

# Update of Global Severe asthma Registry

한양대학교 의과대학  
호흡기알레르기 내과  
이현

# Contents

- **Global severe asthma registry**
- **National severe asthma registry**
- **International severe asthma registry**

# Contents

- **Global severe asthma registry**
- National severe asthma registry
- International severe asthma registry

Name	Country	Organization
<b>National: Europe</b>		
<b>UK Severe Asthma Registry (UKSAR)</b>	United Kingdom	BTS
<b>Severe Asthma Network in Italy (SANI) registry</b>	Italy	SANI
<b>COhort of BRonchial obstruction and Asthma (COBRA)</b>		
Belgian Severe Asthma Registry (BSAR)	Belgium	Belgian Thoracic Society
Spanish Registry of Severe Asthma	Spain	
Portuguese Severe Asthma Registry	Portugal	REAG
Austrian Severe Asthma Registry	Austria	Austrian Severe Asthma Net (ASA-Net)
<b>German Severe Asthma Registry (GAN)</b>	Germany	German Asthma Net
Russian Severe Asthma Registry (RSAR)	Russia	Russian Respiratory Society
<b>National: North America</b>		
<b>CHRONICLE</b>	United States	
<b>Severe Asthma Research Program (SARP)</b>	United States	
<b>National: Asia-Pacific</b>		
<b>ISAR-Korea</b>	Korea	KATRD
<b>Korean Severe Asthma Registry (KoSAR)</b>	Korea	KAAACI
Australian Severe Asthma Registry (ASAR)	Australia	Australian Severe Asthma Network (ASAN), TSANZ
<b>International</b>		
<b>Severe Heterogeneous Asthma Research collaboration, Patient-centred (SHARP)</b>	Europe	ERS
African Severe Asthma Project (ASAP)	Africa	
<b>International Severe Asthma Registry (ISAR)</b>	World	
<b>Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes (U-BIOPRED)</b>	Europe	

# Contents

- Global severe asthma registry
- **National severe asthma registry**
  - UKSAR
- International severe asthma registry

**UKSAR**



OPEN ACCESS

Original research

# Characterisation of patients with severe asthma in the UK Severe Asthma Registry in the biologic era

David J Jackson,<sup>1,2</sup> John Busby,<sup>3</sup> Paul E Pfeffer ,<sup>4</sup> Andrew Menzies-Gow,<sup>5</sup> Thomas Brown,<sup>6</sup> Robin Gore,<sup>7</sup> Martin Doherty,<sup>8</sup> Adel H Mansur ,<sup>9,10</sup> Simon Message,<sup>11</sup> Robert Niven,<sup>12</sup> Mitesh Patel,<sup>13</sup> Liam G Heaney,<sup>14,15</sup> on behalf of the UK Severe Asthma Registry

**Table 3** Biologic population versus non-biologic population\*

	No biologic therapy (n=687)	Biologic therapy (n=1524)	P value
Age at first assessment	49.1 (14.3)	49.7 (14.3)	0.332
18–34	118 (17.2%)	257 (16.9%)	
35–54	315 (45.9%)	659 (43.3%)	
55–79	251 (36.5%)	599 (39.4%)	
80+	3 (0.4%)	7 (0.5%)	
Age at onset of symptoms	23.6 (18.9)	24.5 (19.2)	0.321
<12	230 (37.3%)	481 (35.7%)	
12–18	57 (9.3%)	124 (9.2%)	
>18	329 (53.4%)	742 (55.1%)	
Gender			0.964
Female	428 (62.3%)	951 (62.4%)	
Male	259 (37.7%)	573 (37.6%)	
Ethnicity			0.024
Caucasian	514 (75.5%)	1218 (80.6%)	
Non-Caucasian	167 (24.5%)	293 (19.4%)	
BMI (kg/m <sup>2</sup> )	30.8 (7.4)	30.9 (6.9)	0.747
Smoking status			<0.001
Never smoked	428 (62.7%)	1053 (70.8%)	
Ex-smoker	211 (30.9%)	403 (27.1%)	
Current smoker	44 (6.4%)	32 (2.2%)	

Atopic disease	457 (66.7%)	912 (60.9%)	<0.001
Spinal bone density (T-Score)	−0.7 (1.4)	−0.7 (1.4)	0.912
Femoral neck bone density (T-Score)	−0.5 (1.1)	−0.4 (1.1)	0.446
FEV <sub>1</sub> (% predicted)	67.7 (22.0)	64.2 (20.8)	0.001
FVC (% predicted)	83.2 (20.0)	83.0 (19.5)	0.814
FEV <sub>1</sub> /FVC	65.0 (14.8)	62.7 (18.4)	0.007
Residual volume (% predicted)	120.7 (43.7)	136.3 (43.7)	<0.001
Total lung capacity (% predicted)	100.5 (17.6)	105.0 (19.1)	0.007
ACQ6 Score	3.0 (1.4)	2.9 (1.4)	0.060
Rescue steroids in last year	4 (2, 6)	4 (2, 7)	0.005
Hospital admissions for asthma in last year	0 (0, 2)	0 (0, 1)	0.190
Invasive ventilations (ever)	35 (7.2%)	158 (11.0%)	<0.001
Eczema	32 (4.9%)	30 (2.0%)	<0.001
Nasal polyps	80 (12.3%)	273 (18.2%)	<0.001
Gastro-oesophageal reflux	166 (25.4%)	198 (13.2%)	<0.001
Depression or anxiety	85 (13.0%)	93 (6.2%)	<0.001

**Table 3** Biologic population versus non-biologic population\*

	No biologic therapy (n=687)	Biologic therapy (n=1524)	P value
Blood eosinophil count (N/10 <sup>9</sup> L)	0.22 (0.10, 0.50)	0.40 (0.20, 0.68)	<0.001
Highest blood eosinophil count (N/10 <sup>9</sup> L)†	0.50 (0.30, 0.80)	0.72 (0.50, 1.10)	<0.001
FeNO (ppb)	31.0 (18.0, 61.0)	44.0 (24.0, 81.0)	<0.001
IgE (IU/mL)	294 (151, 485)	143 (47, 407)	<0.001
Maintenance oral steroids	145 (44.6%)	723 (65.0%)	<0.001
Maintenance oral steroid dose (mg)	10 (5, 15)	10 (8, 18)	0.054
Inhaled steroid dose (mcg, BDP equivalent)	2000 (1600, 2000)	2000 (1600, 2000)	0.029
LAMA	176 (55.0%)	589 (54.4%)	0.859
Theophylline	102 (31.4%)	289 (26.4%)	0.106

	No biologic therapy (n=687)	Biologic therapy (n=1524)	P value
Theophylline	177 (25.9%)	414 (27.7%)	0.015
SABA	644 (94.0%)	1434 (95.7%)	0.007
Leukotriene receptor antagonist	378 (56.2%)	662 (45.4%)	<0.001
Maintenance macrolide	64 (9.6%)	135 (9.3%)	0.077
Nebuliser	154 (22.7%)	377 (25.4%)	0.044
Prior anti-IgE therapy	0 (0.0%)	251 (16.8%)	<0.001

\*Mean (SD), median (IQR) or count (%) as appropriate.

†Highest blood count is the highest recorded in available prior medical records.

ACQ, Asthma Control Questionnaire; BMI, body mass index; FeNO, fractional exhaled nitric oxide; LAMA, long-acting antimuscarinic antagonist; SABA, short acting  $\beta$ 2-agonist.

Received: 11 April 2022

Revised: 5 July 2022


Accepted: 15 August 2022

DOI: 10.1111/cea.14222

ORIGINAL ARTICLE

WILEY

# Biologic therapy practices in severe asthma; outcomes from the UK Severe Asthma Registry and survey of specialist opinion

Adel H. Mansur<sup>1</sup>  | Sherif Gonem<sup>2</sup> | Thomas Brown<sup>3</sup> | Hassan Burhan<sup>4</sup> |  
Rekha Chaudhuri<sup>5</sup> | James W. Dodd<sup>6</sup> | Thomas Pantin<sup>7</sup> | Robin Gore<sup>8</sup> |  
David Jackson<sup>9,10</sup> | Andrew Menzies-Gow<sup>11</sup> | Mitesh Patel<sup>12</sup> | Ian Pavord<sup>13</sup> |  
Paul Pfeffer<sup>14,15</sup> | Salman Siddiqui<sup>16,17</sup> | John Busby<sup>18</sup> | Liam G. Heaney<sup>19</sup> |  
on behalf of UK Severe Asthma Registry

# Criteria used to select first biologic

FIGURE 3 Comparisons of biologic therapy responses of individual severe asthma centres

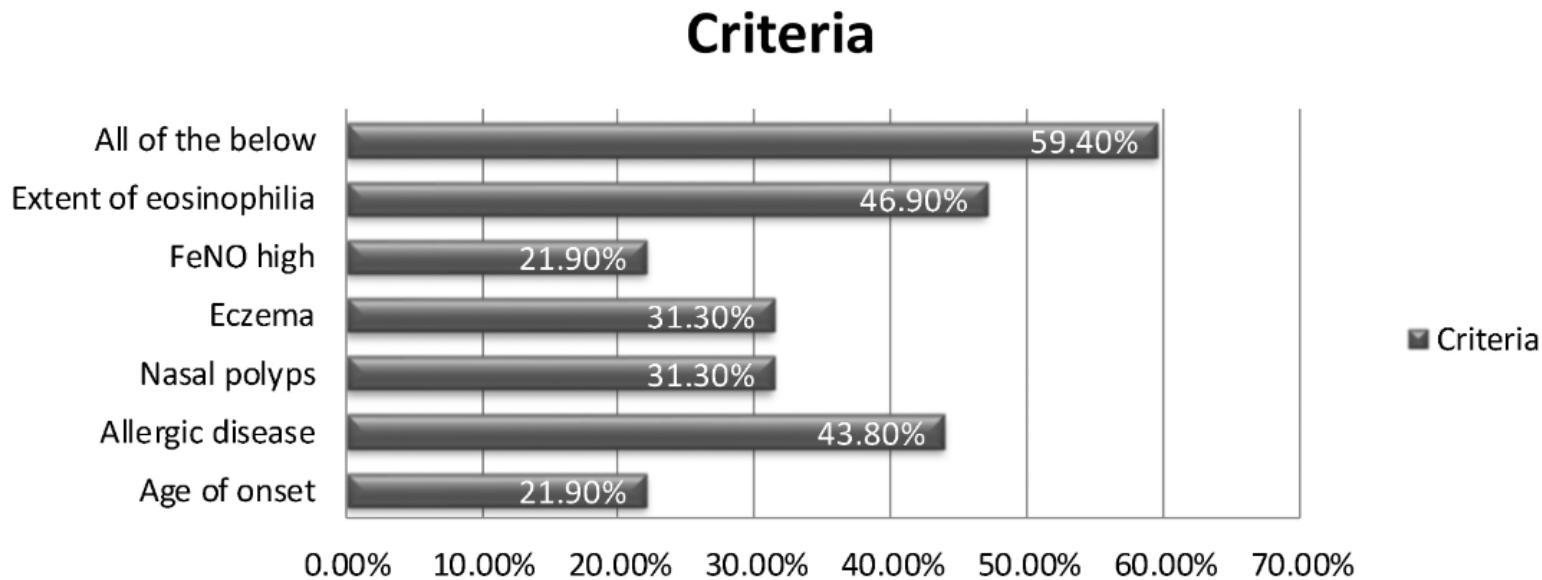
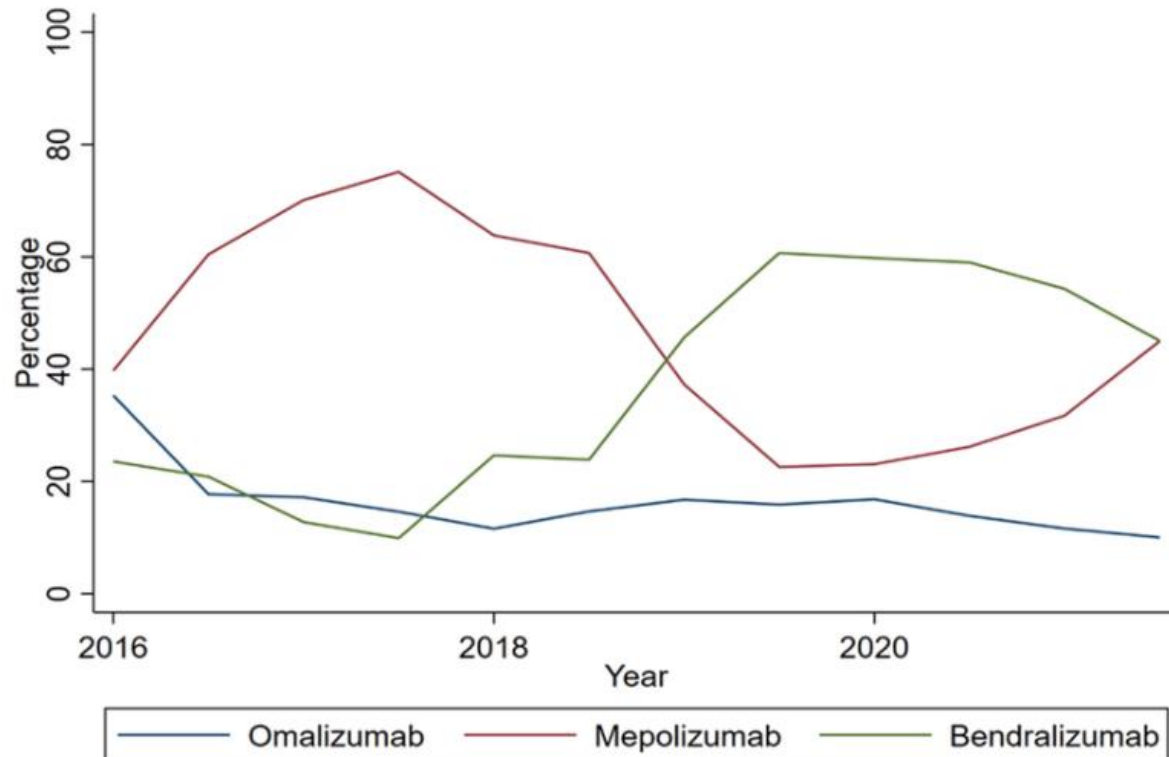


FIGURE 4 Specialists' survey responses on the clinical criteria used to select the first-choice biologic (32 responses from 39 surveyed)

# Prescription trends of biologics



\*Restricted to sites with at least 10 biologic patients, at least 10 in each quarter shown

## Continuation of treatment after one year

- Benralizumab - 94%
- Mepolizumab - 80%
- Omalizumab - 70%

**TABLE 4** Clinical and demographic features in patients who *continued* biologic therapy by treatment at clinical follow-up – 6 patients on reslizumab and dupilumab are not displayed

	Entire cohort	Omalizumab	Mepolizumab	Benralizumab	p-Value
ACQ6 Score	-0.8 (-1.8, -0.2)	-1.0 (-1.8, -0.3)	-0.8 (-1.7, 0.0)	-1.0 (-2.3, -0.2)	.050
Maintenance OCS (mg)	-5 (-7, 0)	-2 (-5, 0)	-5 (-7, 0)	-4 (-7, 0)	.059
OCS change					
Discontinue	99 (24.9%)	4 (12.5%)	72 (24.4%)	23 (32.9%)	.023
Decrease dose	211 (53.1%)	15 (46.9%)	165 (55.9%)	31 (44.3%)	
Maintain/increase dose	87 (21.9%)	13 (40.6%)	58 (19.7%)	16 (22.9%)	

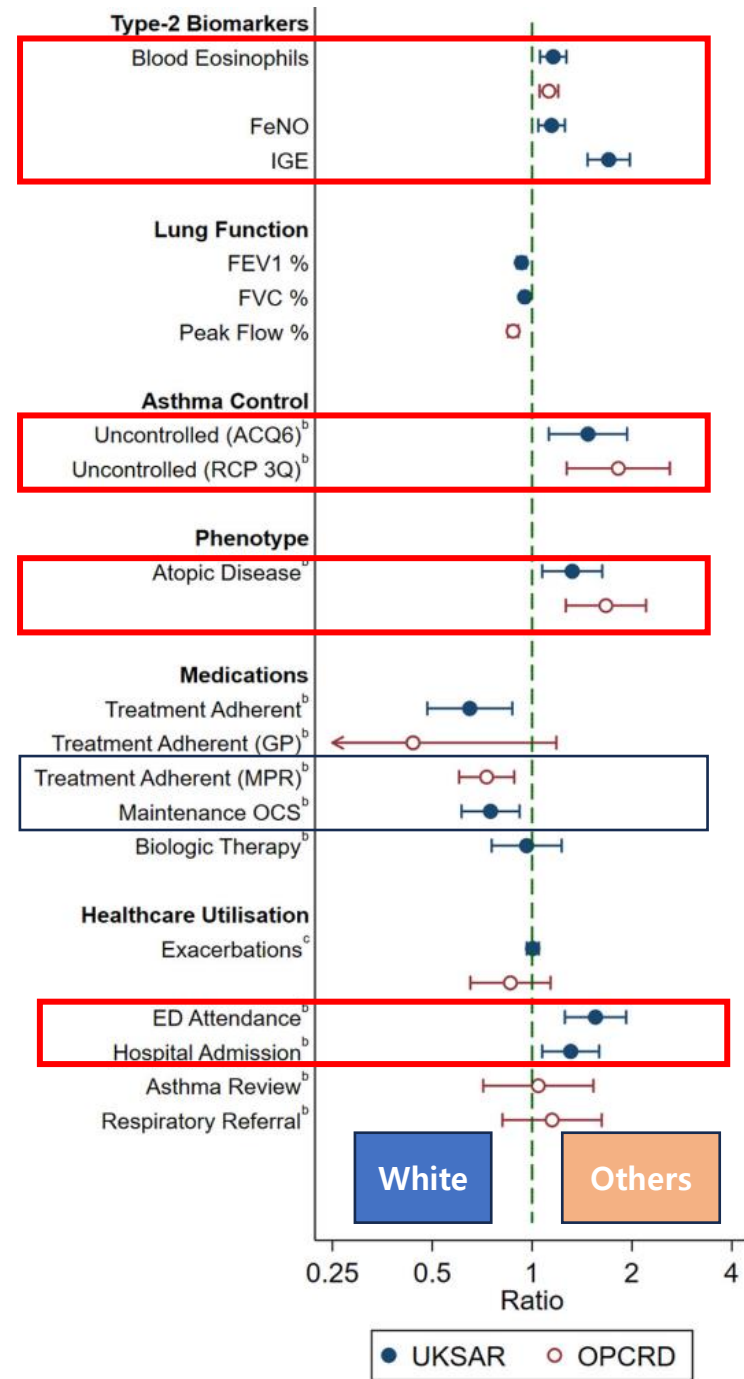
Note: Data depicted as number (%), median IQR or mean SD as appropriate.

Abbreviations: ACQ6, asthma control questionnaire-6 'comprised of 6 items with score range from 0-6 and score  $\leq 1.5$  is indicative of good control',

# Ethnic Differences in Severe Asthma Clinical Care and Outcomes: An Analysis of United Kingdom Primary and Specialist Care

John Busby, PhD<sup>a</sup>, Liam G. Heaney, MRCP, MD<sup>a,b</sup>, Thomas Brown, FRCP<sup>c</sup>, Rekha Chaudhuri, MD<sup>d</sup>, Paddy Dennison, MRCP, PhD<sup>e</sup>, Robin Gore, MD, PhD<sup>f</sup>, David J. Jackson, FRCP, PhD<sup>g,h</sup>, Adel H. Mansur, FRCP, PhD<sup>i</sup>, Andrew Menzies-Gow, FRCP, PhD<sup>j</sup>, Simon Message, FRCP<sup>k</sup>, Rob Niven, FRCP, MD<sup>l</sup>, Mitesh Patel, MRCP, PhD<sup>m</sup>, David Price, FRCGP<sup>n,o</sup>, Salman Siddiqui, FRCP, PhD<sup>p</sup>, Robert Stone, FRCP, PhD<sup>q</sup>, and Paul E. Pfeffer, MRCP, PhD<sup>r,s</sup>, on behalf of the UK Severe Asthma Registry *Aberdeen, Belfast, Birmingham, Cambridge, Glasgow, Gloucester, Leicester, London, Plymouth, Portsmouth, Somerset, and Southampton, United Kingdom; and Singapore*

- UKSAR + OPCRD (Optimum Patient Care Research Database)
- A total of 3,637 patients
- Analysis according to **race/ethnicity**



# Contents

- Global severe asthma registry
- **National severe asthma registry**
  - UKSAR
  - **SANI (Italy)**
- International severe asthma registry

**SANI – “phenotyping”**

Original Article

---

# The Severe Asthma Network in Italy: Findings and Perspectives

---



Enrico Heffler, MD, PhD<sup>a,b</sup>, Francesco Blasi, MD, PhD<sup>c,d</sup>, Manuela Latorre, MD<sup>e</sup>, Francesco Menzella, MD<sup>f</sup>, Pierluigi Paggiaro, MD<sup>e</sup>, Girolamo Pelaia, MD<sup>g</sup>, Gianenrico Senna, MD<sup>h</sup>, and Giorgio Walter Canonica, MD<sup>a,b</sup>; on behalf of the SANI Network\* *Milan, Pisa, Reggio Emilia, Catanzaro, Verona, Italy*

**TABLE I.** Demographic and clinical characteristics of 437 patients with SA

Parameter	Value
Age (y), mean $\pm$ SD	54.1 $\pm$ 13.7
Sex, females (%)	250 (57.2%)
Atopics, n (%)	309 (70.7%)
Sensitized to perennial allergens, n (%)	272 (62.2%)
Active smokers, n (%)	12 (2.7%)
Past smokers, n (%)	88 (20.1%)
BMI, mean $\pm$ SD	26.2 $\pm$ 5.0
BMI classes, n (%)	
<18.5	7 (1.6%)
18.5-24.9	190 (43.5%)
25-29.9	153 (35.0%)
$\geq$ 30	87 (19.9%)
Age of onset (y), mean $\pm$ SD	32.4 $\pm$ 17.1
Late onset,* n (%)	167 (38.2%)
Exacerbations/y, mean $\pm$ SD	3.75 $\pm$ 7.2
Exacerbations in the last 12 mo	
0	76 (17.4%)
1	49 (11.2%)
2	99 (22.7%)
>2	213 (48.7%)
Emergency dept/y, mean $\pm$ SD	0.49 $\pm$ 0.97
Hospitalizations/y, mean $\pm$ SD	0.25 $\pm$ 0.70
Intubation or mechanical ventilation/y, mean $\pm$ SD	0.06 $\pm$ 0.39

BMI, Body mass index; SA, severe asthma; SD, standard deviation.

\*Late onset is defined as age of diagnosis >40 y.

**TABLE II.** Comorbidities of 437 patients with SA

Comorbidity	
Atopics, n (%)	309 (70.7%)
Sensitized to perennial allergens, n (%)	272 (62.2%)
Any kind of rhinitis, n (%)	298 (68.2%)
Allergic rhinitis, n (%)	195 (44.6)
Food allergy, n (%)	38 (8.7%)
CRSwNP, n (%)	186 (42.6%)
Atopic eczema, n (%)	42 (9.6%)
Bronchiectasis, n (%)	70 (16.0%)

CRSwNP, Chronic rhinosinusitis with nasal polyps; SA, severe asthma.

