The pharmacological management of COPD

Professor Dave Singh

Professor of Clinical Pharmacology and Respiratory Medicine, University of Manchester

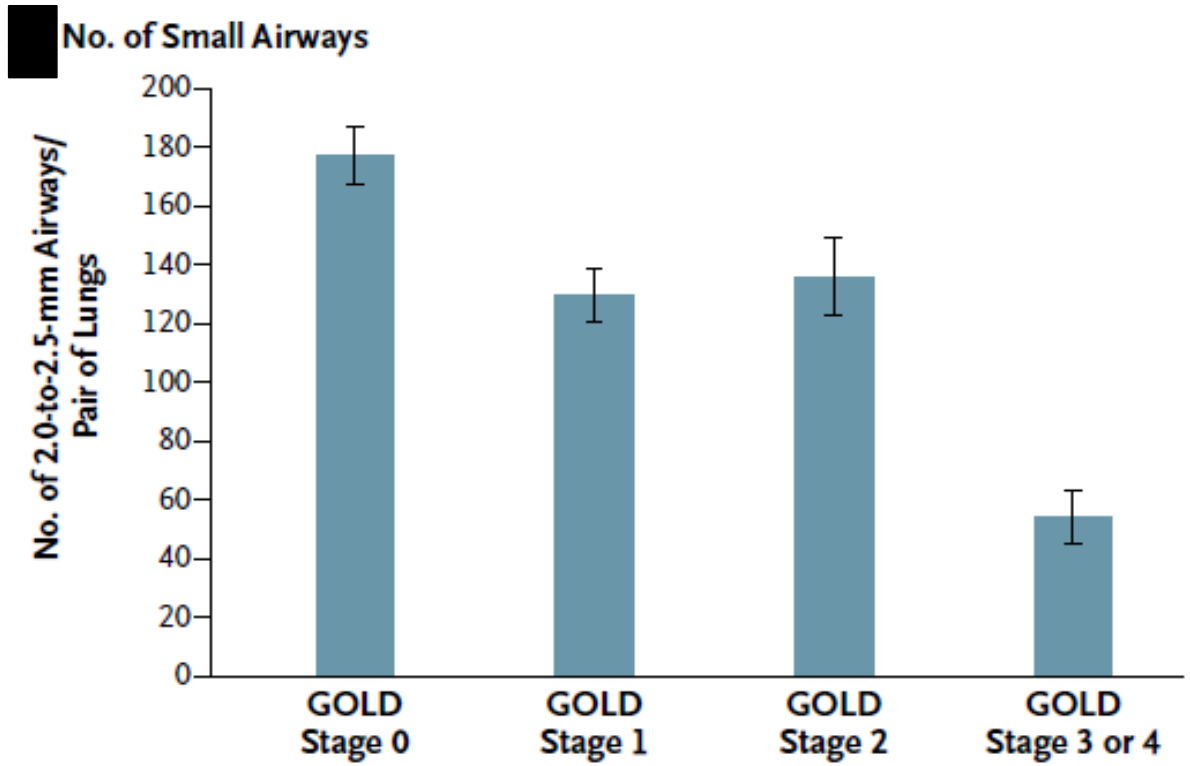
Medical Director, Medicines Evaluation Unit an IQVIA Business, Manchester, UK

Disclosure of interest

Received sponsorship to attend and speak at international meetings, honoraria for lecturing or attending advisory boards from the following companies:

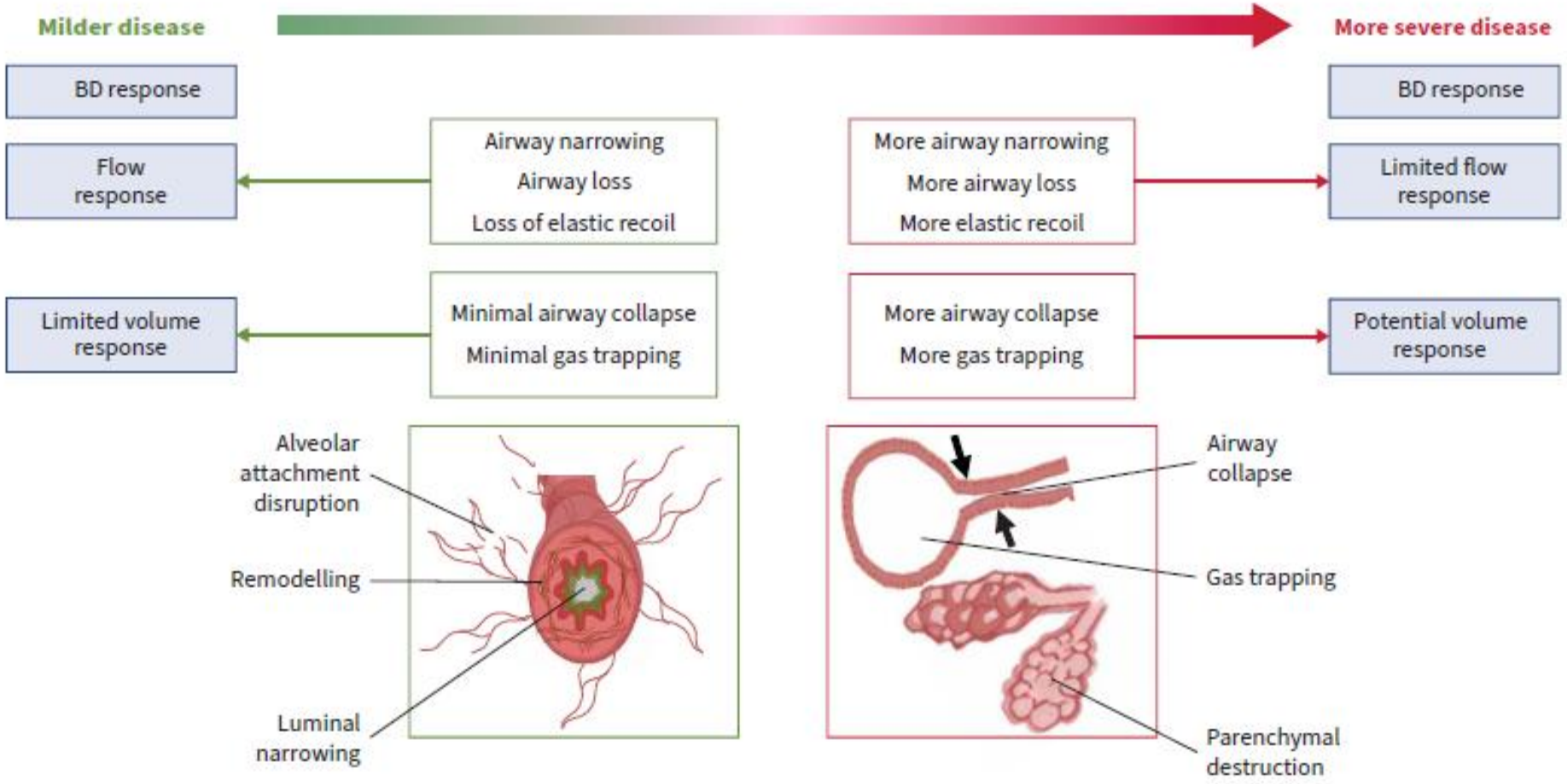
- Adovate, Aerogen, Almirall, Apogee, Arrowhead, AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, Cipla, CONNECT Biopharm, Covis, CSL Behring, DevPro Biopharma LCC, Elpen, Empirico, EpiEndo, Genentech, Generate Biomedicines, GlaxoSmithKline, Glenmark, Kamada, Kinaset Therapeutics, Kymera, Menarini, MicroA, OM Pharma, Orion, Pieris Pharmaceuticals, Pulmatrix, Revolo, Roivant Sciences, Sanofi, Synairgen, Tetherex, Teva, Theravance Biopharma, Upstream and Verona Pharma

