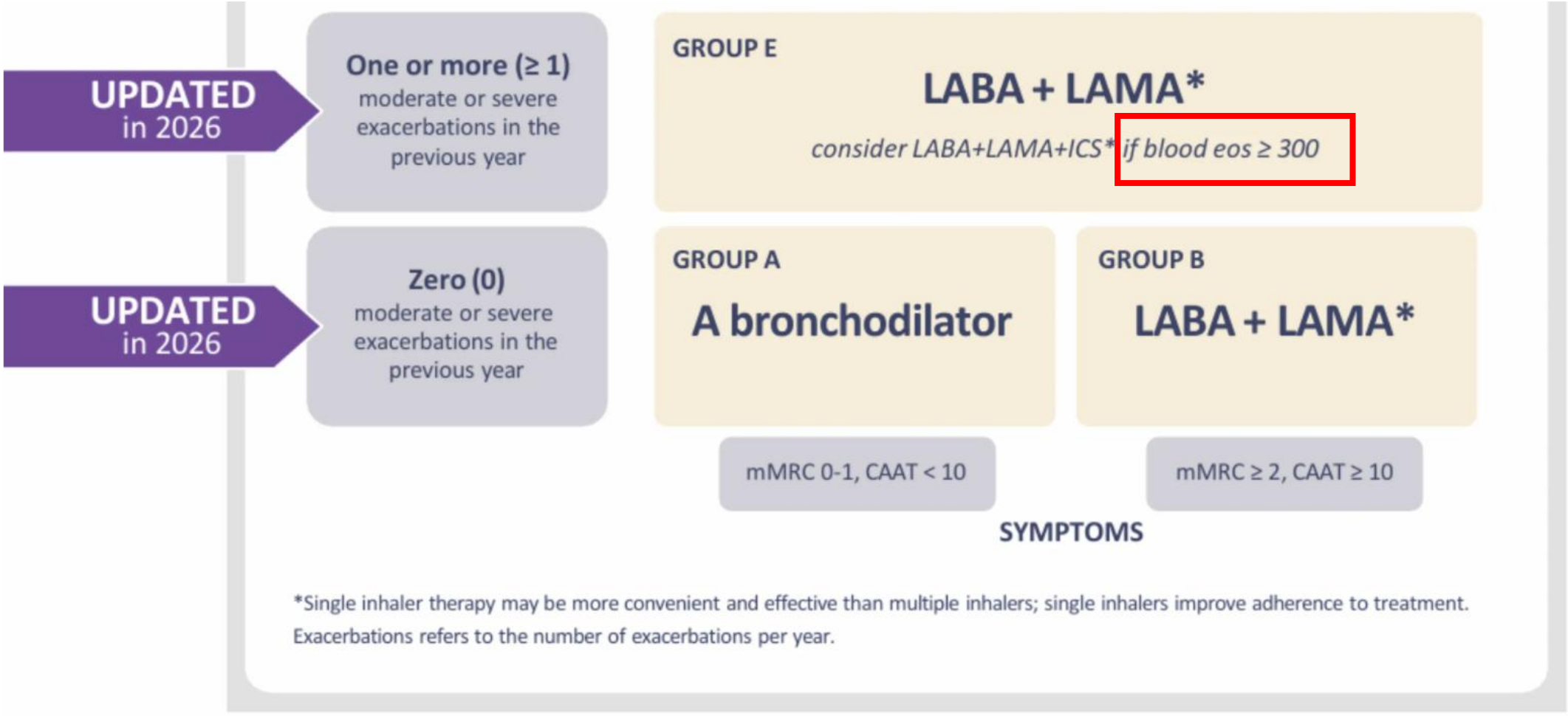
# Eosinophilic COPD: Endotyping and Comprehensive Treatment Strategies

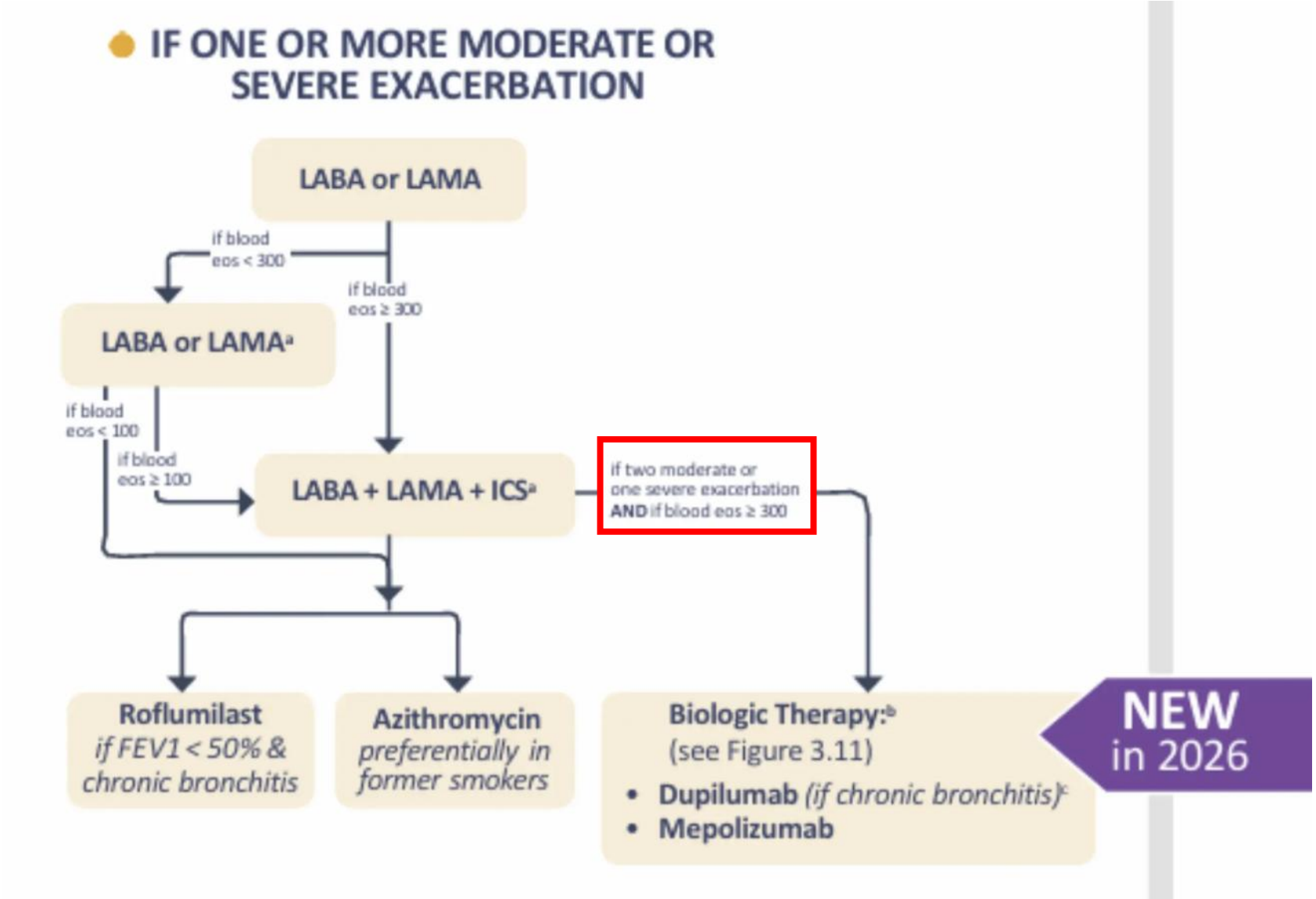
고려대학교구로병원
김상혁

# Eosinophil in COPD




GOLD 2026

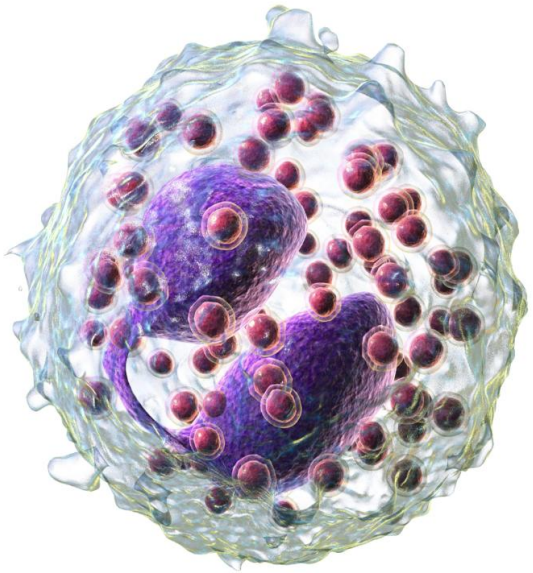
# Eosinophil in COPD




GOLD 2026

Difference with eosinophil in asthma

Biological characteristics



Endotyping and Treatment

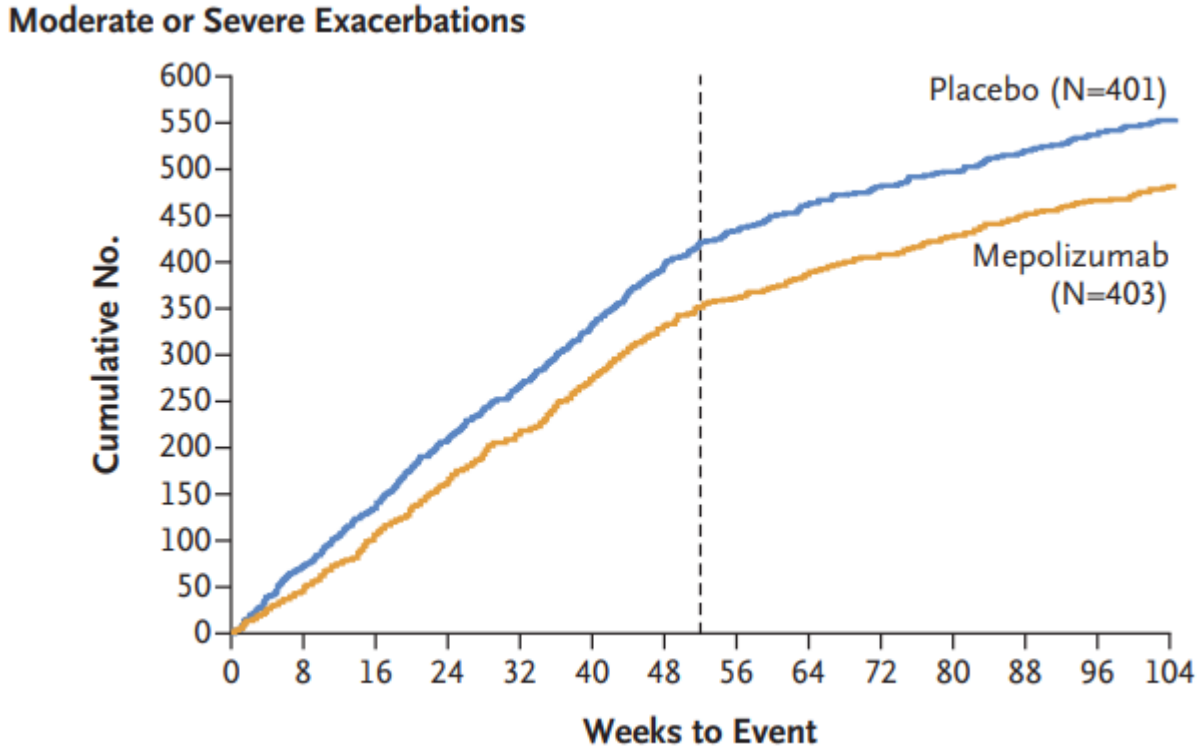
# Eosinophilic COPD is present

ORIGINAL ARTICLE

## Mepolizumab to Prevent Exacerbations of COPD with an Eosinophilic Phenotype

F.C. Sciurba,[1] G.J. Criner,[2] S.A. Christenson,[3] F.J. Martinez,[4] A. Papi,[5] N. Roche,[6] J. Bourbeau,[7] S. Korn,[8] M. Bafadhel,[9] M.L.K. Han,[10] S. Kolterer,[11] K. Miller,[12] D. Mouneimne,[13] J. Fletcher,[13] B. Mayer,[14] J. Min,[15] and I.D. Pavord,[16] for the MATINEE Study Investigators*

All the patients were current or former smokers with a smoking history of at least 10 pack-years. Patients with concurrent or previous asthma (including childhood asthma) were excluded.




*Sciurba FC et al. N Engl J Med. 2025*

# Histopathology studies

| Study (chronological order) | Staining method | Subject groups | Between-group difference | Area of quantification | Additional comments |
|---|---|---|---|---|---|
| **Large airway studies** | | | | | |
| Lacoste et al. 1993[36] | EG2 | COPD vs NS | ↑ | Subepithelium | Minimal degranulation in COPD |
| DiStefano et al. 1998[37] | Eosin | COPD vs S | = | Subepithelium | |
| Pesci et al. 1998[38] | Eosin | COPD vs S | ↑ | Subepithelium | |
| Rutgers et al. 2000[35] | EG2 | COPD vs S | ↑ | Subepithelium | All ex-smokers |
| Lofdahl et al. 2008[39] | EG2 | COPD vs S and NS | = | Intraepithelium | |
| Eltboli et al. 2015[40] | MBP | COPD $eos^{high}$ vs COPD $eos^{low}$ | ↑ | Subepithelium | Correlation with blood eosinophils |
| Kolsum et al. 2017[41] | Luna | COPD $eos^{high}$ vs COPD $eos^{low}$ | ↑ | Subepithelium | |
| Dey et al. 2023[42] | ECP | COPD vs S and NS | ↓ vs NS<br>= vs S | Subepithelium | |
| **Small airway studies** | | | | | |
| Hogg et al. 2002[6] | Hansel's | COPD vs S | = | Number of airways positive | |
| Turato et al. 2018[43] | EG2 | COPD vs S | = | Subepithelium | No correlation with blood eosinophils |
| Jogdand et al. 2020[44] | ECP | [a]COPD vs S<br>[b]GOLD 4 vs GOLD2/3 | [a]=<br>[b]↑ | Intra- and subepithelium | T2-rich neighborhoods |
| Maetani et al. 2023[45] | MBP | COPD vs S | = | Subepithelium | Correlation with blood eosinophils |
| Beech et al. 2023[46] | Luna | COPD vs S | ↑ | Intraepithelium | Effect of current smoking |

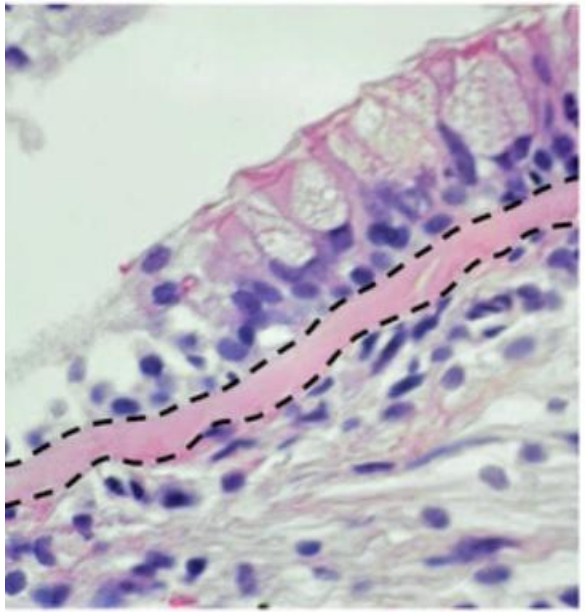
*Higham et al. JLB. 2024*

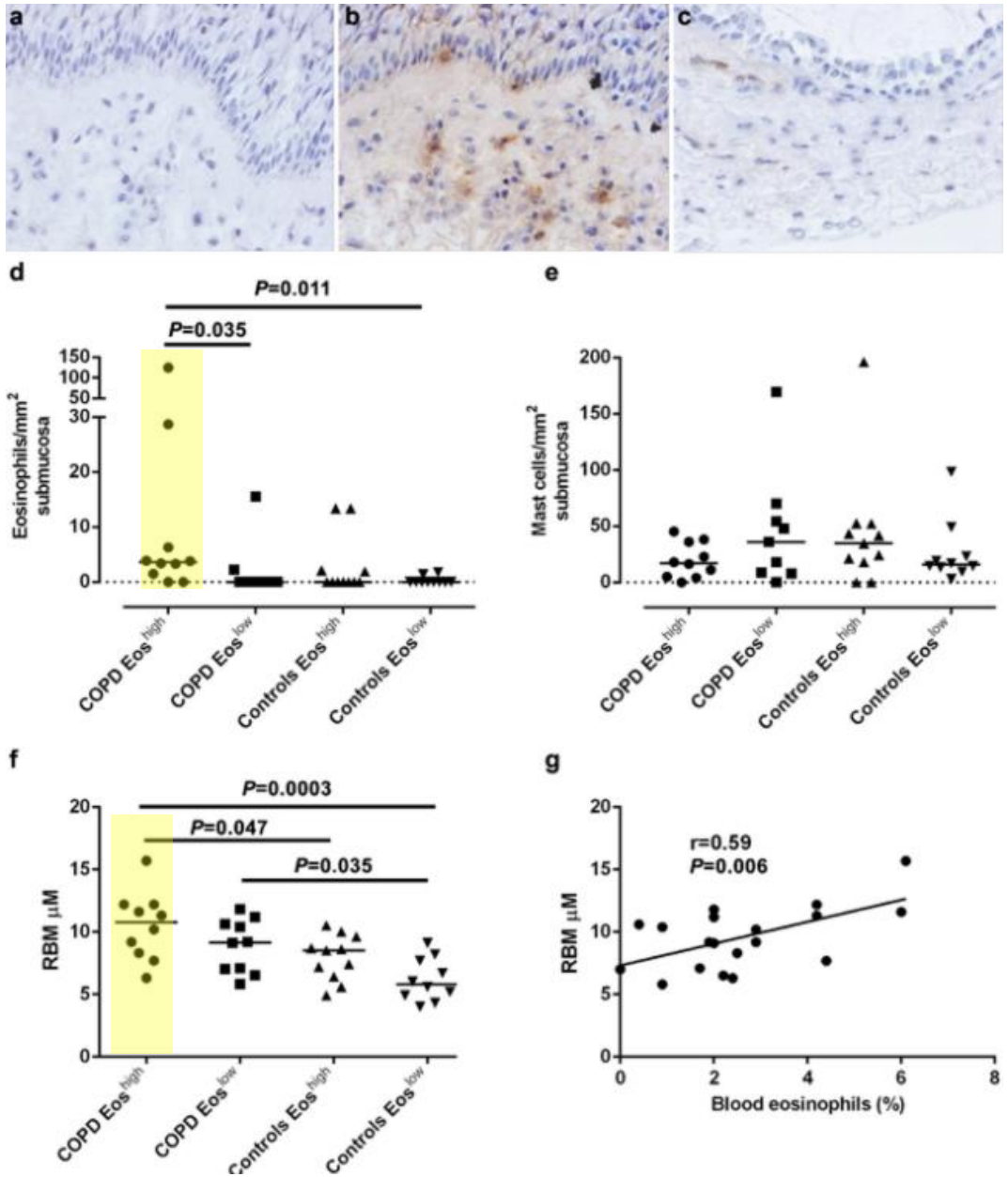
Official Journal of the Asian Pacific Society of Respirology
Respirology
APSR

