Addressing COPD in the Black Community: Risks, Resources, and Health Equity

Black People Like Me

Addressing COPD in the Black Community: Risks, Resources, and Health Equity

Presented by: Allergy & Asthma Network

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Thank you, Genentech, and Viatris for providing funding support to make this webinar possible.

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Today's Speakers

Moderator
Catherine Blackwell, RN
Chief Health Equity Officer,
Allergy & Asthma Network

Patient Speaker
Misako Bonner

Physician Speaker
Cedric "Jamie" Rutland
MD FCCP

Understanding Chronic Obstructive Pulmonary Disease (COPD)

Presented by: Cedric “Jamie” Rutland MD FCCP

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Objectives

- **Identify Different COPD Phenotypes:** Participants will be able to accurately identify and categorize various COPD phenotypes based on clinical characteristics and presentation
- **Describe the Role of Type 2 Inflammation in COPD:** Participants will accurately describe the pathophysiological mechanisms of Type 2 inflammation in COPD and its impact on disease progression and management
- **Evaluate Advanced Therapies for COPD:** Participants will critically evaluate the efficacy and applicability of advanced therapies for Type 2 inflammation in COPD, using evidence-based criteria

COPD Overview

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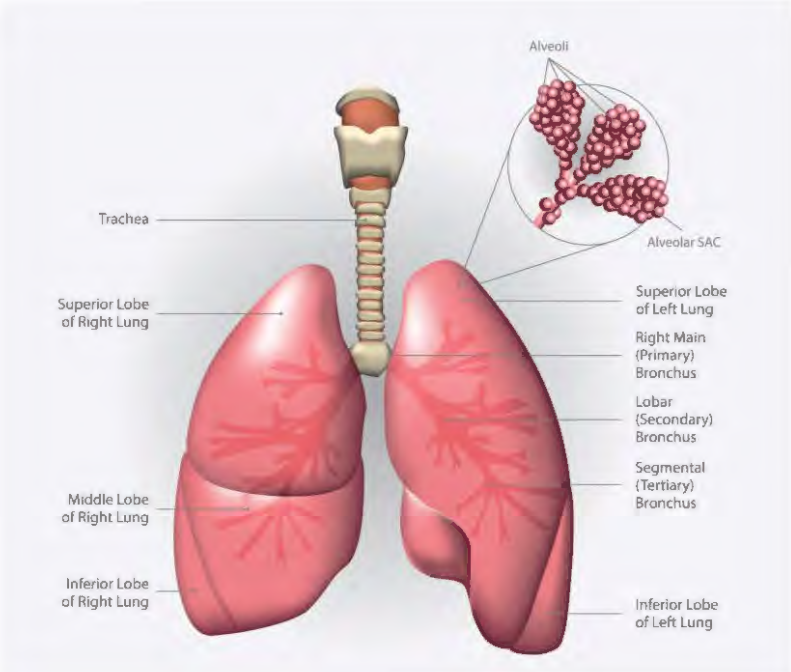
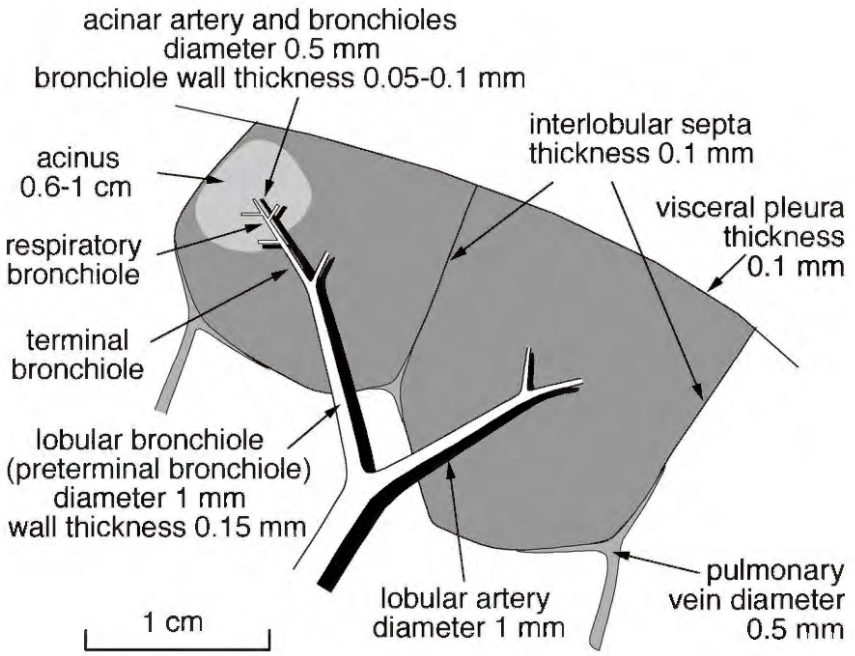
The Lung