Small airway narrowing and destruction



McDonough et al. N Engl J Med 2011; 365: 1567–75

Airway pathophysiology in COPD

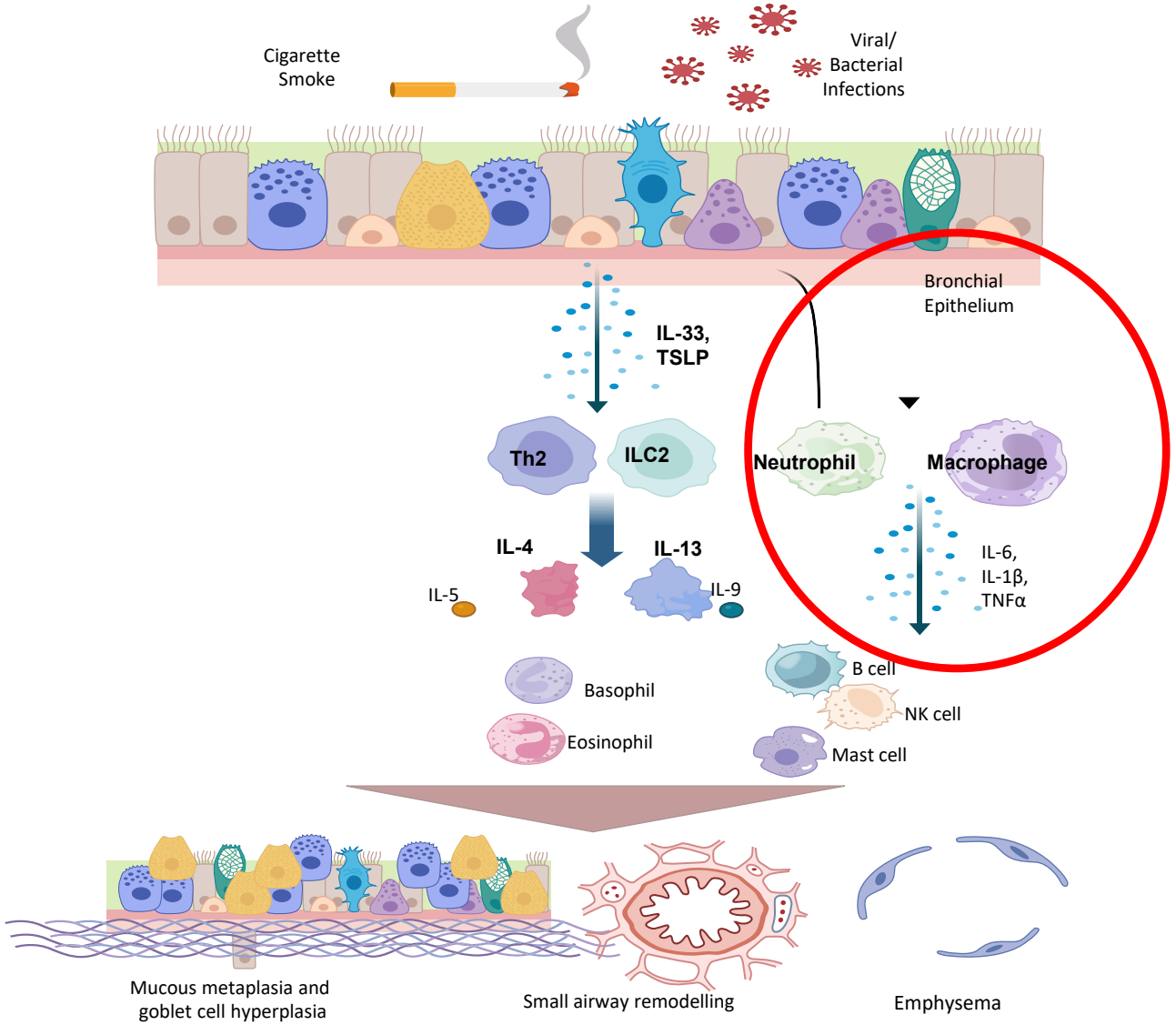


Singh D et al Eur Respir J 2025; 65: 2401603

Diagnosis of COPD

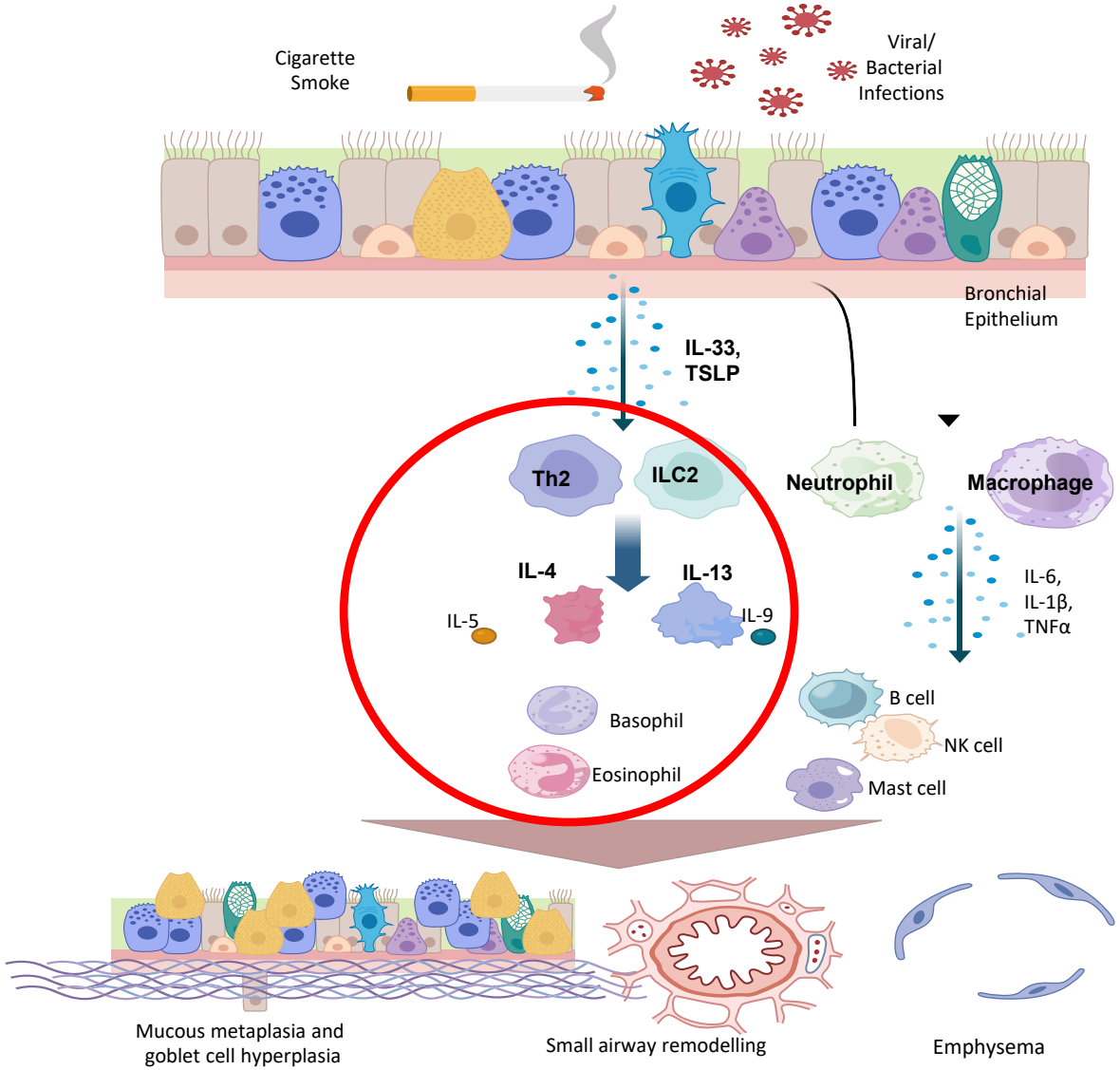
- Risk factors
- Symptoms
- Spirometry using FEV1/FVC < 0.7

Inflammation in COPD



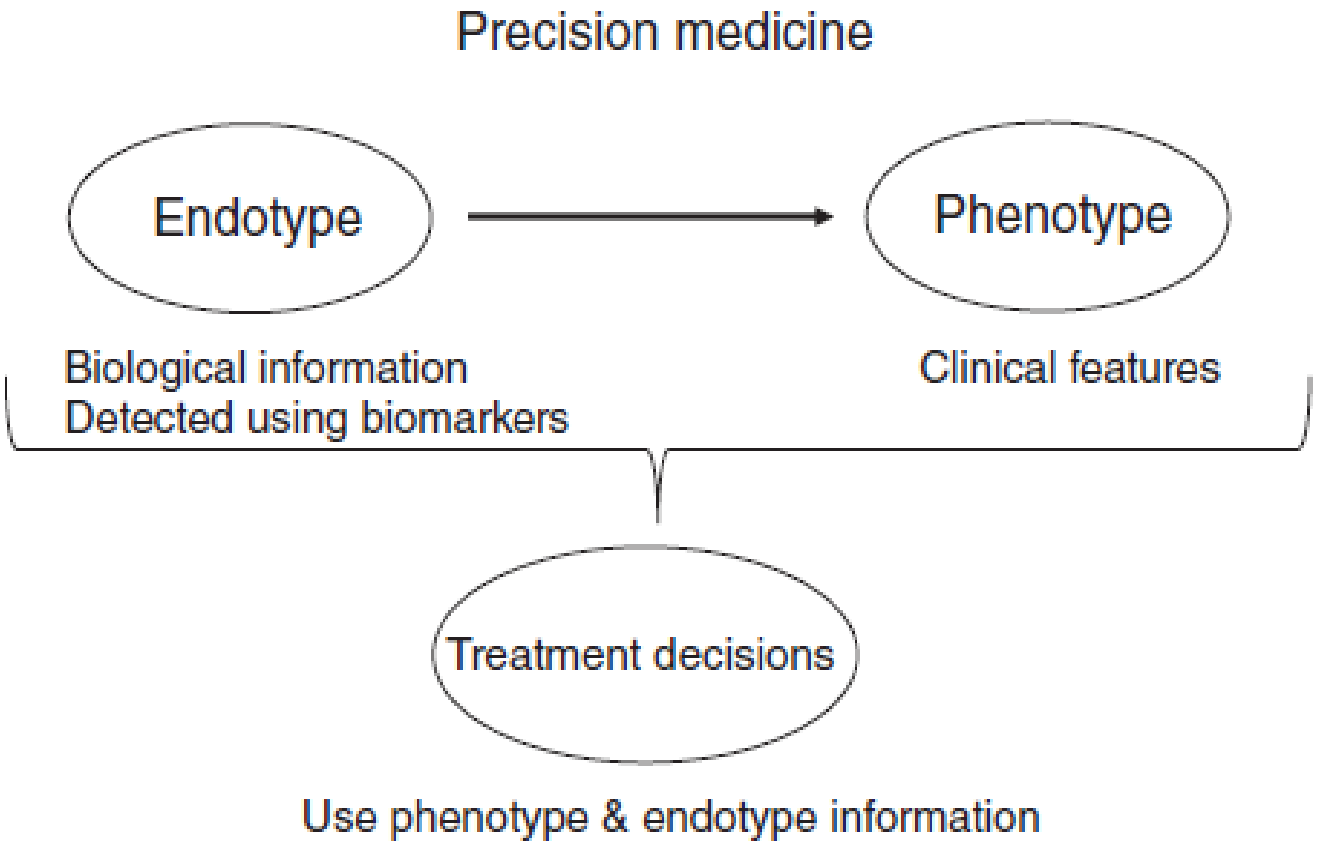
Polverino F, Sin DD. Type 2 airway inflammation in chronic obstructive pulmonary disease. Eur Respir J. 2024; in press (https://doi.org/10.1183/13993003.00150-2024).