**TABLE III.** Functional and biological features of patients with SA

<b>Parameter</b>	
ACT, mean $\pm$ SD	17.2 $\pm$ 5.4
ACT classes	
<20	158 (36.2%)
20-24	86 (19.6%)
25	193 (44.2%)
Exhaled nitric oxide (FeNO) (ppb), mean $\pm$ SD	48.0 $\pm$ 46.3
Distribution of patients according to FeNO	
$\leq$ 25 ppb	40.9%
25-40 ppb	18.2%
>40 ppb	40.9%
FEV <sub>1</sub> % predicted, mean $\pm$ SD	71.4 $\pm$ 20.2
FVC % predicted, mean $\pm$ SD	85.7 $\pm$ 21.1
FEV <sub>1</sub> /FVC, mean $\pm$ SD	65.3 $\pm$ 14.2
Blood eosinophils (mm <sup>3</sup> ), mean $\pm$ SD	536.7 $\pm$ 650.9
Distribution of patients according to blood eosinophils	
$\leq$ 150/mm <sup>3</sup>	20.2%
>150/mm <sup>3</sup>	79.8%
>300/mm <sup>3</sup>	58.8%
Total IgE (kU/L), mean $\pm$ SD	470.3 $\pm$ 812.9

ACT, Asthma control test; FeNO, fractional exhaled nitric oxide; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; SA, severe asthma; SD, standard deviation.

**TABLE IV.** Concomitant treatments

Patients chronically taking OCS, n (%)	280 (64.1%)
Mean OCS dose (prednisone equivalents) (mg) $\pm$ SD	10.7 $\pm$ 8.3
Patients taking LTRA, n (%)	203 (46.4%)
Patients taking LAMA, n (%)	156 (35.7%)
Patients taking omalizumab, n (%)	249 (57.0%)
Patients taking mepolizumab, n (%)	49 (11.2%)



Contents lists available at [ScienceDirect](#)

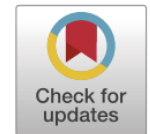
## Respiratory Medicine

journal homepage: <http://www.elsevier.com/locate/rmed>

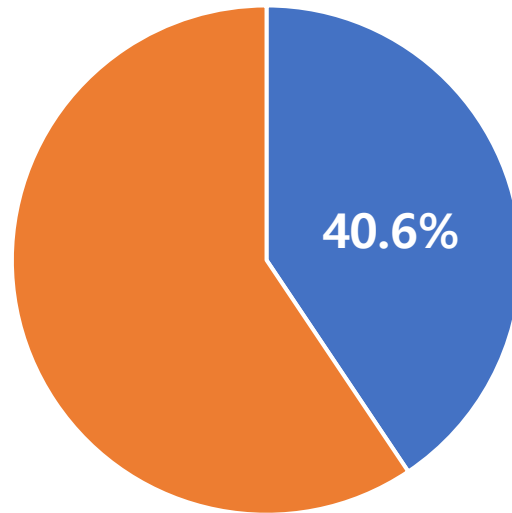


# Chronic rhinosinusitis with nasal polyps impact in severe asthma patients: Evidences from the Severe Asthma Network Italy (SANI) registry

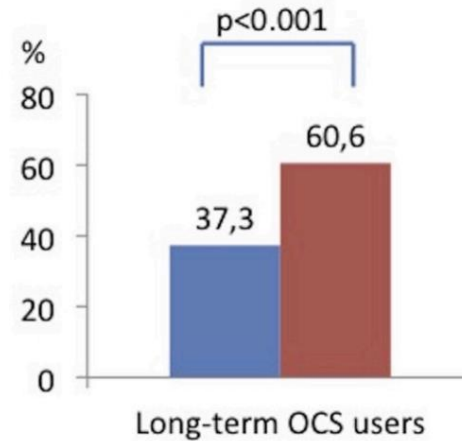
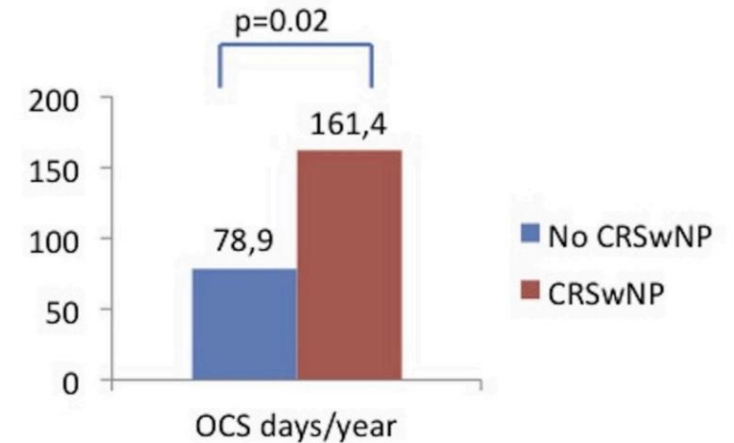
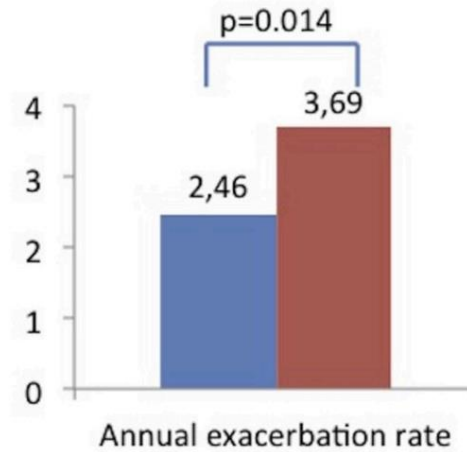
Giorgio Walter Canonica<sup>a,b,\*</sup>, Luca Malvezzi<sup>c</sup>, Francesco Blasi<sup>d</sup>, Pierluigi Paggiaro<sup>e</sup>,  
Marco Mantero<sup>d</sup>, Gianenrico Senna<sup>f</sup>, Enrico Heffler<sup>a,b</sup>, on behalf Severe Asthma Network Italy  
(SANI)



# Severe asthma with CRSwNP







■ CRSwNP ■ No CRSwNP



Original Article



# Sex Differences in Severe Asthma: Results From Severe Asthma Network in Italy-SANI

Gianenrico Senna <sup>1</sup> Manuela Latorre <sup>2</sup> Massimo Bugiani <sup>3</sup> Marco Caminati <sup>1</sup>  
Enrico Heffler <sup>4,5</sup> Daniela Morrone,<sup>4</sup> Giovanni Paoletti <sup>4,5</sup> Paola Parronchi <sup>6</sup>  
Francesca Puggioni <sup>4,5</sup> Francesco Blasi <sup>7,8</sup> Giorgio Walter Canonica <sup>4,5</sup>  
Pierluigi Paggiaro <sup>2\*</sup> and on behalf of SANI Network

**Table 1.** Main clinical features of severe asthmatics according to sex

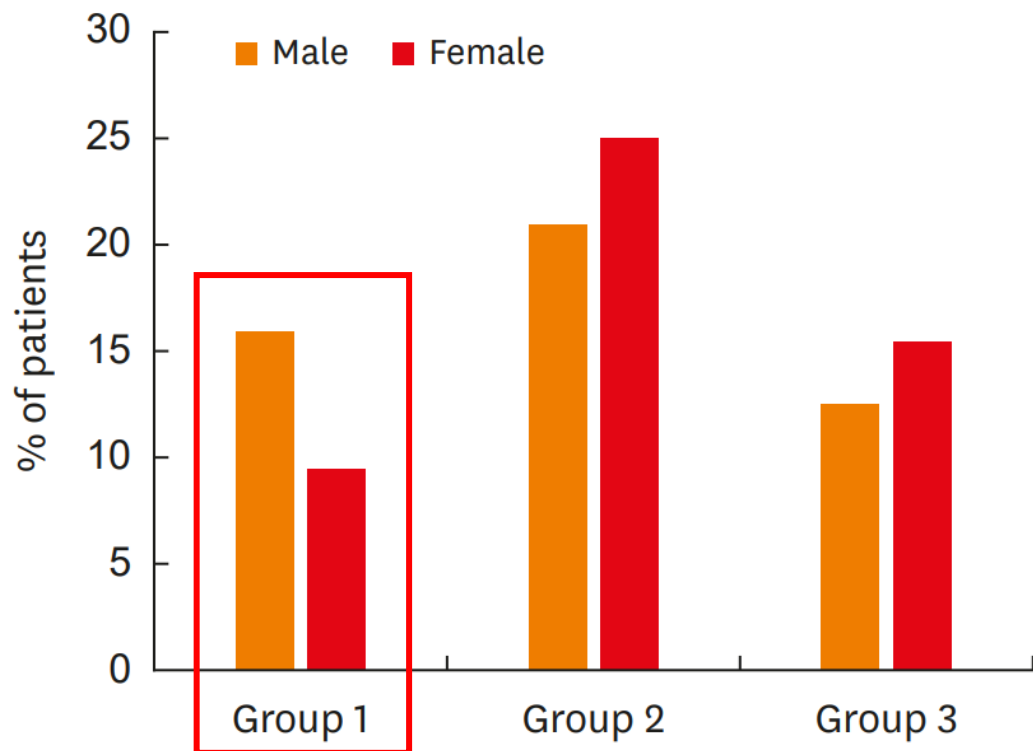
	Male	Female	P value
No.	433 (38.2)	690 (61.8)	
Mean age (yr)	56.1 ± 13.1	55.6 ± 13.2	NS
Age of asthma onset (yr)	35.1 ± 16.8	33.4 ± 16.7	NS
Onset of asthma			
Early onset	12.9	13.9	
Intermediate onset	47.2	52.7	
Late onset	39.9	33.4	NS
Smoking habits			
Non smokers	69.1	76.2	
Ex-smokers	27.3	20.4	
Current smokers	3.6	3.4	< 0.004
BMI			
< 25	45.0	47.9	
25–30	42.3	30.0	
> 30	12.8	22.1	< 0.0001
Comorbidities			
Bronchiectasis (conf + susp)	16.9	15.1	NS
GERD (conf + susp)	28.5	39.9	< 0.002
Polyposis (conf + susp)	47.5	41.5	< 0.05
Rhinitis (prev + curr)	64.3	61.6	NS
Atopy (by SPT)	69.2	67.7	NS
Treatment			
ICS-LABA	95.5	93.7	NS
Mean ICS dose			
LAMA	35.3	36.9	NS
Montelukast	60.9	64.6	NS
OCS (regular or frequent courses)	42.2	41.1	NS

**Table 2.** Asthma control, PB-FEV1 and biomarkers in severe asthmatics according to sex

	Male	Female	P value
ACT (median [IQR])	19 (8)	18 (8)	NS
ACQ (median [IQR])	2.3 (2.3)	2.4 (2.2)	NS
Severe exacerbations (No./yr, mean)	2.3 (3.3)	2.5 (3.6)	NS
ED attendancy (No./yr, mean)	0.32 (1.4)	0.3 (0.8)	NS
Hospitalization (No./yr, mean)	0.17 (.61)	0.22 (.61)	0.07
PB-FEV1 (L, mean)	2.54 (0.87)	1.83 (0.66)	0.005
PB-FEV1 (%pred)	72.4 (21)	76.0 (23)	NS
Blood eosinophils (median [IQR])	360 (510)	300 (490)	NS
Blood eosinophils	6.06	5.69	NS
Blood eosinophils > 150/ $\mu$ L	74.3	66.0	< 0.002
Blood eosinophils > 300/ $\mu$ L	56.3	49.8	NS
Blood eosinophils > 400/ $\mu$ L	41.5	40.9	NS
FeNO	49.9 $\pm$ 44.5	40.3 $\pm$ 38.7	0.001
FeNO > 25 ppb	62.8	53.9	0.05
FeNO > 50 ppb	35.1	27.9	< 0.005
Serum IgE (median [IQR])	508 (686)	352 (503)	0.02
Serum IgE > 150 U/ $\mu$ L	67.3	56.1	0.006
Serum IgE > 700 U/ $\mu$ L	22.05	12.96	< 0.005

Data are shown as mean  $\pm$  standard deviation or number (%).

ACT, asthma control test; ACQ, asthma control questionnaire; IQR, interquartile range; ED, emergency department; PB-FEV1, pre-bronchodilator forced expiratory volume in the first second; FeNO, fractional exhaled nitric oxide; IgE, immunoglobulin E; NS, not significant.



- Group I IgE > 150 Eosinophils > 300
- Group II IgE < 150 Eosinophils > 300
- Group III IgE > 150 Eosinophils < 300

**Table 3.** Multivariate analysis for type 2 endotype (defined as criterion No.1: IgE > 150 and/or BE > 300 and/or FeNO > 25) in severe asthmatic patients

Variable	OR	95% CI	P value
Sex (male vs. female)	1.28	0.96–1.69	0.087
BMI (< 25 vs. ≥ 25)	1.82	1.37–2.42	0.001
Age (yr)			
41–60 vs. < 40	1.23	0.81–1.89	0.329
> 60 vs. < 40	1.69	1.08–2.65	0.022
Age of onset (vs. early < 12)			
Intermediate (12–40)	1.39	0.91–2.10	0.122
Late (> 40)	1.89	1.17–3.04	0.009
(trend)			0.008

IgE, immunoglobulin E; BE, blood eosinophils; FeNO, fractional exhaled nitric oxide; OR, odds ratio; CI, confidence interval; BMI, body mass index.

# Contents

- Global severe asthma registry
- **National severe asthma registry**
  - UKSAR
  - SANI
  - **COBRA (France)**
- International severe asthma registry

**COBRA**

# Characteristics of patients with severe, uncontrolled, eosinophilic asthma enrolled in a French cohort

Eligibility for benralizumab

This article was published in the following Dove Press journal:  
Journal of Asthma and Allergy

Michel Aubier<sup>1-4</sup>

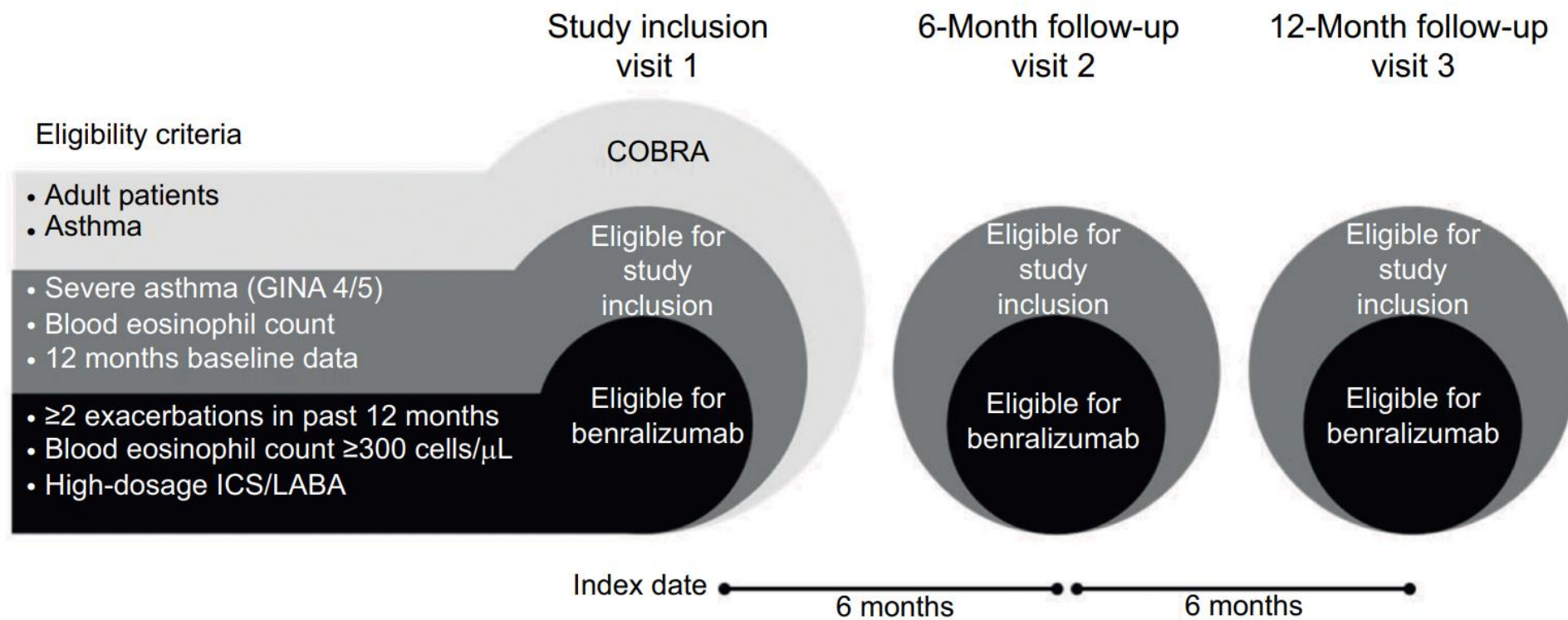
Gabriel Thabut<sup>1-3,5</sup>

Caroline Fabry-Vendrand<sup>6</sup>

**Background and objective:** Benralizumab (Fasenra™) has recently been approved as add-on maintenance treatment for adult patients with severe eosinophilic asthma inadequately controlled despite high-dosage inhaled corticosteroids plus long-acting  $\beta_2$ -agonists. We aimed to identify

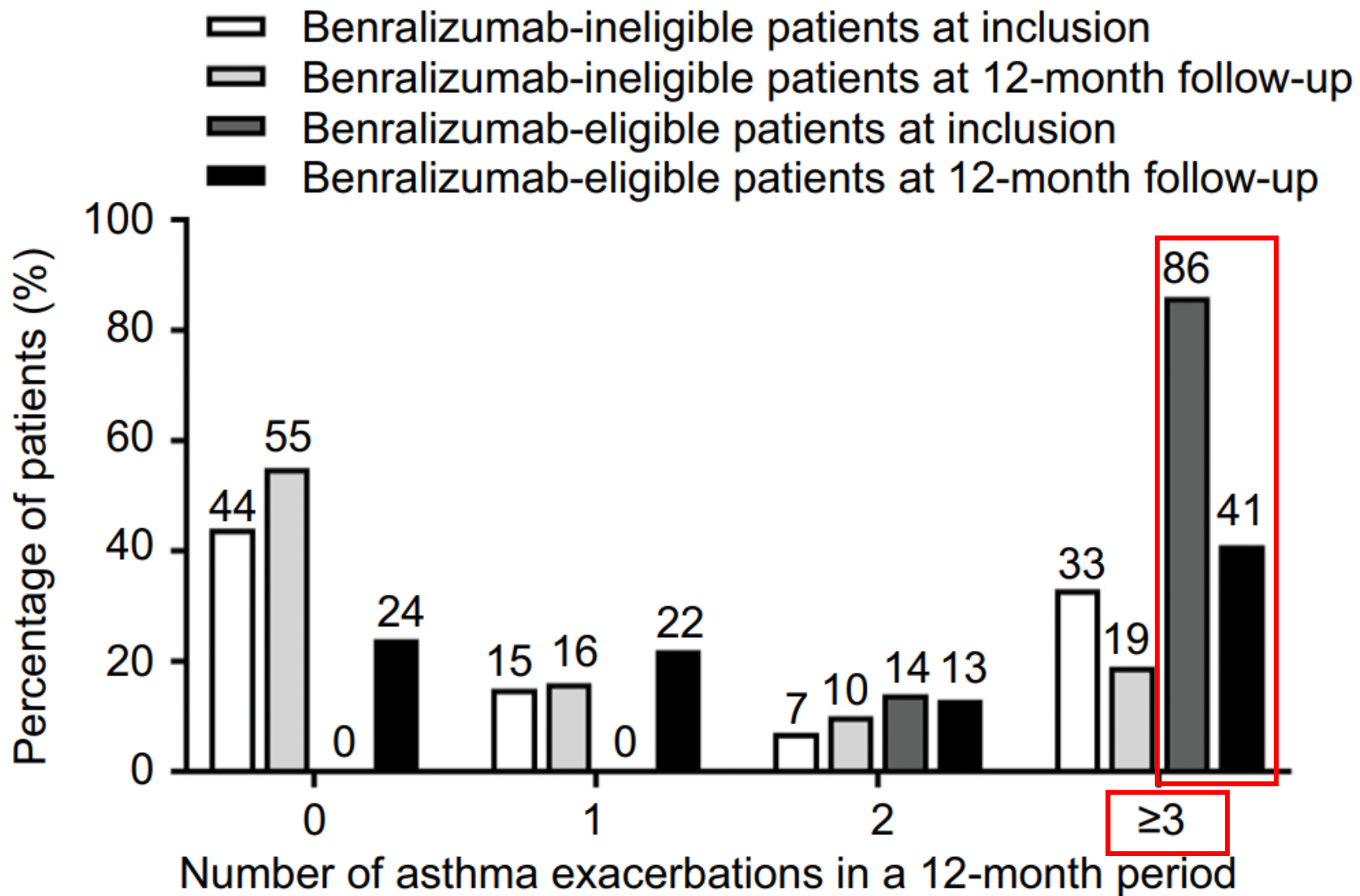
## Acknowledgments

Editorial support was provided by Francis J Golder, BVSc, PhD, of JK Associates, Inc., and Michael A Nissen, ELS, of AstraZeneca. This study was funded by AstraZeneca.



**Figure 1** Eligibility criteria and study design.

**Abbreviations:** COBRA, Asthma and Bronchial Obstruction Cohort; GINA, Global Initiative for Asthma; ICS, inhaled corticosteroids; LABA, long-acting  $\beta_2$ -agonists.