The Anatomy

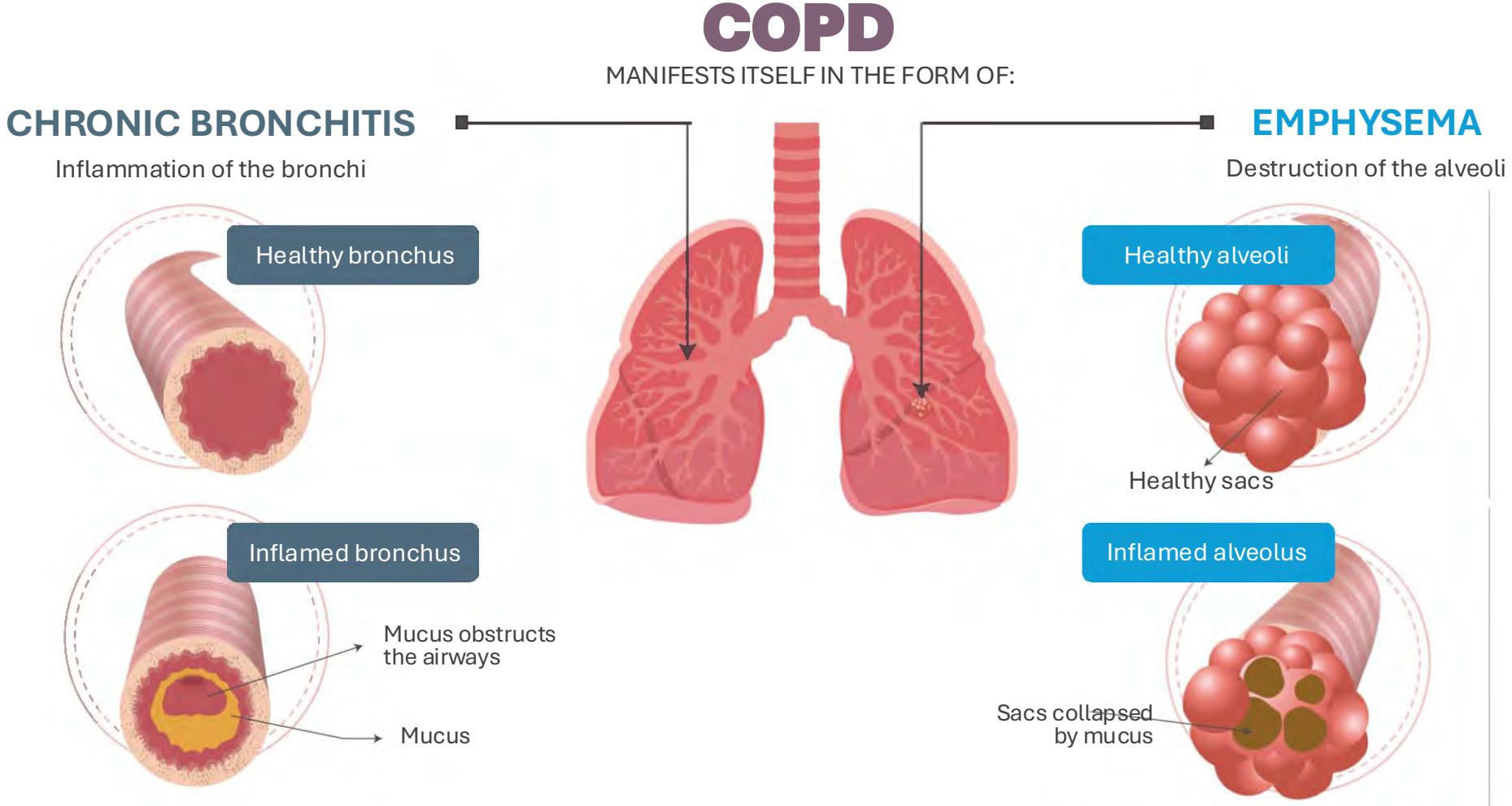


Secondary lobule and pulmonary acinus



1. Webb, WR. *Radiology* 2006: 322-38. doi:10.1148/radiol.2392041968

COPD is characterized by airflow limitation that is usually progressive and associated with abnormal inflammatory response of the lungs