Inflammation in COPD



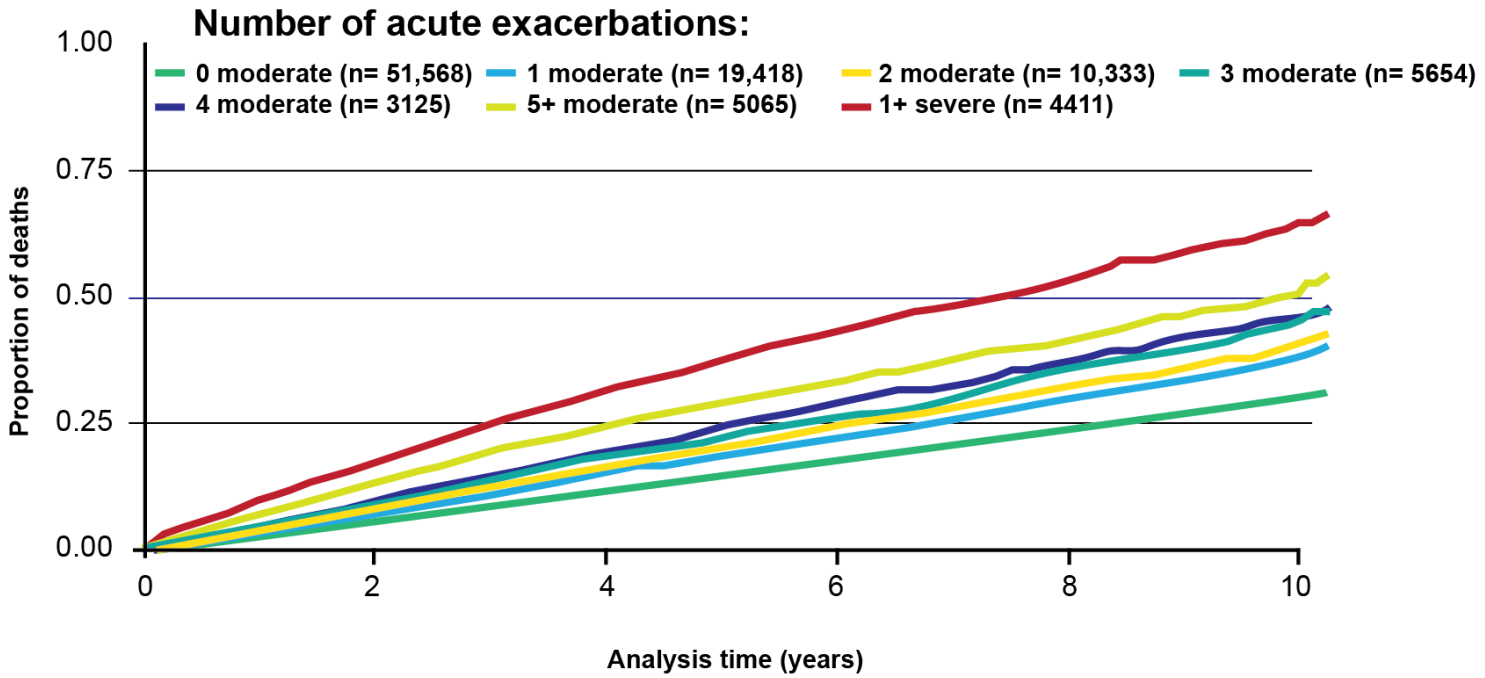
Polverino F, Sin DD. Type 2 airway inflammation in chronic obstructive pulmonary disease. Eur Respir J. 2024; in press (https://doi.org/10.1183/13993003.00150-2024).

Phenotype and Endotype



Singh, D., 2022. New Drugs for Airway Diseases. In: Janes, S.M. (Ed.), Encyclopedia of Respiratory Medicine, vol. 2. Elsevier, Academic Press, pp. 741–753. https://dx.doi.org/10.1016/B978-0-08-102723-3.00170-0.

Severity and frequency of exacerbations are associated with an increased risk of death*[1]



This figure is reproduced with the permission of the American Thoracic Society.
It was first published in Rothnie *et al. 2002.*

Time to death was assessed using a Cox proportional hazards model.[2]

*Based on a population-based study (N=99,574).
1. Rothnie KJ, *et al. Am J Respir Crit Care Med* 2018;198:464–471.

IMPROVEMENT

Goals for Treatment of Stable COPD

Figure 3.1

- Relieve Symptoms
- Improve Exercise Tolerance
- Improve Health Status

→ **REDUCE SYMPTOMS**

AND

- Prevent Disease Progression
- Prevent and Treat Exacerbations
- Reduce Mortality

→ **REDUCE RISK**

PREVENTION

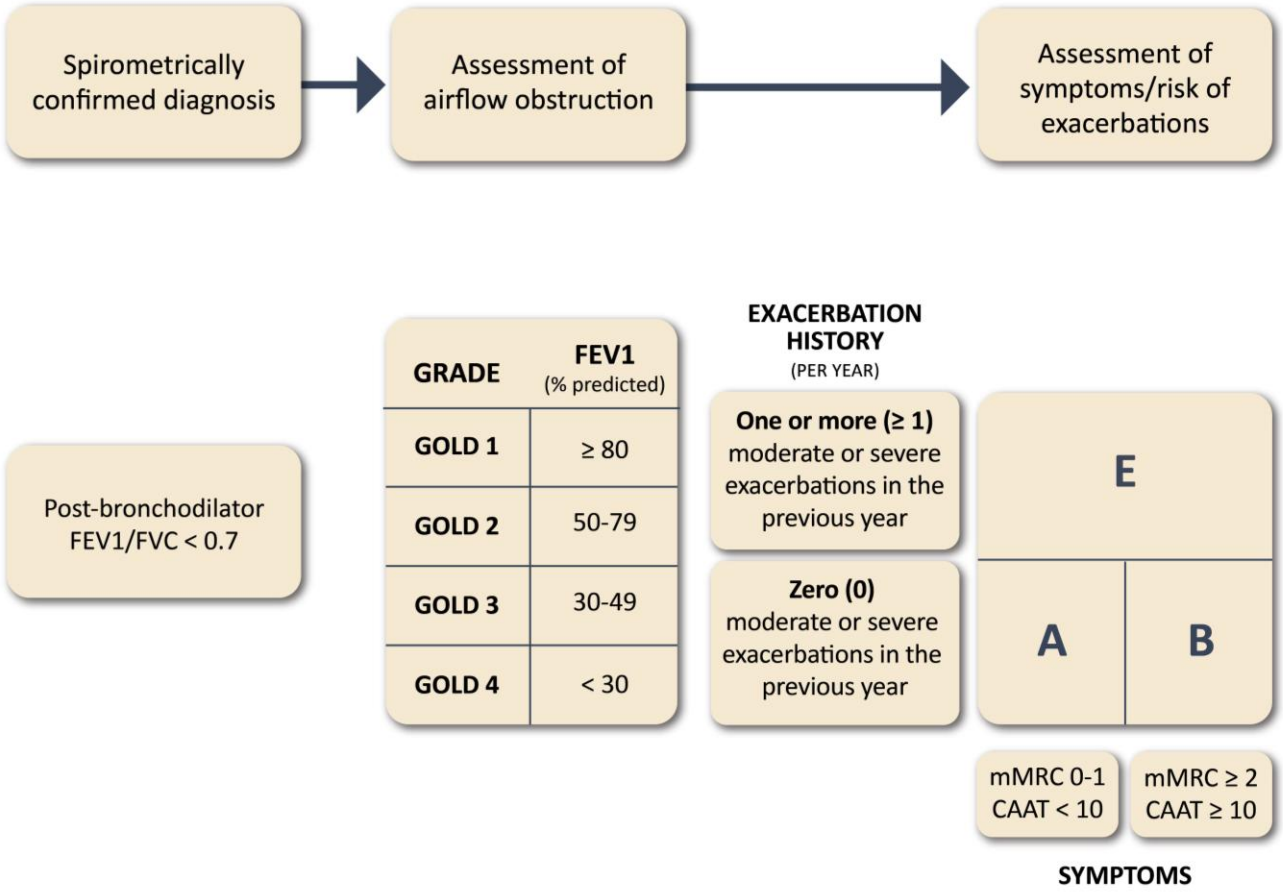
GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™

with the aim to prevent any exacerbations over both the short and long term.