# **Type 2-high asthma is associated with a specific indoor mycobiome and microbiome**

---



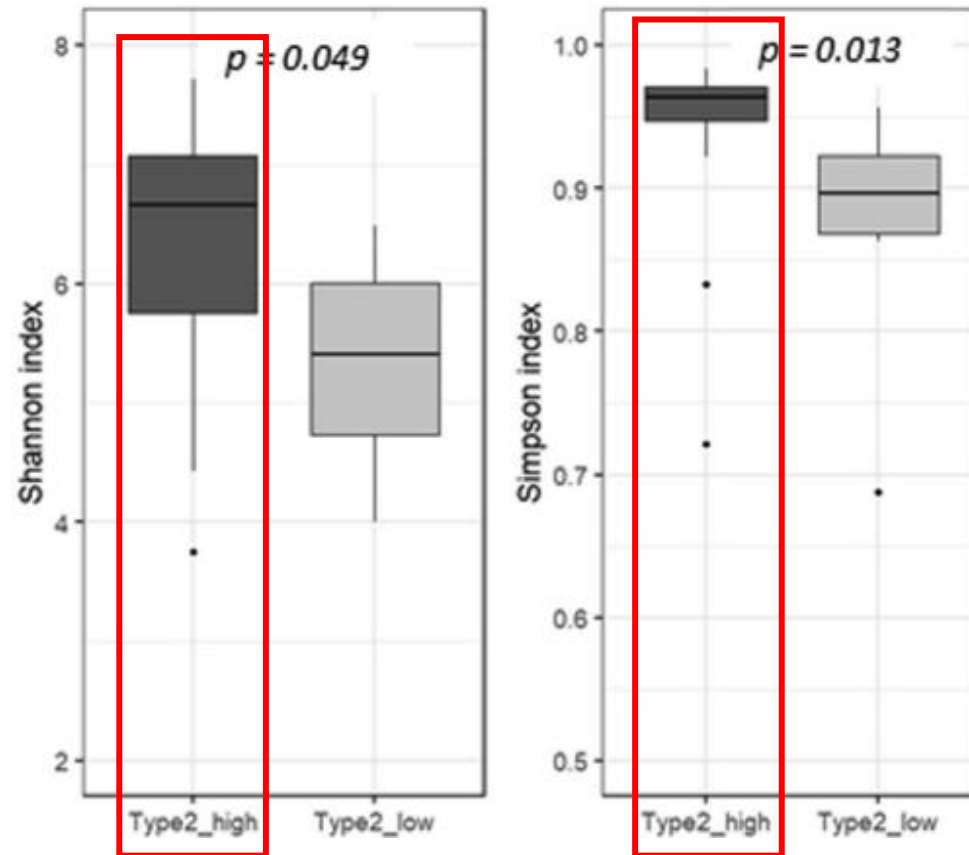
Louise-Eva Vandenberght, PhD,<sup>a,b,c</sup> Raphaël Enaud, MD,<sup>a,b,d</sup> Charlotte Urien, PhD,<sup>c</sup> Noémie Coron, MD,<sup>d</sup>  
Pierre-Olivier Girodet, MD, PhD,<sup>a,b,d</sup> Stéphanie Ferreira, PhD,<sup>c</sup> Patrick Berger, MD, PhD,<sup>a,b,d</sup> and  
Laurence Delhaes, MD, PhD<sup>a,b,d</sup> *Bordeaux, Lille, and Pessac, France*



Dust  
samples

# Bacterial diversity in dust correlates with T2 phenotype

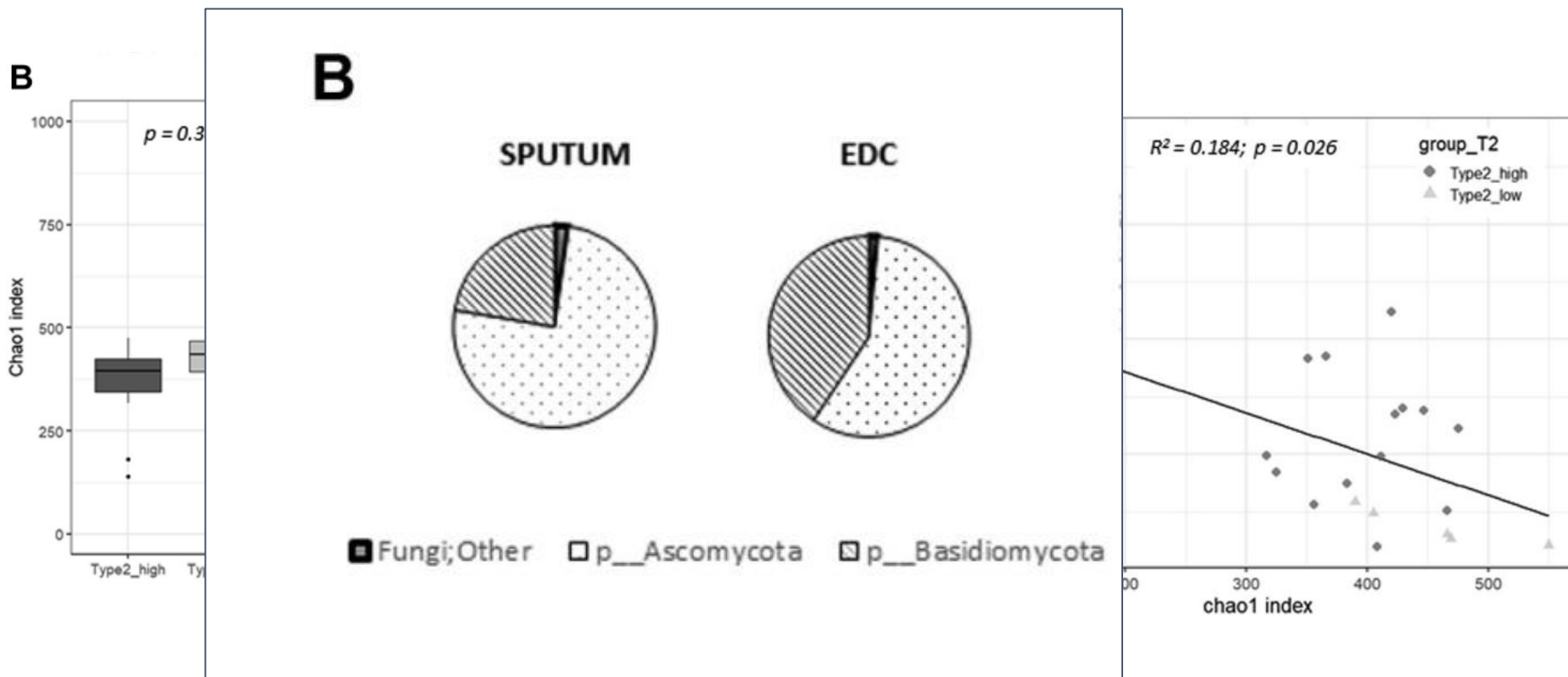
Bacteria



Dust samples

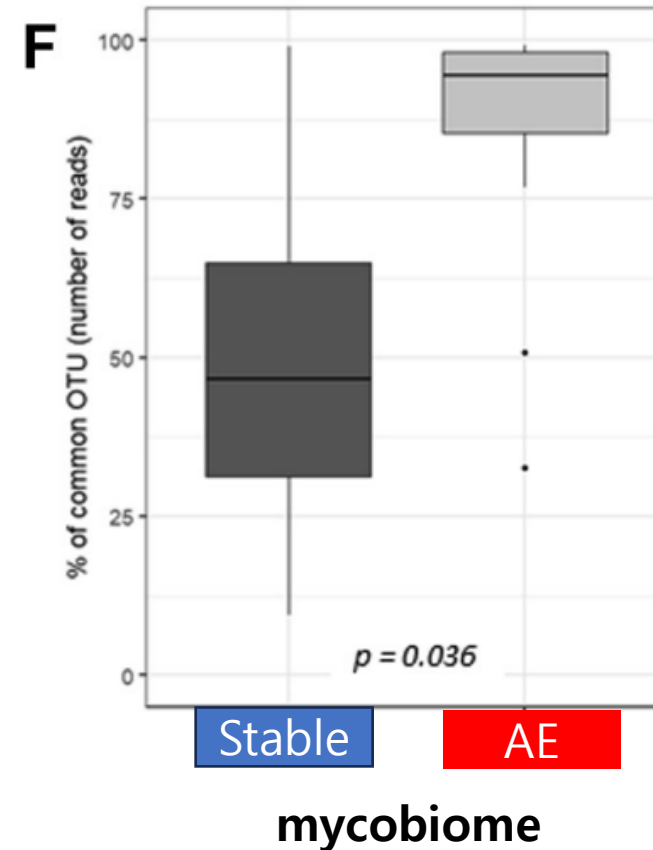
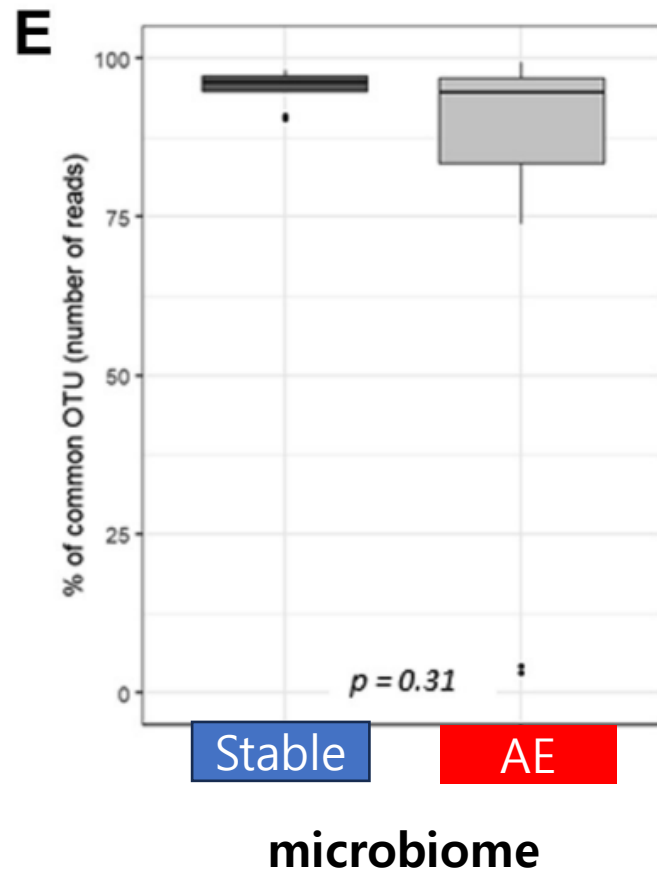
# Fungal diversity in dust inversely correlates with T2 phenotype

Fungi



# AE status & common micro- and mycobiome in sputum vs. dust

Common  
taxa  
(sputum  
and dust)



# Contents

- Global severe asthma registry
- **National severe asthma registry**
  - UKSAR
  - SANI
  - COBRA
  - **GAN (Germany)**
- International severe asthma registry

**GAN**

## Response to Biologics and Clinical Remission in the Adult German Asthma Net Severe Asthma Registry Cohort

---

Katrin Milger, MD<sup>a,b</sup>, Hendrik Suhling, MD<sup>c</sup>, Dirk Skowasch, MD<sup>d</sup>, Annette Holtdirk, MA<sup>e</sup>, Nikolaus Kneidinger, MD, PhD<sup>a,b</sup>, Jürgen Behr, MD<sup>a,b</sup>, Hartmut Timmermann, MD<sup>f</sup>, Christian Schulz, MD<sup>g</sup>, Olaf Schmidt, MD<sup>h</sup>, Rainer Ehmann, MD<sup>i</sup>, Eckard Hamelmann, MD<sup>j</sup>, Marco Idzko, MD<sup>k</sup>, Christian Taube, MD<sup>l</sup>, Marek Lommatzsch, MD<sup>m</sup>, Roland Buhl, MD<sup>n</sup>, and Stephanie Korn, MD<sup>o,p</sup> *Munich, Hannover, Bonn, Hamm, Hamburg, Regensburg, Koblenz, Stuttgart, Bielefeld, Essen, Rosstock, Mainz, and Heidelberg, Germany; and Vienna, Austria*

**What is already known about this topic?** Clinical remission on treatment, defined as more than 1 year of good symptom control in the absence of exacerbations and oral corticosteroid therapy, has recently been proposed as a possible treatment goal even in severe asthma.

**What does this article add to our knowledge?** It provides first real-life data from a severe asthma cohort, showing a remission rate of one-third after start of a biologic. Patients treated without a biologic had lower remission rates despite less severe disease at baseline.

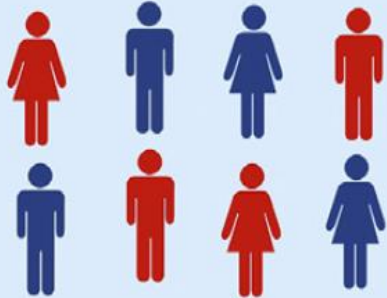
**How does this study impact current management guidelines?** Clinical remission can be achieved in a proportion of patients with severe asthma, and the concept might help improve outcomes in the future; biologics are an important factor for achieving remission.

### Clinical remission

- 1) absence of significant symptoms (ACT  $\geq$  20) &
- 2) Absence of exacerbations &
- 3) Absence of oral corticosteroid therapy

## Severe Asthma Registry

 German Asthma Net (GAN)



Adult Cohort

## Patient groups

Group A (n=233)



Baseline Visit V0:  
No biologic

Group B (n=210)



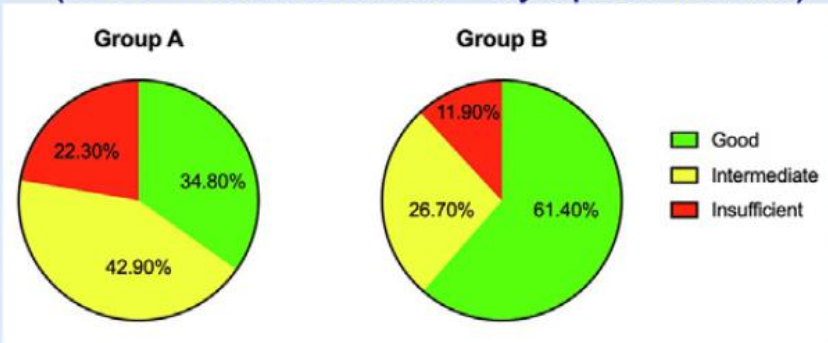
Treated without biologic

Treated with biologic

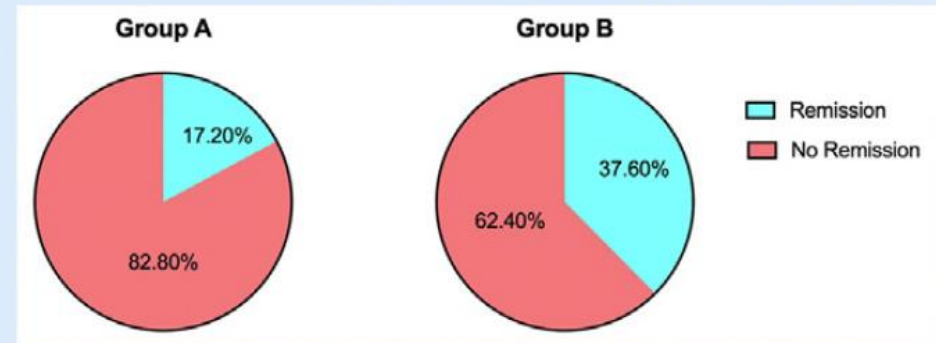


1-year Visit V1:  
Outcomes

Response Biologic Asthma Response Score  
(OCS + exacerbations + symptom control)



Clinical Remission under therapy  
(No OCS + no exacerbations + good symptom control)



1-year Outcomes: Response and Clinical Remission

# Contents

- Global severe asthma registry
- **National severe asthma registry**
  - UKSAR
  - SANI
  - COBRA
  - GAN
  - **SARP (North America)**
- International severe asthma registry

**SARP**

## Original Article

---

# Baseline Features of the Severe Asthma Research Program (SARP III) Cohort: Differences with Age

---



W. Gerald Teague, MD<sup>a</sup>, Brenda R. Phillips, MS<sup>b</sup>, John V. Fahy, MD, MSc<sup>c</sup>, Sally E. Wenzel, MD<sup>d</sup>, Anne M. Fitzpatrick, PhD<sup>e</sup>, Wendy C. Moore, MD<sup>f</sup>, Annette T. Hastie, PhD<sup>f</sup>, Eugene R. Bleecker, MD<sup>f</sup>, Deborah A. Meyers, PhD<sup>f</sup>, Stephen P. Peters, MD, PhD<sup>f</sup>, Mario Castro, MD, MPH<sup>g</sup>, Andrea M. Coverstone, MD<sup>g</sup>, Leonard B. Bacharier, MD<sup>g</sup>, Ngoc P. Ly, MD, MPH<sup>c</sup>, Michael C. Peters, MD<sup>c</sup>, Loren C. Denlinger, MD<sup>h</sup>, Sima Ramratnam, MD<sup>h</sup>, Ronald L. Sorkness, PhD<sup>h</sup>, Benjamin M. Gaston, MD<sup>i</sup>, Serpil C. Erzurum, MD<sup>j</sup>, Suzy A.A. Comhair, PhD<sup>j</sup>, Ross E. Myers, MD<sup>i</sup>, Joe Zein, MD<sup>j</sup>, Mark D. DeBoer, MD<sup>a</sup>, Anne-Marie Irani, MD<sup>k</sup>, Elliot Israel, MD<sup>l</sup>, Bruce Levy, MD<sup>l</sup>, Juan Carlos Cardet, MD<sup>l</sup>, Wanda Phipatanakul, MD, MS<sup>l</sup>, Jonathan M. Gaffin, MD, MMsc<sup>l</sup>, Fernando Holguin, MD, MPH<sup>d</sup>, Merritt L. Fajt, MD<sup>d</sup>, Shean J. Aujla, MD<sup>d</sup>, David T. Mauger, PhD<sup>b</sup>, and Nizar N. Jarjour, MD<sup>h</sup> *Charlottesville and Richmond, Va; Hershey and Pittsburgh, Pa; San Francisco, Calif; Atlanta, Ga; Winston-Salem, NC; St. Louis, Mo; Madison, Wis; Cleveland, Ohio; and Boston, Mass*

# NIH/NHLBI Severe Asthma Research Program (SARP)

7 Partnerships/14 Enrollment Sites + Data Coordinating Center  
1028 potential enrollees screened by telephone

808 criteria met

948 airway physiology tested

140 did not meet criteria

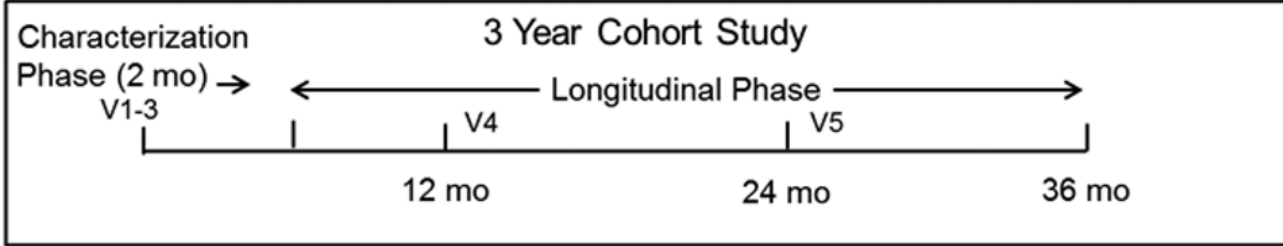
94 eligible but not enrolled:  
- 37 declined participation  
- 1 death pre-enrollment  
- 26 lost to follow up  
- 29 other reasons  
- 1 re-classified

714 enrolled:  
- 451  $\geq$  12% albuterol response  
- 250  $PC_{20} < 16$  mg/ml  
- 13 confirmed by PI

526 adults

188 children

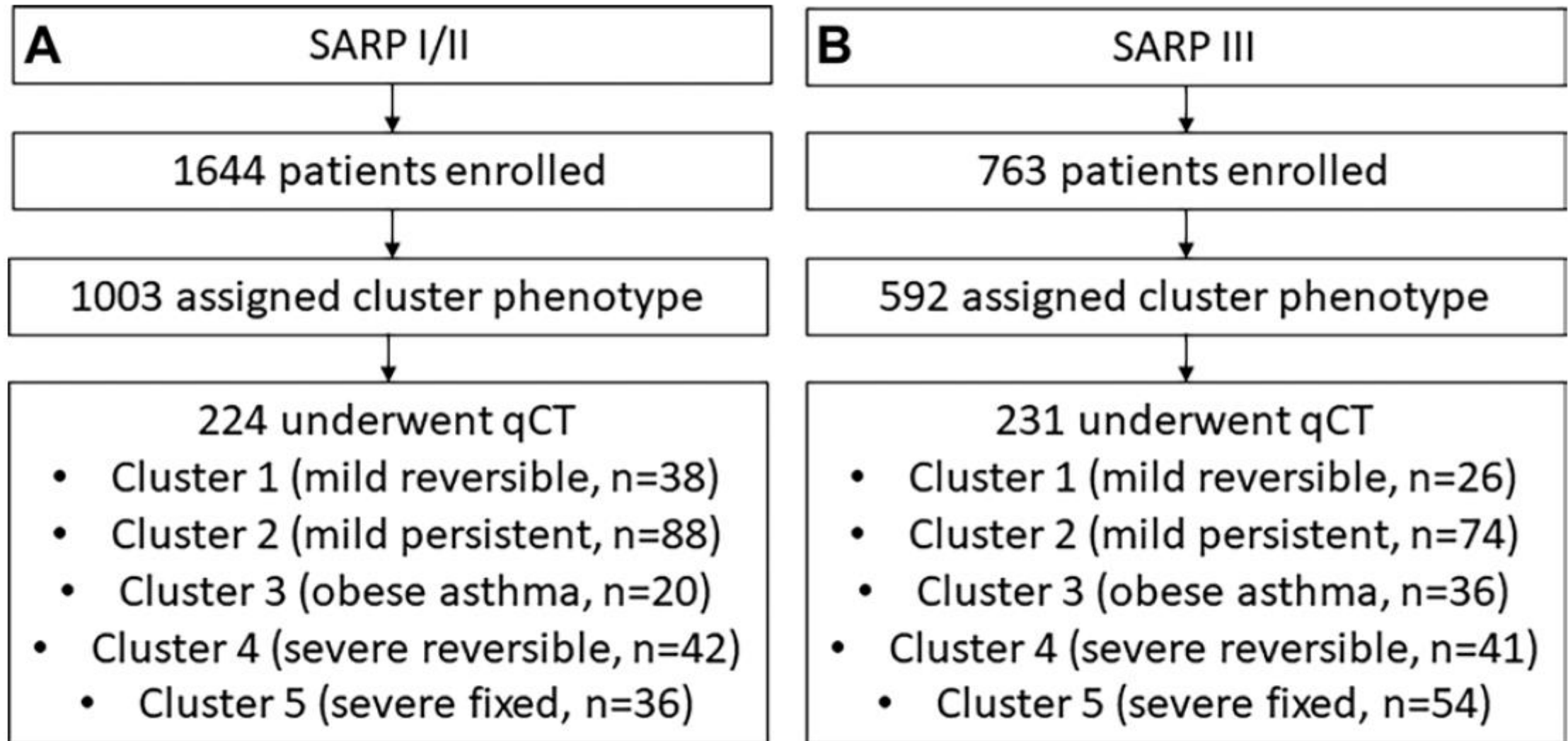
- Baseline characterization procedures:
- Anthropometrics/Questionnaires
  - Maximum bronchodilator testing
  - Allergen-specific IgE and blood eos
  - Sputum, blood, exhaled biomarkers (FeNO)



## Quantitative CT Characteristics of Cluster Phenotypes in the Severe Asthma Research Program Cohorts

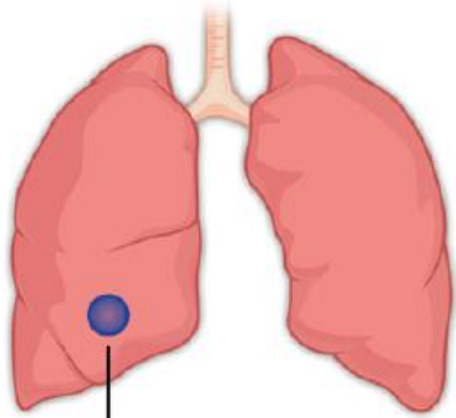
*Abhaya P. Trivedi, MD • Chase Hall, MD • Charles W. Goss, PhD • Daphne Lew, MPH • James G. Krings, MD • Mary Clare McGregor, MD • Maanasi Samant, MD • Jered P. Sieren, BS • Huashi Li, MS • Ken B. Schechtman, PhD • Joshua Schirm, BS • Stephen McEleney, BS • Sam Peterson, MS • Wendy C. Moore, MD • Eugene R. Bleecker, MD • Deborah A. Meyers, PhD • Elliot Israel, MD • George R. Washko, MD • Bruce D. Levy, MD • Joseph K. Leader, PhD • Sally E. Wenzel, MD • John V. Fahy, MD, MSc • Mark L. Schiebler, MD • Sean B. Fain, PhD • Nizar N. Jarjour, MD • David T. Mauger, PhD • Joseph M. Reinhardt, PhD • John D. Newell, Jr, MD • Eric A. Hoffman, PhD • Mario Castro, MD • Ajay Sheshadri, MD • for the NHLBI Severe Asthma Research Program (SARP)<sup>1</sup>*

From the Division of Pulmonary, Critical Care, and Sleep Medicine, Rush University Medical Center, Chicago, Ill (A.P.T.); Division of Pulmonary and Critical Care Medicine, University of Kansas School of Medicine, Kansas City, KS 66103-2937 (C.H., M.C.); Division of Biostatistics (C.W.G., D.L., K.B.S.), Division of Pulmonary and Critical Care Medicine (J.G.K., M.C.M., M.S.), Washington University School of Medicine, St Louis, Mo; Department of Radiology, University of Iowa, Iowa City, Iowa (J.P.S., J.M.R., J.D.N., E.A.H.); Department of Medicine, University of Arizona, Tucson, Ariz (H.L., E.R.B., D.A.M.); VIDA Diagnostics, Coralville, Iowa (J.S., S.M., S.P.); Section of Pulmonary, Critical Care, Allergy and Immunologic Diseases, Wake Forest University School of Medicine, Winston-Salem, NC (W.C.M.); Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Boston, Mass (E.I., G.R.W., B.D.L.); Department of Radiology (J.K.L.) and Division of Pulmonary, Allergy and Critical Care Medicine (S.E.W.), University of Pittsburgh, Pittsburgh, Pa; Division of Pulmonary and Critical Care Medicine, University of California, San Francisco, San Francisco, Calif (J.V.F.); Department of Radiology (M.L.S., S.B.F.) and Division of Allergy, Pulmonary and Critical Care Medicine (N.N.J.), University of Wisconsin, Madison, Wis; Department of Public Health Sciences, Penn State Eberly College of Science, University Park, Pa (D.T.M.); and Department of Pulmonary Medicine, The University of Texas MD Anderson Cancer Center, Houston, Tex (A.S.). Received February 25, 2021; revision requested April 7; revision received December 27; accepted February 17, 2022. **Address correspondence to** M.C. (email: [mcastro2@kumc.edu](mailto:mcastro2@kumc.edu)).