Scientific Letter | Open Access

# Relationship between blood and bronchial submucosal eosinophilia and reticular basement membrane thickening in chronic obstructive pulmonary disease

Osama Eltboli, Vijay Mistry, Bethan Barker, Chris E. Brightling

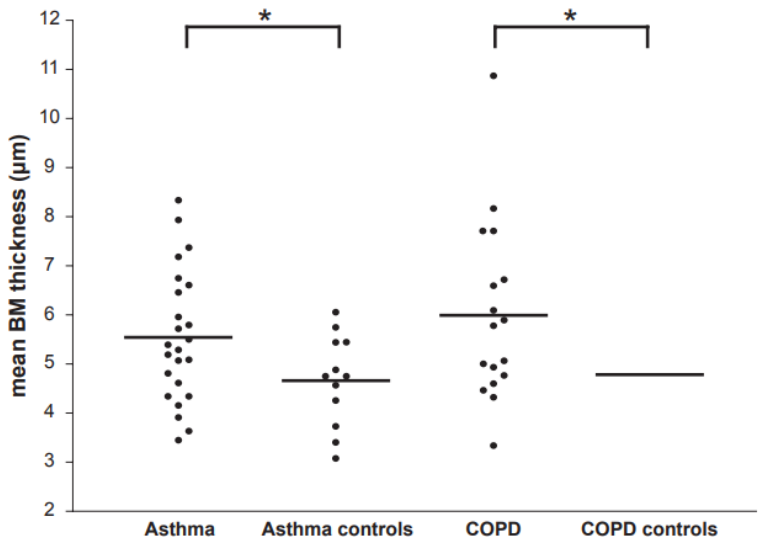



**BEC provides histopathological evidence of submucosal eosinophilia and remodeling**

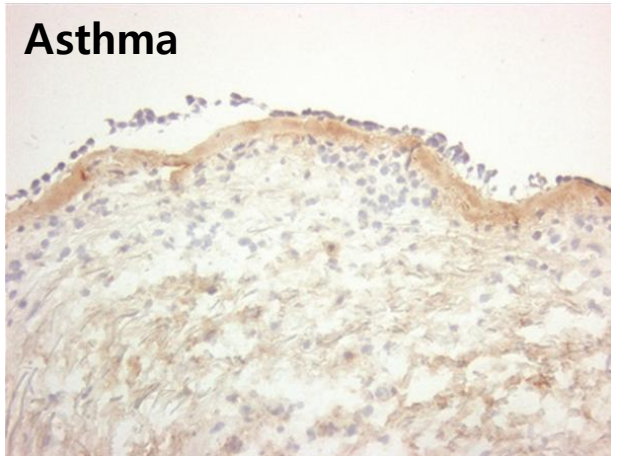
*Eltboli et al, Respirology, 2015*

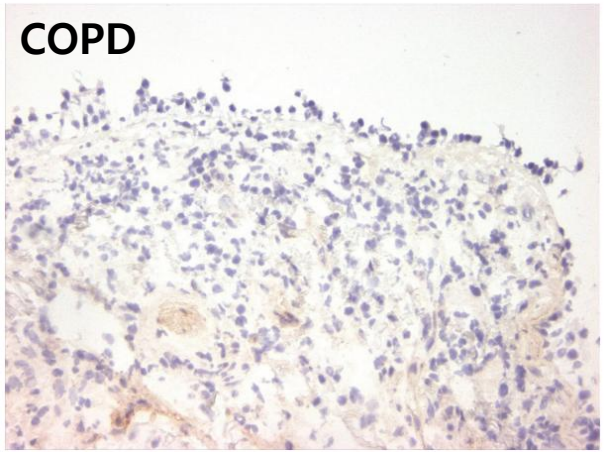
# Reticular basement membrane in asthma and COPD: Similar thickness, yet different composition

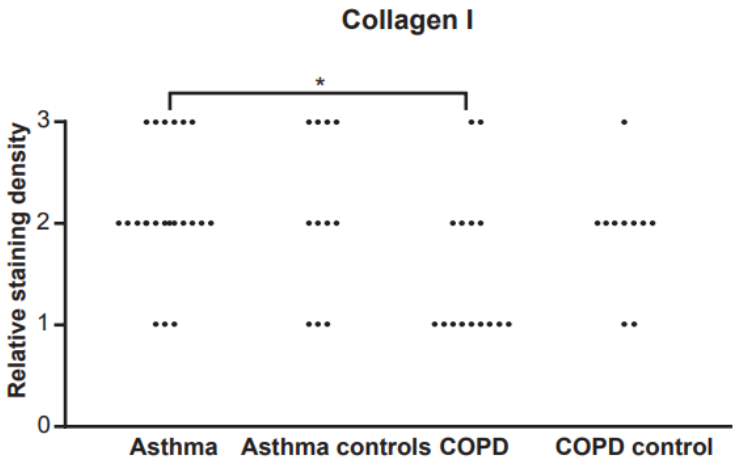


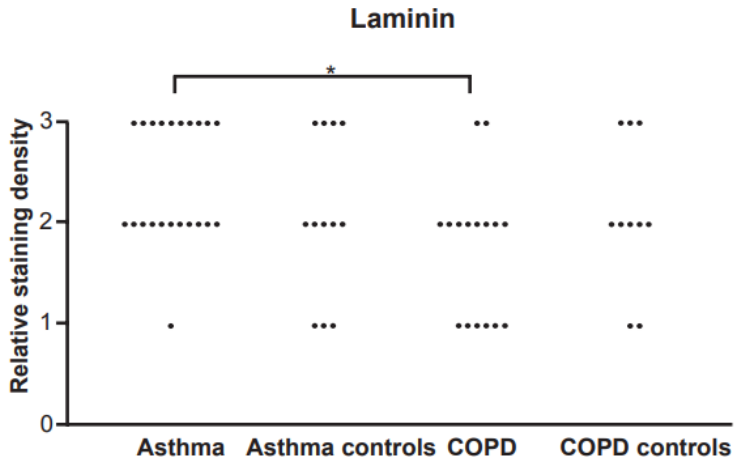

**Asthma: Hyper-repairing**
**- Tissue-level fibrogenesis**
**COPD: Chronic injury & impaired repair**
**- Tissue destruction & Incomplete synthesis**

## Collagen I staining




*Liesker et al. IJCOPD. 2009*

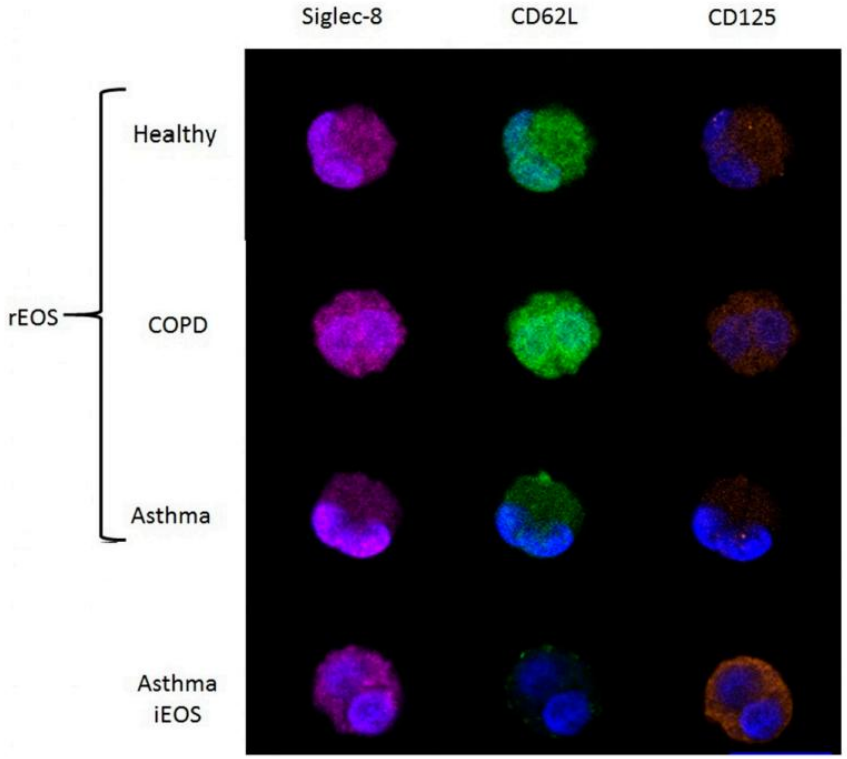
# Differences in Eosinophil Subtypes

ORIGINAL ARTICLE

## Eosinophil Subtypes in Adults with Asthma and Adults with Chronic Obstructive Pulmonary Disease

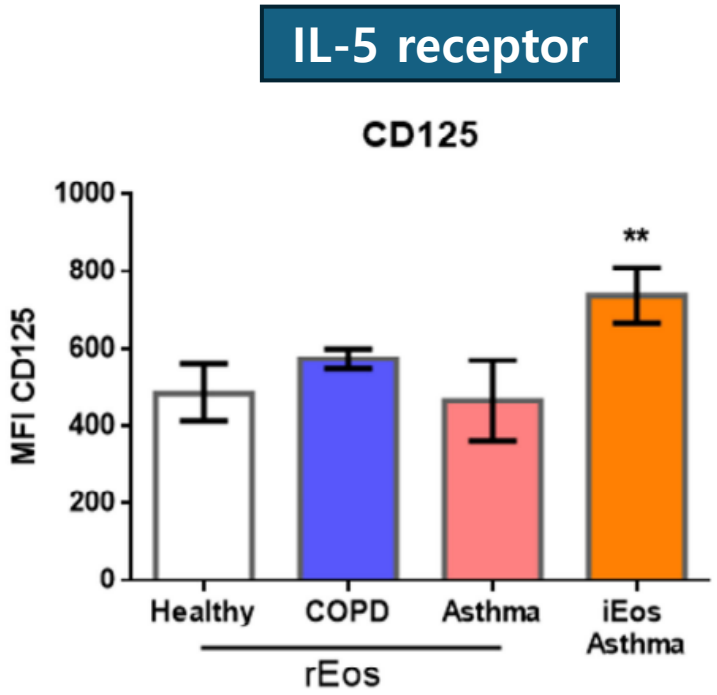
Carlos Cabrera López[1], Alejandra Sánchez Santos[2], Angelina Lemes Castellano[3], Sara Cazorla Rivero[2,4], Joaquín Breña Atienza[5], Enrique González Dávila[6], Bartolomé Celli[7], and Ciro Casanova Macario[8]

| | Group | | | |
|---|---|---|---|---|
| | COPD Matched Group ($n=10$) | Smokers without COPD ($n=10$) | Patients with Asthma ($n=10$) | Healthy Subjects ($n=10$) |
| Eosinophils, cells/μl | 200 ± 98 | 192 ± 135 | 607 ± 429 | 203 ± 92 |
| ≤150 | 3 (30) | 4 (40) | — | 3 (30) |
| 150–299 | 6 (60) | 5 (50) | 5 (50) | 6 (60) |
| 300–499 | 1 (10) | — | — | 1 (10) |
| ≥500 | — | 1 (10) | 5 (50) | — |
| Eosinophils, % | 2.7 ± 1.3 | 2.6 ± 1.8 | 8.4 ± 7.5 | 3.0 ± 1.8 |
| rEos, %* | 99.3 ± 1.1 | 99.9 ± 0.2 | 74.4 ± 15.4 | 99.3 ± 1.7 |
| iEos, %* | 0.70 ± 1.10 | 0.14 ± 0.24 | 25.59 ± 15.38 | 0.67 ± 1.72 |




*López et al, AJRCCM 2023*

# Differences in Eosinophil Subtypes




√ These results tell us why IL-5 treatment responses are different between asthma and COPD