2026
Teaching Slide Set

GOLD ABE Assessment Tool

Figure 2.13

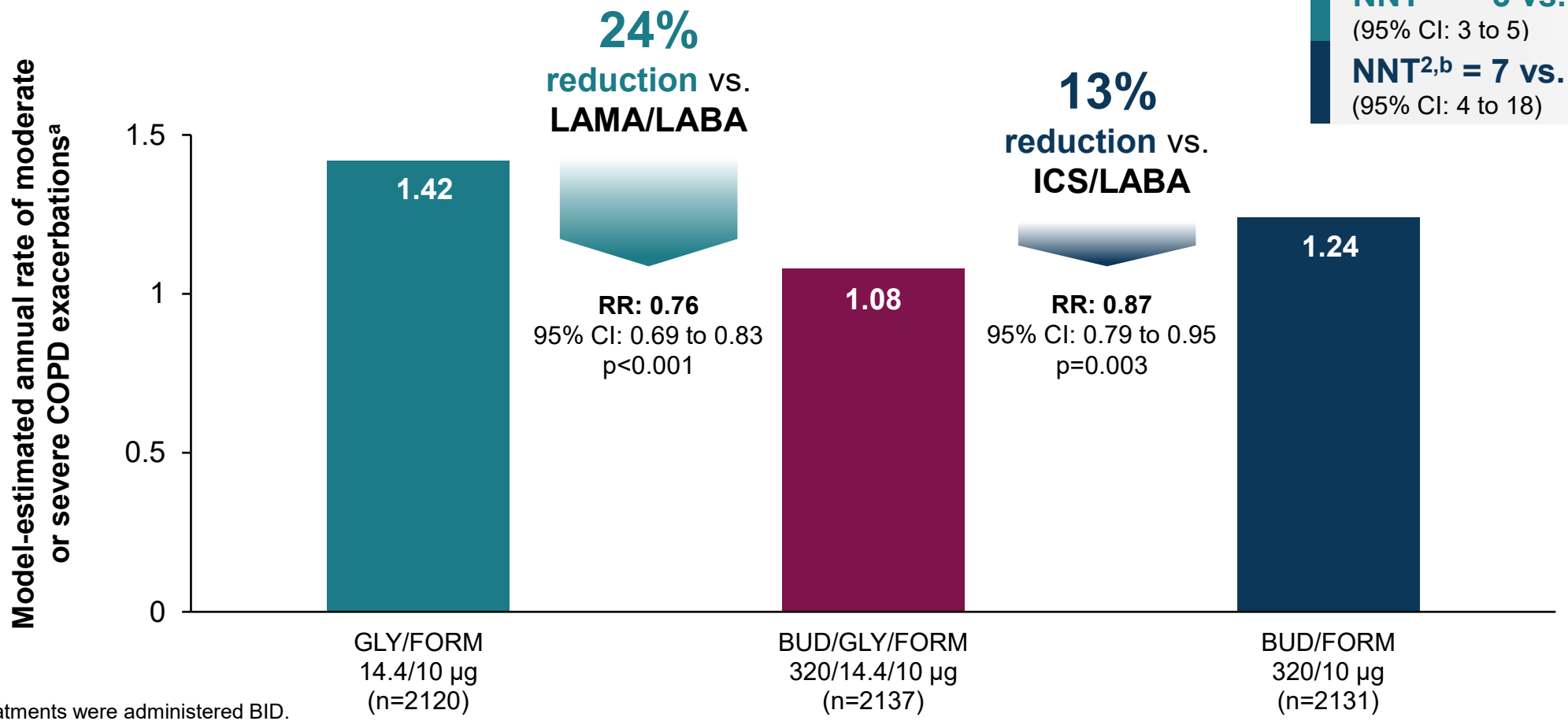


BUD/GLY/FORM significantly reduced the rate of moderate or severe exacerbations vs. dual therapies[1]

ETHOS
Primary endpoint

In the 52-week ETHOS study, **BUD/GLY/FORM** demonstrated a:

NNT[2,b] = 3 vs. LAMA/LABA
(95% CI: 3 to 5)
NNT[2,b] = 7 vs. ICS/LABA
(95% CI: 4 to 18)



Note: All treatments were administered BID.

[a]mITT population; [b]Representing the number of patients that would need to be treated for 1 year with BUD/GLY/FORM to prevent 1 additional moderate or severe COPD exacerbation compared with dual therapies (NNT calculated using $1/[rate_{BUD/GLY/FORM} - rate_{comparator}]$).

1. Rabe KF et al. Article and supplementary appendix. *N Engl J Med*. 2020;383:35-48; 2. Rabe KF et al. Abstract. *Eur Respir J*. 2020;56(64):5230.

FF/UMEC/VI significantly reduces all-cause mortality vs UMEC/VI[1,2]

IMPACT clinical trial*

25% fewer
moderate/severe exacerbations
per year vs UMEC/VI†

(ARR: 0.3/year; $p<0.001$)

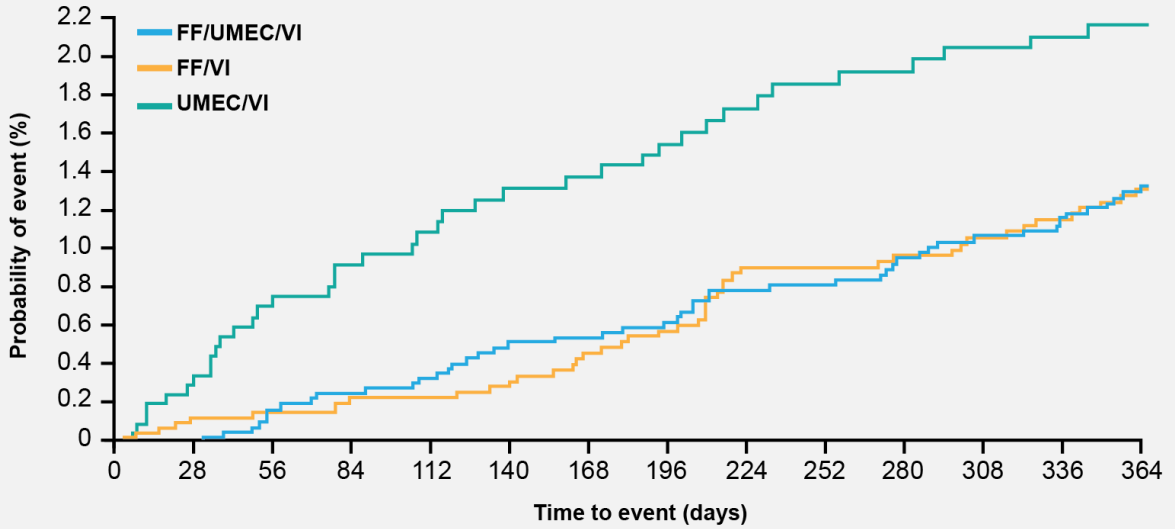
34% fewer
severe exacerbations
per year vs UMEC/VI‡

(ARR: 0.06/year; 0.13 vs 0.19, respectively; RR 0.66, 95% CI: 0.56, 0.78; $p<0.001$)

42% lower
relative risk in all-cause mortality
with vs UMEC/VI§

(ARR: 0.68%; 1.20% vs 1.88%, respectively; HR 0.58, 95% CI: 0.38, 0.88; $p=0.01$)