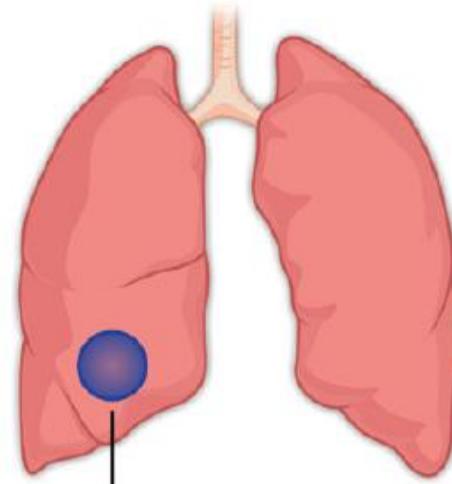


**Figure 1:** Flowcharts show the enrollment of the study cohort from the overall **(A)** Severe Asthma Research Program (SARP) I and II and **(B)** SARP III cohorts. qCT = quantitative CT.

expiration



inspiration



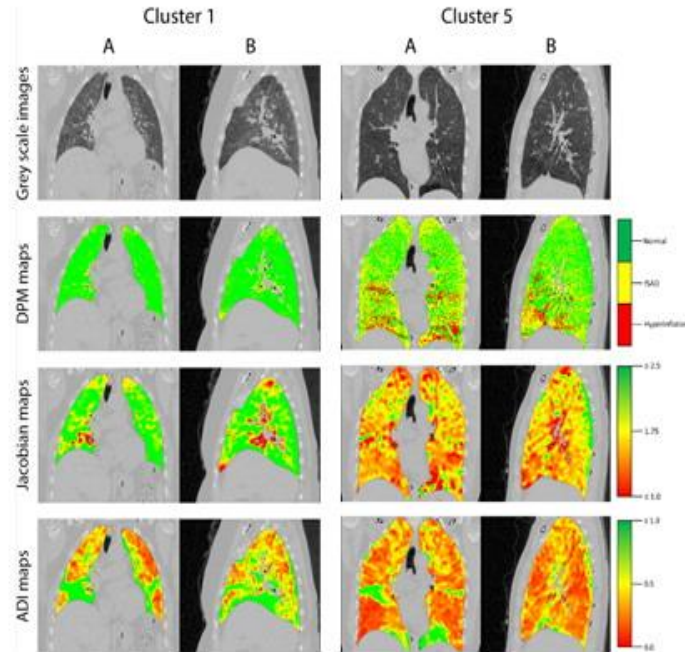
Jacobian measures **volume change**

- $J > 1 \rightarrow$  expansion
- $J = 1 \rightarrow$  no volume change
- $J < 1 \rightarrow$  contraction

ADI measures **shape change**

- ADI = 0  $\rightarrow$  no shape change
- ADI > 0  $\rightarrow$  anisotropic shape change
- Bigger ADI  $\rightarrow$  more pronounced anisotropic shape change

# Quantitative CT Characteristics of Cluster Phenotypes in the Severe Asthma Research Program Cohorts



Expansion/Anisotropic change- Green

- In an analysis of 455 participants with asthma, lung expansion on chest CT was 31% smaller in those with severe asthma compared to participants with mild asthma (Jacobian: 1.61 vs 2.31,  $P < .001$ ) and 34% more isotropic (anisotropic deformation index [ADI]: 0.40 vs 0.61,  $P < .001$ ).
- Airway morphometry and air trapping could identify severe asthma phenotypes.

# Contents

- Global severe asthma registry
- **National severe asthma registry**
  - UKSAR
  - SANI
  - COBRA
  - GAN
  - SARP
  - **CHRONICLE (North America)**
- International severe asthma registry

# CHRONICLE

– Biologic use and pattern change

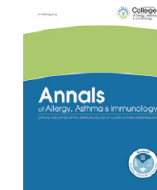
# The CHRONICLE Study of US Adults with Subspecialist-Treated Severe Asthma: Objectives, Design, and Initial Results

Ann Allergy Asthma Immunol 125 (2020) 294–303



ELSEVIER

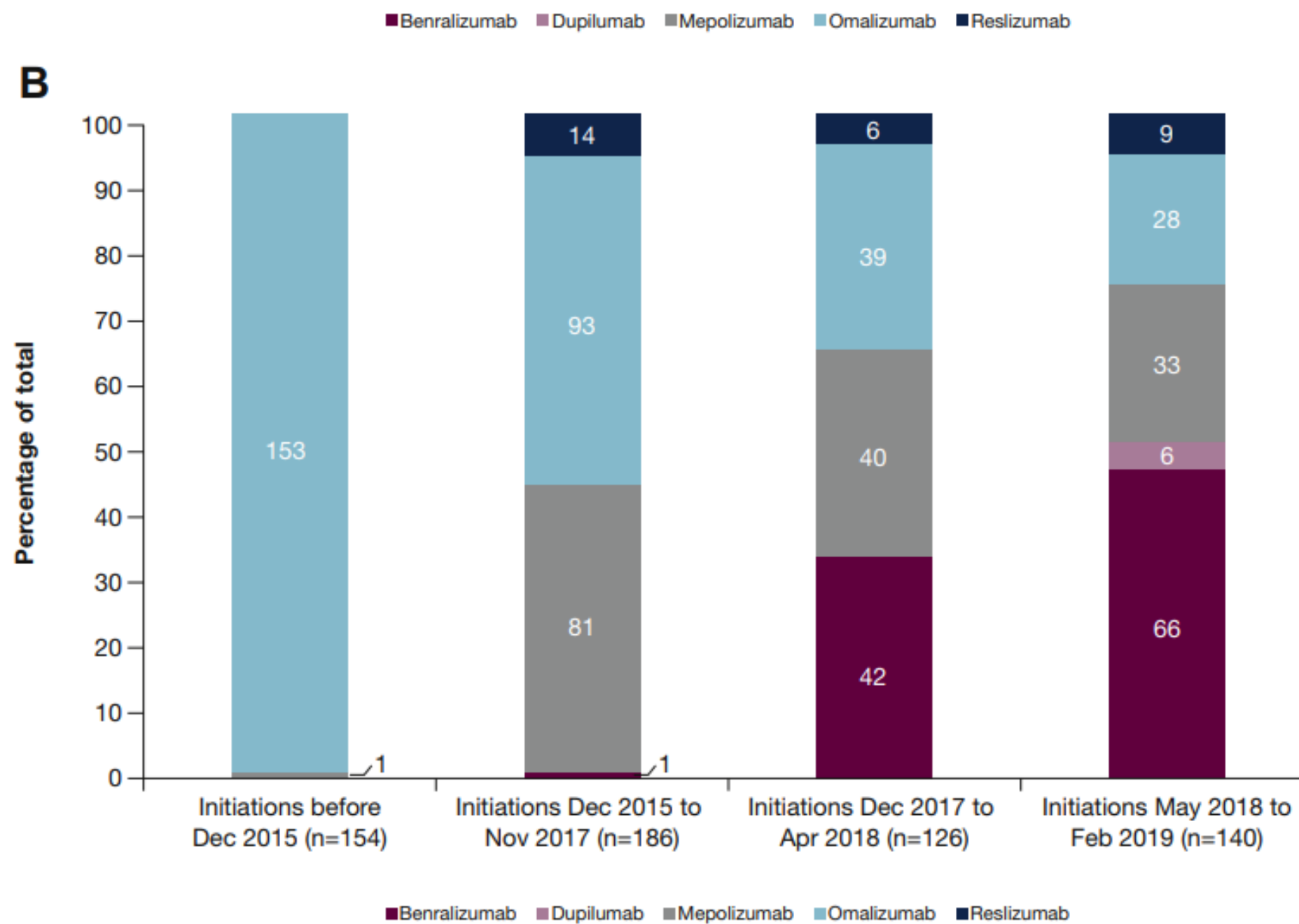
Contents lists available at ScienceDirect



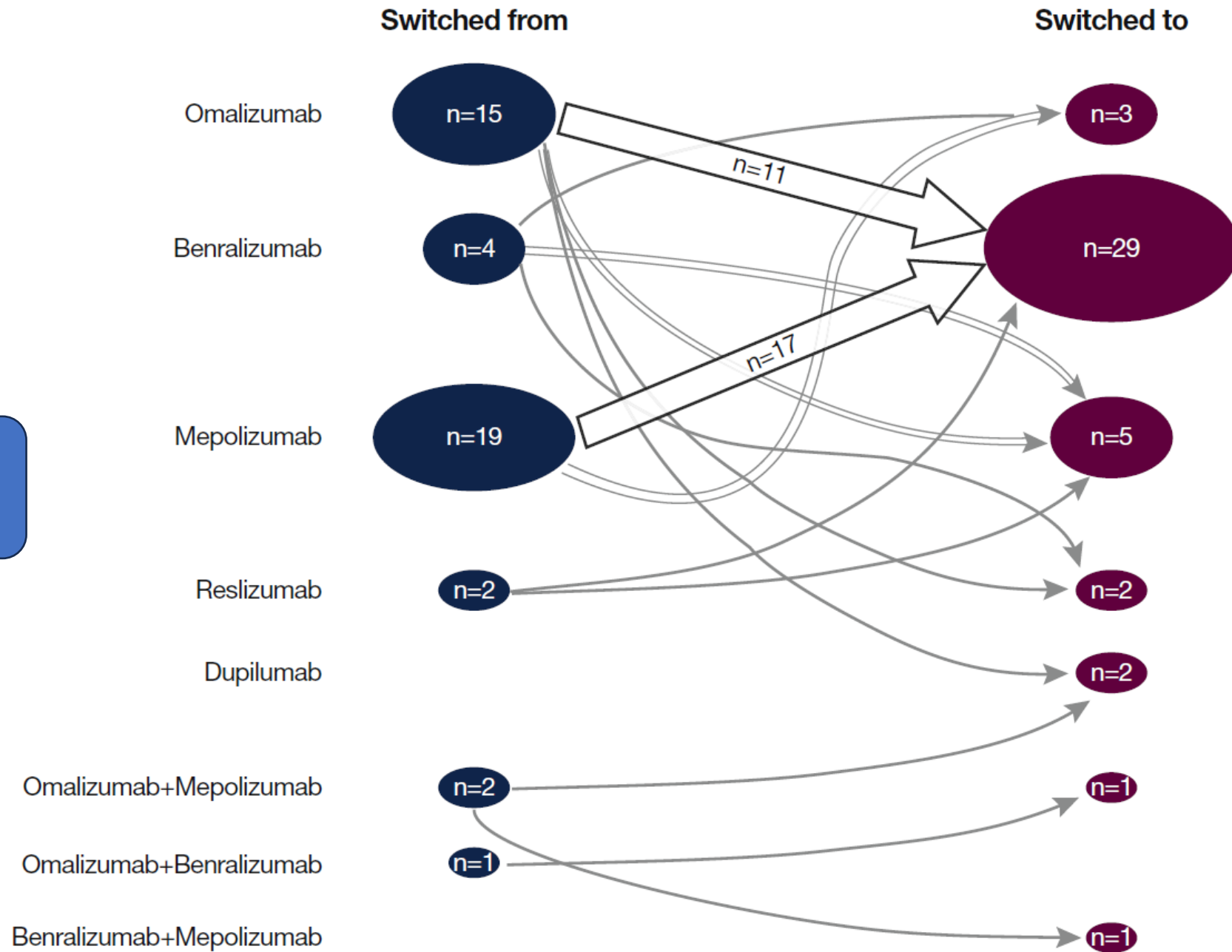
Biologic and maintenance systemic corticosteroid therapy among US subspecialist-treated patients with severe asthma



Wendy C. Moore, MD<sup>\*</sup>; Reynold A. Panettieri Jr., MD<sup>†</sup>; Jennifer Trevor, MD<sup>‡</sup>;  
Dennis K. Ledford, MD<sup>§</sup>; Njira Lugogo, MD<sup>||</sup>; Weily Soong, MD<sup>¶</sup>;  
Bradley E. Chipps, MD<sup>#</sup>; Warner Carr, MD<sup>\*\*</sup>; Laura Belton, MSc<sup>††</sup>;  
Hitesh Gandhi, MBBS, MHA, MAS<sup>‡‡</sup>; Frank Trudo, MD, MBA<sup>††</sup>;  
Christopher S. Ambrose, MD, MBA<sup>§§</sup>

**B****2018.02 – 2019.02**

Switching pattern

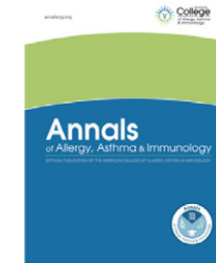


Factors associated with biologics  
*Receiver operating curve AUC of 0.70*

Factor	OR (95% CI)
Health insurance (vs no insurance)	5.5 (2.4, 12.7)
Eosinophilic comorbidity	4.5 (1.6, 13.4)
No recorded COPD diagnosis	1.9 (0.9, 3.7)
Nonhospital-based clinic (vs hospital-based)	1.7 (1.0, 2.9)
Multispecialty practice (vs single specialty)	1.7 (1.1, 2.7)
More nonphysician staff per physician (ratio of counts)	1.2 (1.0, 1.4)
More physicians treating severe asthma (each additional)	1.1 (1.1, 1.2)
Years since first receipt of HD ICS (each additional)	1.02 (1.0, 1.1)



Contents lists available at ScienceDirect



## Biologic use and outcomes among adults with severe asthma treated by US subspecialists



Reynold A. Panettieri Jr, MD<sup>\*</sup>; Dennis K. Ledford, MD<sup>†</sup>; Bradley E. Chipps, MD<sup>‡</sup>;  
Weily Soong, MD<sup>§</sup>; Njira Lugogo, MD<sup>||</sup>; Warner Carr, MD<sup>¶</sup>; Arjun Mohan, MD<sup>#</sup>; Donna Carstens, MD<sup>\*\*</sup>;  
Eduardo Genofre, MD, PhD<sup>\*\*</sup>; Frank Trudo, MD<sup>\*\*</sup>; Christopher S. Ambrose, MD, MBA<sup>††</sup>

<sup>\*</sup> Rutgers Institute for Translational Medicine and Science, The State University of New Jersey, New Brunswick, New Jersey

<sup>†</sup> Division of Allergy and Immunology, Department of Internal Medicine, Morsani College of Medicine, University of South Florida, Tampa, Florida

<sup>‡</sup> Capital Allergy & Respiratory Disease Center, Sacramento, California

<sup>§</sup> AllerVie Health—Alabama Allergy & Asthma Center, Birmingham, Alabama

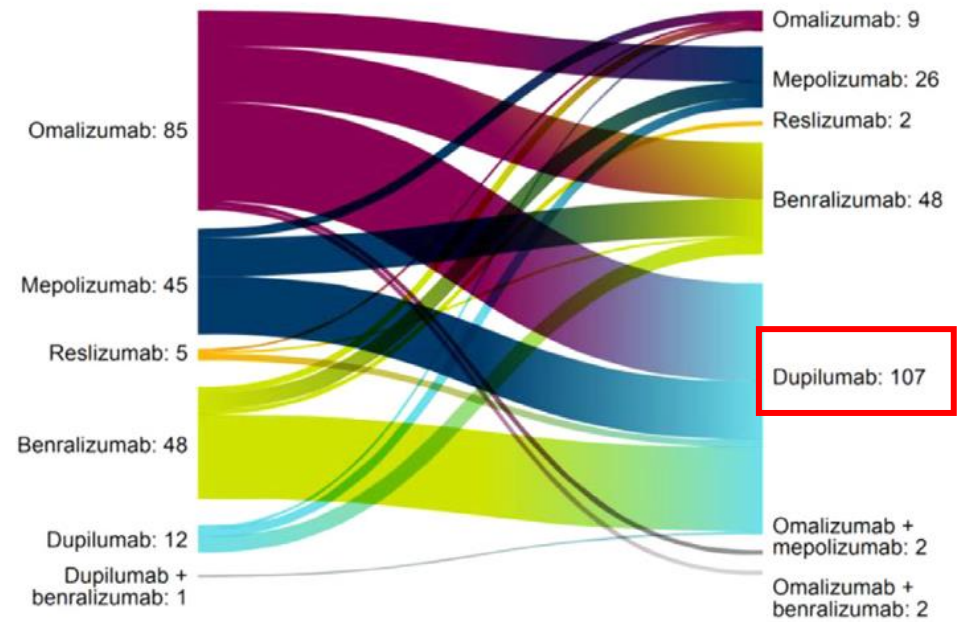
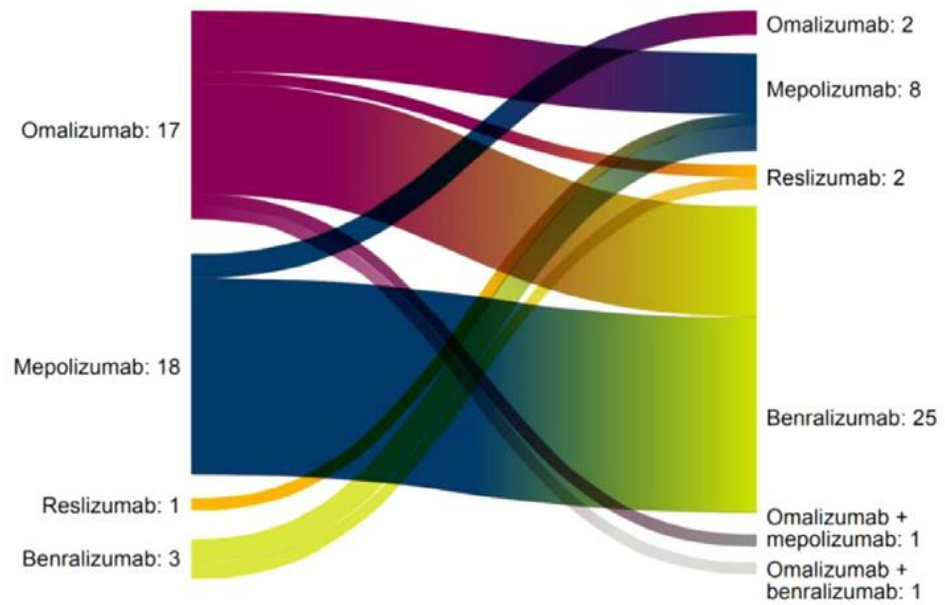
<sup>||</sup> Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan

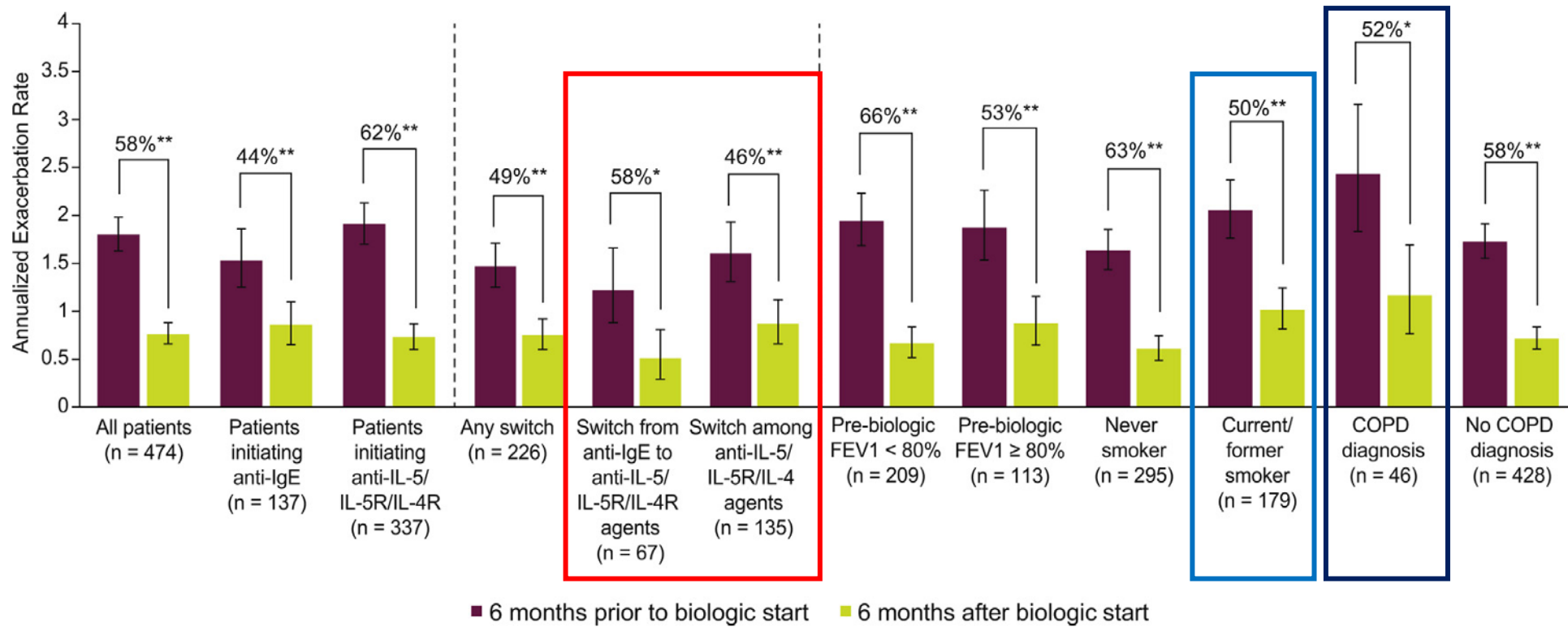
<sup>¶</sup> Allergy & Asthma Associates of Southern California, Mission Viejo, California