√ However, some COPD patients were responded to IL-5 treatment

√ Stable status, blood flow cytometry, phenotypic plasticity…

*López et al, AJRCCM 2023*

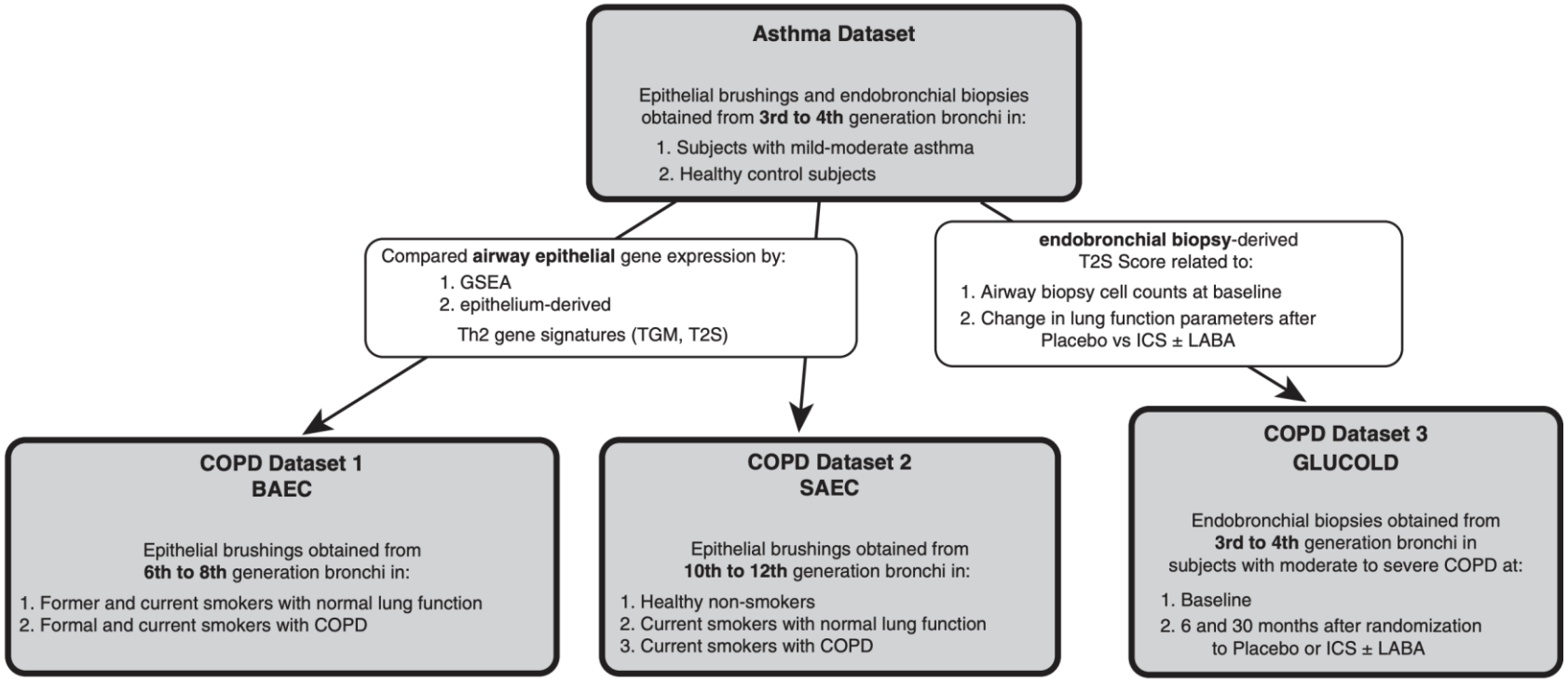
# Gene and Transcriptome

ORIGINAL ARTICLE

**Asthma–COPD Overlap**

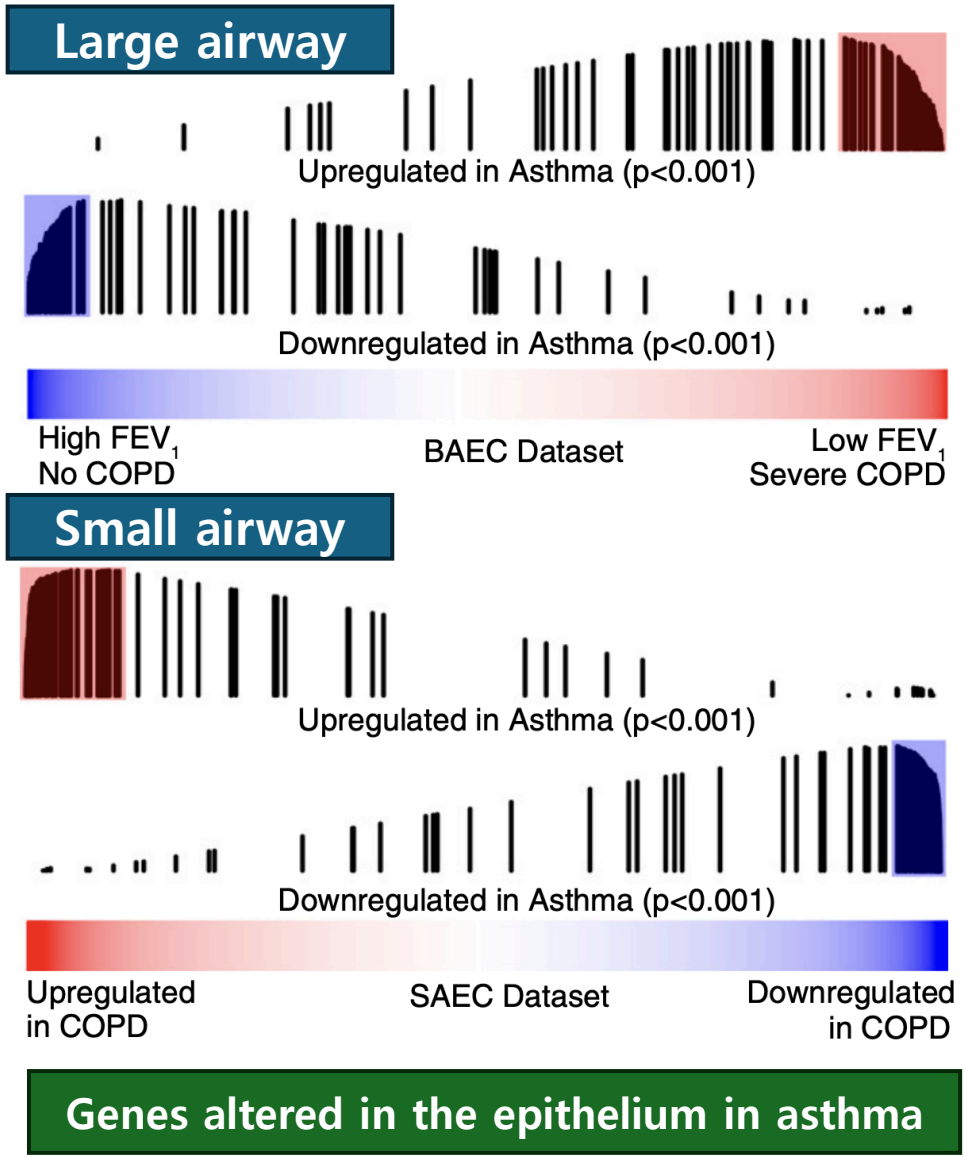
Clinical Relevance of Genomic Signatures of Type 2 Inflammation in Chronic Obstructive Pulmonary Disease

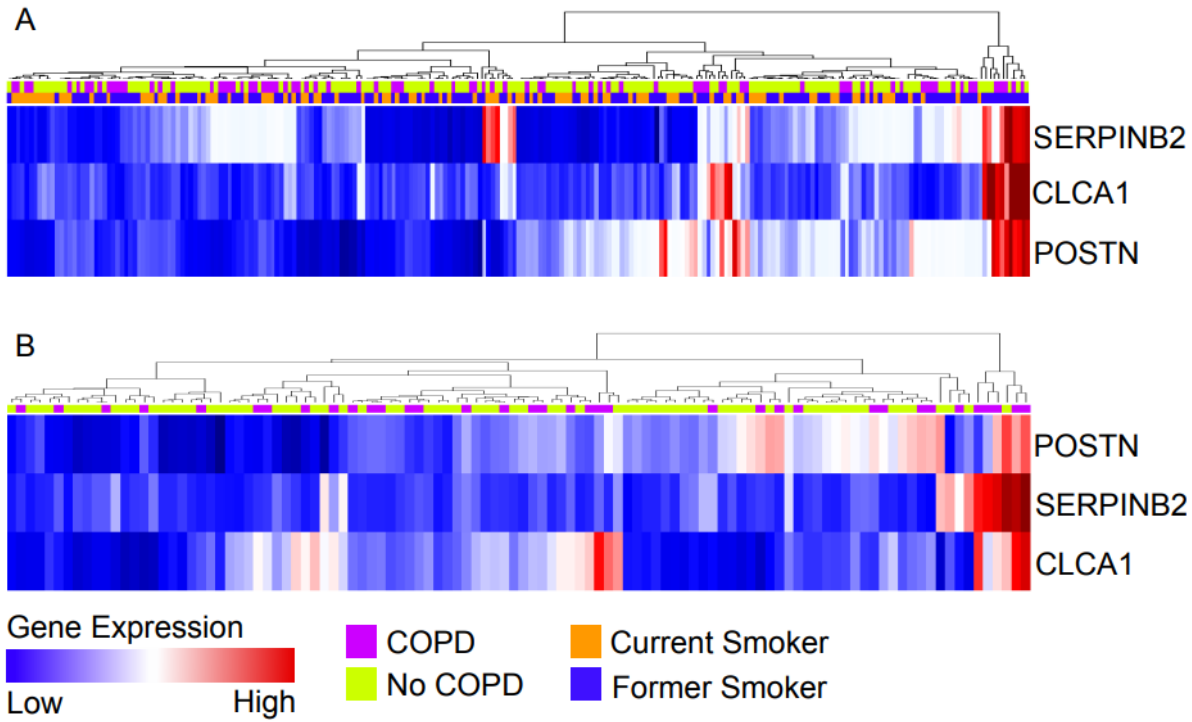
Stephanie A. Christenson[1,2], Katrina Steiling[3,4], Maarten van den Berge[5,6], Kahkeshan Hijazi[7], Pieter S. Hiemstra[8], Dirkje S. Postma[5,6], Marc E. Lenburg[3,4,9], Avrum Spira[3,4,9], and Prescott G. Woodruff[1,2]




*Christenson et al. AJRCCM. 2015*

# Gene and Transcriptome



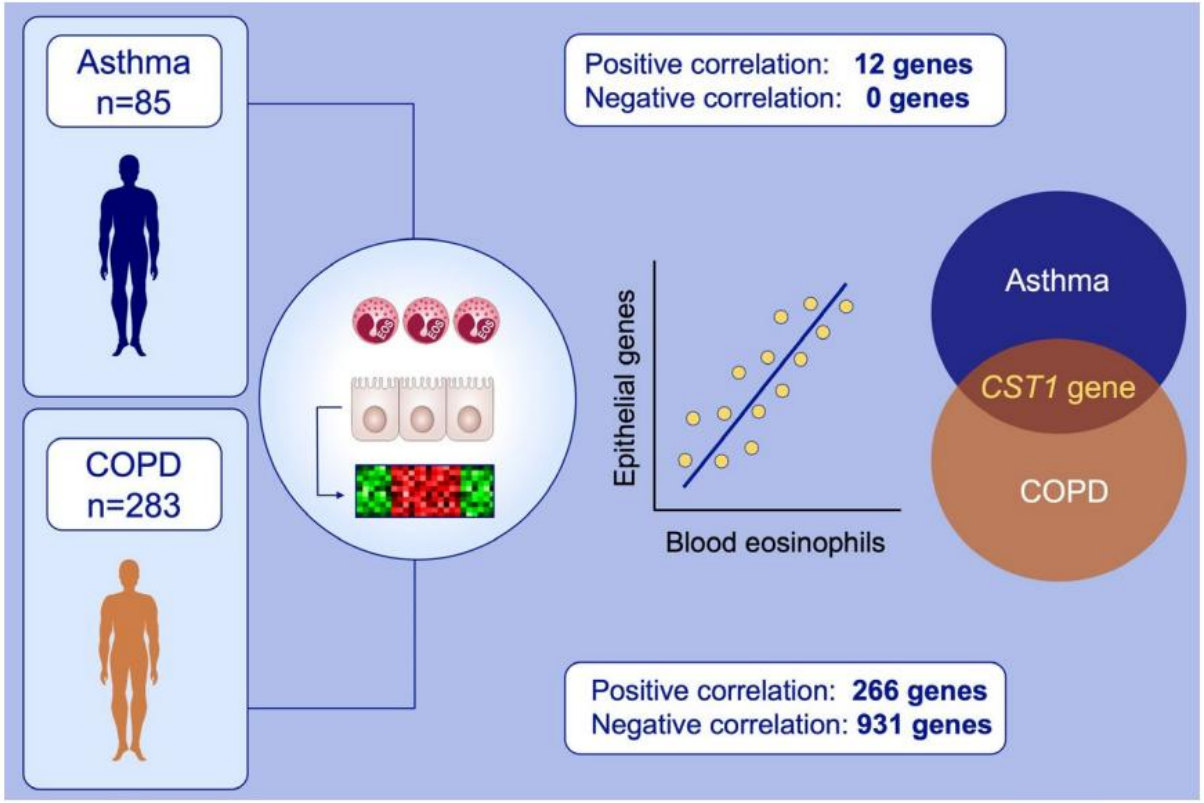



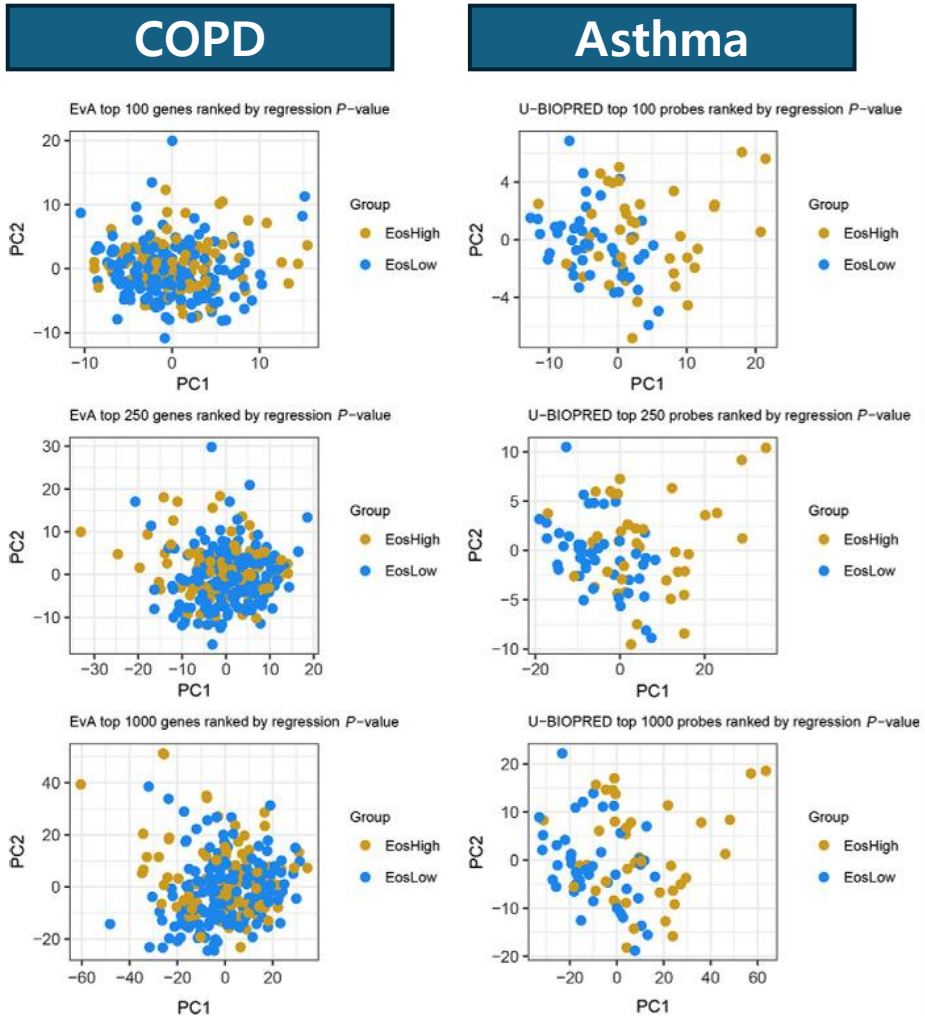

**√ T2-related gene expression was associated with worse COPD.**

**√ However, some typical asthma-related genes (like SERPINB2) were repressed by active smoking in these patients.**

*Christenson et al. AJRCCM. 2015*

# Gene and Transcriptome



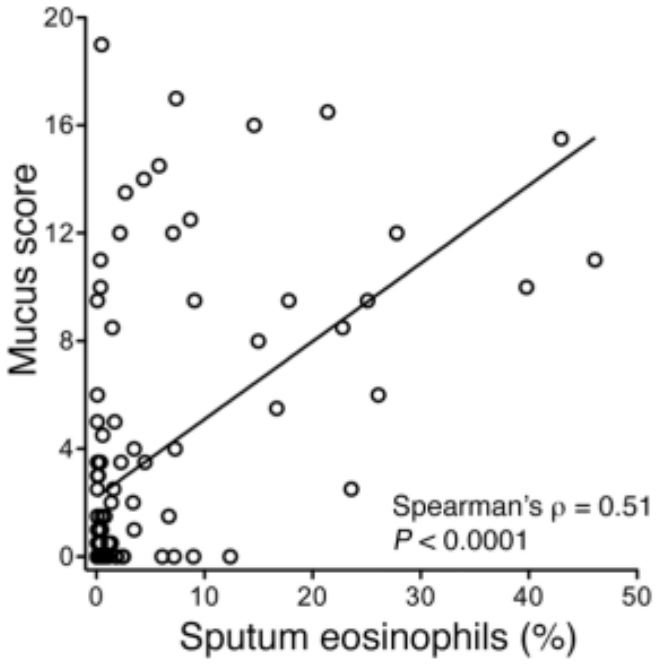




**Unlike in asthma, elevated blood eosinophils in COPD did not show significant differences in the airway epithelial transcriptome**