On-treatment all-cause mortality with FF/UMEC/VI, FF/VI and UMEC/VI



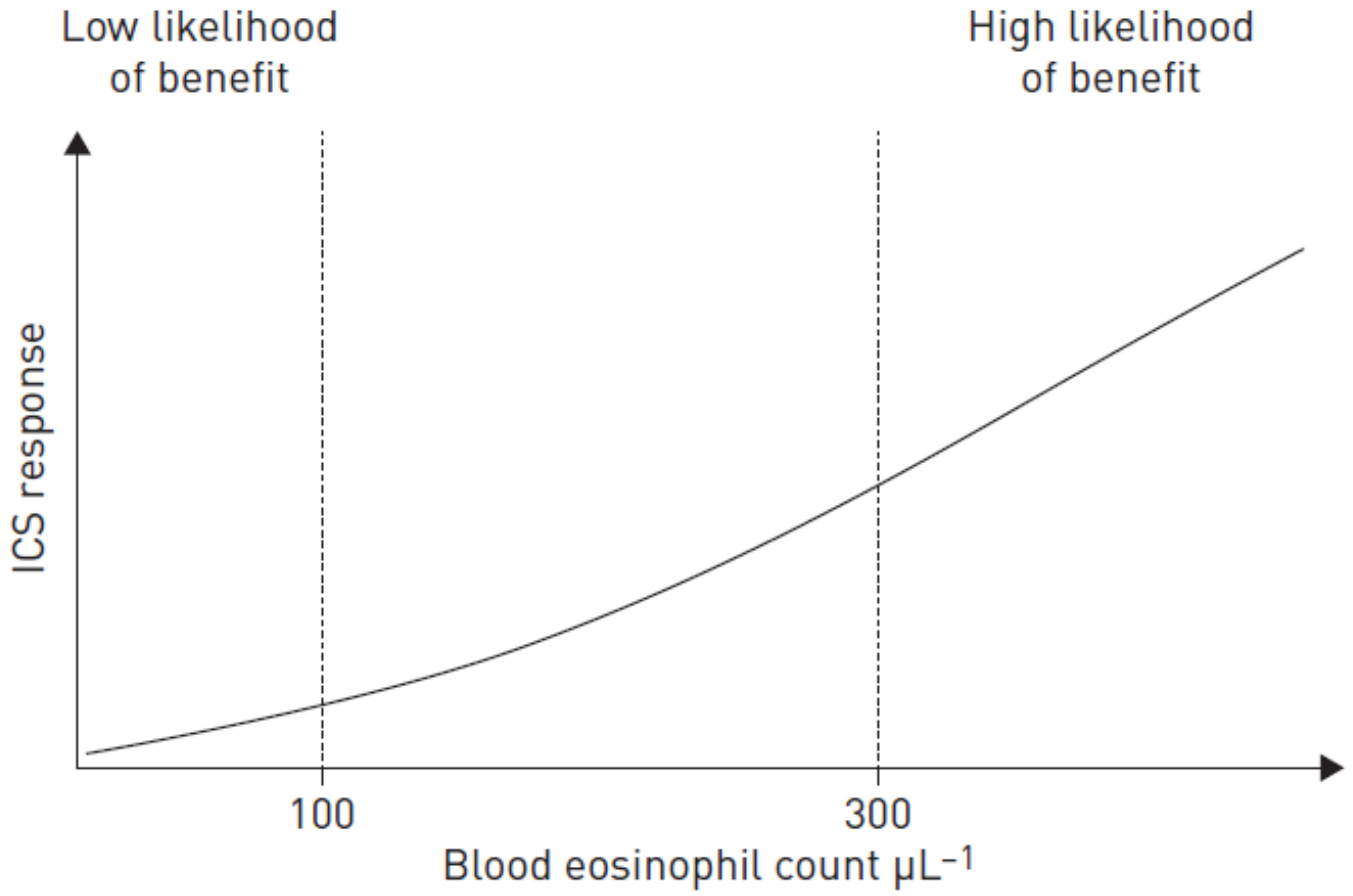
FF/UMEC/VI	4,151	4,082	3,968	3,898	3,838	3,752	3,714	3,690	3,613	3,581	3,545	3,486	3,454	3,346
FF/VI	4,134	3,984	3,798	3,694	3,619	3,496	3,443	3,391	3,291	3,258	3,230	3,182	3,152	3,044
UMEC/VI	2,070	1,993	1,880	1,820	1,769	1,713	1,685	1,656	1,612	1,595	1,578	1,548	1,531	1,485

This figure has been adapted from Lipson DA *et al. Am J Respir Crit Care Med* 2020;201(12):1508–1516. under a Creative Commons license (CC BY 4.0. Available at: http://creativecommons.org/licenses/by/4.0/).

*Phase 3 RCT involving 10,355 patients with COPD with primary objective to evaluate the effects of 52 weeks of a once-daily combination of FF/UMEC/VI compared with UMEC/VI and FF/VI on the rate of moderate/severe exacerbations.[3] †Rate reduction: 0.75 (95% CI: 0.70, 0.81); ‡Rate reduction: 0.66 (95% CI: 0.56, 0.78); §Pre-specified other endpoint of the IMPACT study; on treatment deaths: 1.2% (n=50/4151) vs 1.88% (n=39/2070); HR for all-cause mortality: 0.58 (95% CI: 0.38, 0.88).
ARR, absolute rate reduction; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FF, fluticasone furoate; HR, hazard ratio; RCT, randomised controlled trial; UMEC, umeclidinium; VI, vilanterol.

1. Lipson DA, *et al. N Engl J Med* 2018;378:1671–1680; 2. Lipson DA, *et al. Am J Respir Crit Care Med* 2020;201:1508–1516.

GOLD Science committee report 2019

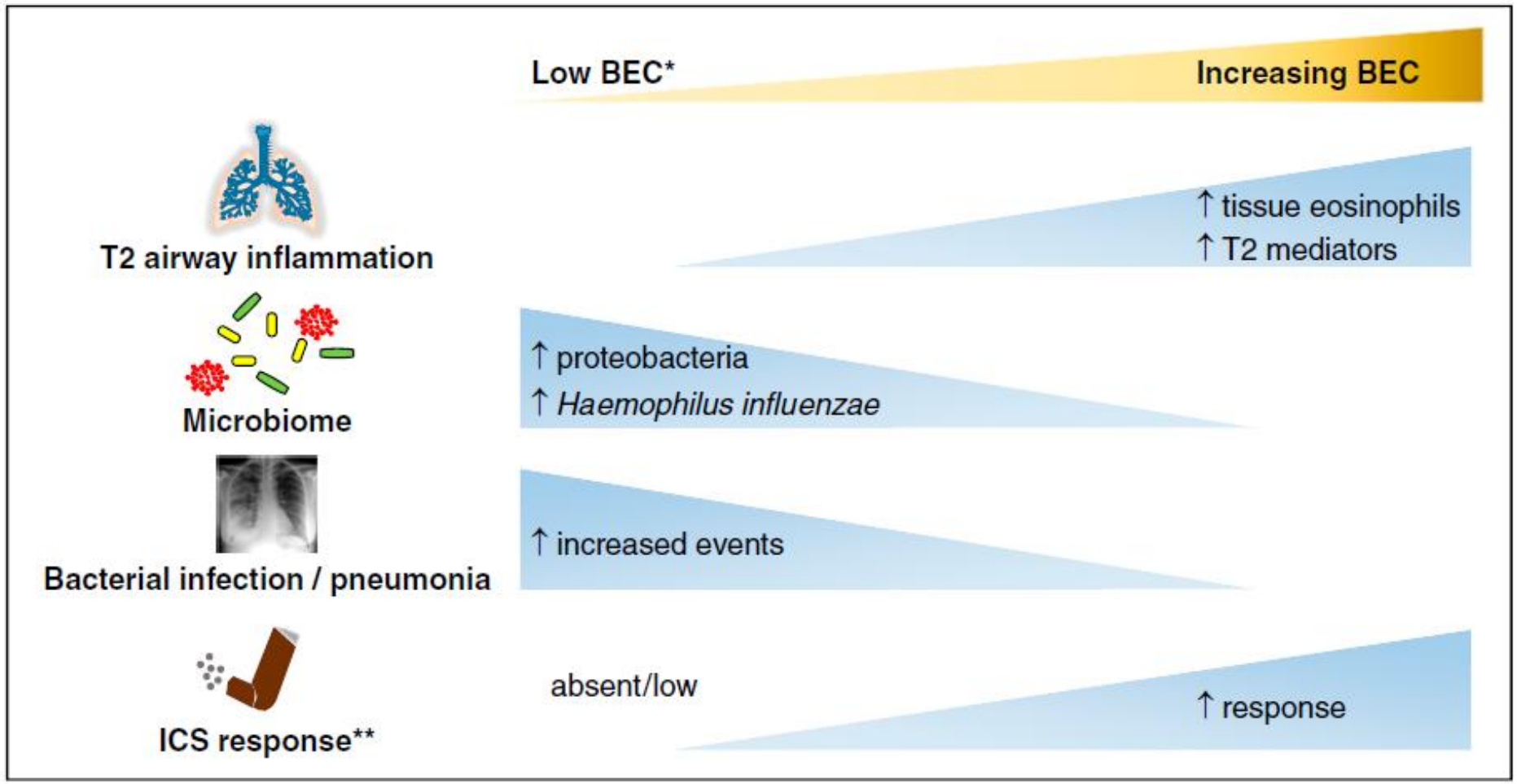


Singh D et al Eur Respir J 2019; 53: 1900164

Blood Eosinophils and Chronic Obstructive Pulmonary Disease

A Global Initiative for Chronic Obstructive Lung Disease Science Committee 2022 Review

Dave Singh[1], Alvar Agusti[2], Fernando J. Martinez[3], Alberto Papi[4], Ian D. Pavord[5], Jadwiga A. Wedzicha[6], Claus F. Vogelmeier[7], and David M. G. Halpin[8]



Am J Respir Crit Care Med Vol 206, Iss 1, pp 17–24, Jul 1, 2022

Initial Pharmacological Treatment

Figure 3.8

1 Initiate Treatment

INITIAL treatment - for patients with COPD who are naïve to maintenance pharmacological treatment

EXACERBATION HISTORY
(PER YEAR)