<sup>#</sup> Pulmonary Disease & Critical Care Medicine, Virginia Commonwealth University, Richmond, Virginia

<sup>\*\*</sup> BioPharmaceuticals Medical, AstraZeneca, Wilmington, Delaware

<sup>††</sup> BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, Maryland





# ISAR + CHRONICLE

Journal of Asthma and Allergy

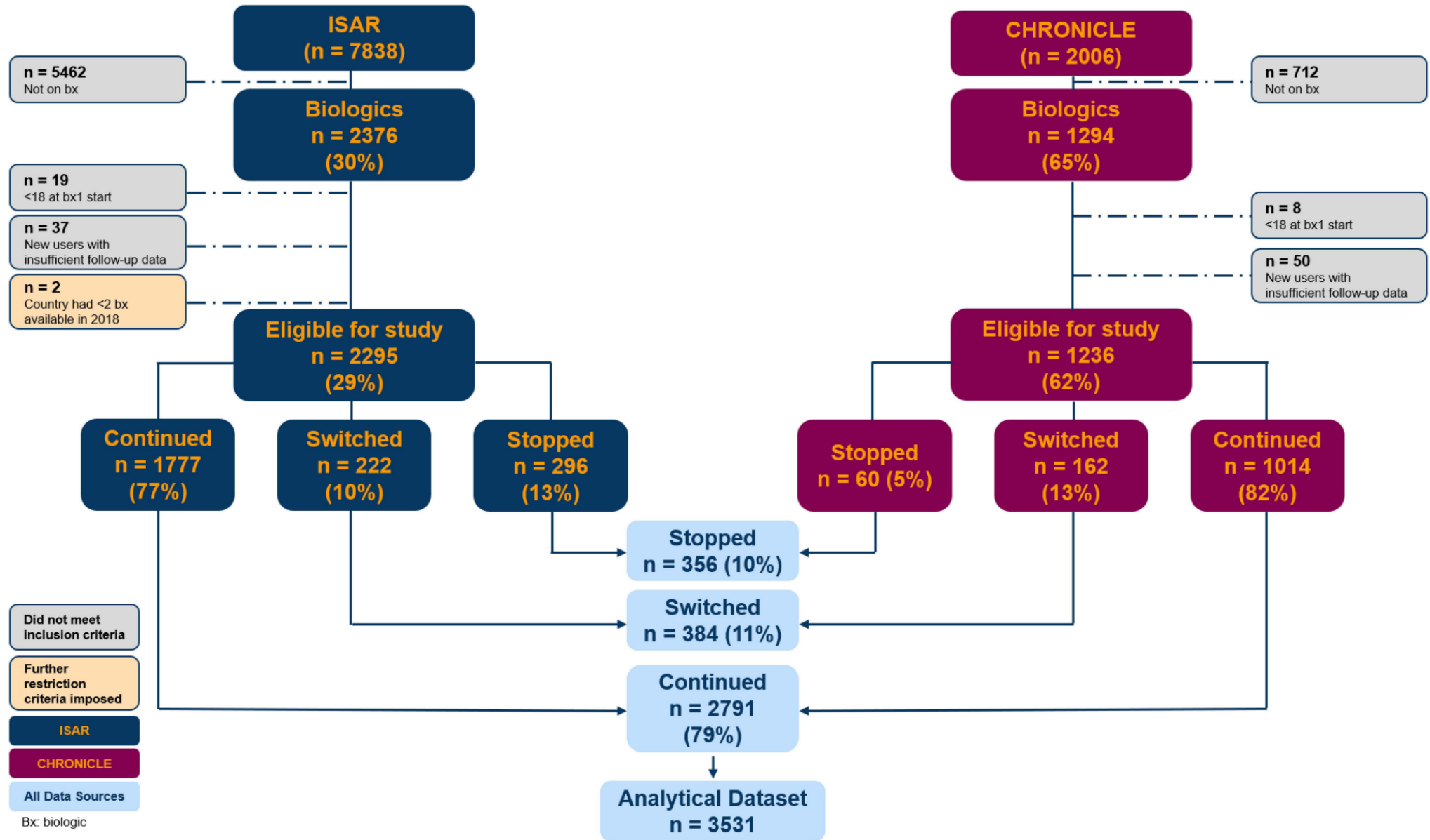
Dovepress

open access to scientific and medical research

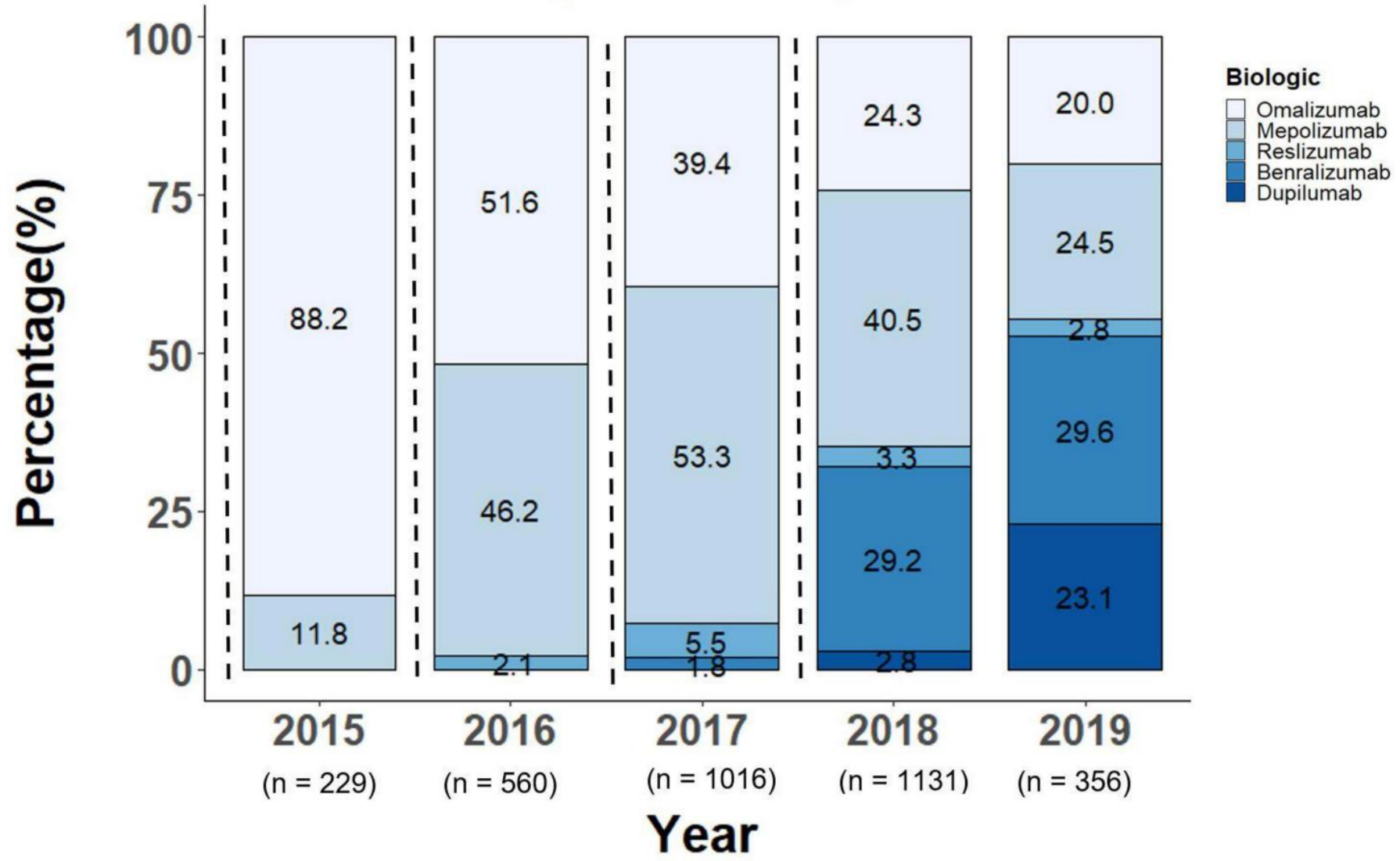
 Open Access Full Text Article

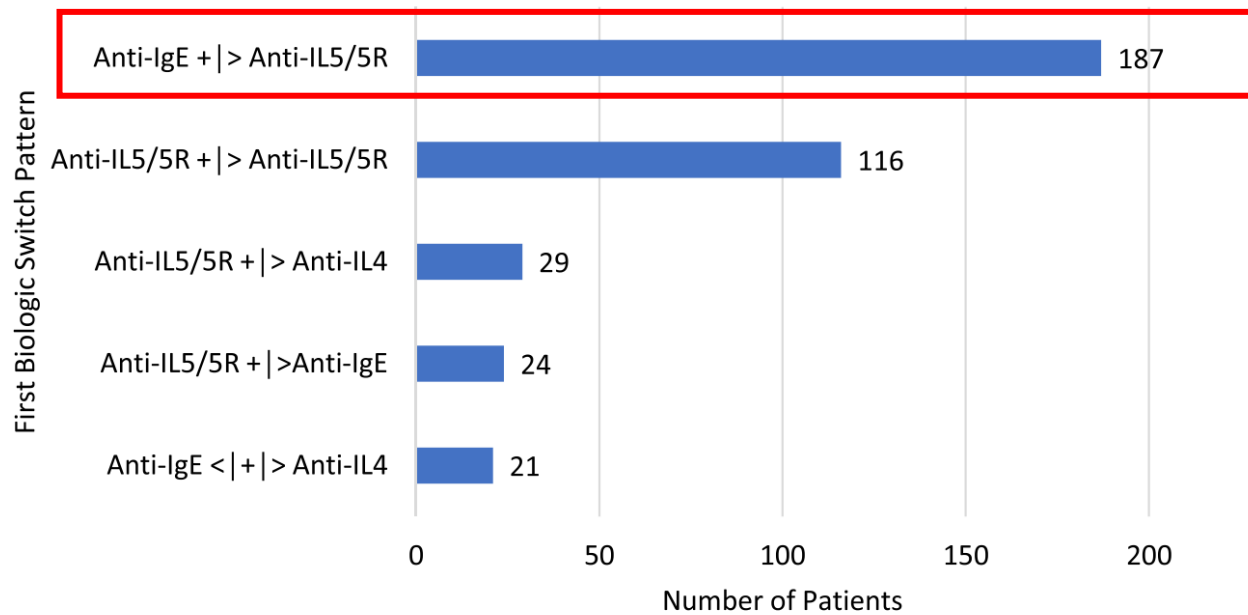
ORIGINAL RESEARCH

Real World Biologic Use and **Switch** Patterns in Severe Asthma: Data from the International Severe Asthma Registry and the US CHRONICLE Study



## Biologic Initiation by Year





**Table 3** Reasons Why eCRF Patients with Severe Asthma Enrolled into ISAR or CHRONICLE Stopped or Switched Their First Prescribed Biologic

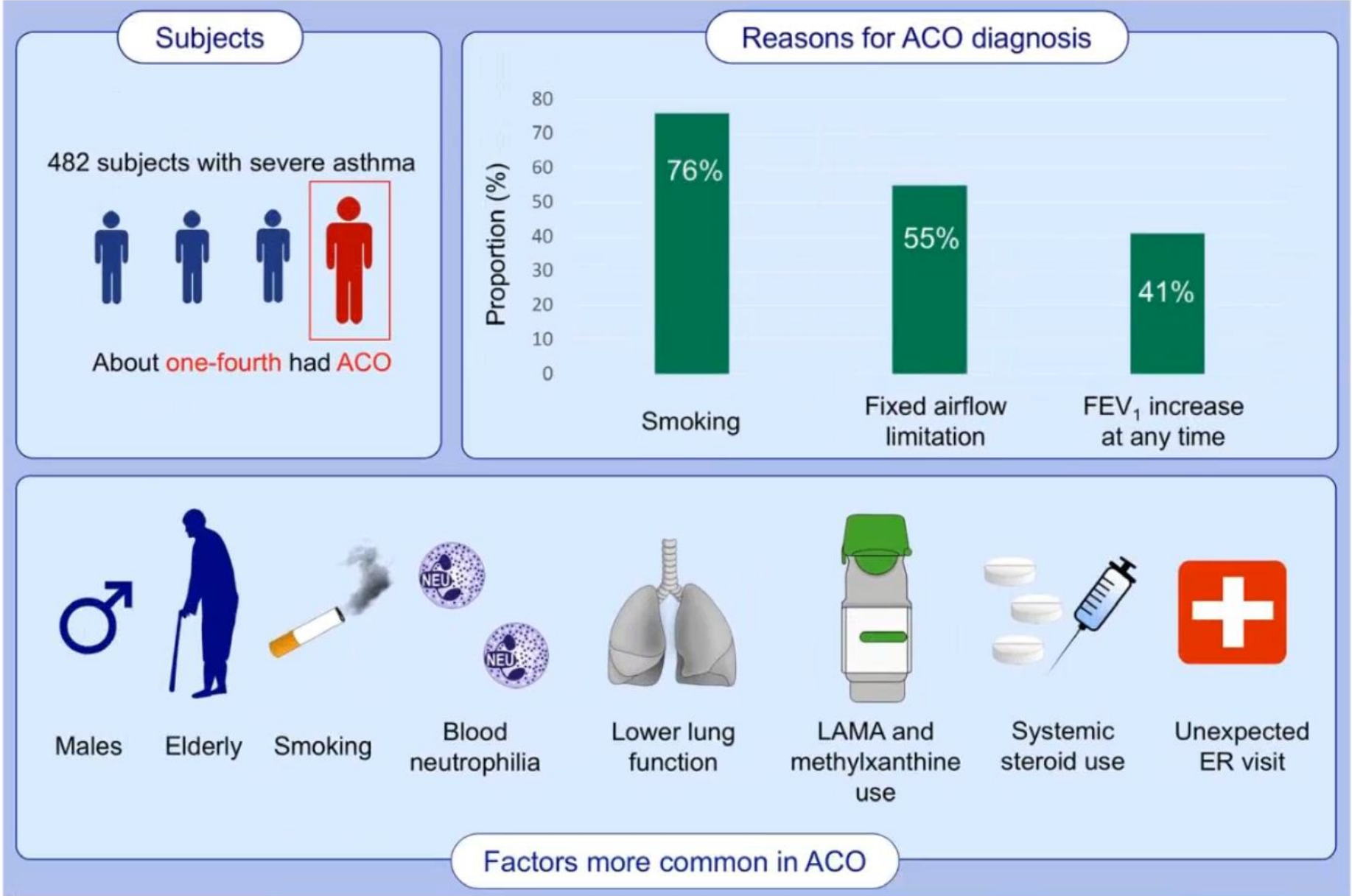
Reason	Stopped (n=139)	Switched (n=280)
Reason available n (%)	113	183
Insufficient Clinical Efficacy	72 (63.7)	158 (86.3)
Potential adverse outcomes	18 (15.9)	14 (7.7)
Biologic Access Restriction	8 (7.1)	5 (2.7)
Patient Preference	4 (3.5)	3 (1.6)
Other	12 (10.6)	11 (6.0)

**Abbreviations:** eCRF, electronic case report form; ISAR, International Severe Asthma Registry.

# Contents

- Global severe asthma registry
- **National severe asthma registry**
  - UKSAR
  - SANI
  - COBRA
  - GAN
  - SARP
  - CHRONICLE
  - **KoSAR (Korea)**
- International severe asthma registry

**KoSAR**



### Patients



Severe asthma  
(KoSAR patients)



Chronic obstructive pulmonary disease  
(KOCOSS patients)

### Outcome

**ACO definition**

In the COPD cohort

- BDR  $\geq$  15% and  $\geq$  400 mL from baseline or
- blood eosinophil count (BEC)  $\geq$  300 cells/ $\mu$ L.

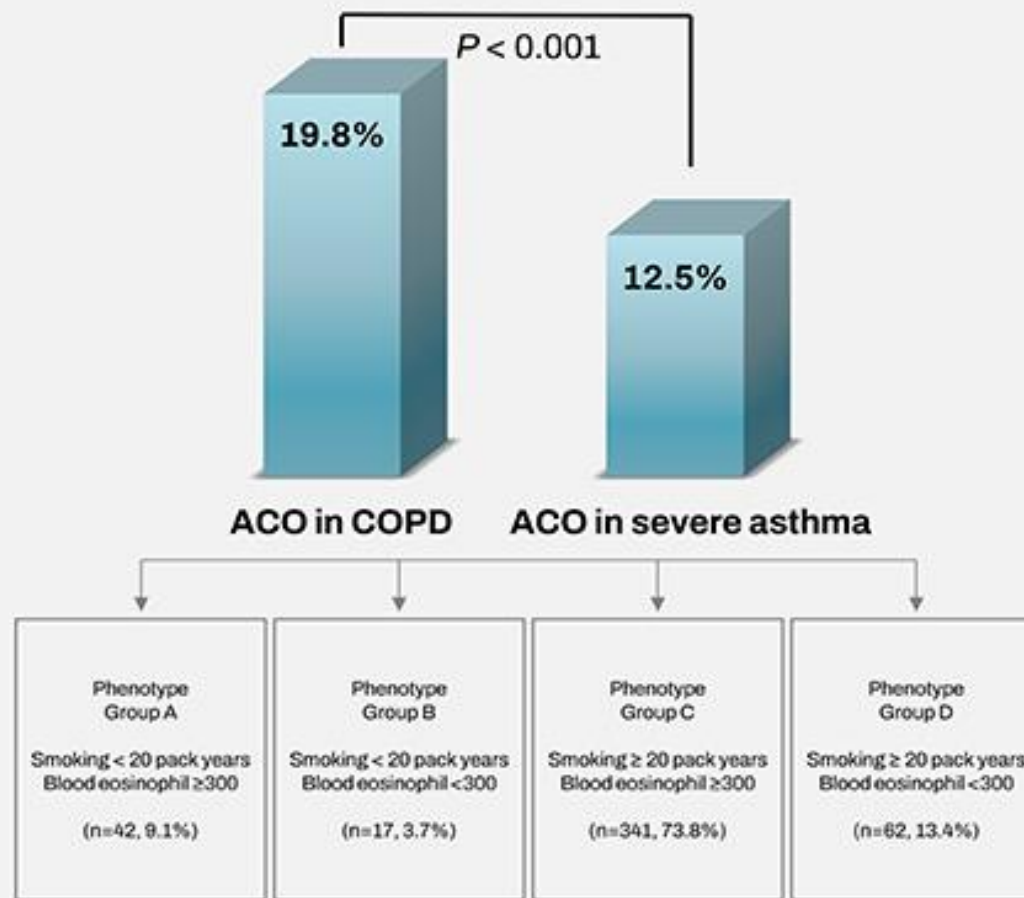
In the severe asthma cohort

- Age  $\geq$  35 years, smoking  $\geq$  10 pack-years, and
- post-BD FEV1/FVC  $<$  0.7



Prevalence of  
Asthma-COPD overlap (ACO)

### Result



### Conclusion

The prevalence of ACO differed between COPD and severe asthma cohorts. ACO patients can be classified into four phenotype groups, such that each phenotype exhibits distinct characteristics.