*George et al. Allergy. 2019*

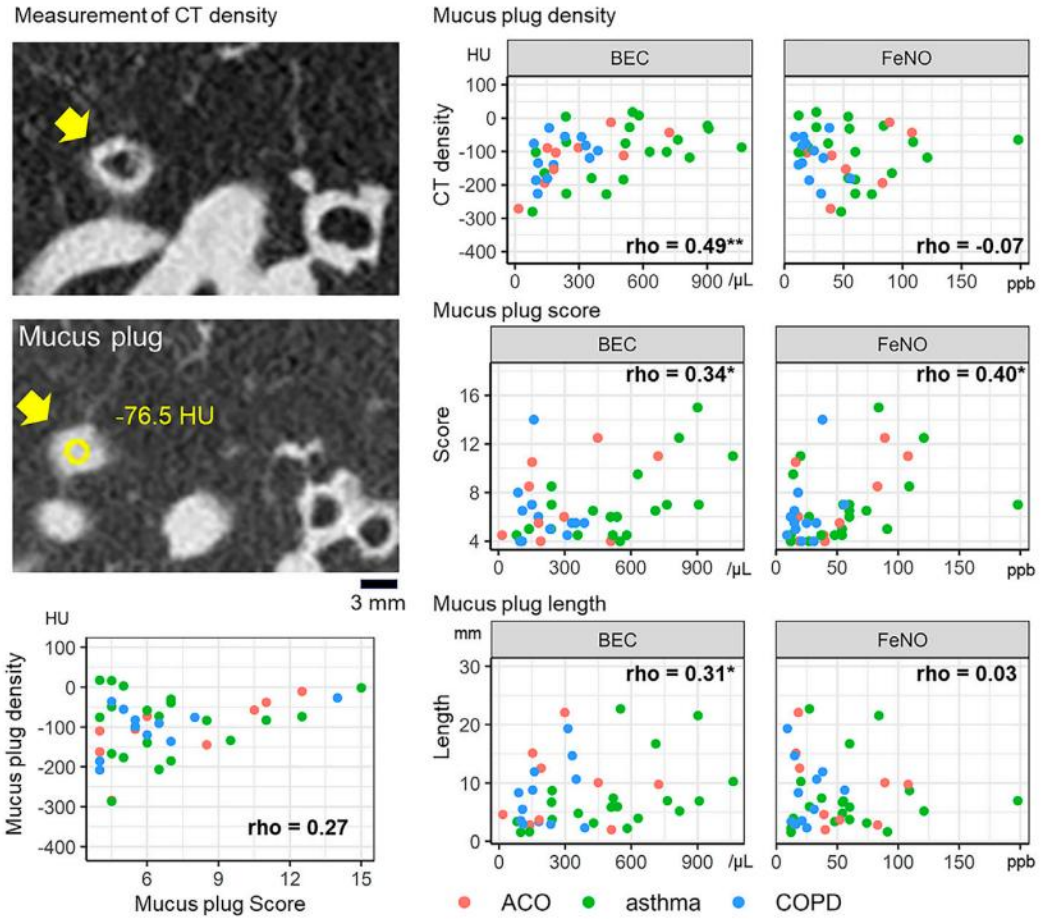
# Mucus plug and Eosinophil

## Asthma




## COPD

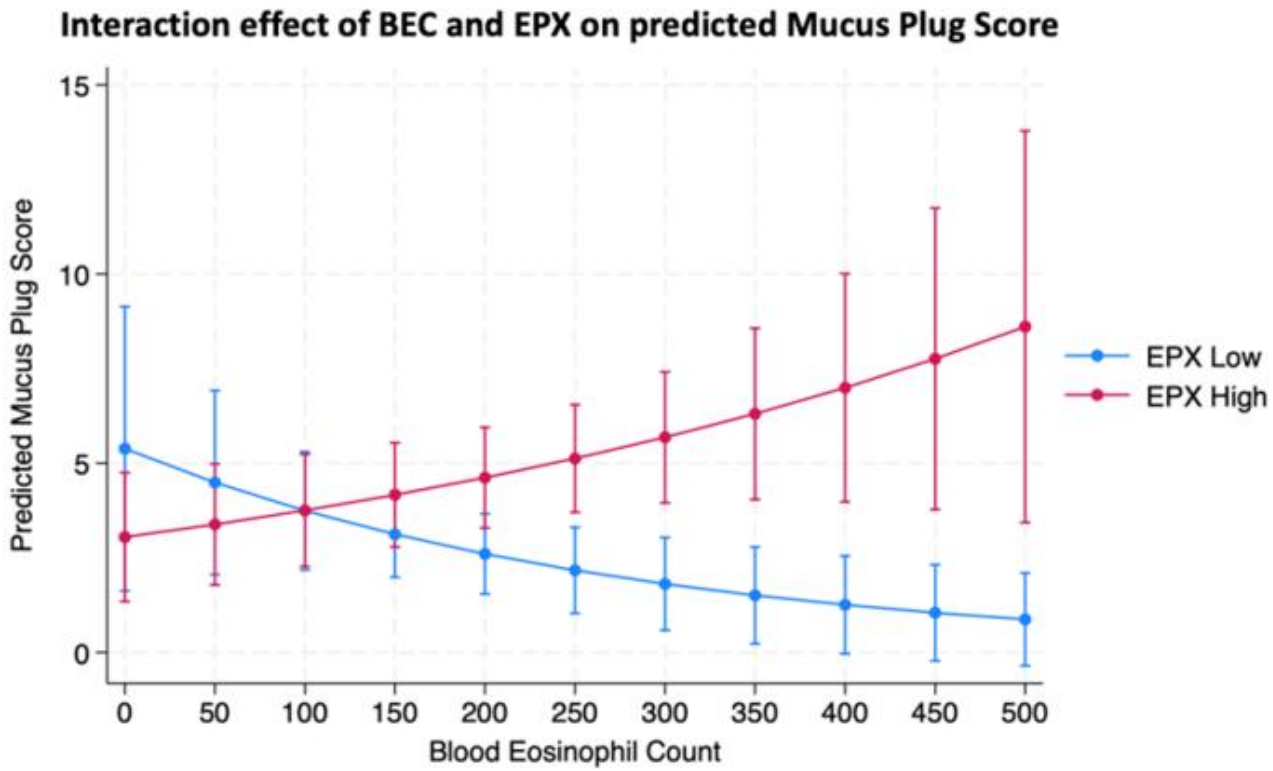
Among the 400 smokers, 127 had data for neutrophil percentage and eosinophil percentage in induced sputum. The median [interquartile range] sputum neutrophil percentage was higher in patients with a high mucus plug score than in those with a low score (86% [71–94%] vs. 72% [52–83%]; $P < 0.001$). The median [interquartile range] sputum neutrophil number ($\times 10^6$/ml) was also higher in patients with a high mucus plug score than in those with a low score (1.12 [0.27–3.62] vs. 0.24 [0.09–0.59]; $P = 0.0002$). The sputum eosinophil percentage was similar in both subgroups (0.1 [0–1.1] vs. 0.3% [0–1.0]; $P = 0.55$), and the sputum eosinophil number was also similar (data not shown).




*Dunican et al. J Clin Invest. 2018; Dunican et al. AJRCCM. 2022; Tanabe AJRCCM 2025*

**Mucus Plug Formation is Associated with Eosinophilic Activation in Chronic Obstructive Pulmonary Disease**

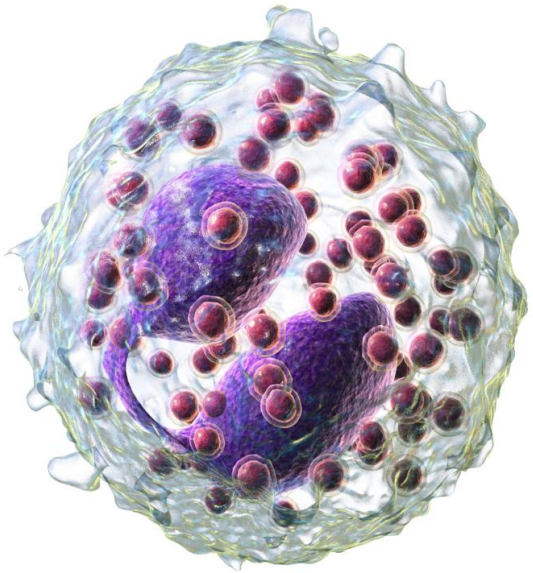
Federico Baraldi[1,2], Jordina S Y Mah[1], Abdulrahman Almuhanna[1], Aaron Braddy-Green[1], Sam Bartlett-Pestell[1], Mairi A MacLeod[1], Chloe I Bloom[1], Andrew I Ritchie[1,3], Dexter J Wiseman[1,4], James P Allinson[1], Eric A Hoffman[5], Alberto Papi[2], Jadwiga A Wedzicha[1], Lydia J Finney[1]




*Baraldi et al 2026 AJRCCM*

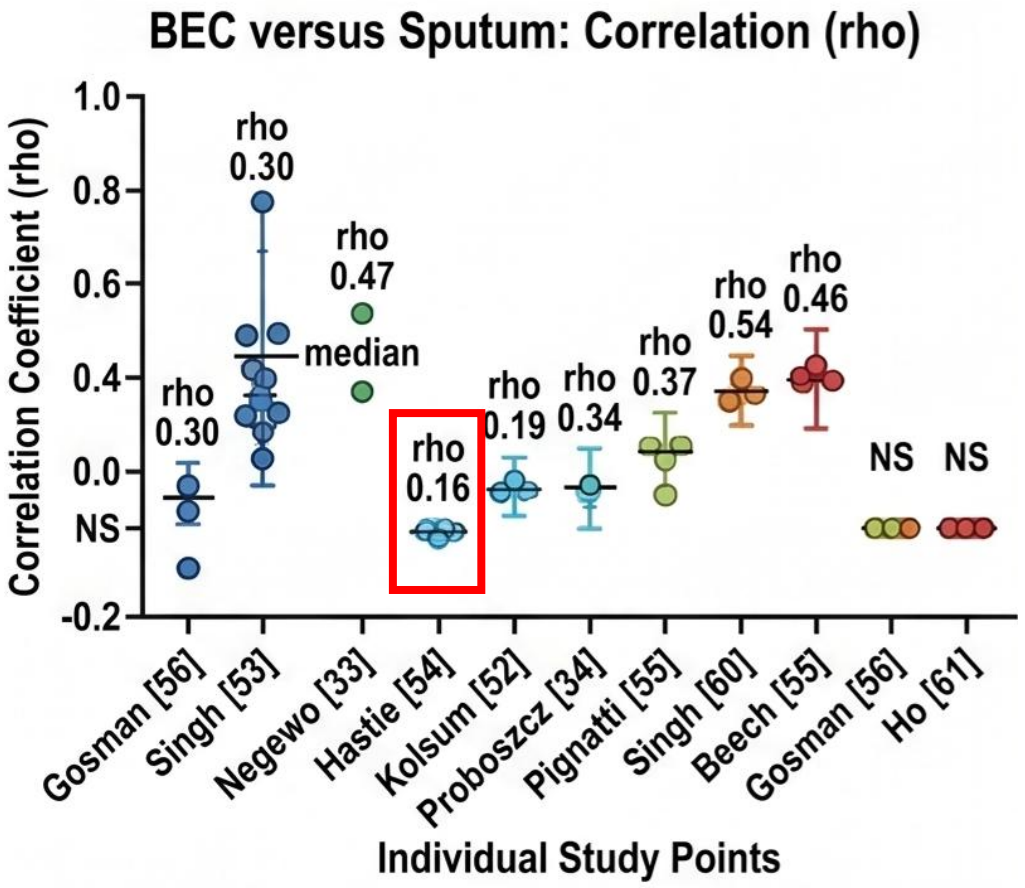
Difference with eosinophil in asthma

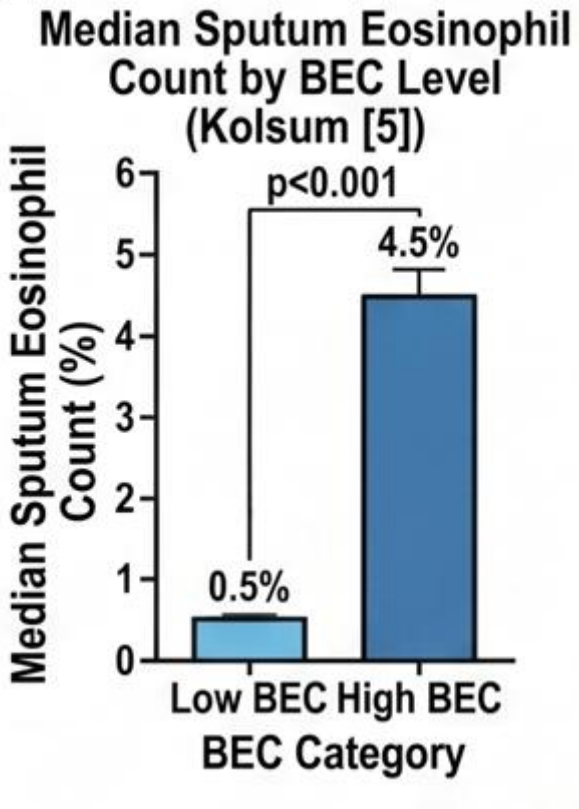
Biological characteristics



Endotyping and Treatment

# Pulmonary eosinophils



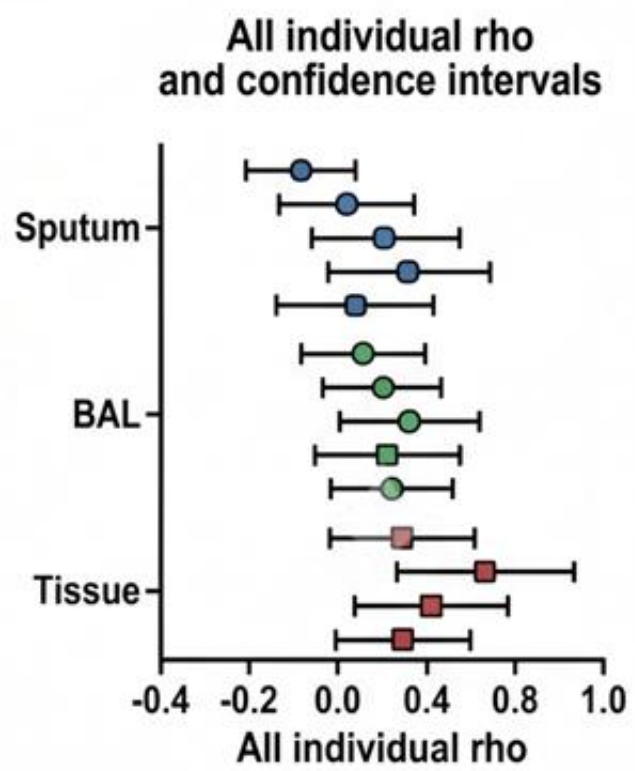
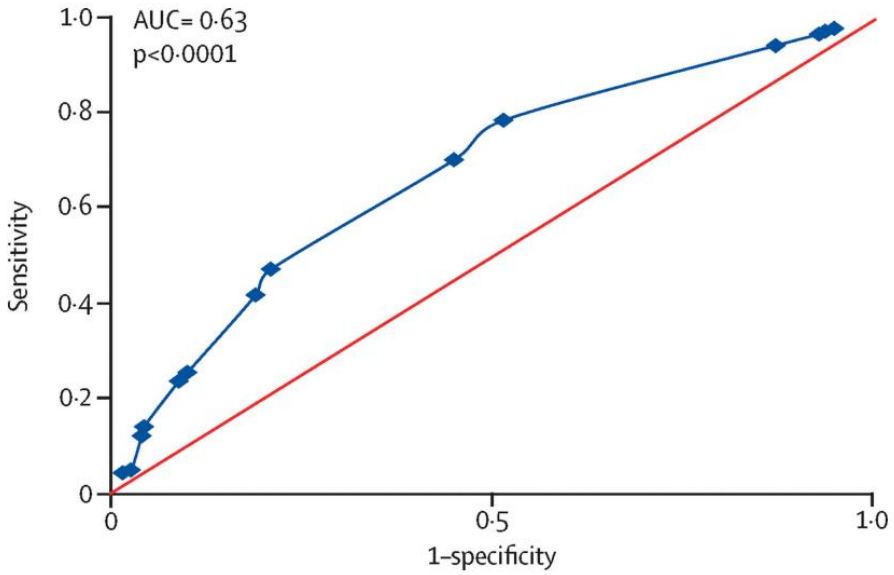



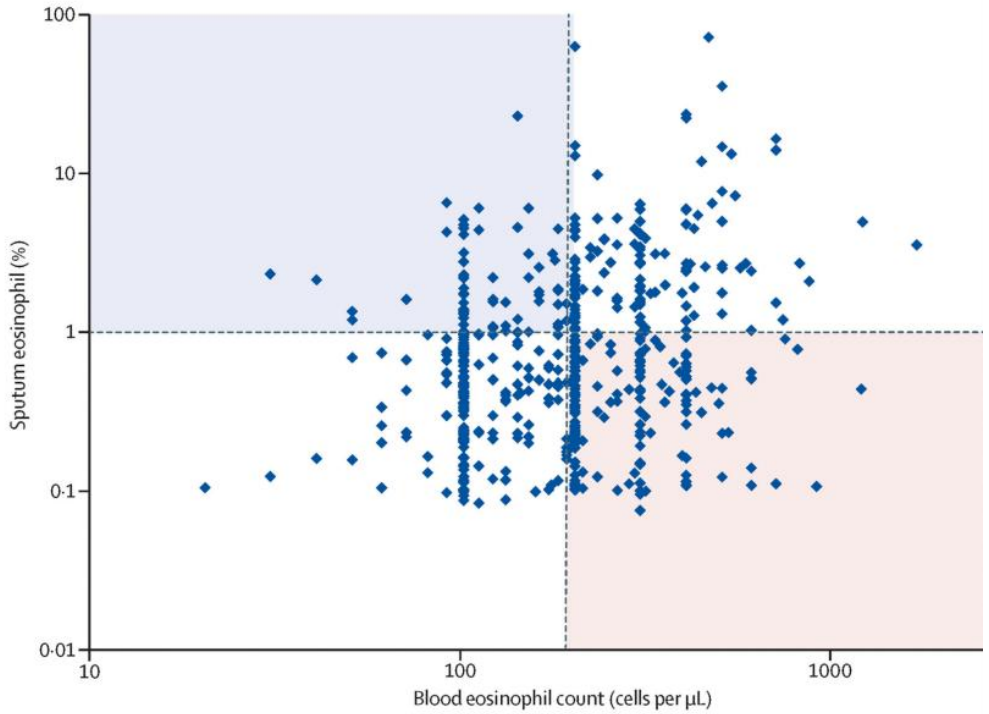

*Image was generated by Gemini from Table 1*
*Beech A et al. ERS monograph 2025*

# BEC vs. Sputum eosinophil in COPD

## Association of sputum and blood eosinophil concentrations with clinical measures of COPD severity: an analysis of the SPIROMICS cohort