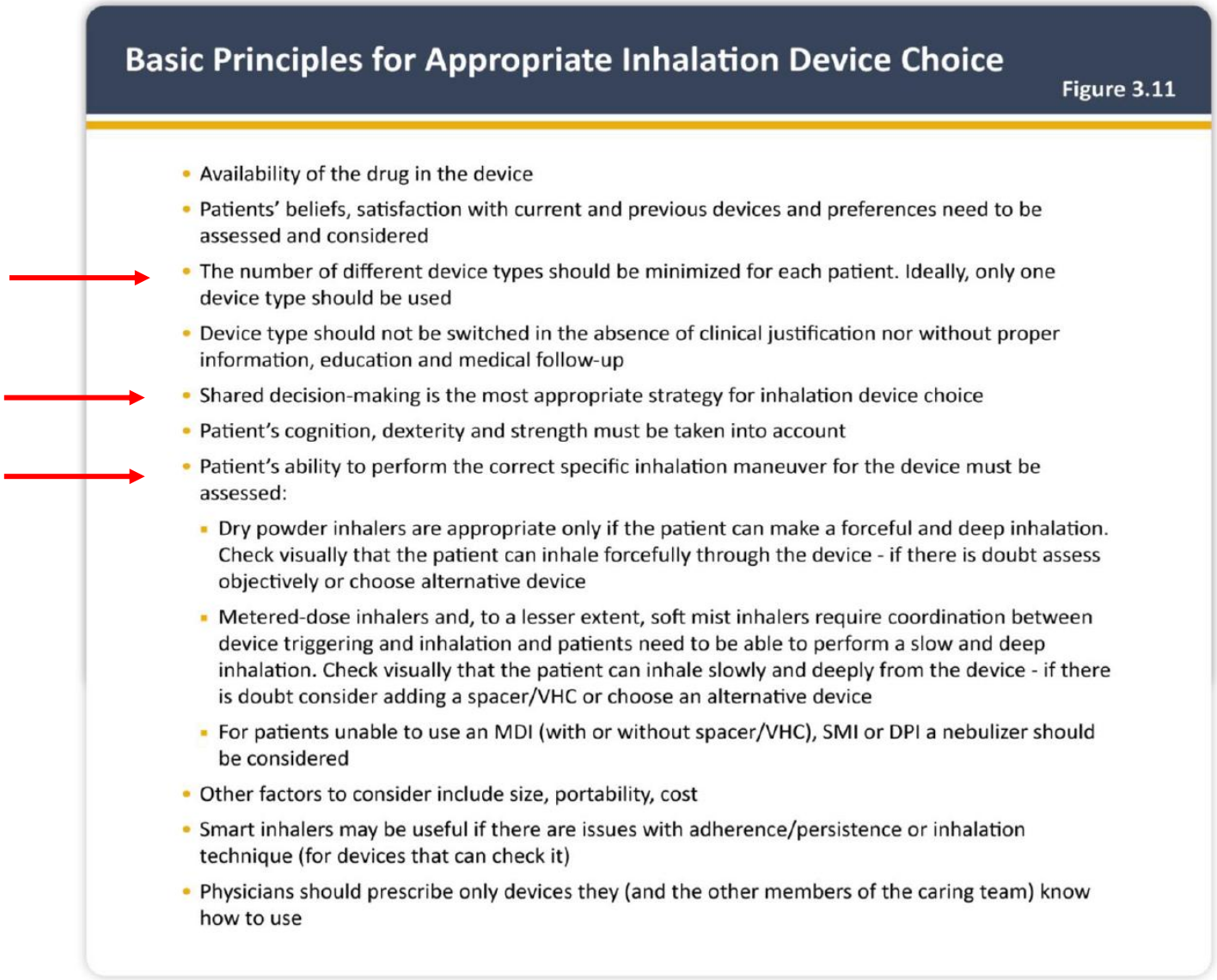
	SYMPTOMS: mMRC 0-1, CAAT < 10	SYMPTOMS: mMRC ≥ 2, CAAT ≥ 10
One or more (≥ 1) moderate or severe exacerbations in the previous year	**GROUP E** **LABA + LAMA*** *consider LABA+LAMA+ICS* if blood eos ≥ 300*	
Zero (0) moderate or severe exacerbations in the previous year	**GROUP A** **A bronchodilator**	**GROUP B** **LABA + LAMA***

*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAAT™: Chronic Airways Assessment Test™.

2026 Teaching Slide Set

Device considerations

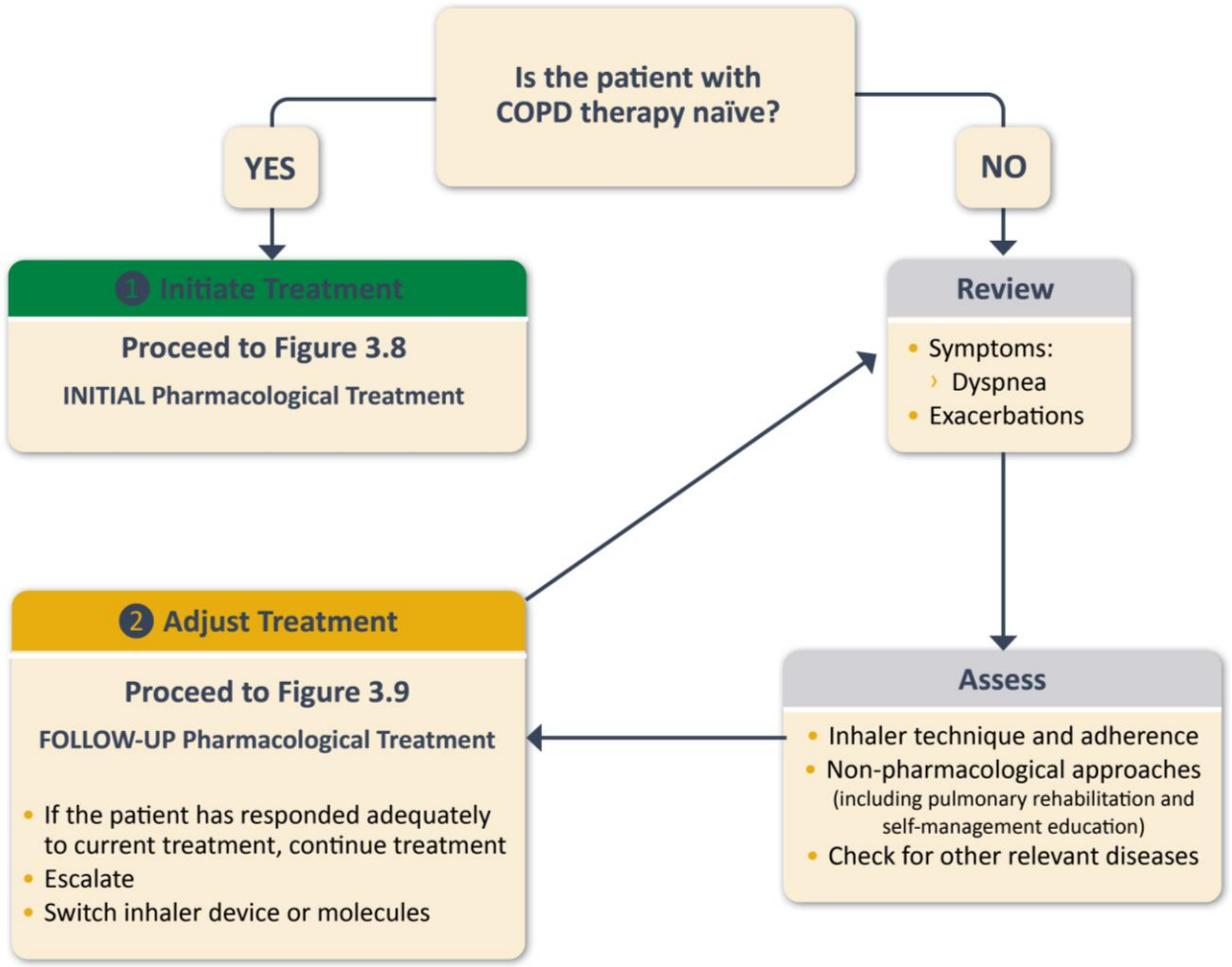


GOLD 2024

2026
Teaching
Slide Set

Diagnosis and Management Cycle

Figure 3.7



Follow-up Pharmacological Treatment

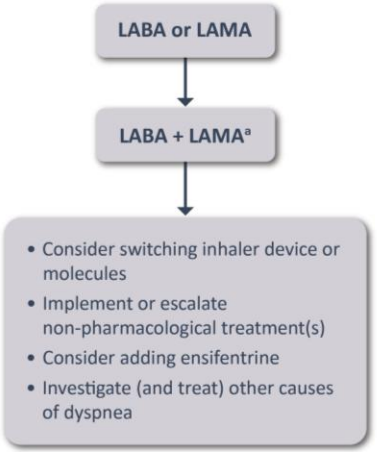
Figure 3.9

2 Adjust Treatment

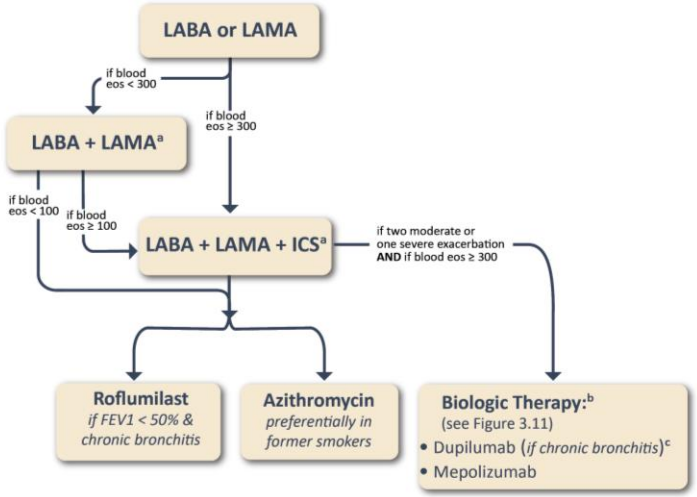
CONTINUE CURRENT TREATMENT

unless dyspnea or exacerbation(s) require optimization

• IF PERSISTENT DYSPNEA



• IF ONE OR MORE MODERATE OR SEVERE EXACERBATION



[a]Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment.