# Contents

- Global severe asthma registry
- **National severe asthma registry**
  - UKSAR
  - SANI
  - COBRA
  - GAN
  - SARP
  - CHRONICLE
  - KoSAR (Korea)
  - **ISAR-Korea**
- International severe asthma registry

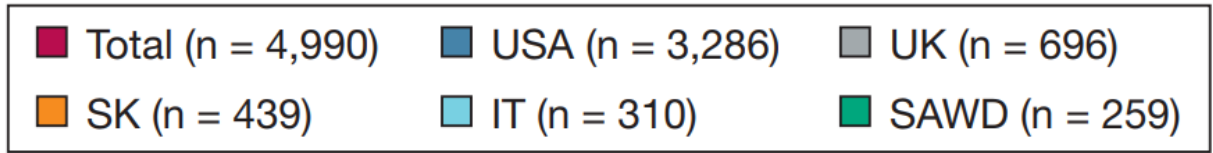
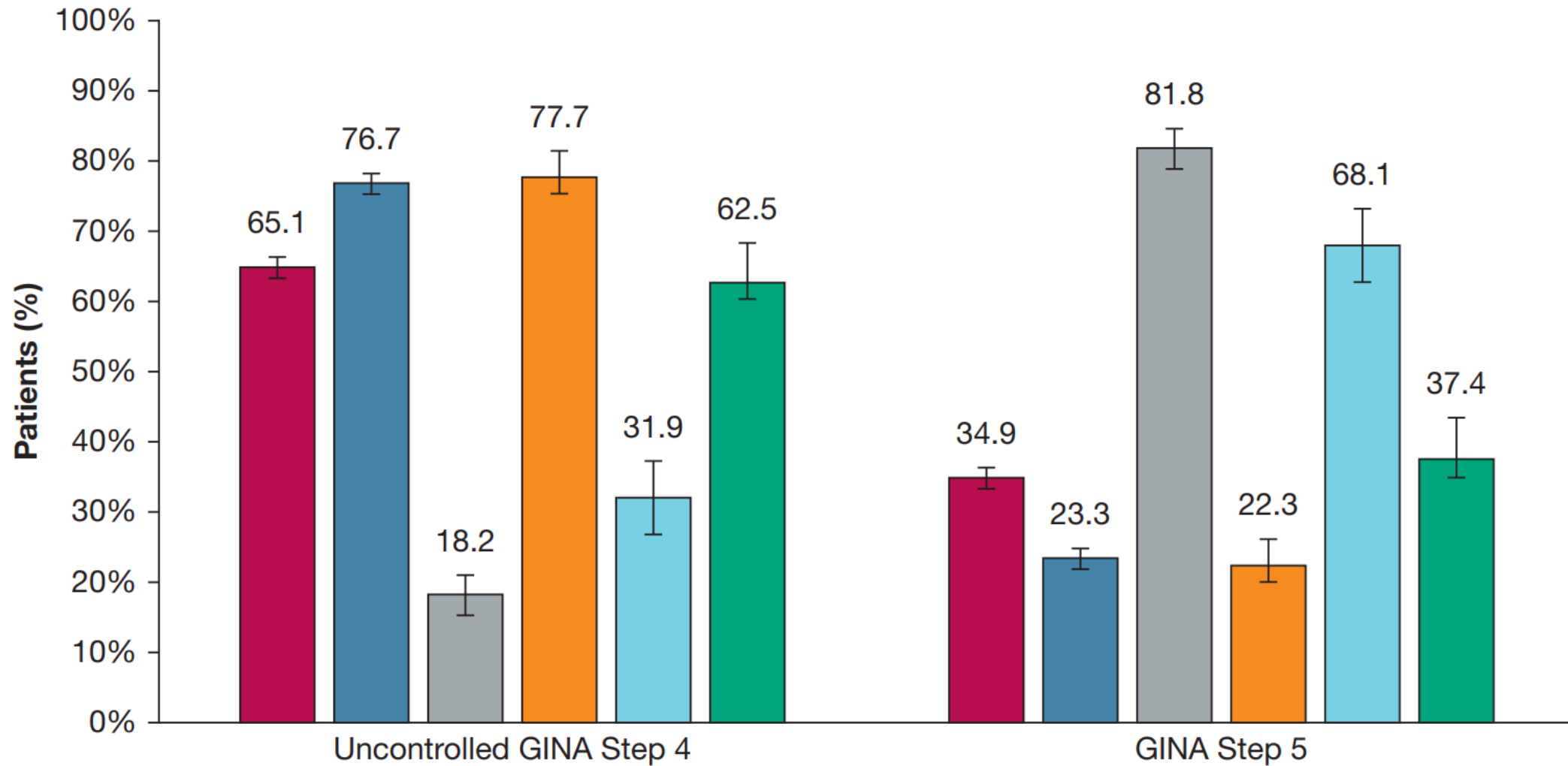
ISAR-Korea

# Characterization of Severe Asthma Worldwide

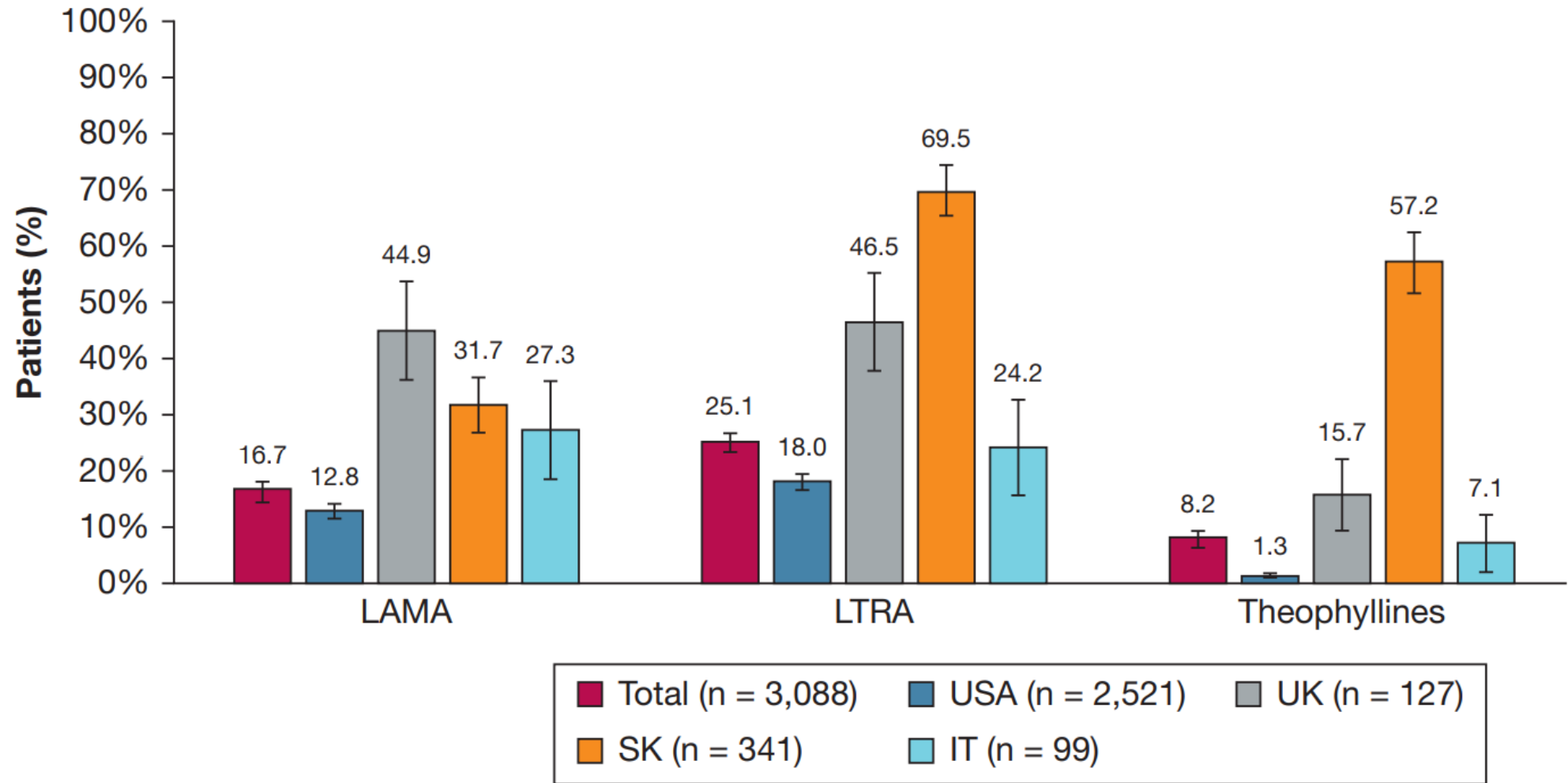


## Data From the International Severe Asthma Registry

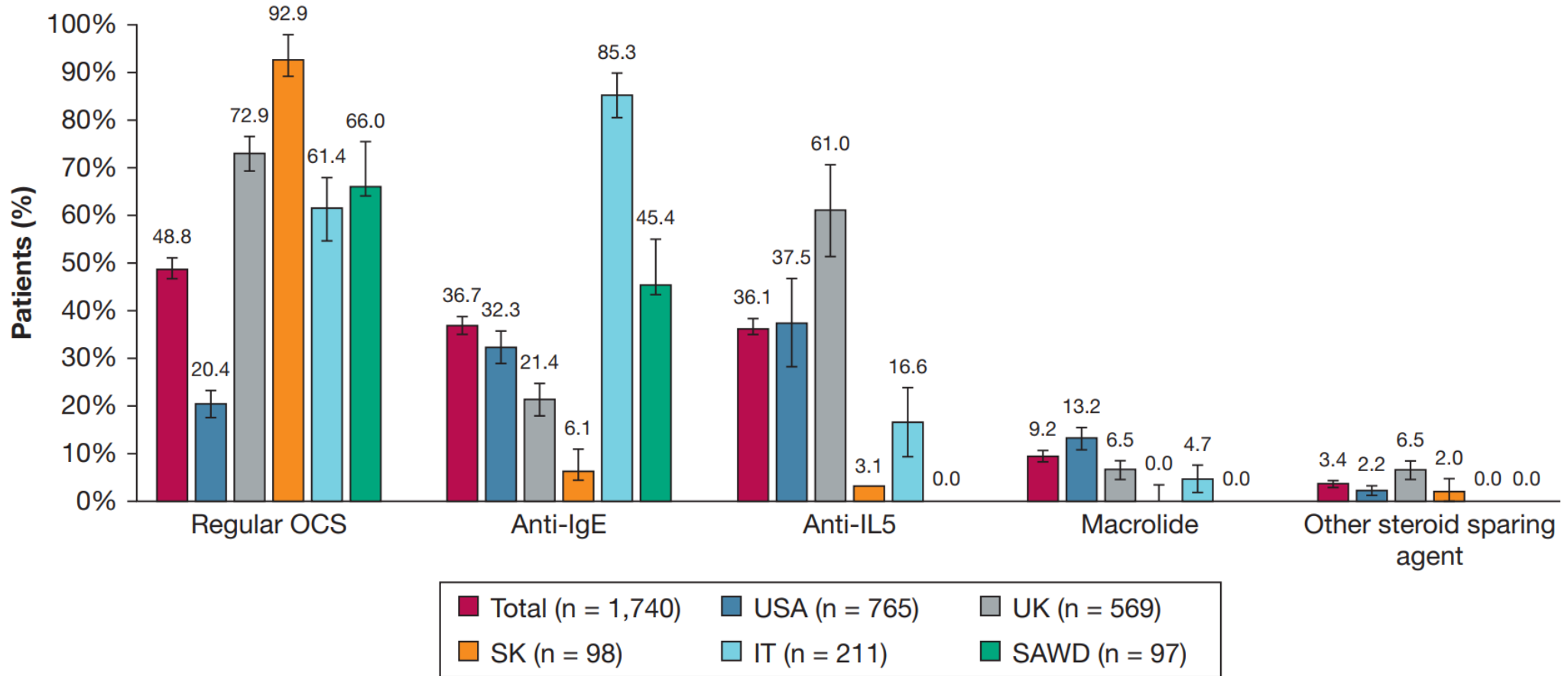
*Eileen Wang, MD, MPH; Michael E. Wechsler, MD; Trung N. Tran, MD, PhD; Liam G. Heaney, MD; Rupert C. Jones, MD; Andrew N. Menzies-Gow, MD; John Busby, PhD; David J. Jackson, MD, PhD; Paul E. Pfeffer, MD, PhD; Chin Kook Rhee, MD, PhD; You Sook Cho, MD, PhD; G. Walter Canonica, MD; Enrico Heffler, MD, PhD; Peter G. Gibson, D Med; Mark Hew, PhD; Matthew Peters, MD, PhD; Erin S. Harvey, PhD; Marianna Alacqua, MD, PhD; James Zangrilli, MD; Lakmini Bulathsinhala, MPH; Victoria A. Carter, BSc; Isha Chaudhry, MSc; Neva Eleangovan, BSc; Naeimeh Hosseini, MD; Ruth B. Murray, PhD; and David B. Price, MD*



A



B



# Contents

- Global severe asthma registry
- National severe asthma registry
- **International severe asthma registry**
  - **ISAR**

ISAR



The **International Severe Asthma Registry** is a global collaborative initiative to gather **anonymous, longitudinal, real-life data for patients with severe asthma**. ISAR offers a rich source of real-life data for scientific research to understand and improve symptoms, treatments, and patient outcomes for severe asthma. The database will also provide an international platform for research collaboration in respiratory medicine and patient care.

[Contact Us to Learn More](#)

## Our numbers

Our Numbers: At ISAR, we are committed to collecting real-life data from patients with severe asthma around the world. Here, we share some key numbers that highlight the impact of our global collaborative initiative.

**17,000+**

Total number of patients

**15,000+**

Prospective  
patient-level data

**13**

Published articles

**40**

Abstracts accepted

**330+**

Total number of registries

**23**

Research Projects

**26**

Total number of countries

# Protocol

FitzGerald et al. *BMC Medical Research Methodology* (2020) 20:212  
<https://doi.org/10.1186/s12874-020-01065-0>

BMC Medical Research  
Methodology

RESEARCH ARTICLE

Open Access

## International severe asthma registry (ISAR): protocol for a global registry



J. Mark FitzGerald<sup>1</sup>, Trung N. Tran<sup>2</sup>, Marianna Alacqua<sup>2</sup>, Alan Altraja<sup>3</sup>, Vibeke Backer<sup>4</sup>, Leif Bjermer<sup>5</sup>, Unnur Bjornsdottir<sup>6</sup>, Arnaud Bourdin<sup>7</sup>, Guy Brusselle<sup>8,9</sup>, Lakmini Bulathsinhala<sup>10</sup>, John Busby<sup>11</sup>, Giorgio W. Canonica<sup>12,13</sup>, Victoria Carter<sup>10</sup>, Isha Chaudhry<sup>10</sup>, You Sook Cho<sup>14</sup>, George Christoff<sup>15</sup>, Borja G. Cosio<sup>16</sup>, Richard W. Costello<sup>17</sup>, Neva Eleangovan<sup>10</sup>, Peter G. Gibson<sup>18,19</sup>, Liam G. Heaney<sup>20</sup>, Enrico Heffler<sup>12,13</sup>, Mark Hew<sup>21</sup>, Naeimeh Hosseini<sup>10</sup>, Takashi Iwanaga<sup>22</sup>, David J. Jackson<sup>23</sup>, Rupert Jones<sup>24</sup>, Mariko S. Koh<sup>25</sup>, Thao Le<sup>10</sup>, Lauri Lehtimäki<sup>26</sup>, Dora Ludviksdottir<sup>27</sup>, Anke H. Maitland-van der Zee<sup>28</sup>, Andrew Menzies-Gow<sup>29</sup>, Ruth B. Murray<sup>10</sup>, Nikolaos G. Papadopoulos<sup>30,31</sup>, Luis Perez-de-Llano<sup>32</sup>, Matthew Peters<sup>33</sup>, Paul E. Pfeffer<sup>34</sup>, Todor A. Popov<sup>35</sup>, Celeste M. Porsbjerg<sup>36</sup>, Chris A. Price<sup>10</sup>, Chin K. Rhee<sup>37</sup>, Mohsen Sadatsafavi<sup>38</sup>, Yuji Tohda<sup>22</sup>, Eileen Wang<sup>39</sup>, Michael E. Wechsler<sup>40</sup>, James Zangrilli<sup>2</sup> and David B. Price<sup>10,41,42\*</sup>

# Mission statement

[ Asthma CHEST Reviews ]

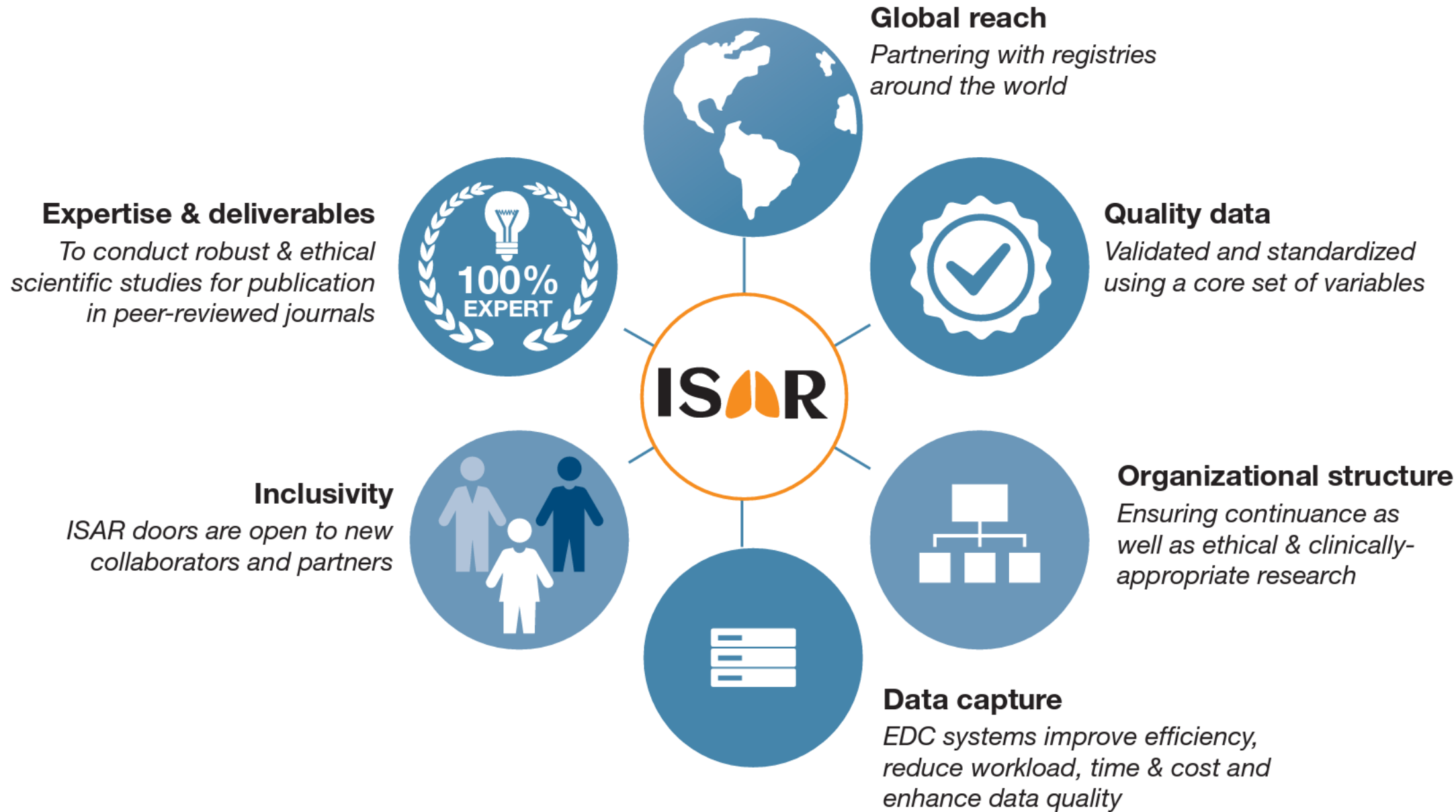


## International Severe Asthma Registry Mission Statement



*The ISAR Study Group\**

Regional and/or national severe asthma registries provide valuable country-specific information. However, they are often limited in scope within the broader definitions of severe asthma, have insufficient statistical power to answer many research questions, lack interoperability to share lessons learned, and have fundamental differences in data collected, making cross comparisons difficult. What is missing is a worldwide registry which brings all severe asthma data together in a cohesive way, under a single umbrella, based on standardized data collection protocols, permitting data to be shared seamlessly. The International Severe Asthma Registry (ISAR; <http://isaregistries.org/>) is the first global adult severe asthma registry. It is a joint initiative where national registries (both newly created and preexisting) retain ownership of their own data but open their borders and share data with ISAR for ethically approved research purposes. Its strength comes from collection of patient-level, anonymous, longitudinal, real-



**TABLE 1 ]** ISAR Global Core Projects and Prioritized Research

Description
<b>Global core projects</b>
Demographic and clinical <b>baseline characteristics</b> of patients with severe asthma worldwide
Characterization and comparison of <b>eosinophilic and noneosinophilic</b> phenotypes
<b>Comparative effectiveness across severe asthma biologic classes</b> (anti-IL-5 vs anti-IgE) in patients eligible for both modalities
<b>Prioritized research</b>
Hidden patients with severe asthma in primary care vs ISAR
Impact of exacerbation burden on lung function trajectory in a broad asthma population and severe asthma population
Biologics in severe asthma: utilization patterns, causes for discontinuation and switching, and adverse outcomes
Biomarker Relatability in the International Severe Asthma Registry
Identification of predictors (ie, biomarkers) of response to biologics
Hidden chronic asthma within the COPD/ACO population
Age at onset of asthma in patients with severe asthma
Relationship between socioeconomic status and asthma outcomes
Describe the OCS landscape: annual consumption, prevalence, outcomes, and side effects of long-term OCS users
Characterization of health disparities (burden of illness or mortality) across countries
Criteria for choosing and switching between similar biologic treatment options in patients with atopic and nonatopic severe eosinophilic asthma
Describe the characteristics of patients with severe asthma with inflammatory phenotypes and $FEV_1 < 40\%$

ACO = asthma-COPD overlap; ISAR = International Severe Asthma Registry; OCS = oral corticosteroid.

# Cluster Analysis of Inflammatory Biomarker Expression in the International Severe Asthma Registry



Eve Denton, MBBS, MPH, FRACP<sup>a,b</sup>, David B. Price, FRCGP<sup>c,d,e</sup>, Trung N. Tran, MD, PhD<sup>f</sup>, G. Walter Canonica, MD<sup>g,h</sup>, Andrew Menzies-Gow, PhD, FRCP<sup>i</sup>, J. Mark FitzGerald, MD, FRCPC<sup>j</sup>, Mohsen Sadatsafavi, MD, PhD<sup>k</sup>, Luis Perez de Llano, MD, PhD<sup>l</sup>, George Christoff, MD, PhD, MPH<sup>m</sup>, Anna Quinton, MS<sup>n</sup>, Chin Kook Rhee, MD, PhD<sup>o</sup>, Guy Brusselle, MD, PhD<sup>p,q</sup>, Charlotte Ulrik, MD, DMS, FERS<sup>r</sup>, Njira Lugogo, MD<sup>s</sup>, Fiona Hore-Lacy, BNutSci<sup>a,b</sup>, Isha Chaudhry, MS<sup>c</sup>, Lakmini Bulathsinhala, MPH<sup>c</sup>, Ruth B. Murray, PhD<sup>c</sup>, Victoria A. Carter, BS<sup>c</sup>, and Mark Hew, MBBS, PhD, FRACP<sup>a,b</sup> Melbourne, Australia; Cambridge, Aberdeen, and London, United Kingdom; Singapore; Gaithersburg, Md; Milan, Italy; Vancouver, BC, Canada; Lugo, Spain; Sofia, Bulgaria; Seoul, South Korea; Ghent, Belgium; Rotterdam, The Netherlands; Hvidovre, Denmark; Ann Arbor, Mich

**What is already known about this topic?** Asthma is now understood to encompass a variety of distinct clinical phenotypes, likely arising from different pathological mechanisms.

**What does this article add to our knowledge?** In a large international severe asthma cohort, distinct clusters according to biomarker expression exhibited unique clinical characteristics, suggesting the occurrence of discrete patterns of underlying inflammatory pathway activation.

**How does this study impact current management guidelines?** Understanding more about distinct patterns of underlying inflammatory pathway activation in individual severe asthma patients allows clinicians to tailor targeted severe asthma therapies such as monoclonal biologics, furthering precision medicine for severe asthma.