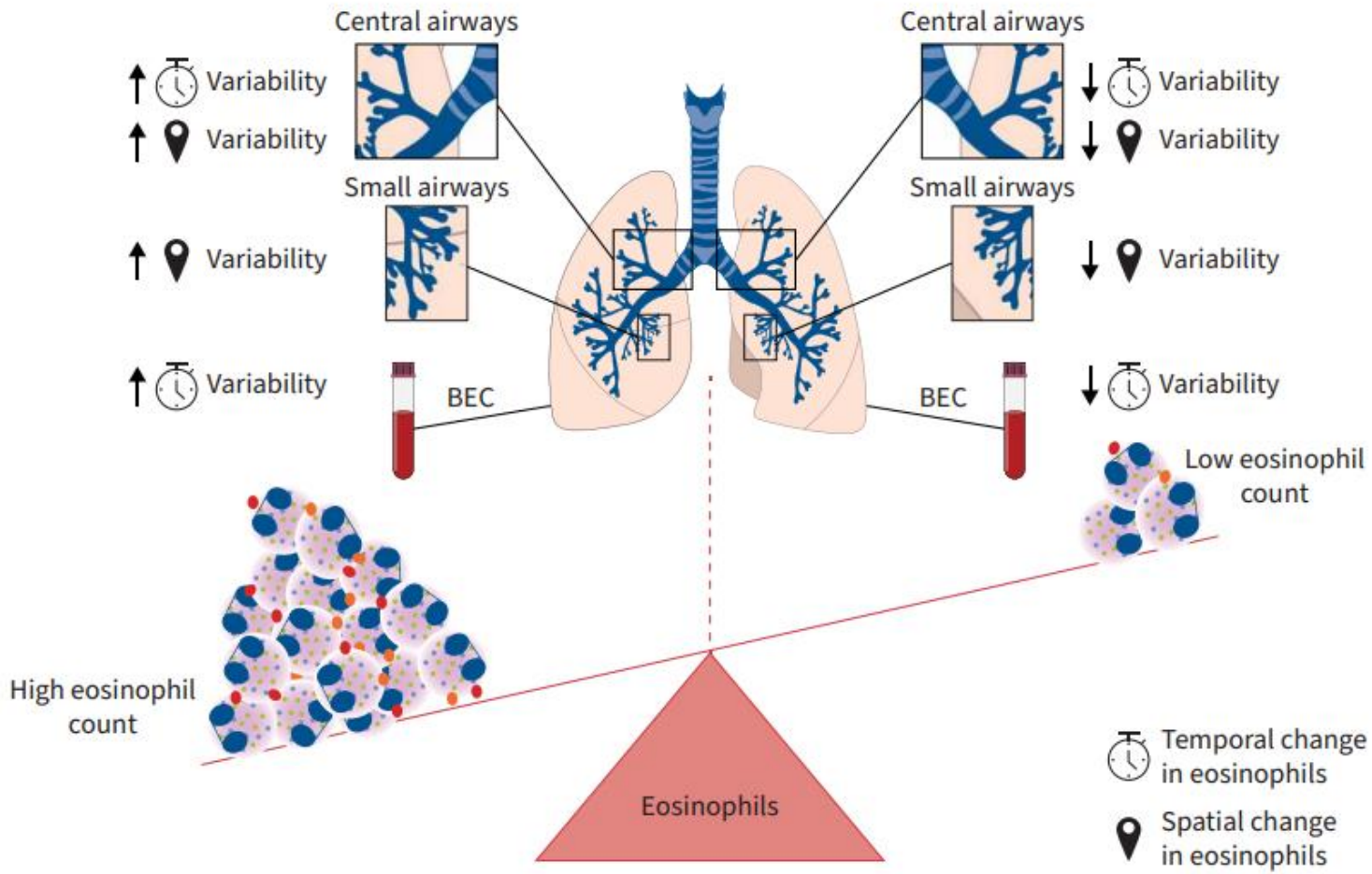
*Annette T Hastie, Fernando J Martinez, Jeffrey L Curtis, Claire M Doerschuk, Nadia N Hansel, Stephanie Christenson, Nirupama Putcha, Victor E Ortega, Xingnan Li, R Graham Barr, Elizabeth E Carretta, David J Couper, Christopher B Cooper, Eric A Hoffman, Richard E Kanner, Eric Kleerup, Wanda K O'Neal, Richard Paine III, Stephen P Peters, Neil E Alexis, Prescott G Woodruff, MeiLan K Han, Deborah A Meyers, Eugene R Bleecker, for the SPIROMICS investigators**




*Hastie et al. Lancet Resp Med. 2017*

# Variability in eosinophil count in COPD




*Beech A et al. ERS monograph 2025*

# Microbiome: association with eosinophil

**STABLE**

*biomedicines*

MDPI

*Article*

## Airway Bacteria Quantification Using Polymerase Chain Reaction Combined with Neutrophil and Eosinophil Counts Identifies Distinct COPD Endotypes

Augusta Beech [1,2,*], Simon Lea [1], Jian Li [1], Natalie Jackson [2], Alex Mulvanny [1,2] and Dave Singh [1,2]

| | Sputum Eos Persistently ≥3% ($n$ = 7) | | Sputum Eos ≥3% at One Visit Only ($n$ = 8) | | Sputum Eos <3% at Both Visits ($n$ = 33) | |
|---|---|---|---|---|---|---|
| | Baseline | 6 months | Baseline | 6 months | Baseline | 6 months |
| No PPM | 6 | 6 | 6 | 6 | 12 | 11 |
| HI | 0 | 0 | 1 | 1 | 7 | 7 |
| PA | 0 | 0 | 0 | 0 | 1 | 0 |
| SP | 0 | 0 | 0 | 0 | 0 | 1 |
| MC | 0 | 1 | 0 | 1 | 0 | 1 |
| [a] >1 PPM | 0 | 0 | 0 | 0 | 1 | 2 |
| Any bacterial colonisation | 0/6 (0.0%) | 1/7 (14.3%) | 1/7 (14.3%) | 2/8 (25.0%) | 9/21 (42.9%) | 11/22 (50.0%) |
| * No data | 1 | 0 | 1 | 0 | 12 | 11 |

*Beech et al. Biomedicines. 2021*

# Microbiome: association with eosinophil

**STABLE**

*biomedicines*

MDPI

*Article*

## Identification of COPD Inflammatory Endotypes Using Repeated Sputum Eosinophil Counts

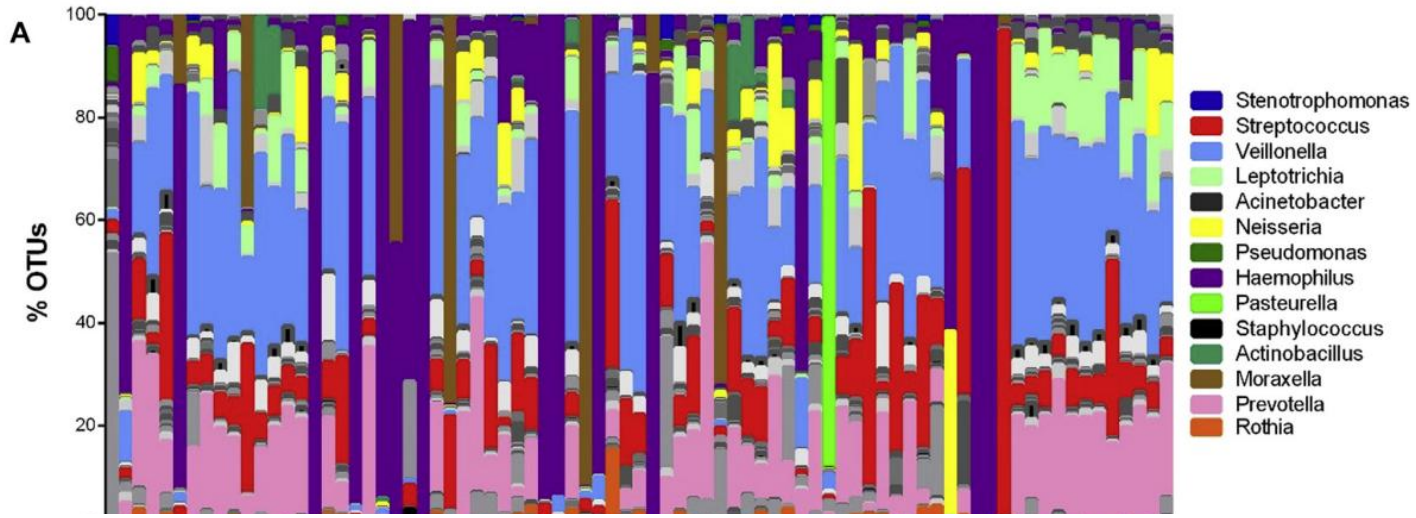
Augusta Beech [1,2,*], Natalie Jackson [2] and Dave Singh [1]

| Baseline sputum characteristic | Eosinophil$^{LOW}$ n=13 | Eosinophil$^{INT}$ n=12 | Eosinophil$^{HIGH}$ n=9 | p-value |
|---|---|---|---|---|
| **Total PPM Load (genome copies/ml)** | 8.12E+05 [0.00E+00-9.25E+07] | 2.03E+05 [2.48E+02-1.58E+08] | 8.73E+03 [0.00E+00-5.12E+06] | 0.25 |
| ***H.influenzae* Load (genome copies/ml)** | **2.67E+04 [0.00E+00-9.05E+07]** | **4.12E+03 [0.00E+00-1.58E+08]** | ***2.75E+02 [0.00E+00-1.63E+04]** | **0.03** |
| ***S.pneumoniae* Load (genome copies/ml)** | 2.42E+05 [0.00E+00-2.02E+06] | 2.81E+04 [0.00-1.25E+06] | 8.53E+03 [0.00E+00-5.12E+06] | 0.99 |
| ***M.catarrhalis* Load (genome copies/ml)** | 0.00E+00 [0.00E+00-5.63E+02] | 0.00E+00 [0.00E+00-1.34E+04] | 0.00E+00 [0.00E+00-3.27E+02] | 0.30 |
| ***P.aeruginosa* Load (genome copies/ml)** | 0.00E+00 [0.00E+00-5.88E+06] | 0.00E+00 [0.00E+00-0.00E+00] | 0.00E+00 [0.00E+00-0.00E+00] | 0.46 |
| **No colonisation (% of patients)** | 53.8 | 66.7 | 100.0 | 0.06 |