[b]Listed in order of approval in the US.

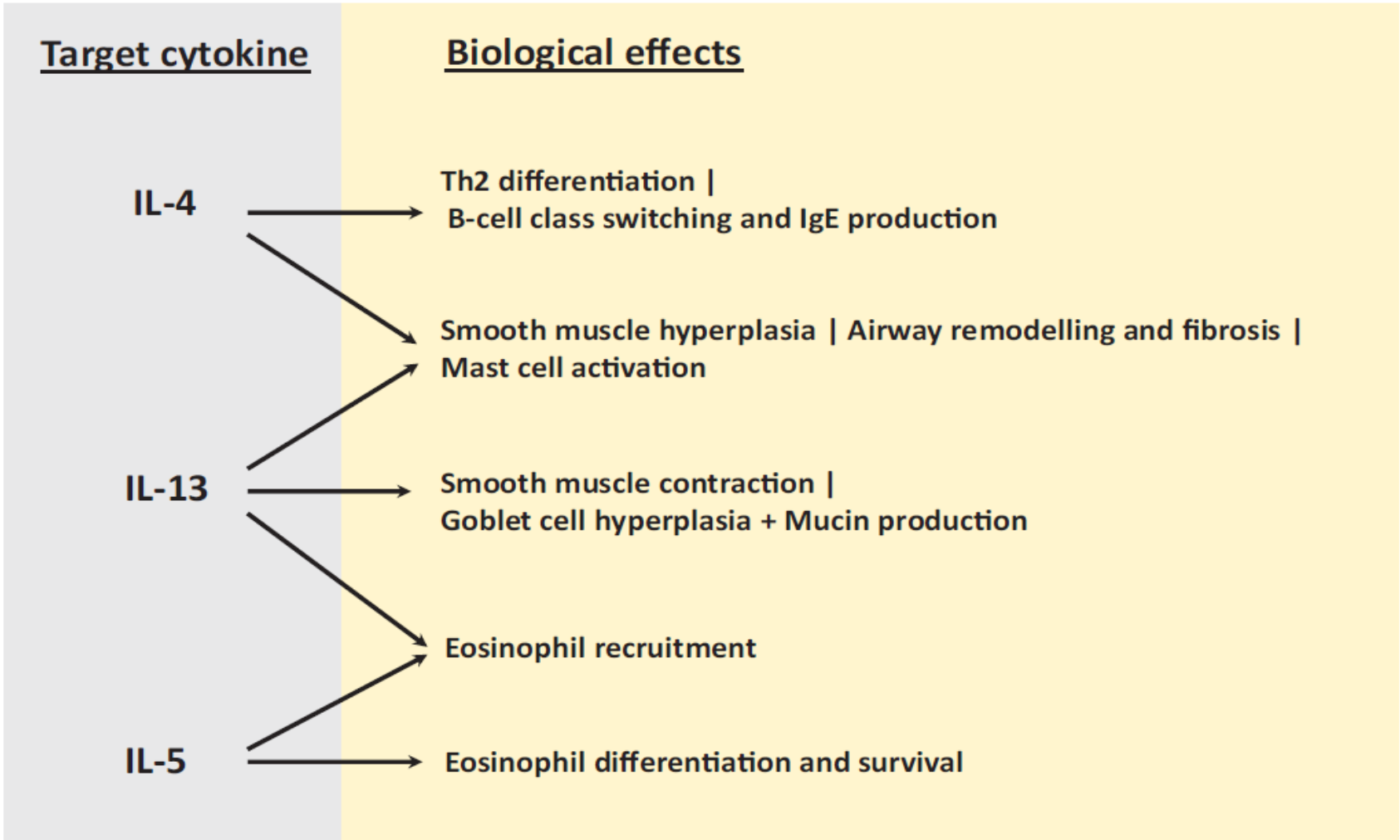
[c]Patient-reported history of chronic bronchitis (chronic productive cough) for 3 months in the year up to screening, absent other known causes.

Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eosinophils ≥ 300 cells/µl de-escalation is more likely to be associated with the development of exacerbations.

2026 Teaching Slide Set

Biological Therapy in COPD Management: Current Evidence, Challenges and Opportunities

Dave Singh [a,b,*], Antonio Menéndez Lobo [c], Andrew Higham [a], Bernardino Alcázar Navarrete [d,e]



https://doi.org/10.1016/j.arbres.2025.07.017

Dupilumab for chronic obstructive pulmonary disease with type 2 inflammation: a pooled analysis of two phase 3, randomised, double-blind, placebo-controlled trials

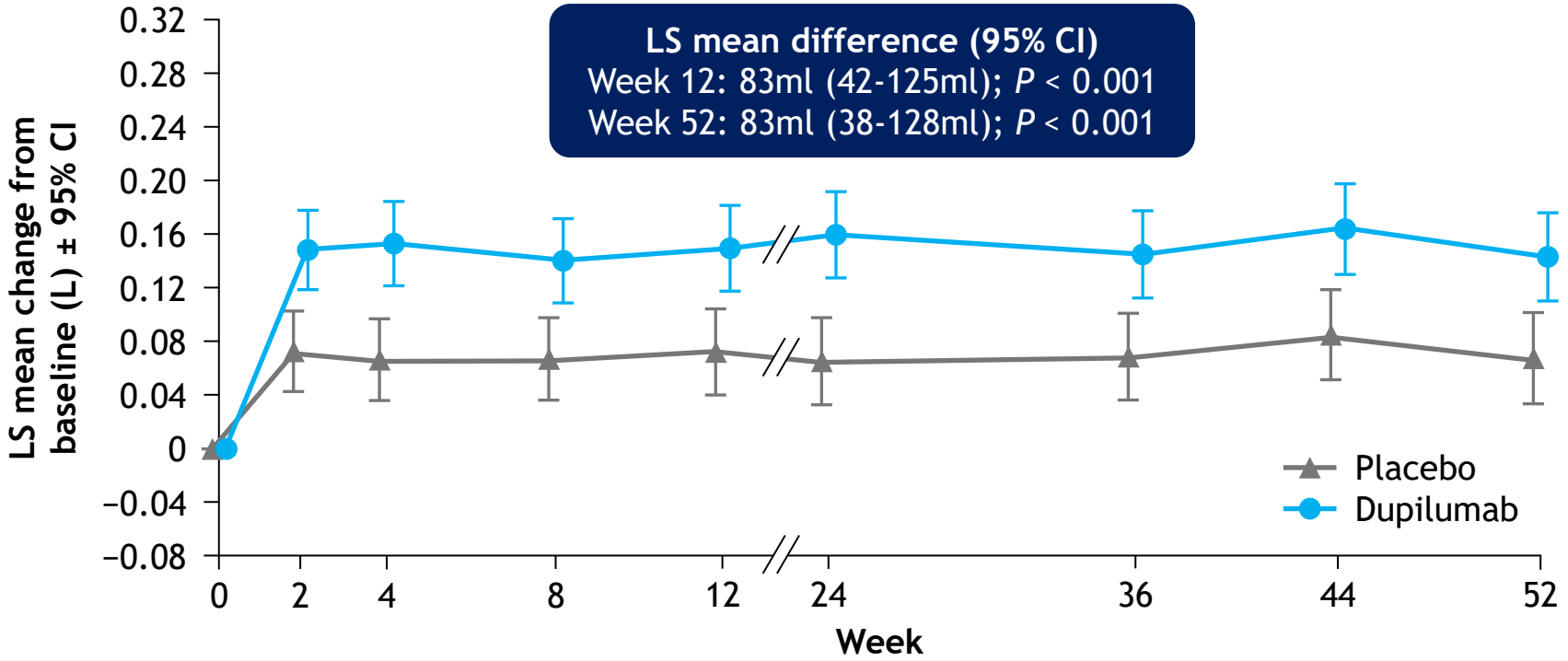
	Placebo (n=936)*	Dupilumab (n=938)*	Difference *vs* placebo (95% CI)†	Nominal p value‡
Primary outcome				
Annualised rate of moderate or severe COPD exacerbation during the 52-week treatment period§	1·156	0·794	0·687 (0·595 to 0·793)	<0·0001

Inclusion: Triple therapy, ≥ 2 exacerbations, blood eosinophils ≥ 300 / uL

Bhatt et al *Lancet Respir Med* 2025; 13: 234–43

Dupilumab Phase 3 BOREAS: Effect on Prebronchodilator FEV_1

BOREAS: Change in prebronchodilator FEV_1 over time*
(FEV_1 < 0.70, postbronchodilator FEV_1 30% to 70% predicted normal)



No. of participants with observed change from baseline									
Placebo	471	455	459	439	439	435	415	404	420
Dupilumab	467	457	454	446	449	443	415	410	426

Improvement in FEV_1 observed within 2 weeks and sustained throughout the study period in BOREAS

*LS mean difference at Week 12 of 83 mL (95% CI: 42-125; P < 0.001) and Week 52 of 83 mL (95% CI: 38-128; P < 0.001). FEV_1, forced expiratory volume in 1 second; LS, least squares.
Bhatt SP, Rabe KF, et al. *N Engl J Med*. 2023;389(3):205-214.

