Eosinophilic and Noneosinophilic Asthma:
An Expert Consensus To Characterize Phenotypes in a Global Real-life Severe Asthma Cohort

Liam G. Heaney, Luis Perez de Llano, Mona Al-Ahmad, Vibeke Backer, John Busby, Giorgio Walter Canonica, George C. Christoff, Borja G. Cosio, J. Mark FitzGerald, Enrico Heffler, Takashi Iwanaga, David J. Jackson, Andrew N. Menzies-Gow, Nikolaos G. Papadopoulos, Andriana I. Papaioannou, Paul E. Pfeffer, Todor A. Popov, Celeste M. Porsbjerg, Chin Kook Rhee, Mohsen Sadatsafavi, Yuji Tohda, Eileen Wang, Michael E. Wechsler, Marianna Alacqua, Alan Altraja, Leif Bjermer, Unnur S. Björnsdóttir, Arnaud Bourdin, Guy G. Brusselle, Roland Buhl, Richard W. Costello, Mark Hew, Mariko Koh Siyue, Sverre Lehmann, Lauri Lehtimäki, Matthew Peters, Camille Taillé, Christian Taube, Trung N. Tran, James Zangrilli, Lakmini Bulathsinhala, Victoria A. Carter, Isha Chaudhry, Neva Eleangovan, Naeimeh Hosseini, Marjan Kerkhof, Ruth B. Murray, Chris A. Price, David B. Price

Heaney LG, et al. *CHEST* 2021; Article in press

The ISAR Initiative

- **A large observational registry with pooled data from multiple countries has the statistical power to better understand severe asthma epidemiology, clinical management and outcomes across international populations.**

The Broad Inclusion Criteria For Enrolment Captures a Diverse Patient Population Rarely Represented in RCTs

Inclusion

- Adult ≥18 years old with severe asthma
- Undergoing GINA Step 5 treatment OR uncontrolled on GINA Step 4 treatment
  - Uncontrolled as defined by ERS/ATS guidelines
- Poor symptom control where ACQ is consistently > 1.5, ACT <20
- Airflow limitation where pre-bronchodilator FEV_1 <80% predicted, with reduced FEV_1/FVC
- Serious exacerbations with ≥1 hospitalization, ICU stay or mechanical ventilation in the previous year
- Frequent severe exacerbations with ≥2 bursts of SCS with each course >3 days in the previous

- ✓ Smokers
- ✓ ACO
- ✓ Moderate-to-severe asthma

Exclusion

- Lack of informed consent for participation

Fitzgerald JM, Price DB et al. BMC Med Res Methodol 2020;20:212

Background[1]

- The term “severe asthma” includes many different phenotypes and endotypes that differ in their clinical presentation, underlying pathways, and response to treatment[2]
- Various classifications for the eosinophilic and non-eosinophilic phenotypes of severe asthma have been suggested, however, the data upon which they are based and their clinical applicability in the real world is limited

There is therefore an urgent need to characterize discrete severe asthma phenotypes using a combination of biomarkers and clinical characteristics, in order to provide effective personalized treatment for patients

1. Heaney LG, et al. *CHEST* 2021; Article in press, 2. Bakakos A et al. *J Clin Med* 2019;8, 3. Carr TF et al. *Am J Crit Care Respir Med* 2018;197:22-37