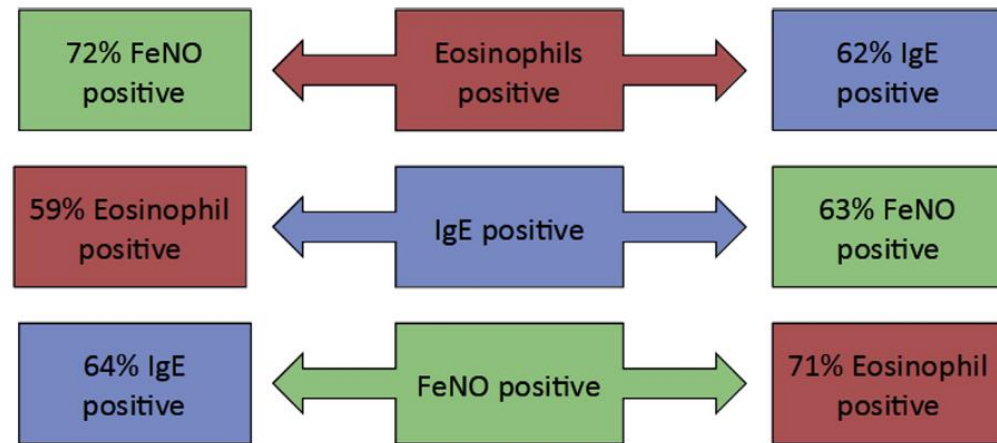
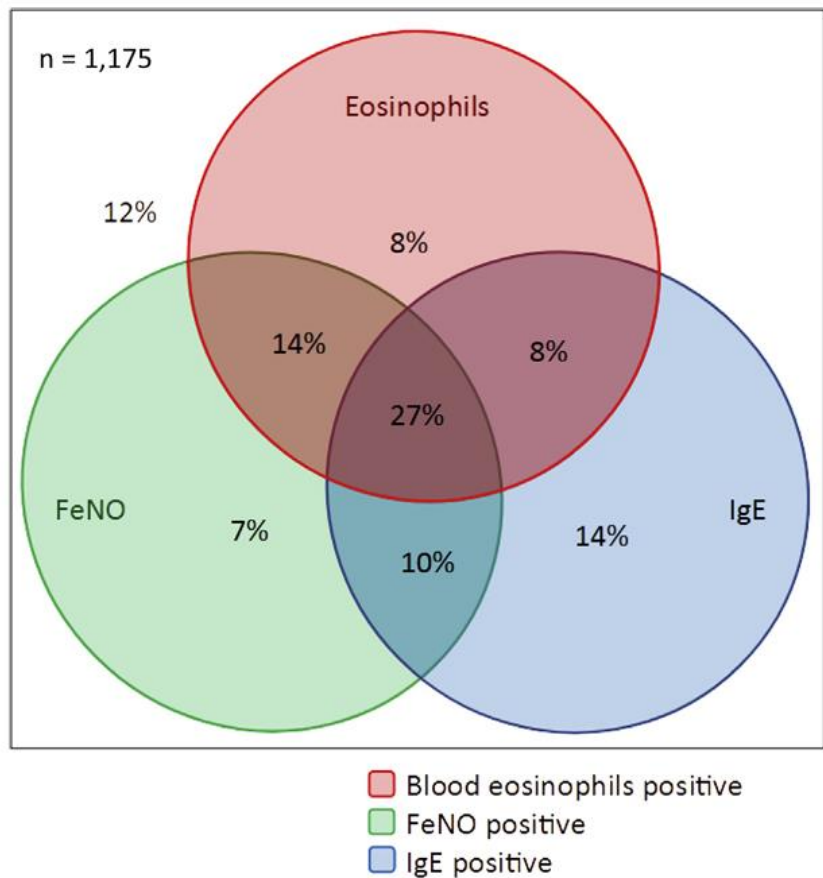
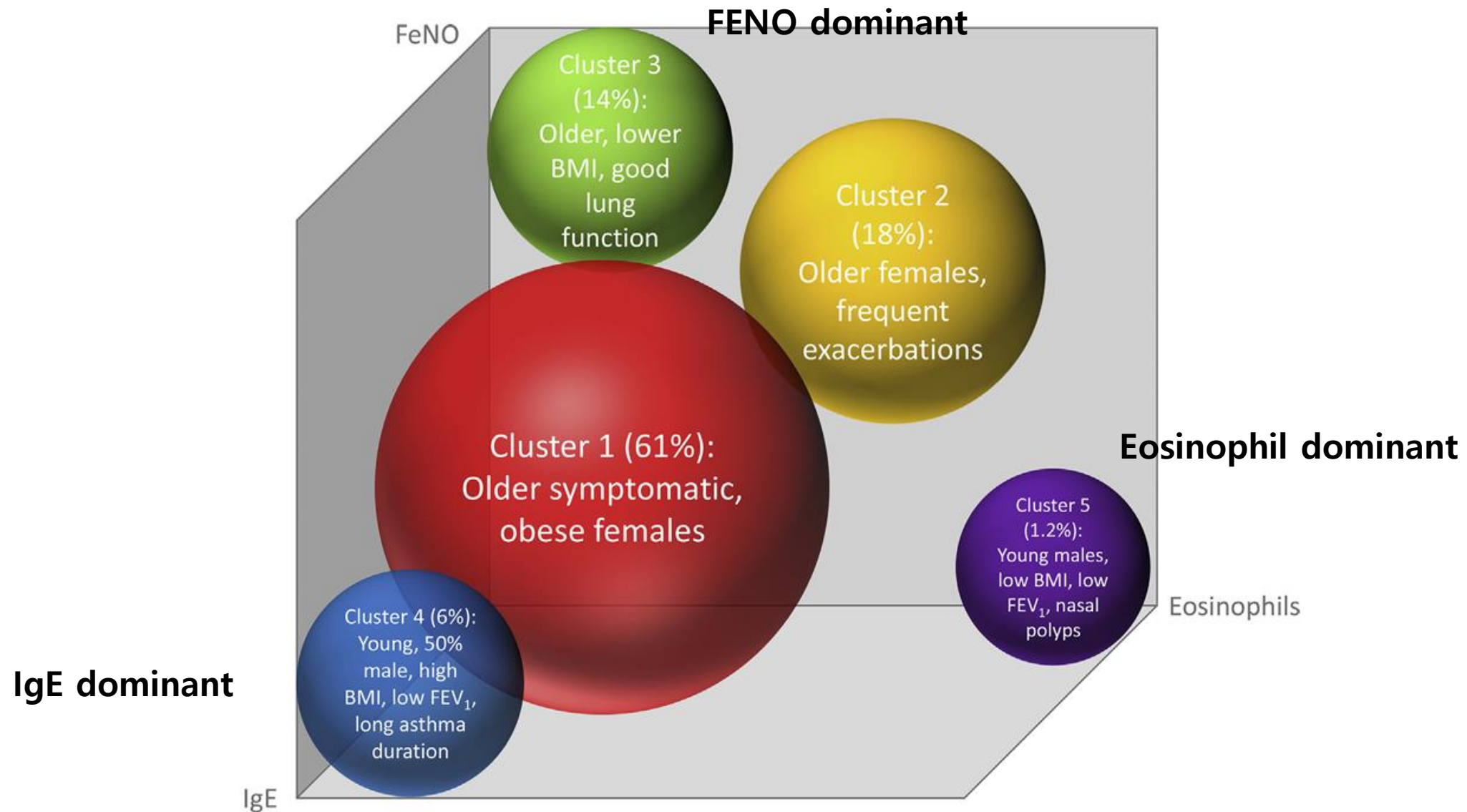
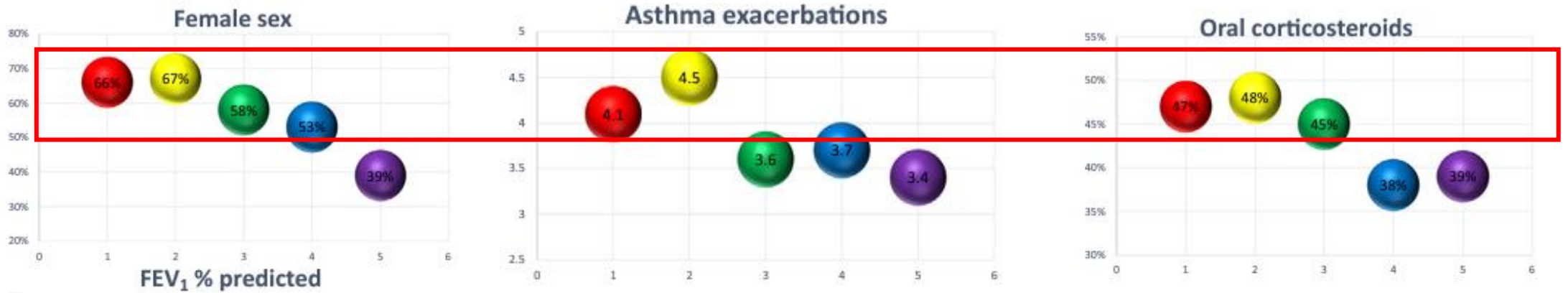


FIGURE 2. Percent likelihood that other biomarkers are positive based on positivity of another biomarker in the ISAR.



**FIGURE 3.** Graphical representation of the clinical characteristics of the 5 severe asthma clusters relating to 3 biomarker levels identified on hierarchical cluster analysis performed with blood eosinophils, total IgE, and FeNO.

# Cluster I & II



# Eosinophilic dominant (cluster 5)



**FIGURE 4.** Clinical characteristics of the 5 severe asthma clusters relating to 3 biomarker levels identified on hierarchical cluster analysis performed with blood eosinophils, total IgE and FeNO. Clusters 1 to 5 along the x axis.

# Eosinophilic and Noneosinophilic Asthma

## An Expert Consensus Framework to Characterize Phenotypes in a Global Real-Life Severe Asthma Cohort



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



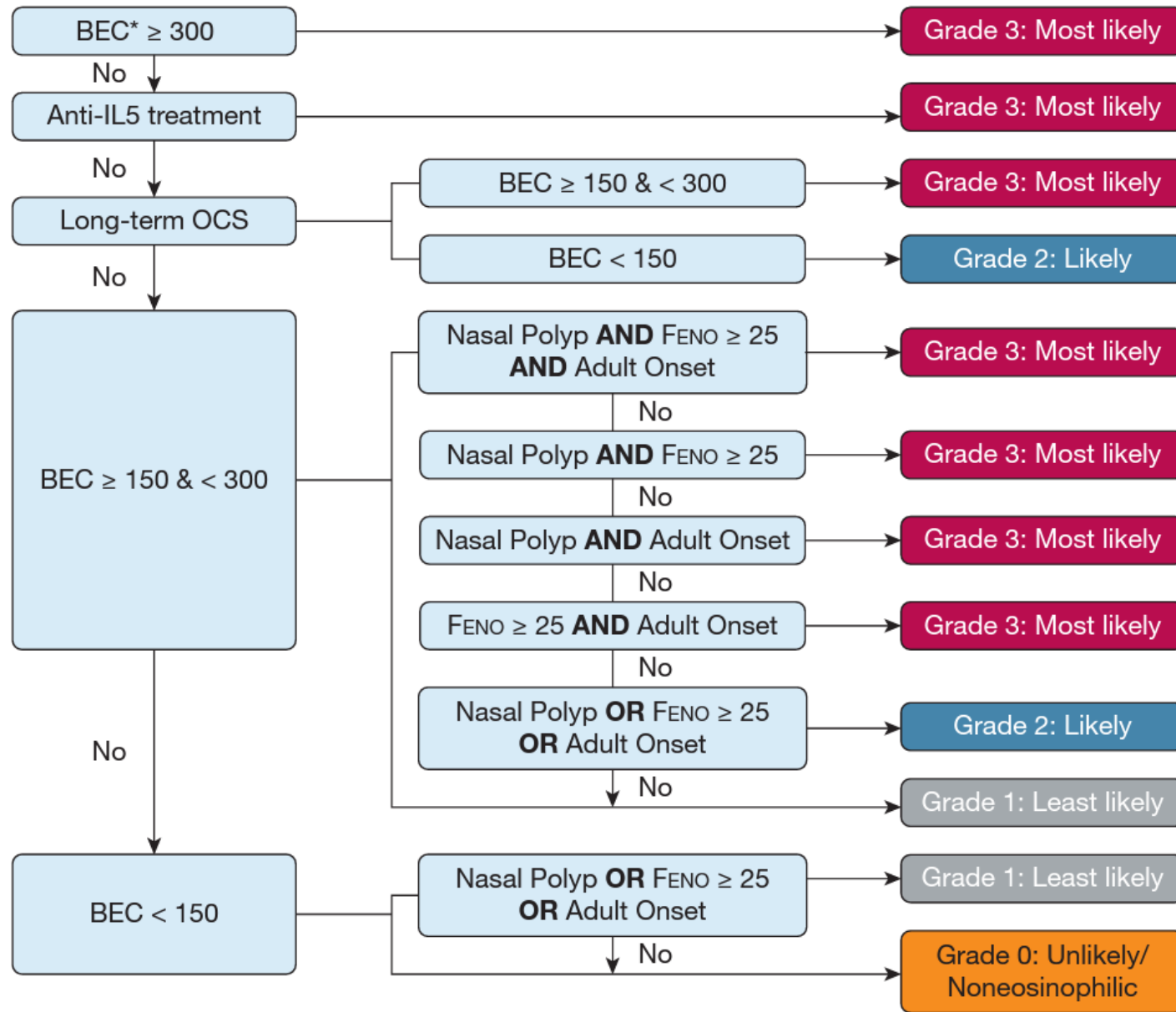


Figure 1 – Flow chart showing original eosinophilic and noneosinophilic severe asthma phenotype algorithm. BEC = blood eosinophil count; FENO = fractional exhaled nitric oxide; OCS = oral corticosteroid.

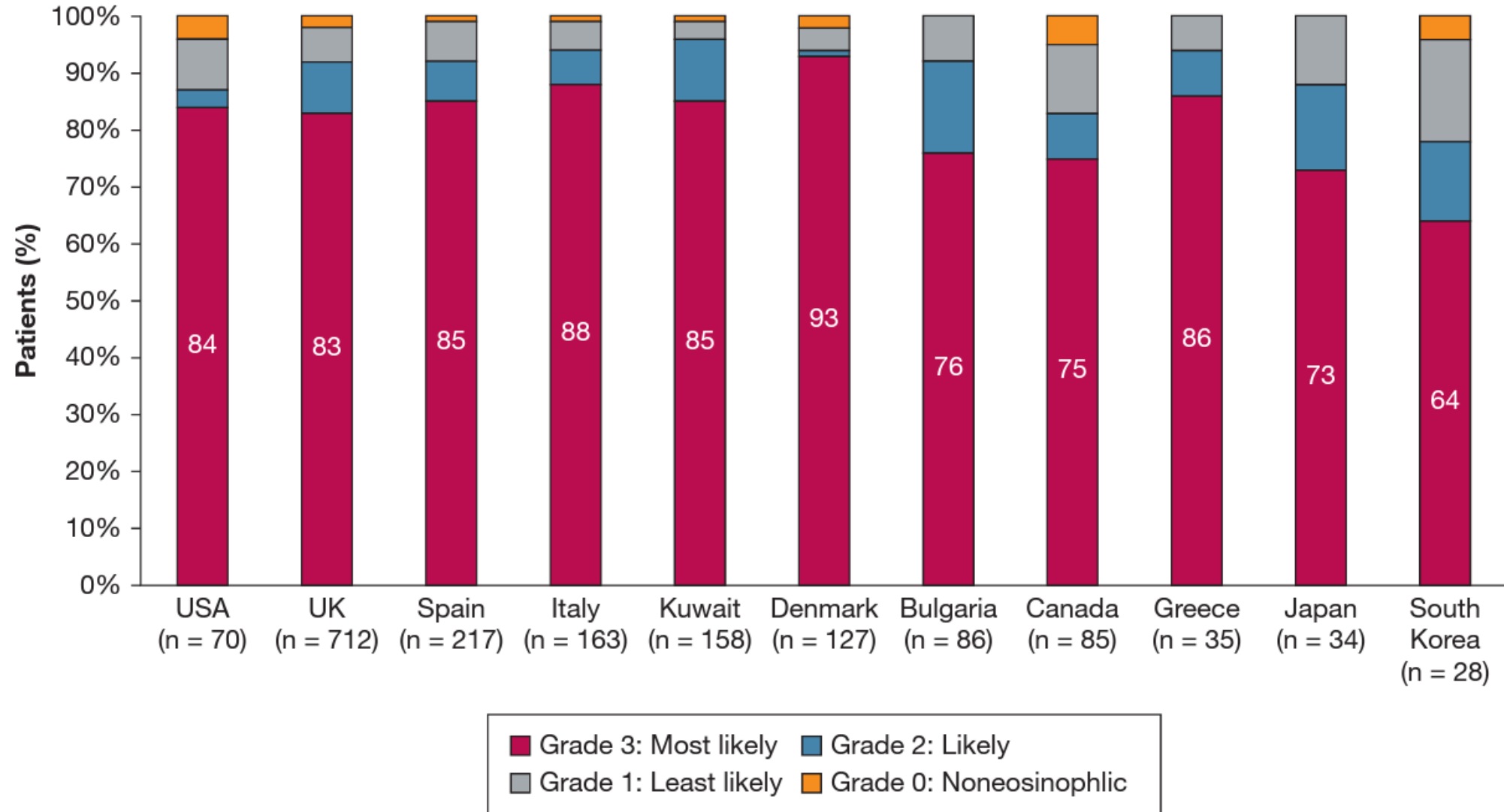
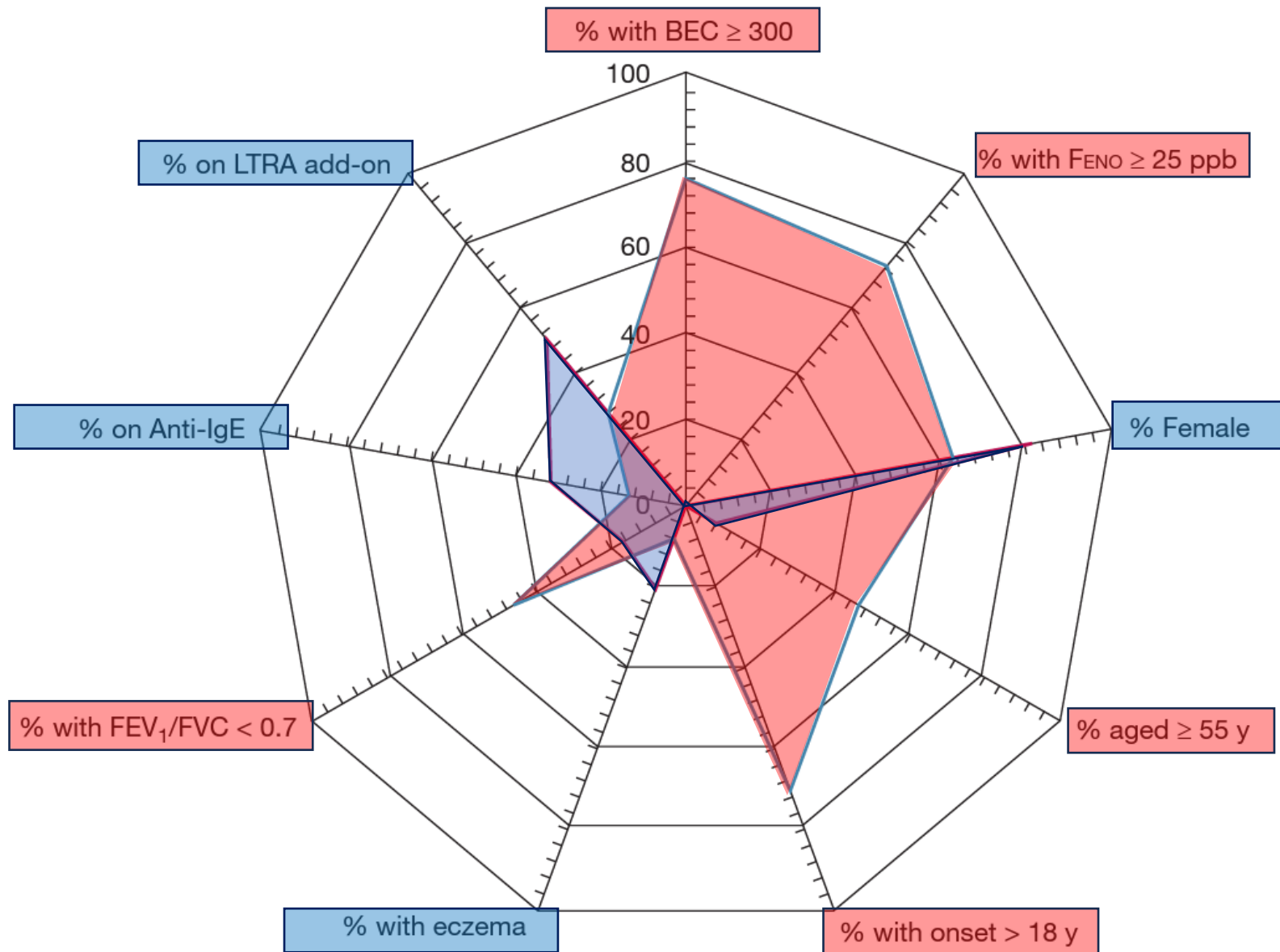


Figure 2 – Bar graph showing eosinophilic severe asthma phenotype distribution by country for prospective International Severe Asthma Registry population (defined according to the original algorithm).