Mepolizumab to Prevent Exacerbations of COPD with an Eosinophilic Phenotype

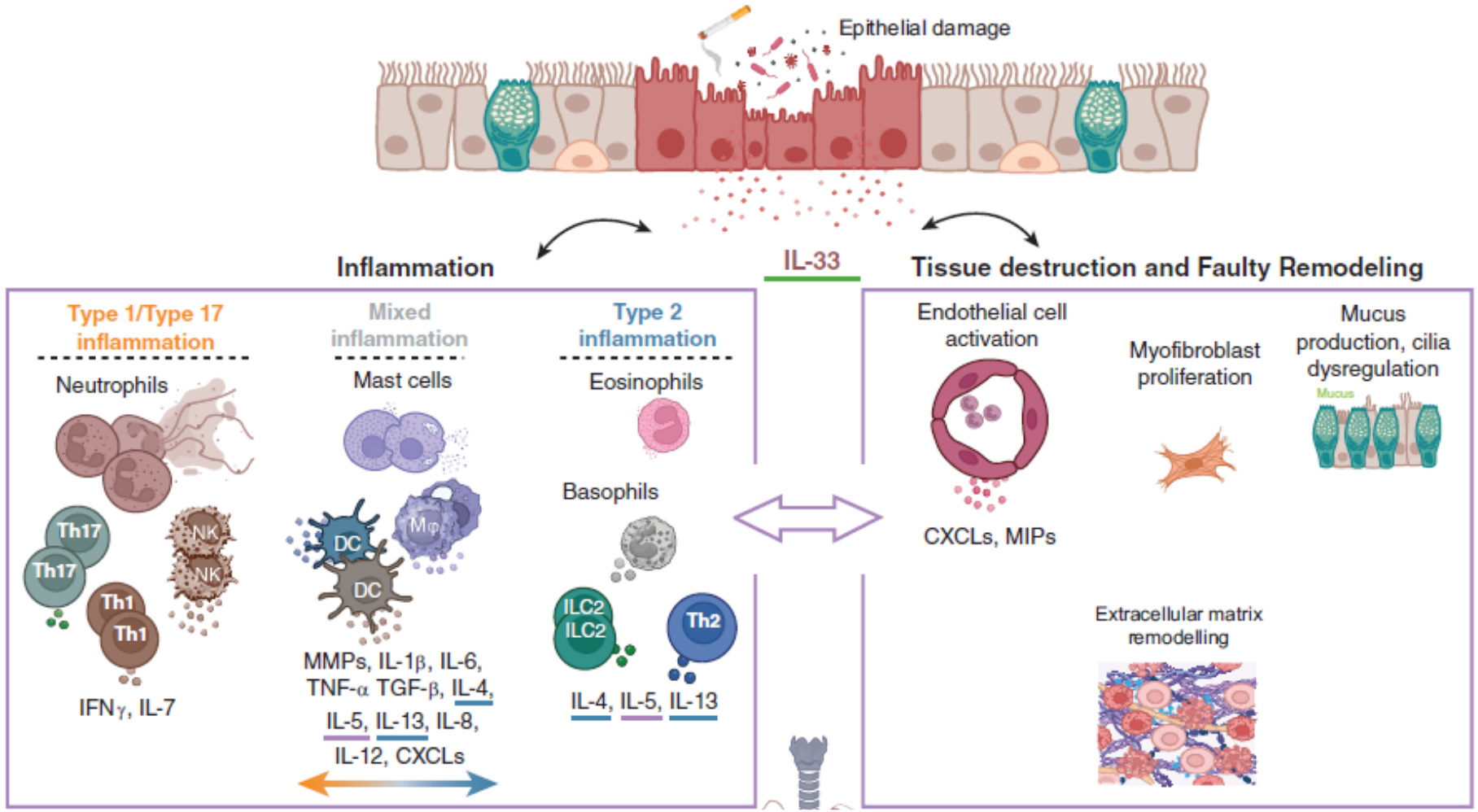
End Point	Mepolizumab (N=403)	Placebo (N=401)
Primary end point		
Annualized rate of moderate or severe exacerbations (95% CI) — events/yr	0.80 (0.70–0.91)	1.01 (0.89–1.15)
Rate ratio vs. placebo (95% CI)	0.79 (0.66–0.94)	—
P value	0.01	—

Inclusion: Triple therapy, ≥ 2 exacerbations, blood eosinophils ≥ 300 / uL

Pavord I et al

The Emerging Role of Alarmin-Targeting Biologics in the Treatment of Patients With COPD

Bartolome R. Celli, MD, FCCP; Antonio Anzueto, MD; Dave Singh, MD; Nicola A. Hanania, MD; Leonardo Fabbri, MD; Fernando J. Martinez, MD; Xavier Soler, MD, PhD; Michel Djandji, MD; Juby A. Jacob-Nara, MD; Paul J. Rowe, MD; Yamo Deniz, MD; and Amr Radwan, MB BChir

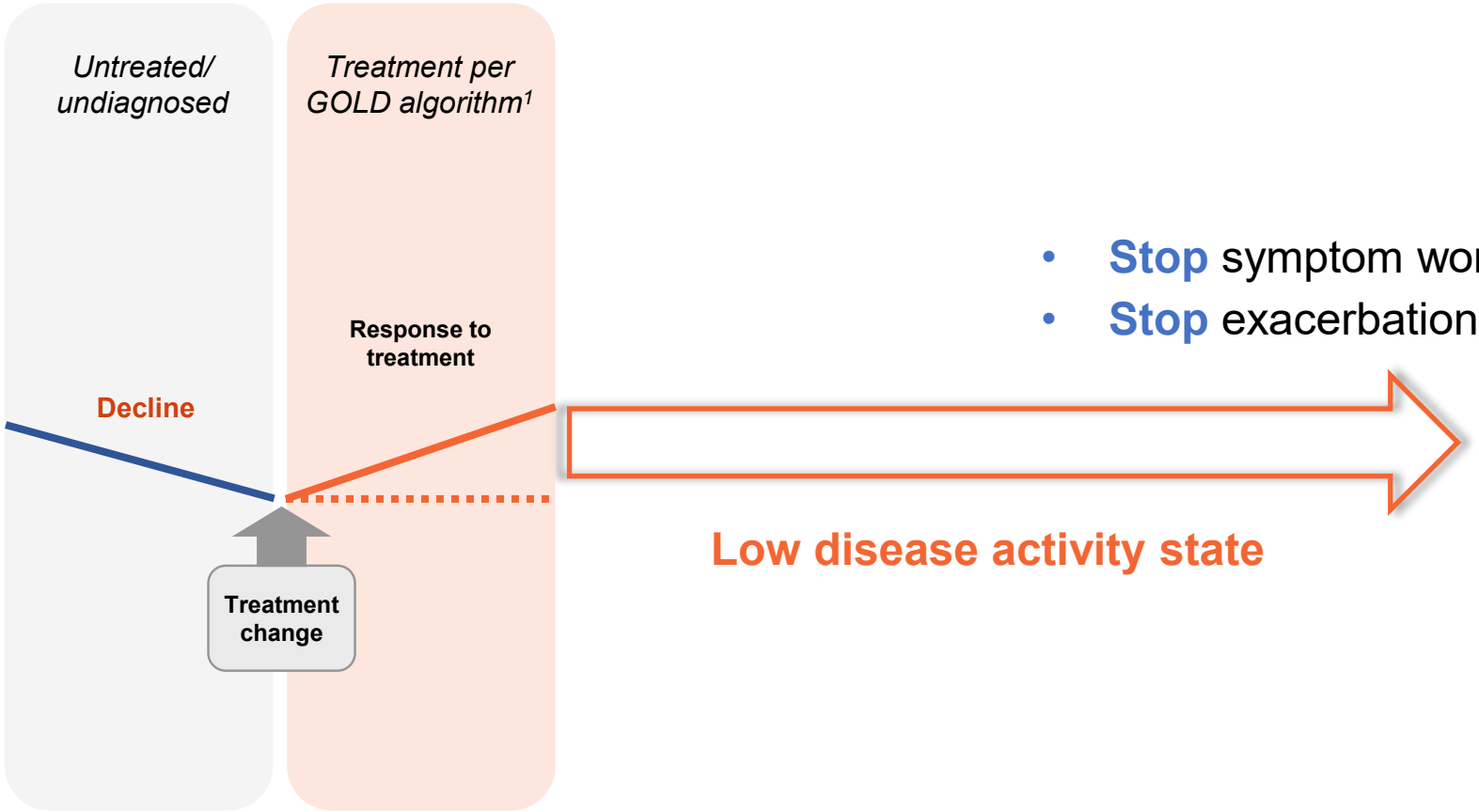


CHEST 2025; 167(5):1346-1355

Striving for Stability in Patients with COPD: A New Way Forward?

MeiLan K. Han · Lowie E. G. W. Vanfleteren · Stefanie Kolterer · Rianne Stacey · Dave Singh

Short and long term goal



- **Stop** symptom worsening
- **Stop** exacerbations

Low disease activity state

Adv Ther
https://doi.org/10.1007/s12325-024-02982-y