Aims & Objectives

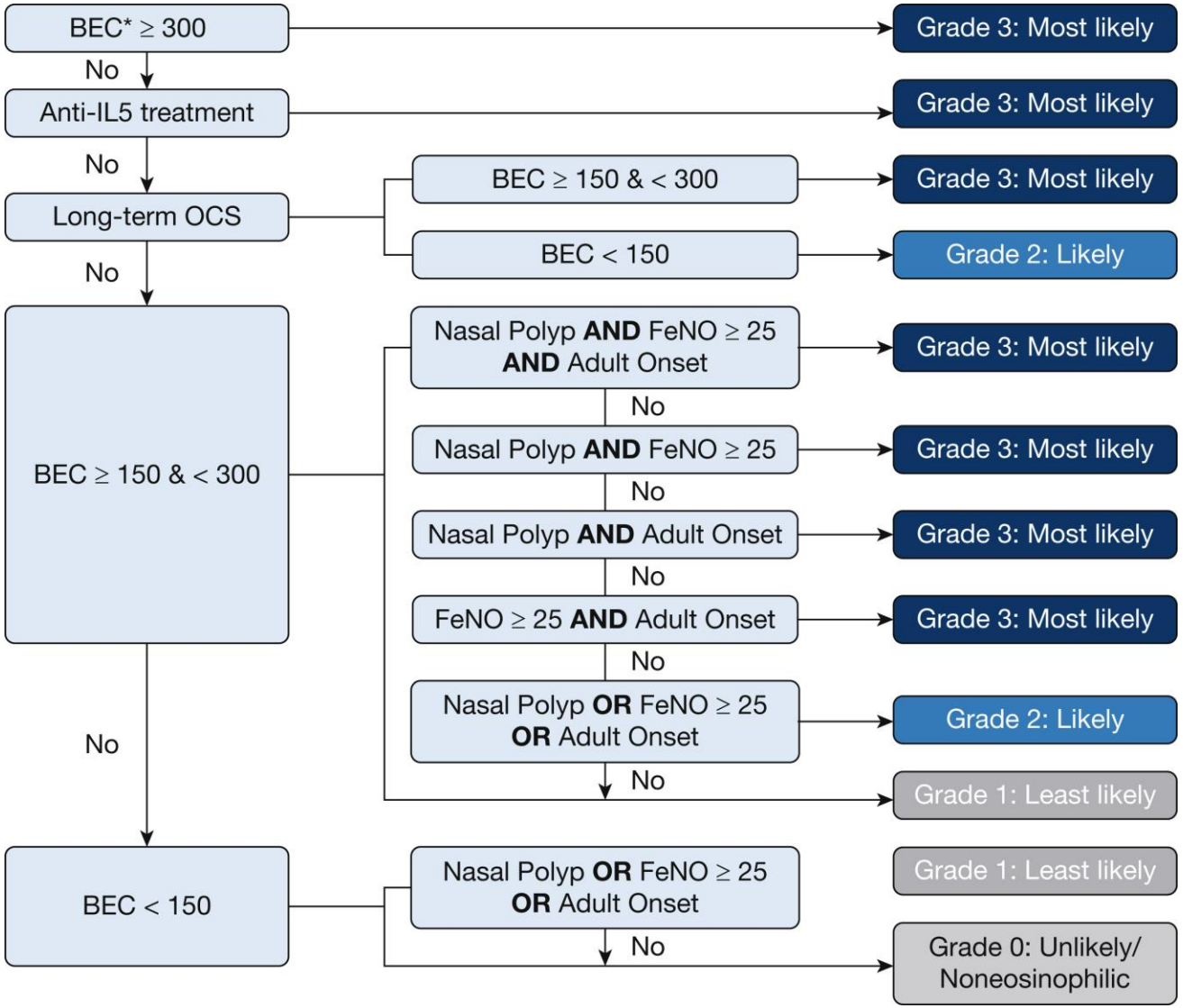
1. Describe an algorithm to better characterize severe eosinophilic and noneosinophilic asthma using both phenotype characteristics and biomarkers

2. To quantify the proportion of patients with severe asthma with these phenotypes in the largest real-life severe asthma cohort in the world – ISAR