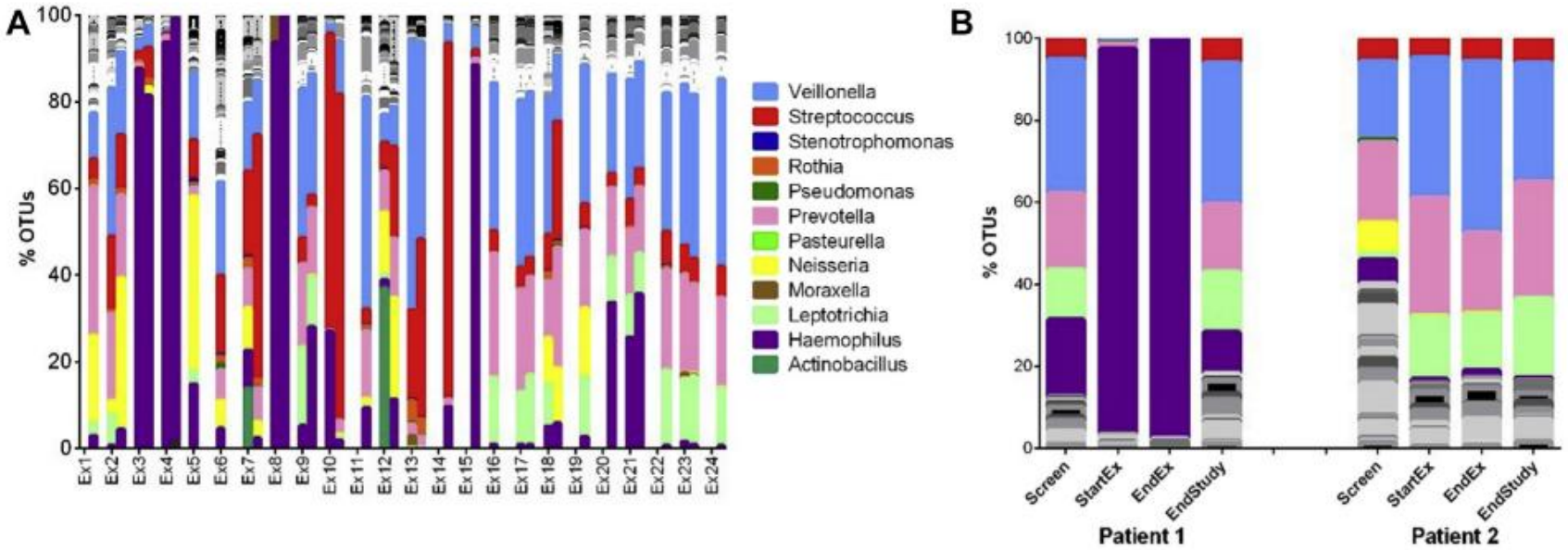
*Beech et al. Biomedicines. 2022*

# Hemophilus colonization-neutrophilic subtype

**STABLE**



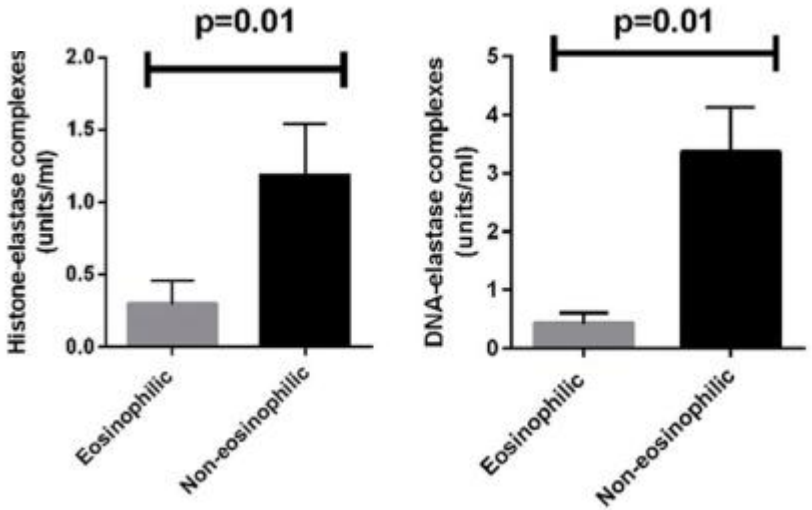

**Exacerbation**



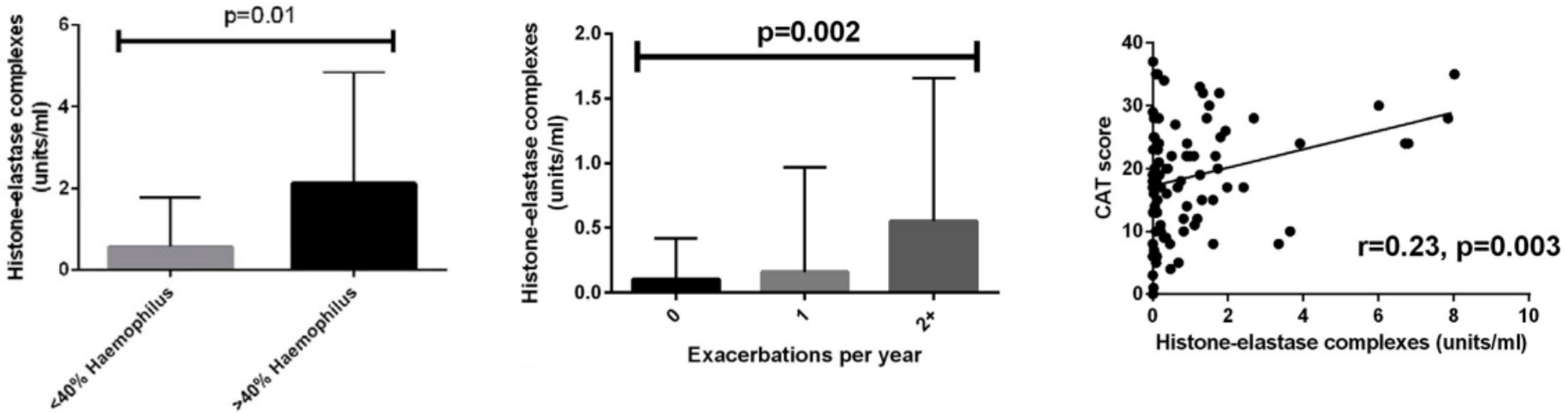

*Dicker et al. JACI. 2018*

# Hemophilus colonization-neutrophilic subtype

**NET / BEC**



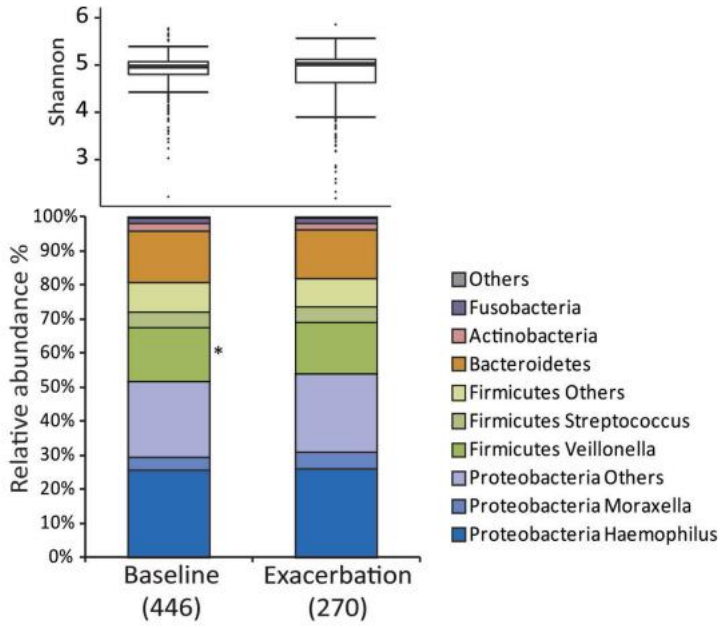

**NET / Hemophilus, Exacerbation, CAT**



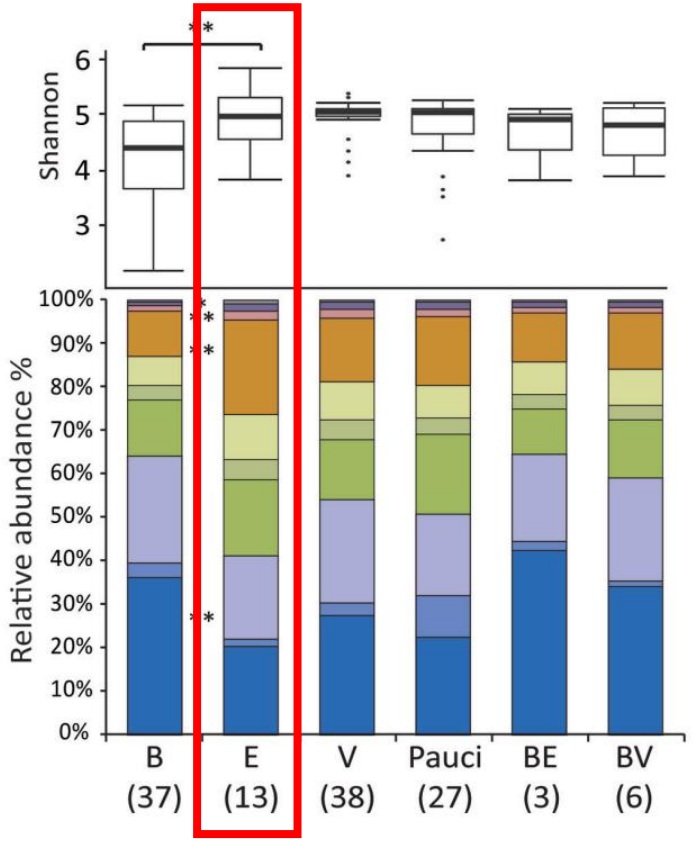

*Dicker et al. JACI. 2018*

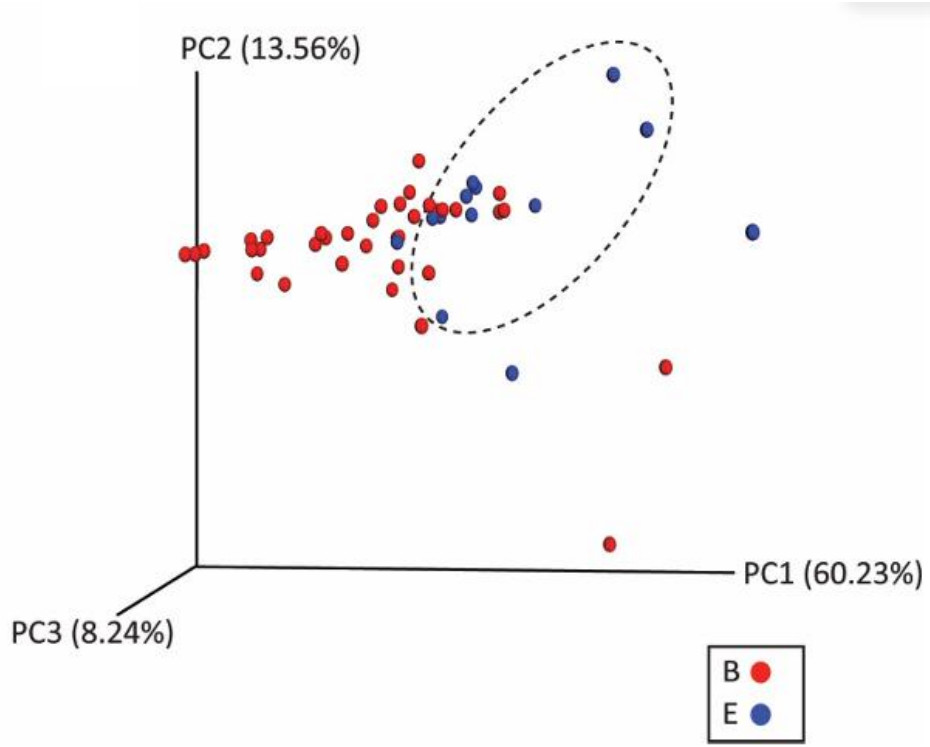
# Microbiome: association with eosinophil

**Exacerbation**




**B vs. E**

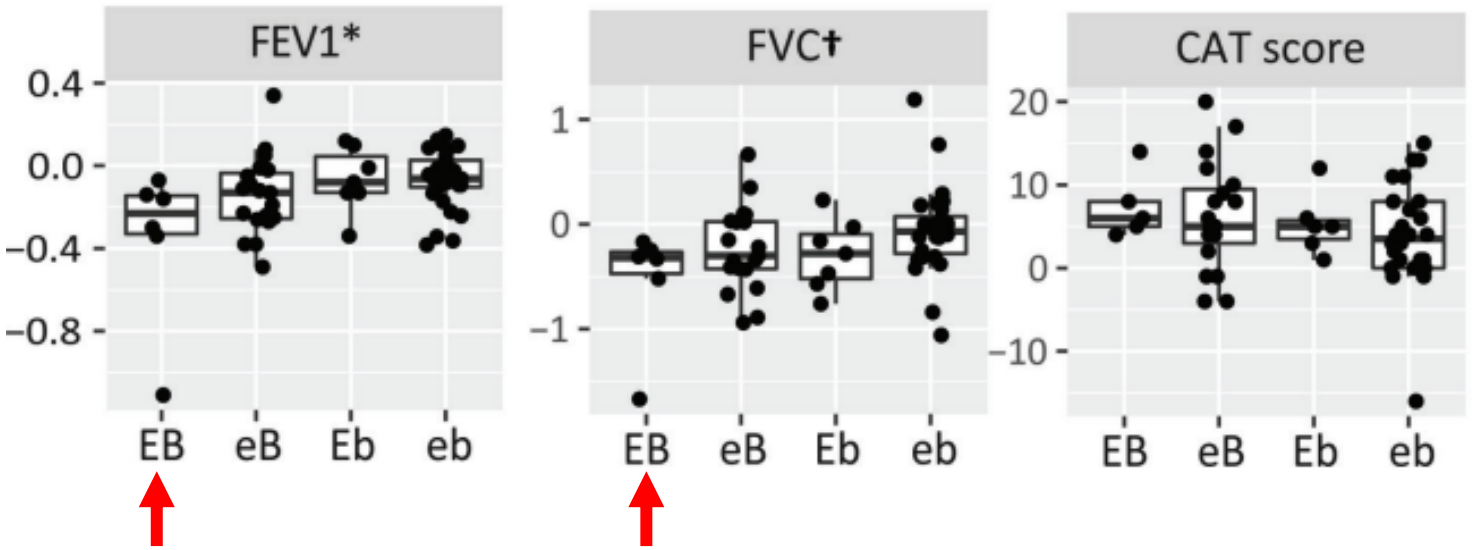



*Wang et al. Thorax. 2018*

# Microbiome: association with eosinophil

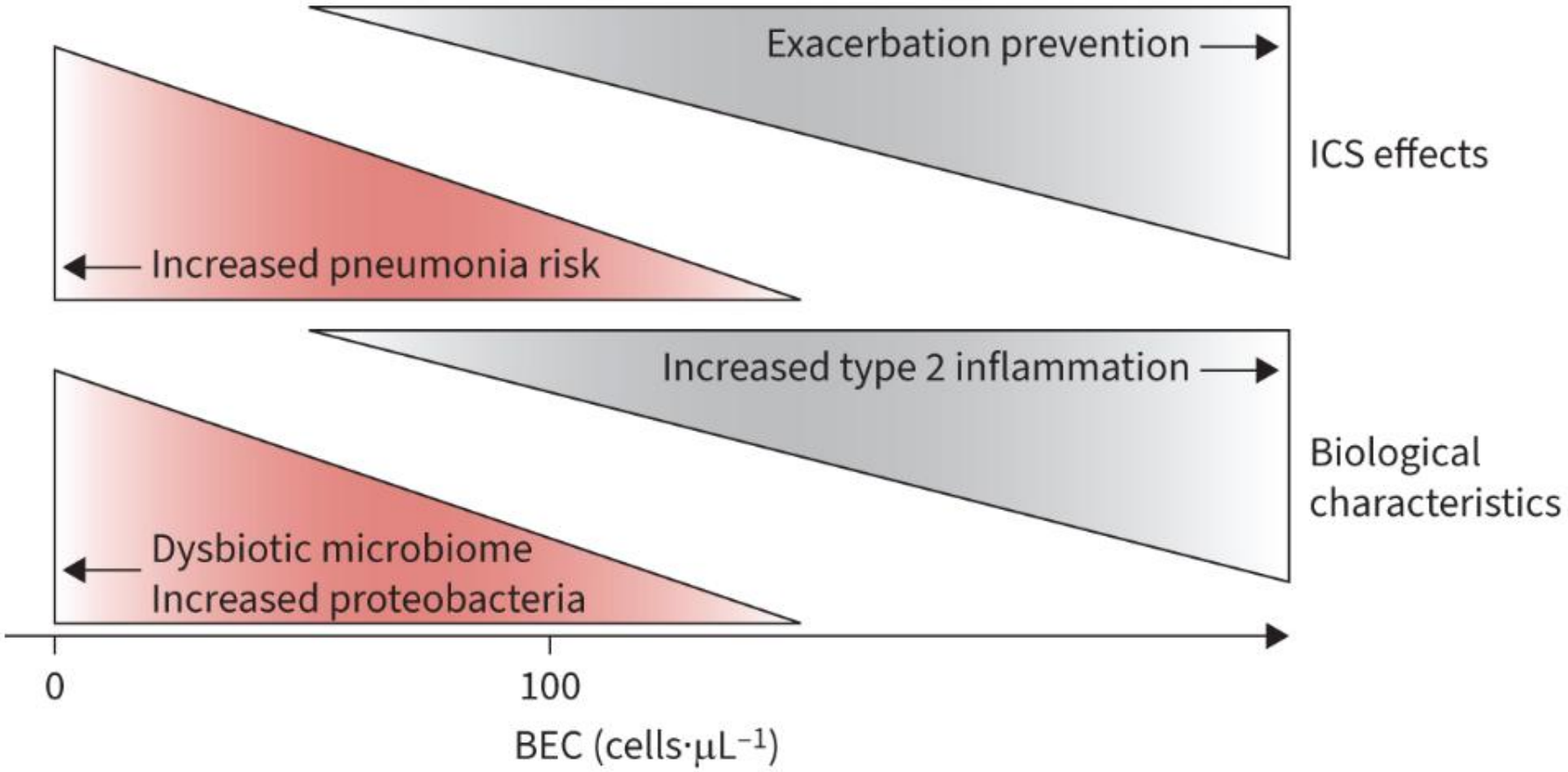
**Exacerbation**




**EB:** Eosinophil+Dysbiosis
**eB:** Non-eosinophil+Dysbiosis
**Eb:** Eosinophil+Non-dysbiosis
**eb:** Non-eosinophil+Non-dysbiosis

*Wang et al. Thorax. 2018*

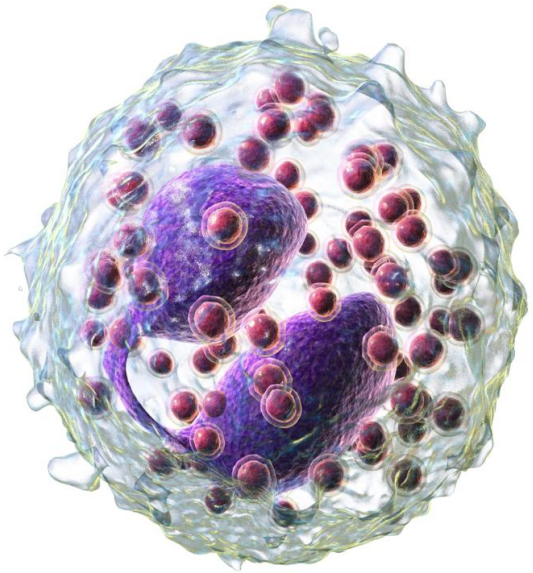
# Relationships between BECs and ICS effects and biological characteristics




*Beech A et al. ERS monograph 2025*

Difference with eosinophil in asthma

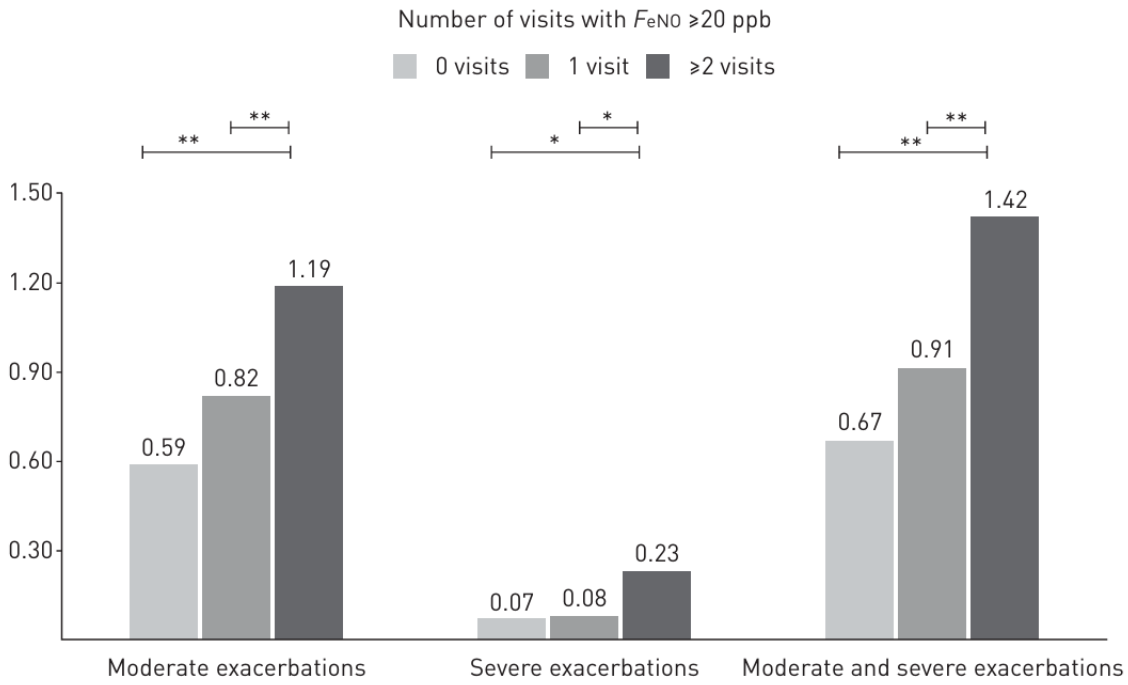
Biological characteristics



Endotyping and Treatment

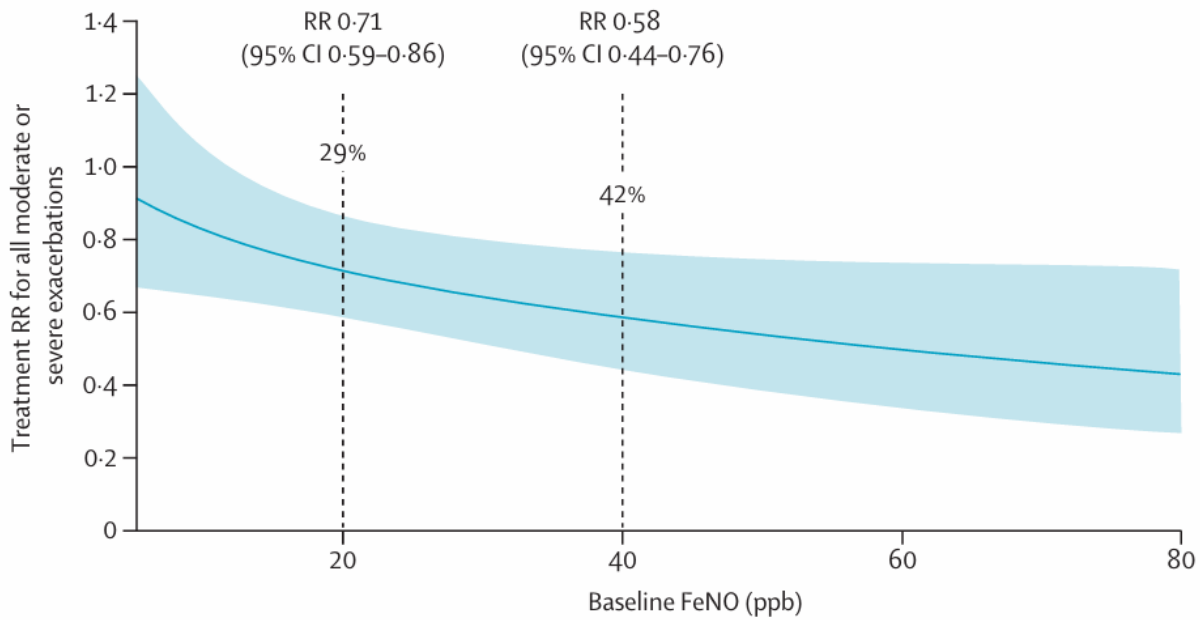
# Persistently elevated exhaled nitric oxide fraction is associated with increased risk of exacerbation in COPD