## ORIGINAL ARTICLE

Asthma and Lower Airway Disease

## Comparative effectiveness of anti-IL5 and anti-IgE biologic classes in patients with severe asthma eligible for both

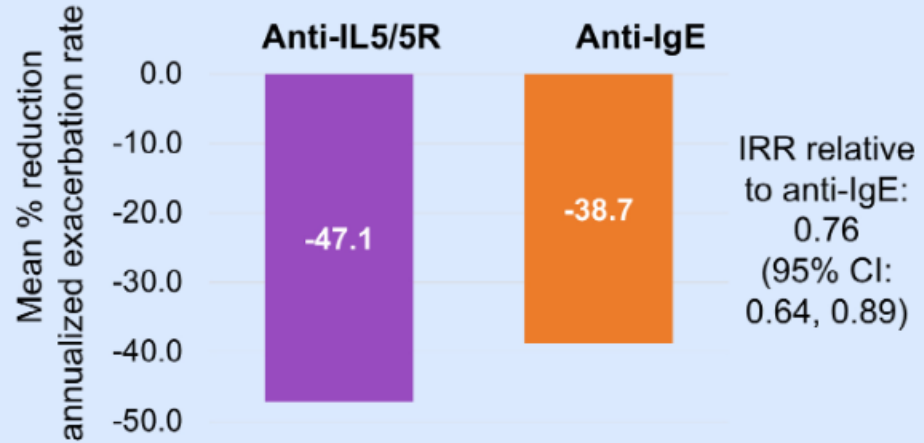
Paul E. Pfeffer<sup>1,2</sup> | Nasloon Ali<sup>3,4</sup> | Ruth Murray<sup>4</sup> | Charlotte Ulrik<sup>5</sup> | Trung N. Tran<sup>6</sup> |  
 Jorge Maspero<sup>7,8</sup> | Matthew Peters<sup>9</sup> | George C. Christoff<sup>10</sup> | Mohsen Sadatsafavi<sup>11</sup> |  
 Carlos A. Torres-Duque<sup>12</sup> | Alan Altraja<sup>13</sup> | Lauri Lehtimäki<sup>14,15</sup> |  
 Nikolaos G. Papadopoulos<sup>16,17</sup>  | Sundeep Salvi<sup>18</sup> | Richard W. Costello<sup>19</sup> |  
 Breda Cushen<sup>20</sup> | Enrico Heffler<sup>21,22</sup>  | Takashi Iwanaga<sup>23</sup> | Mona Al-Ahmad<sup>24</sup> |  
 Désirée Larenas-Linnemann<sup>25</sup>  | Piotr Kuna<sup>26</sup> | João A. Fonseca<sup>27</sup> |  
 Riyad Al-Lehebi<sup>28,29</sup> | Chin Kook Rhee<sup>30</sup> | Luis Perez-de-Llano<sup>31,32</sup>  |  
 Diahn-Warng Perng Steve<sup>33,34</sup> | Bassam Mahboub<sup>35,36</sup> | Eileen Wang<sup>37,38</sup>  |  
 Celine Goh<sup>3,4</sup>  | Juntao Lyu<sup>3,39</sup> | Anthony Newell<sup>3,39</sup> | Marianna Alacqua<sup>40</sup> |  
 Andrey S. Belevskiy<sup>41</sup> | Mohit Bhutani<sup>42</sup> | Leif Bjermer<sup>43</sup> | Unnur Bjornsdottir<sup>44</sup>  |  
 Arnaud Bourdin<sup>45</sup>  | Anna von Bulow<sup>46</sup> | John Busby<sup>47</sup> | Giorgio Walter Canonica<sup>21,22</sup> |  
 Borja G. Cosio<sup>48</sup>  | Delbert R. Dorscheid<sup>49</sup> | Mariana Muñoz-Esquerre<sup>50,51</sup> |  
 J. Mark FitzGerald<sup>52</sup> | Esther Garcia Gil<sup>53</sup> | Peter G. Gibson<sup>54,55</sup> | Liam G. Heaney<sup>56</sup>  |  
 Mark Hew<sup>57,58</sup>  | Ole Hilberg<sup>59</sup> | Flavia Hoyte<sup>37,38</sup> | David J. Jackson<sup>60,61</sup>  |  
 Mariko Siyue Koh<sup>62,63</sup> | Hsin-Kuo Bruce Ko<sup>64</sup>  | Jae Ha Lee<sup>65</sup> | Sverre Lehmann<sup>66,67</sup> |  
 Cláudia Chaves Loureiro<sup>68</sup>  | Dóra Lúðvíksdóttir<sup>69,70</sup> | Andrew N. Menzies-Gow<sup>71</sup> |  
 Patrick Mitchell<sup>72</sup> | Andriana I. Papaioannou<sup>73</sup>  | Todor A. Popov<sup>74</sup> |  
 Celeste M. Porsbjerg<sup>75</sup>  | Laila Salameh<sup>35,36</sup> | Concetta Sirena<sup>76</sup> | Camille Taillé<sup>77</sup> |  
 Christian Taube<sup>78</sup> | Yuji Tohda<sup>79</sup> | Michael E. Wechsler<sup>80</sup> | David B. Price<sup>3,4,81</sup> 

### Global registry

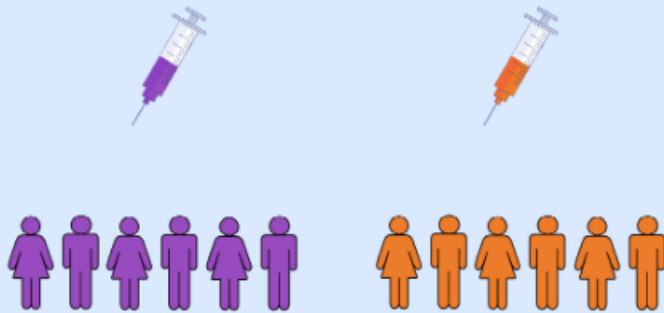


Severe asthma

### Primary Endpoint



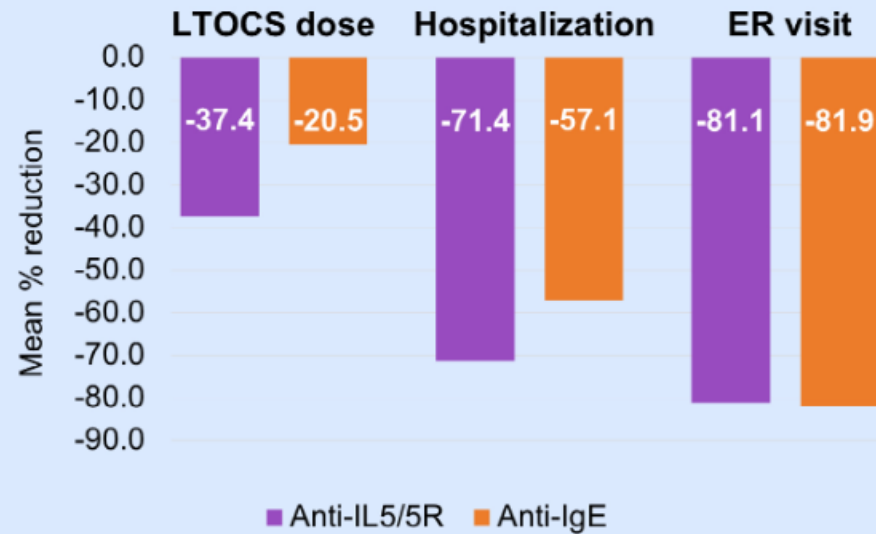
### Eligible for both



Anti-IL5/5R  
n=350

Anti-IgE  
n=350

### Secondary Endpoints






# Contents

- Global severe asthma registry
- National severe asthma registry
- International severe asthma registry
  - ISAR
  - **U-BIOPRED**

**U-BIOPRED**

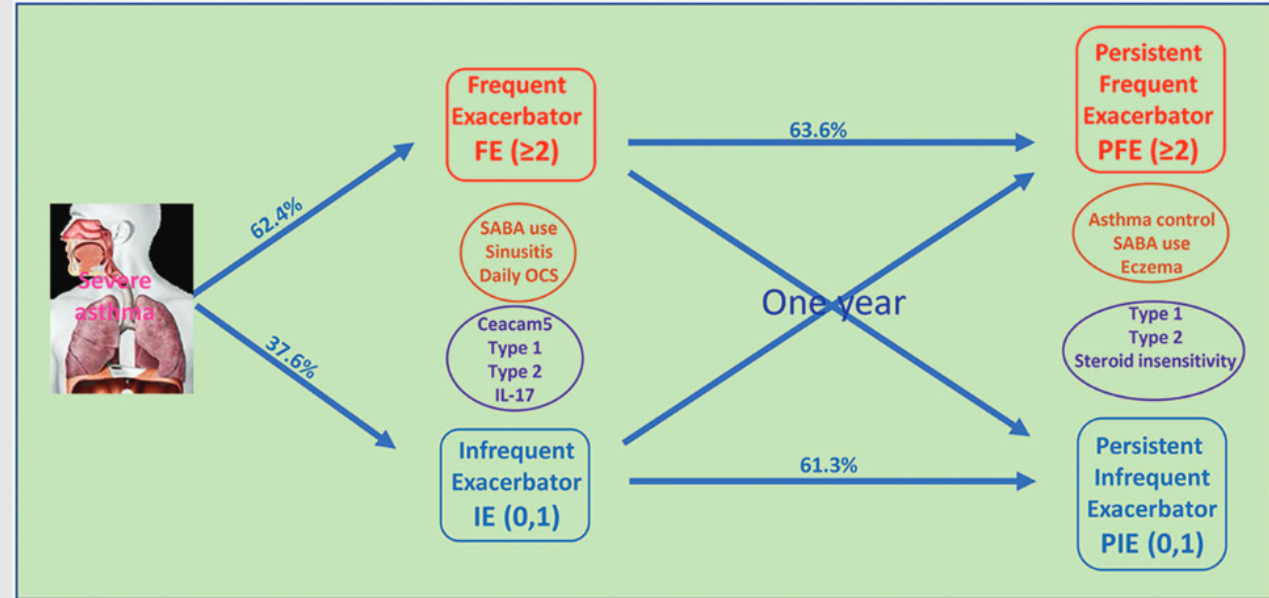
RESEARCH ARTICLE

# Clinical and transcriptomic features of persistent exacerbation-prone severe asthma in U-BIOPRED cohort

Uruj Hoda<sup>1</sup> | Stelios Pavlidis<sup>2</sup> | Aruna T. Bansal<sup>3</sup> | Kentaro Takahashi<sup>1,4</sup> |  
Sile Hu<sup>3</sup> | Francois Ng Kee Kwong<sup>1</sup> | Christos Rossios<sup>1</sup>  | Kai Sun<sup>3</sup> |  
Pankaj Bhavsar<sup>1</sup> | Matthew Loza<sup>5</sup> | Frederic Baribaud<sup>5</sup> | Pascal Chanez<sup>6</sup> |  
Stephen J. Fowler<sup>7</sup> | Ildiko Horvath<sup>8</sup> | Paolo Montuschi<sup>9</sup> | Florian Singer<sup>10</sup>  |  
Jacek Musial<sup>11</sup> | Barbro Dahlen<sup>12</sup> | Norbert Krug<sup>13</sup> | Thomas Sandstrom<sup>14</sup> |  
Dominic E. Shaw<sup>15</sup> | Rene Lutter<sup>16</sup> | Louise J. Fleming<sup>1</sup> | Peter H. Howarth<sup>17</sup> |  
Massimo Caruso<sup>18</sup> | Ana R. Sousa<sup>19</sup> | Julie Corfield<sup>20</sup> | Charles Auffray<sup>21</sup> |  
Bertrand De Meulder<sup>21</sup> | Diane Lefaudeux<sup>21</sup> | Sven-Erik Dahlen<sup>12</sup> |  
Ratko Djukanovic<sup>17</sup> | Peter J. Sterk<sup>16</sup> | Yike Guo<sup>3</sup> | Ian M. Adcock<sup>1</sup> |  
Kian Fan Chung<sup>1</sup>  | on behalf of the U-BIOPRED study group

- 317 patients
- RNA from blood, nasal epithelial brushings, bronchial biopsy, and sputum cells
- Gene set variation analysis for 103 gene signatures

## Graphical Abstract



- In severe asthma, frequent exacerbator (FE) and persistent frequent exacerbator (PFE) are associated with poorer asthma control compared to infrequent exacerbator (IE) and persistent IE, respectively.
- CEACAM5 was the differentially-expressed transcript in bronchial biopsies in FE compared to IE.
- In FE and persistent FE, there was an increase in the expression of type 1 and type 2 inflammatory pathways.

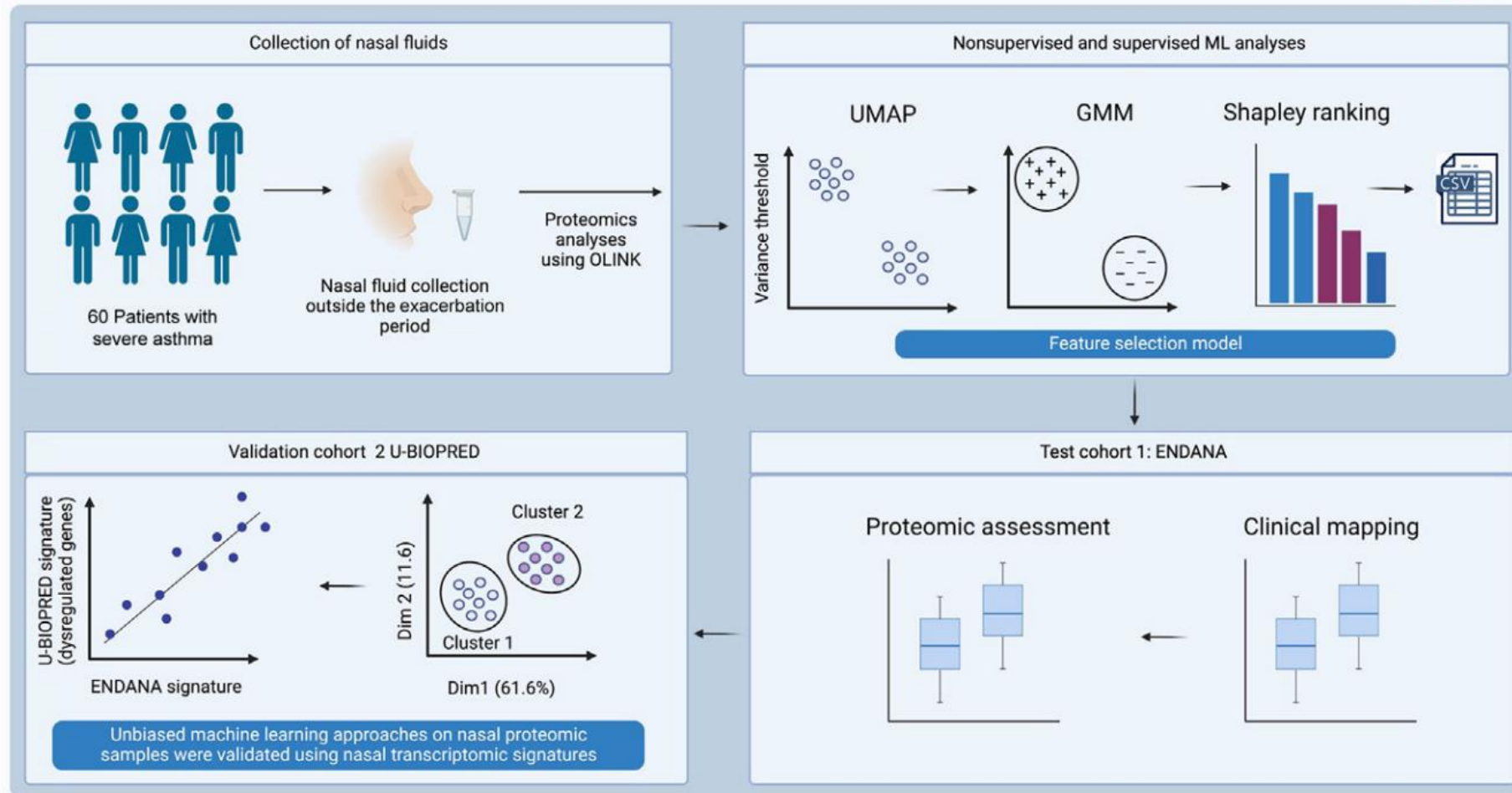
CEA cell adhesion molecule 5 (CEACAM5)

# Multidimensional endotyping using nasal proteomics predicts molecular phenotypes in the asthmatic airways



Ioana Agache, MD, PhD,<sup>a,b\*</sup> Mohamed H. Shamji, PhD, FAAAAI,<sup>c,d\*</sup> Nazanin Zounemat Kermani, PhD,<sup>c,e</sup>  
Giulia Vecchi, PhD,<sup>f</sup> Alberto Favaro, PhD,<sup>f</sup> Janice A. Layhadi, PhD,<sup>c,d</sup> Anja Heider, PhD,<sup>g</sup> Didem Sanver Akbas, PhD,<sup>c,d</sup>  
Paulina Filipaviciute, MSc,<sup>c,d</sup> Lily Y. D. Wu, BSc,<sup>c,d</sup> Catalina Cojanu, MD, PhD,<sup>a,b</sup> Alexandru Laculiceanu, MD,<sup>a,b</sup>  
Cezmi A. Akdis, MD, PhD,<sup>g,h</sup>† and Ian M. Adcock, PhD<sup>c,d</sup>† *Brasov, Romania; London, United Kingdom; and Davos, Switzerland*

# Nasal protein Machine Learning model identified two severe asthma endotypes



Cluster 1 had significant **airway obstruction, small airways disease, air trapping, decreased diffusing capacity, and increased oxidative stress**

→ TH1, TH2, neutrophil, Janus kinase-signal transducer and activator of transcription, TLR, and infection activation

# Contents






- Global severe asthma registry
- National severe asthma registry
- International severe asthma registry
  - ISAR
  - U-BIOPRED
  - **ERS SHARP**

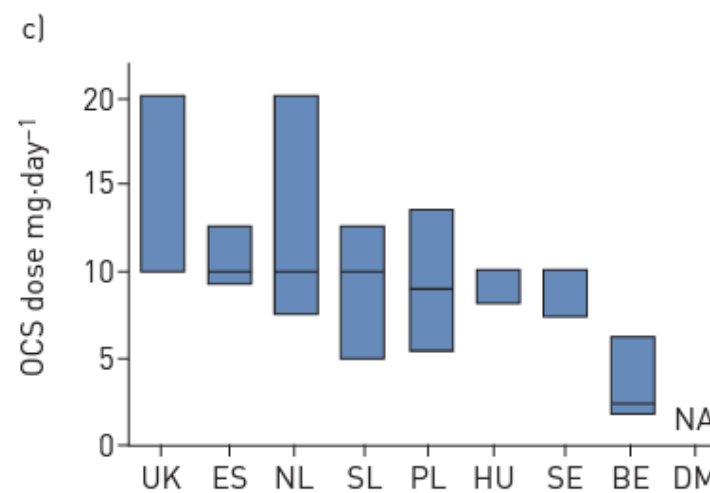
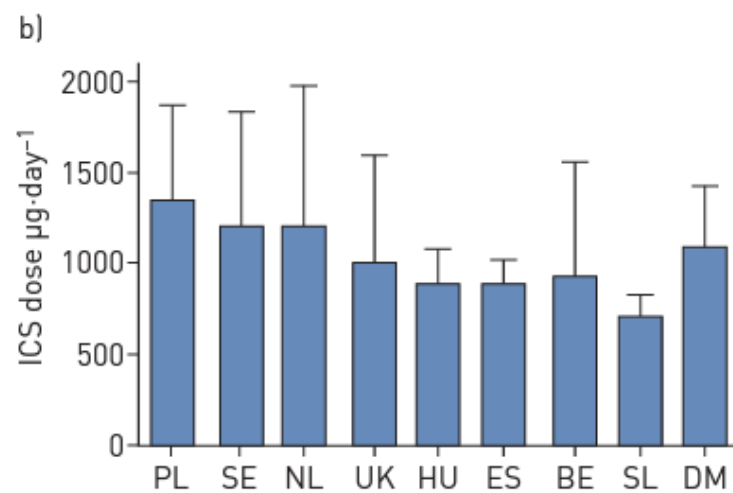
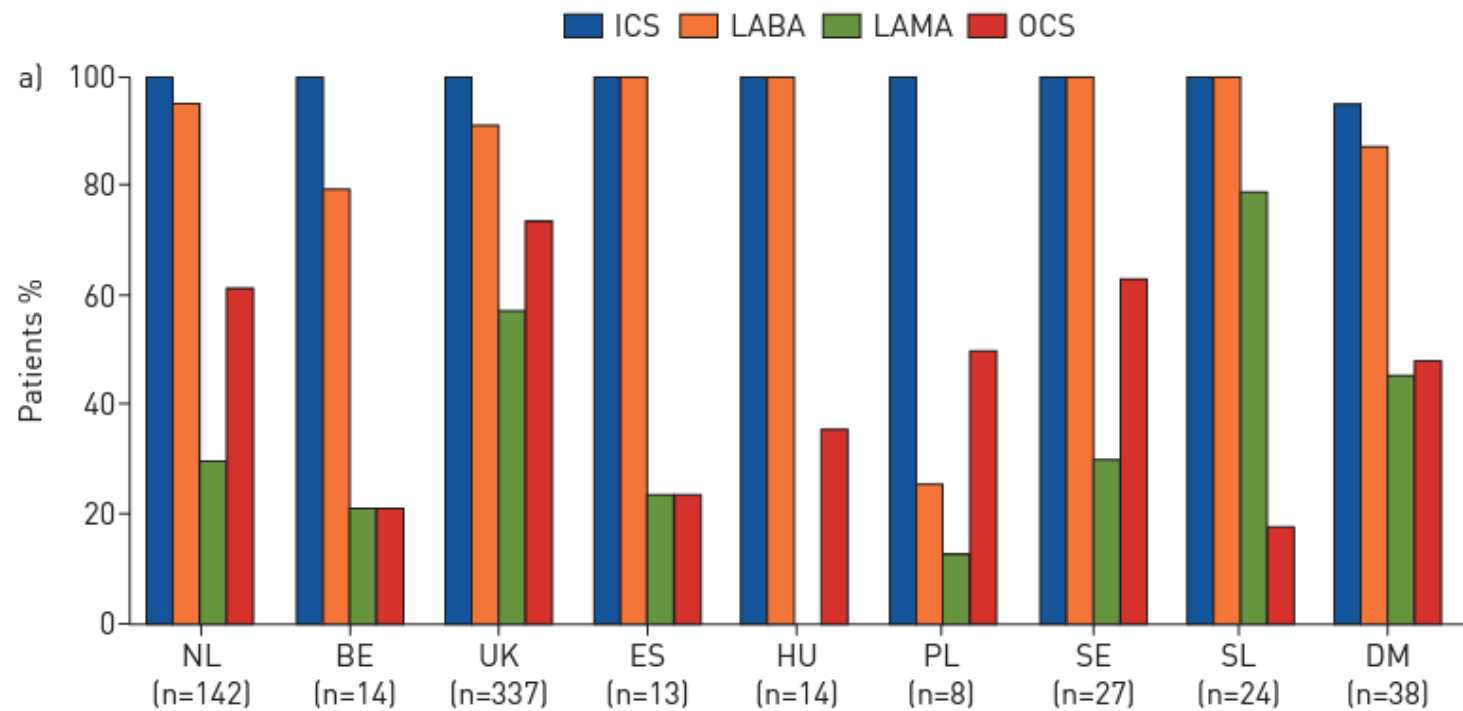
**ERS-SHARP**



CrossMark

# Characteristics and treatment regimens across ERS SHARP severe asthma registries

Job J.M.H. van Bragt <sup>1</sup>, Ian M. Adcock<sup>2</sup>, Elisabeth H.D. Bel<sup>1</sup>, Gert-Jan Braunstahl<sup>3</sup>, Anneke ten Brinke<sup>4</sup>, John Busby<sup>5</sup>, Giorgio W. Canonica<sup>6</sup>, Hui Cao<sup>7</sup>, Kian Fan Chung<sup>8</sup>, Zsuzsanna Csoma<sup>9</sup>, Barbro Dahlén<sup>10</sup>, Elizabeth Davin<sup>11</sup>, Susanne Hansen<sup>12</sup>, Enrico Heffler<sup>6</sup>, Ildiko Horvath<sup>9</sup>, Stephanie Korn<sup>13</sup>, Maxim Kots<sup>14</sup>, Piotr Kuna<sup>15</sup>, Namhee Kwon<sup>16</sup>, Renaud Louis<sup>17</sup>, Vicente Plaza <sup>18</sup>, Celeste Porsbjerg<sup>19</sup>, David Ramos-Barbon<sup>18</sup>, Levi B. Richards <sup>1</sup>, Sabina Škrjat <sup>20</sup>, Jacob K. Sont<sup>21</sup>, Susanne J.H. Vijverberg <sup>1</sup>, Els J.M. Weersink<sup>1</sup>, Valentyna Yasinska<sup>10</sup>, Scott S. Wagers<sup>22</sup>, Ratko Djukanovic<sup>23</sup> and Anke H. Maitland-van der Zee<sup>1</sup> on behalf of the SHARP Clinical Research Collaboration<sup>24</sup>



# Conclusions

- Recent global severe asthma registry studies focused on
  - Phenotypes and endotypes
  - Biologic use, efficacy, and outcomes
  - Clinical remission after biologic use
  - Translational research
    - Blood, nasal biopsy, bronchoscopic epithelial biopsy