3. To describe and compare their demographics and clinical characteristics

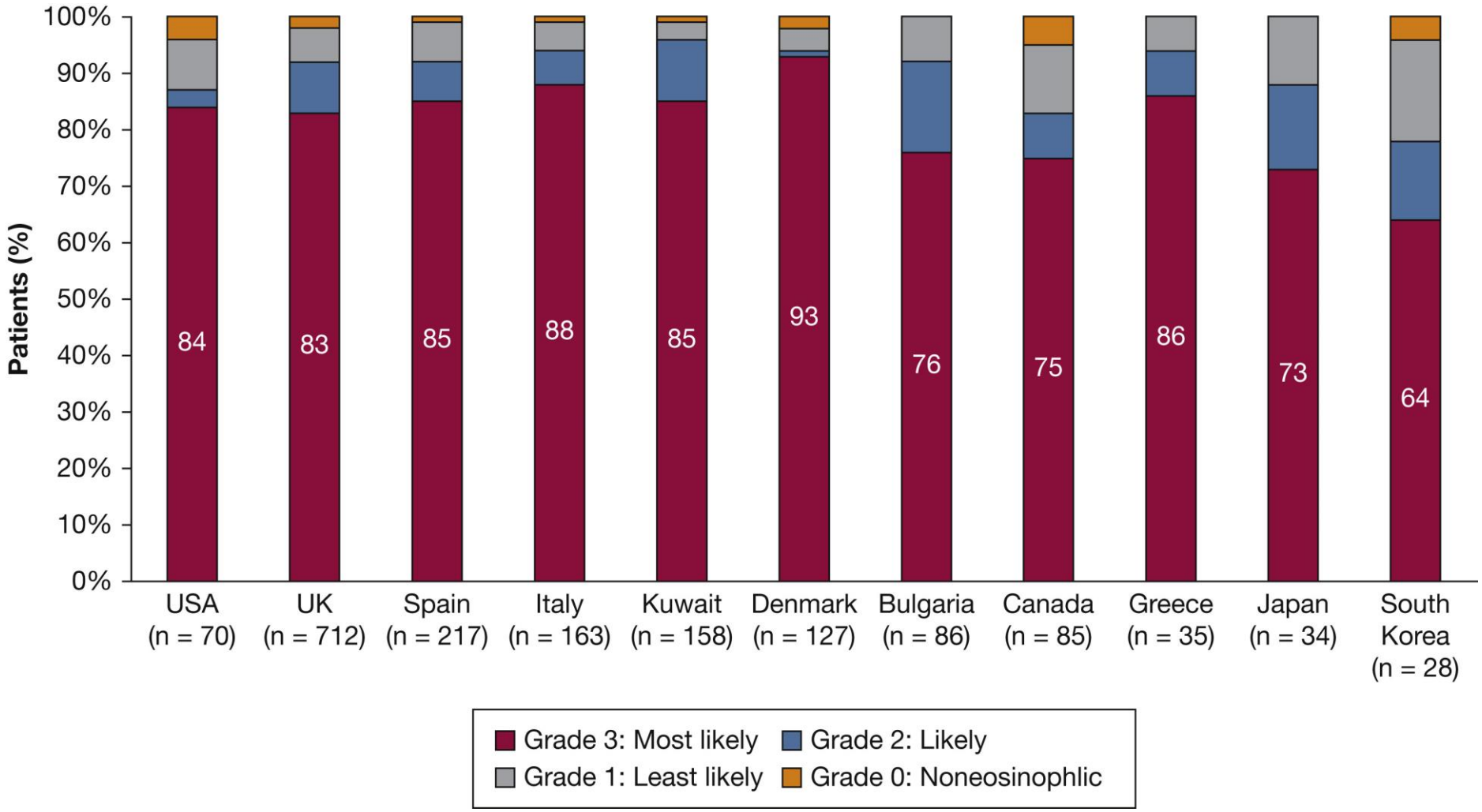
Heaney LG, et al. *CHEST* 2021; Article in press

The Eosinophilic Grade: A New Tool To Characterize Eosinophilic Severe Asthma Phenotypes