Bernardino Alcázar-Navarrete [1,2,3], Oliverio Ruiz Rodríguez[1], Pablo Conde Baena[4], Pedro José Romero Palacios[2] and Alvar Agusti[3,5,6]




# Type 2 inflammation biomarkers and their association with response to dupilumab in COPD (BOREAS): an analysis of a randomised, placebo-controlled, phase 3 trial

*Stephanie A Christenson, Nicola A Hanania, Surya P Bhatt, Mona Bafadhel, Klaus F Rabe, Claus F Vogelmeier, Alberto Papi, Dave Singh, Elizabeth Laws, Paula Dakin, Ashish Bansal, Xin Lu, Deborah Bauer, Jennifer Maloney, Lacey B Robinson, Raolat M Abdulai*



# Endotyping: FeNO

Chronic obstructive pulmonary disease

OPEN ACCESS

Original research

## Eosinophilia and fractional exhaled nitric oxide levels in chronic obstructive lung disease

Srinadh Annangi ,[1] Snigdha Nutalapati,[2] Jamie Sturgill,[1] Eric Flenaugh,[3] Marilyn Foreman[3]

**Table 2** Prevalence of peripheral eosinophilia among subjects with COPD without asthma history and COPD with asthma history, stratified by gender, race, age groups, smoking status and exhaled FeNO levels

| | COPD without asthma history | COPD with asthma history | |
|---|---|---|---|
| Subjects with presence of variables shown to influence FeNO levels were excluded* (N = 3,175,294) | | | |
| and/or vegetables within 3 hours/have used inhaled, | | | |
| oral corticosteroids within 2 days/have had cough, cold | | | |
| Unknown smoking status | 40.6% (40.5% to 40.7%) | 30.7% (30.5% to 30.9%) | <0.001 |
| FeNO levels (ppb) (95% CI) | | | |
| 0–24 | 34.6% (34.6% to 34.7%) | 27.6% (27.5% to 27.8%) | <0.001 |
| 25–50 | 30.4% (30.3% to 30.6%) | 84.4% (84.2% to 84.7%) | <0.001 |
| 51 and above | 42.3% (42.0% to 42.5%) | 0% | NA |

**Table 4** Mean exhaled nitric oxide levels, stratified by clinical status and demographics

| | Total study population | COPD without asthma history | COPD with asthma history | |
|---|---|---|---|---|
| | | | Mean FeNO level (SD) | P value |
| | | | 19.6 (13.2) | <0.001 |
| | | | 16.6 (11.7) | 0.7 |
| | | | 21.7 (13.7) | <0.001 |
| | | | 12.4 (3.8) | <0.001 |
| Non-smoker | 19.2 (16.5) | 18.8 (16.9) | 21.8 (12.6) | <0.001 |
| Unknown smoking status | 18.9 (12.4) | 18.7 (11.8) | 19.6 (13.9) | <0.001 |
| Peripheral eosinophil count | | | | |
| <300 cells/µL | 14.6 (9.6) | 13.9 (8.7) | 18.2 (14.6) | <0.001 |
| ≥300 cells/µL | 19.6 (18.1) | 19.2 (19.2) | 21.7 (10.1) | <0.001 |

*Annangi et al. Thorax. 2021*

# Endotyping: FeNO

Contents lists available at ScienceDirect

Nitric Oxide

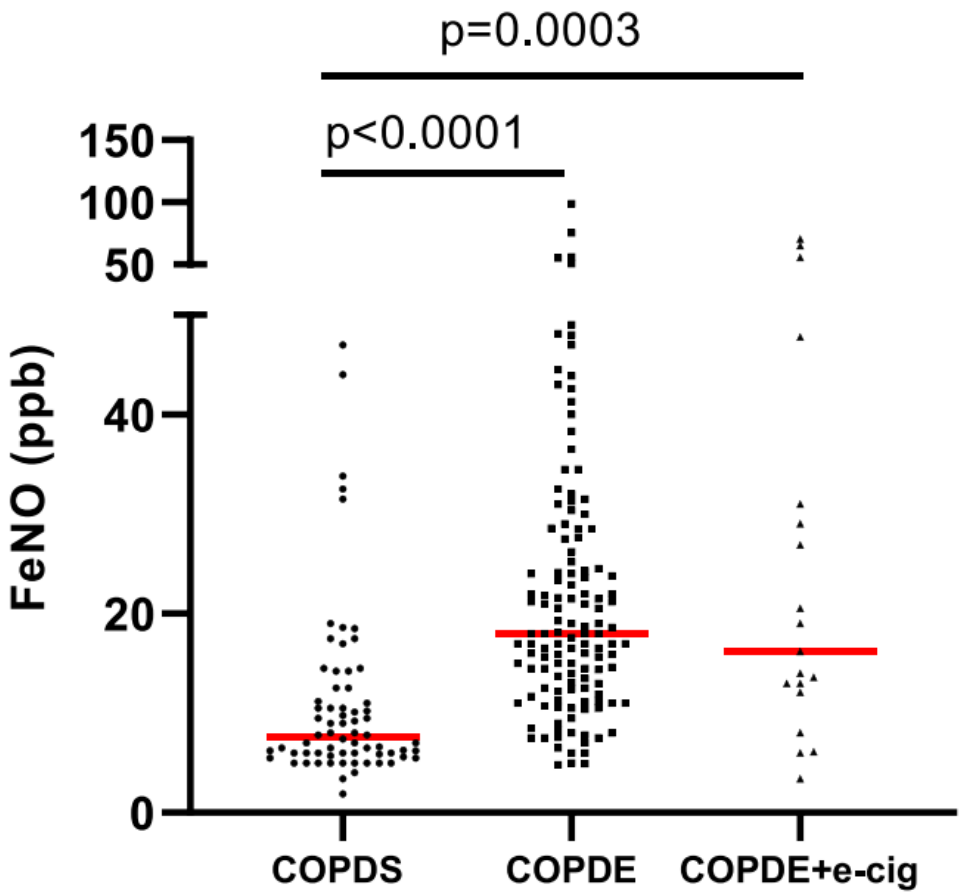
journal homepage: www.elsevier.com/locate/yniox

## Exhaled nitric oxide levels in COPD patients who use electronic cigarettes

Andrew Higham [a,*], Augusta Beech [a,b], Dave Singh [a,b]

[a] Division of Immunology, Immunity to Infection and Respiratory Medicine, School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester and Manchester University NHS Foundation Trust, Manchester, UK
[b] Medicines Evaluation Unit, The Langley Building, Southmoor Road, Manchester, UK

| | COPDS(n=68) | COPDE (n=130) | COPDE+e-cig (n=19) | |
|---|---|---|---|---|
| **ICS users (%)** | 67 | 78 | 76 | 0.3 |
| **FeNO (ppb)** | 7.6 [1.9–47.0] | 18.0 [4.8–99.0] *** | 16.2 [3.4–70.5] *** | <0.0001 |
| **Blood eosinophil count (x10$^9$/L)** | 0.2 [0.04–0.6] | 0.2 [0.02–0.9] | 0.2 [0.06–0.4] | 0.9 |
| **Blood neutrophil count (x10$^9$/L)** | 4.5 [2.2–10.6] | 4.0 [2.0–12.8] | 3.8 [2.4–9.8] | 0.07 |




*Higham et al. Nitric Oxide, 2024*

# Endotyping: FeNO

Contents lists available at ScienceDirect

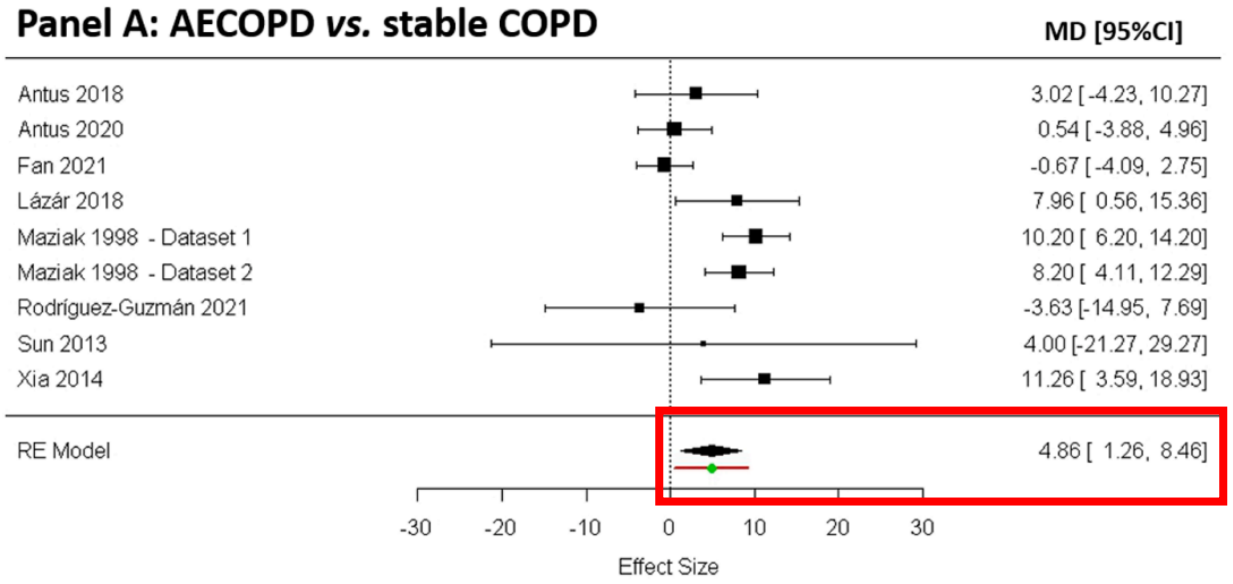
European Journal of Internal Medicine

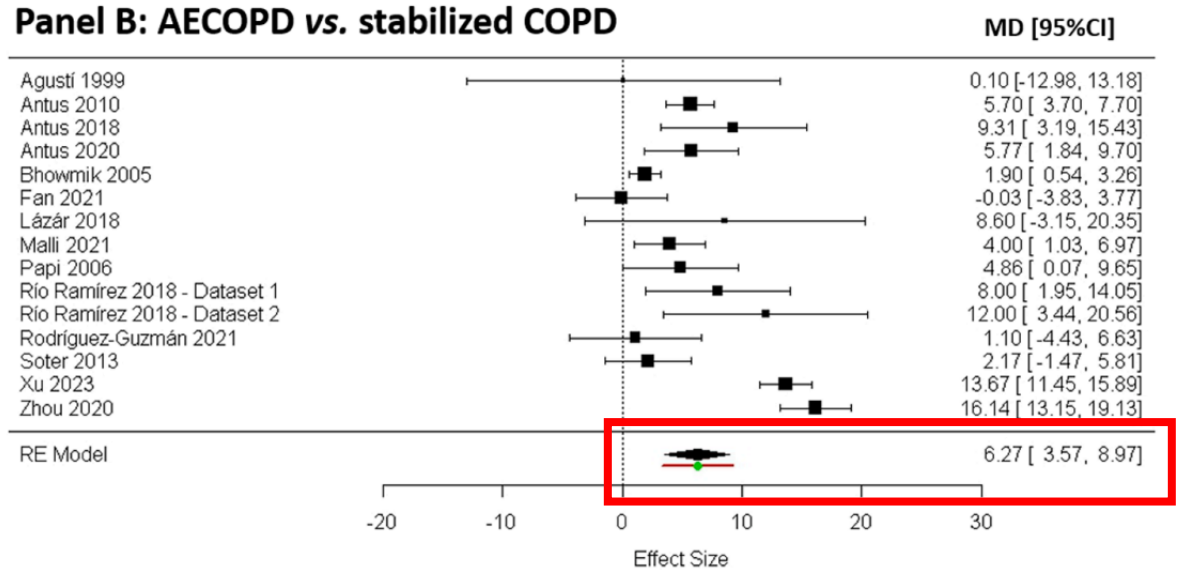
journal homepage: www.elsevier.com/locate/ejim

Original Article

## Fractional exhaled nitric oxide in acute exacerbations of chronic obstructive pulmonary disease: A meta-analysis with meta-regressions

Pasquale Ambrosino [a,1], Claudio Candia [b,1], Stefano Sanduzzi Zamparelli [c], Giuseppina Marcuccio [d], Fabio Manzo [e], Giorgio Alfredo Spedicato [f], Christian Basile [g,h], Costantino Mancusi [i], Ennio Lubrano [d,j], Guido Grassi [k], Andrea Motta [l], Mauro Maniscalco [d,i,*]




*Ambrosino et al. European Journal of Internal Medicine, 2026*

# Endotyping: FeNO

Sociedad Española de Neumología y Cirugía Torácica SEPAR

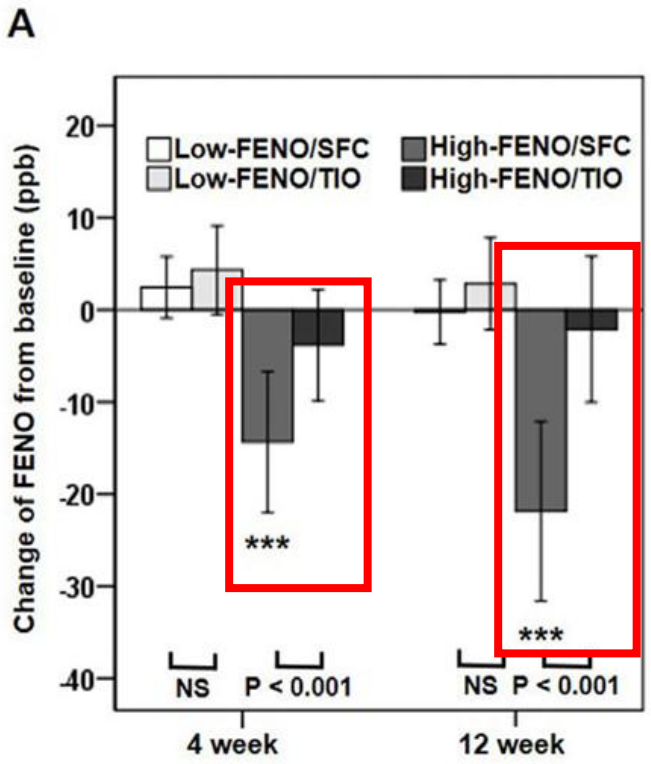
ARCHIVOS DE Bronconeumología

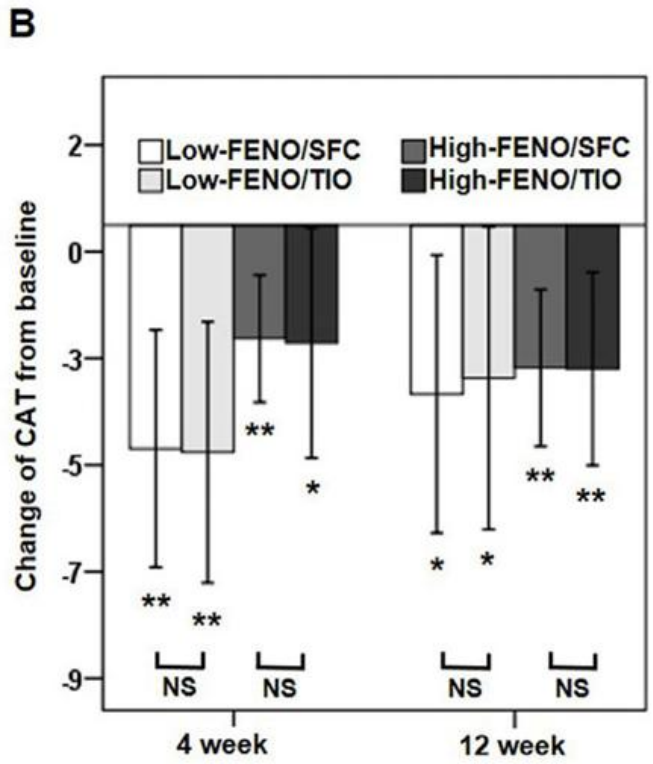
www.archbronconeumol.org

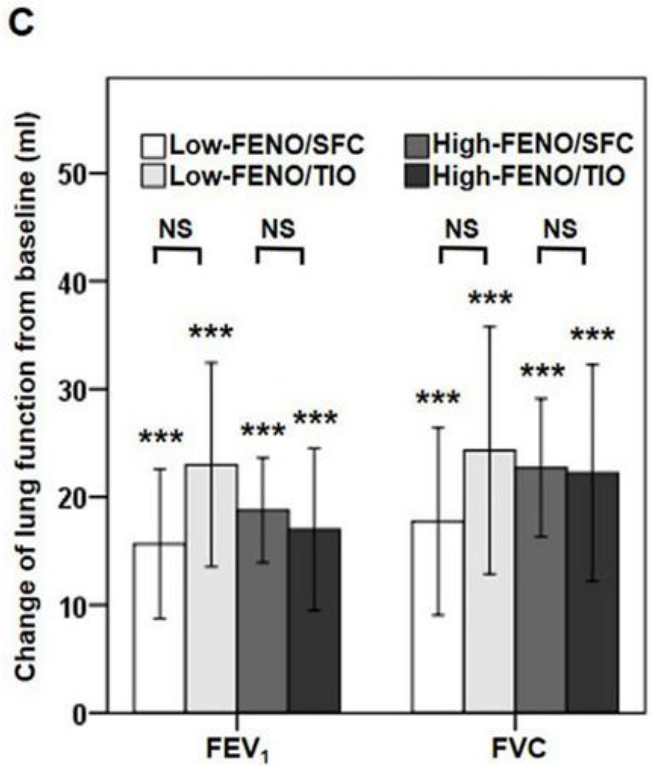
Original Article

## Fractional Exhaled Nitric Oxide Guided-Therapy in Chronic Obstructive Pulmonary Disease: A Stratified, Randomized, Controlled Trial

