Gossamerbio, Kinaset, Menarini, Novartis, Pulmatrix, Sanofi, Teva, Theravance and Verona. |