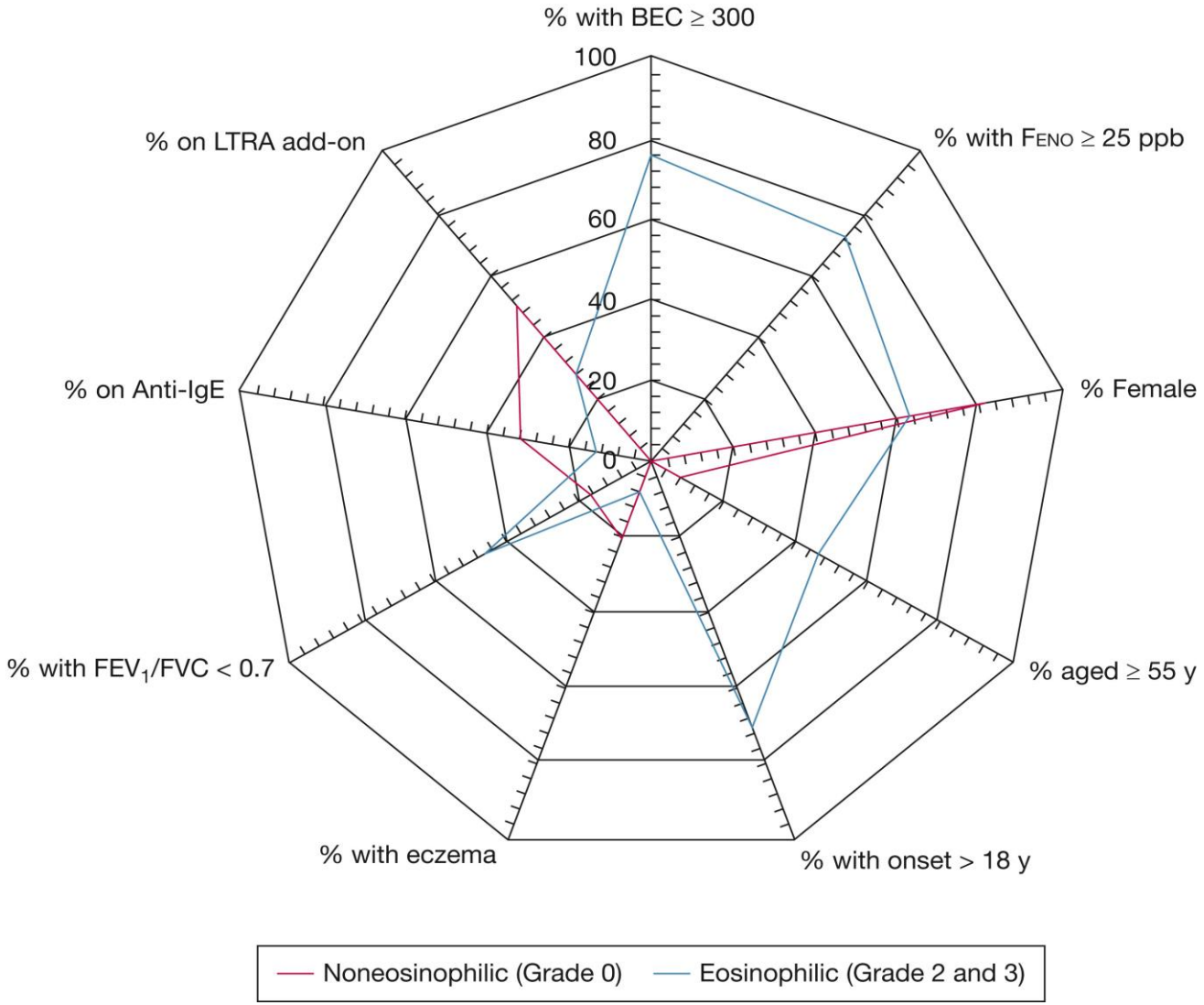
Heaney LG, et al. *CHEST* 2021; Article in press

Eosinophilic Asthma is By Far The Most Common Phenotype In Severe Asthma



Heaney LG, et al. *CHEST* 2021; Article in press

Distinct Demographics and Clinical Characteristics Observed in the Eosinophilic vs Noneosinophilic Phenotypes



Common characteristics of the **eosinophilic** phenotype:

- Older age
- Later asthma onset
- Worse lung function

Common characteristics of the **noneosinophilic** phenotype:

- Female gender
- Eczema
- Anti-IgE and LTRA add-on to ICS/LABA

Heaney LG, et al. *CHEST* 2021; Article in press

Conclusions & Implications for Clinical Practice

- The eosinophilic phenotype is much more common than previously thought – GINA 2021 estimates 50% of the severe asthma population are eosinophilic, however, results show it is >80%
  - This is a distinct severe asthma phenotype that can be defined using variables readily accessible in real-life

- The use of a gradient and multicomponent analysis – as opposed to evaluating eosinophilia based on blood eosinophil count alone – provides a safeguard against phenotypic misclassification

- Characterizing severe asthma patients according to discrete phenotypes will ultimately aid the delivery of precision medicine by shedding more light on treatable traits

Heaney LG, et al. *CHEST* 2021; Article in press