Kang-Cheng Su[a,b,c], Hsin-Kuo Ko[a,c], Yi-Han Hsiao[a,b,c], Kun-Ta Chou[a,b,c], Yen-Wen Chen[a,c], Wen-Kuang Yu[a,c], Sheng-Wei Pan[a,c], Jia-Yih Feng[a,c], Diahn-Warng Perng[a,c,*]




| | | | | |
|---|---|---|---|---|
| Total eosinophils, /μl | 128 (68–202) | 117 (59–189) | 182 (99–346)‡ | 161 (120–222) | .048 |

*Su et al. Archivos de bronconeumologia. 2022*

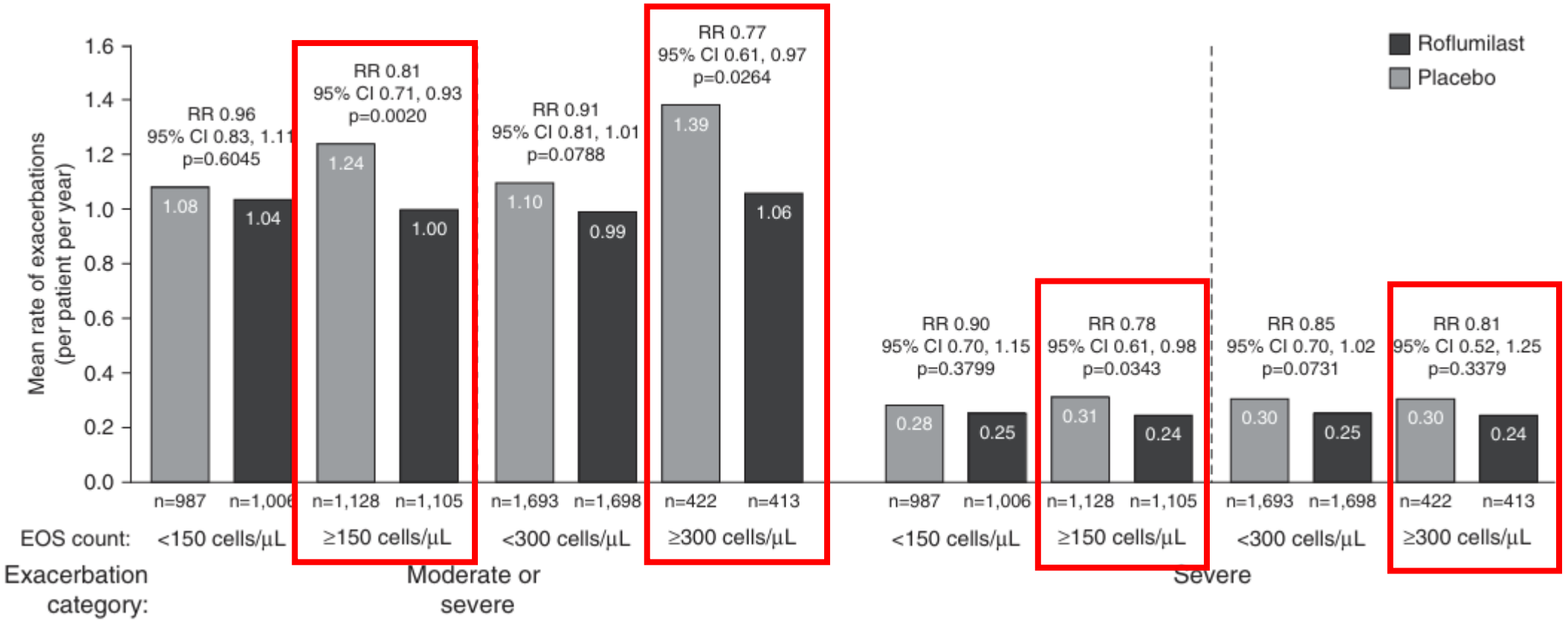
# Treatment: PDE4

ORIGINAL ARTICLE

**Determinants of Response to Roflumilast in Severe Chronic Obstructive Pulmonary Disease**

Pooled Analysis of Two Randomized Trials

Fernando J. Martinez[1], Klaus F. Rabe[2], Peter M. A. Calverley[3], Leonardo M. Fabbri[4,5], Sanjay Sethi[6], Emilio Pizzichini[7], Andrew McIvor[8], Antonio Anzueto[9], Vijay K. T. Alagappan[10], Shahid Siddiqui[10], Colin Reisner[10], Sofia Zetterstrand[11], Jonas Román[11], Debasree Purkayastha[12], Nitin Bagul[13], and Stephen I. Rennard[14,15]




*Martinez et al. AJRCCM. 2018*

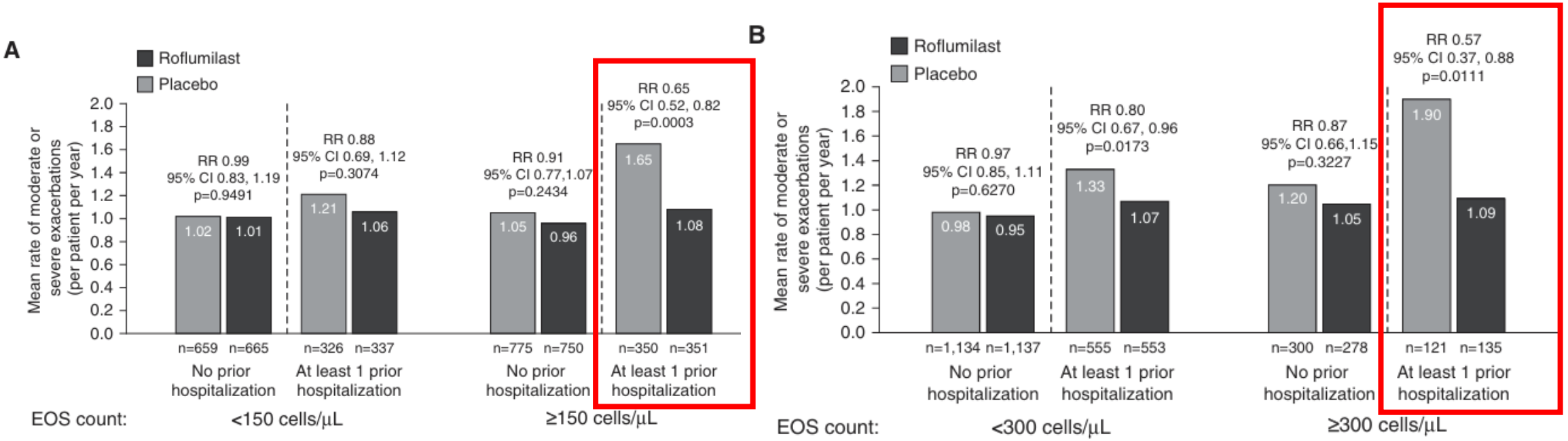
# Treatment: PDE4

ORIGINAL ARTICLE

**Determinants of Response to Roflumilast in Severe Chronic Obstructive Pulmonary Disease**

Pooled Analysis of Two Randomized Trials

Fernando J. Martinez[1], Klaus F. Rabe[2], Peter M. A. Calverley[3], Leonardo M. Fabbri[4,5], Sanjay Sethi[6], Emilio Pizzichini[7], Andrew McIvor[8], Antonio Anzueto[9], Vijay K. T. Alagappan[10], Shahid Siddiqui[10], Colin Reisner[10], Sofia Zetterstrand[11], Jonas Román[11], Debasree Purkayastha[12], Nitin Bagul[13], and Stephen I. Rennard[14,15]



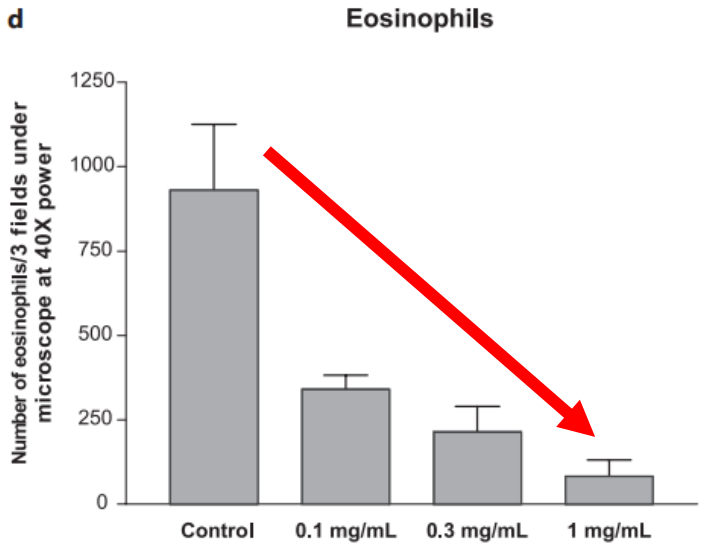

*Martinez et al. AJRCCM. 2018*

# Treatment: Ensifentrine

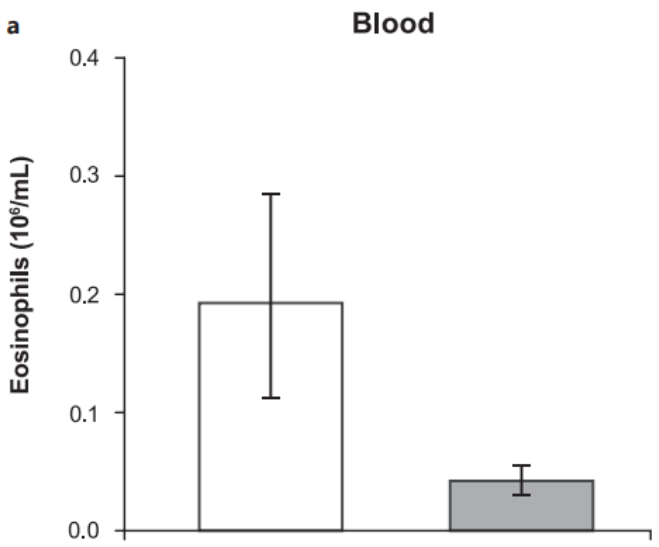
## Anti-Inflammatory Activity of Ensifentrine: A Novel, Selective Dual Inhibitor of Phosphodiesterase 3 and Phosphodiesterase 4

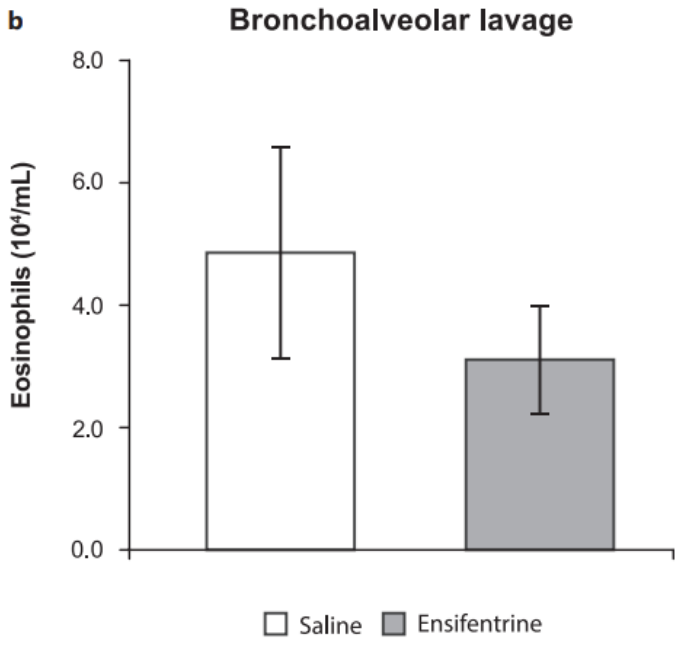
Domenico Spina[a] Lui Franciosi[b] Radhakrishnan Venkatasamy[a,c]
David A. Saint[d,e,f] Margot MacDonald-Berko[g] Tara Rheault[g]

[a]Institute of Pharmaceutical Science, King's College, London, UK; [b]Franciosi Consulting Ltd, Coquitlam, BC, Canada; [c]Pharmidex Pharmaceutical Services Limited, London, UK; [d]University of Adelaide, Adelaide, SA, Australia; [e]Southern Angels Inc., Adelaide, SA, Australia; [f]Gamma Vaccines Pty Ltd, Adelaide, SA, Australia; [g]Verona Pharma, Raleigh, NC, USA




Guinea pig




Non-human primates

*Spina et al. Respiration. 2025*

[ COPD Original Research ]

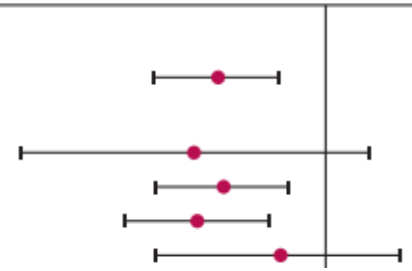
CHEST

# Effect of Dual Phosphodiesterase 3 and 4 Inhibitor Ensifentrine on Exacerbation Rate and Risk in Patients With Moderate to Severe COPD

Frank C. Sciurba, MD; Stephanie A. Christenson, MD; Tara Rheault, PhD, MPH; Thomas Bengtsson, MSc; Kathleen Rickard, MD; and Igor Z. Barjaktarevic, MD, PhD

## Exacerbation

| | Ensifentrine | | Placebo | | | |
|---|---|---|---|---|---|---|
| | Events/No | (%) | Events/No | (%) | HR (95% CI) | *P* Value |
| **Primary analysis** | | | | | | |
| mITT | 84/975 | (8.6) | 81/574 | (14.1) | 0.59 (0.44-0.81) | .001 |
| **Baseline eosinophils** | | | | | | |
| < 100 cell/μL | 10/182 | (5.5) | 11/107 | (10.3) | 0.52 (0.22-1.24) | .141 |
| ≥ 100 cells/μL | 74/791 | (9.4) | 70/467 | (15.0) | 0.60 (0.43-0.83) | .002 |
| < 300 cells/μL | 60/745 | (8.1) | 62/434 | (14.3) | 0.53 (0.37-0.76) | .001 |
| ≥ 300 cells/μL | 24/228 | (10.5) | 19/140 | (13.6) | 0.79 (0.43-1.45) | .453 |



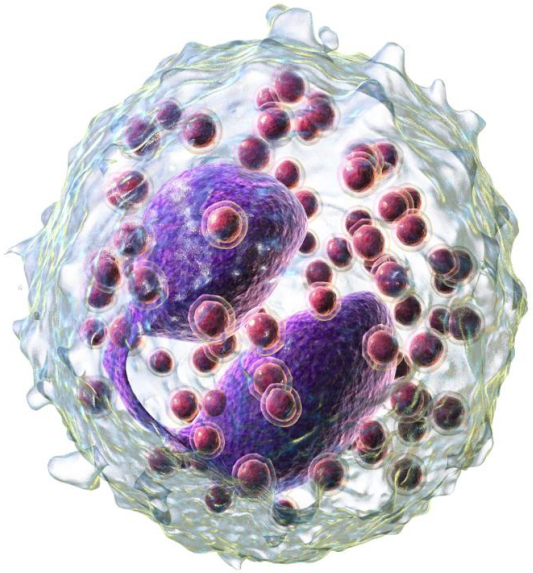
## Dyspnea

| Subgroup | Ensifentrine (n = 975) % responders (n/N) | Placebo (n = 574) % responders (n/N) | Week 24 Ensifentrine-Placebo Responder LSM Odds Ratio (95% CI), *P* value |
|---|---|---|---|
| BEC <300 cells/μL | 63.2 (462/731) | 43.8 (188/429) | 1.76 (1.34, 2.31), <0.001 |
| BEC ≥300 cells/μL | 69.8 (155/222) | 47.8 (64/134) | 2.08 (1.26, 3.43), 0.004 |

*Sciurba et al. Chest. 2025; Mahler et al. Exp. review of medicine. 2024*

# SUMMARY

**Difference with eosinophil in asthma:**
**iEOS, remodeling, gene, mucus plug**



**Biological characteristics**
**: pulmonary eosinophilia, microbiome**

**Endotyping and Treatment**
**: FeNO, PDE**