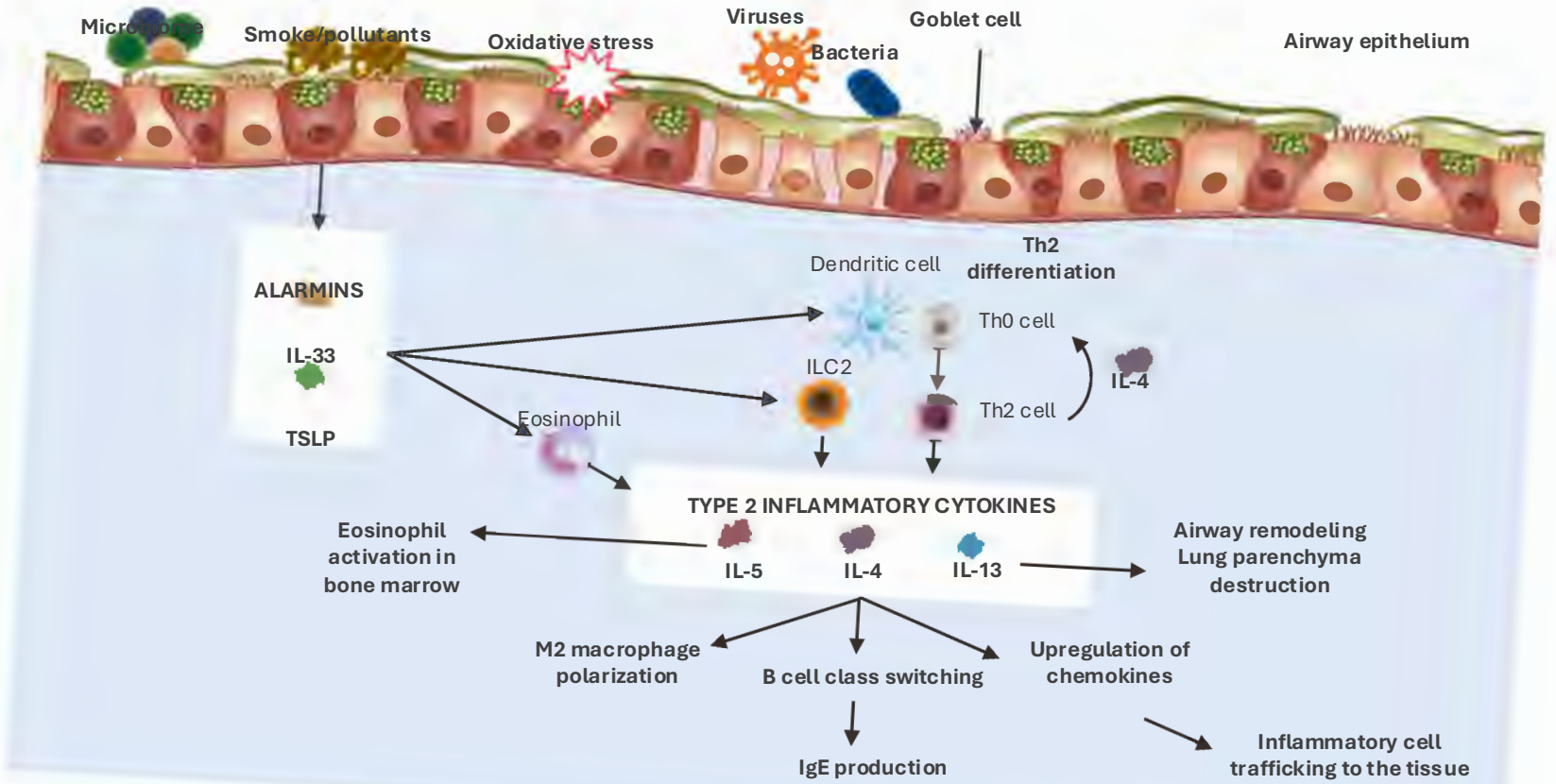


Abbrev: COPD, chronic obstructive pulmonary disease

1. Rabe KF. Delete title. Am J Resp Crit Care Med (itals). 2007;176(6):532-555. doi:10.1164/rccm.200703-456SO

Airway Epithelial Cells and communication

COPD = chronic obstructive pulmonary disease; ILC2 = type 2 innate lymphoid cell; ST2 = suppression of tumorigenicity 2; Th = T-helper cell; TSLP = thymic stromal lymphopoietin



1. Rabe, Klaus F et al. "Targeting Type 2 Inflammation and Epithelial Alarmins in Chronic Obstructive Pulmonary Disease: A Biologics Outlook." American journal of respiratory and critical care medicine vol. 208,4 (2023): 395-405. doi:10.1164/rccm.202303-0455CI

COPD Is a Leading Cause of Morbidity and Mortality[1,2]

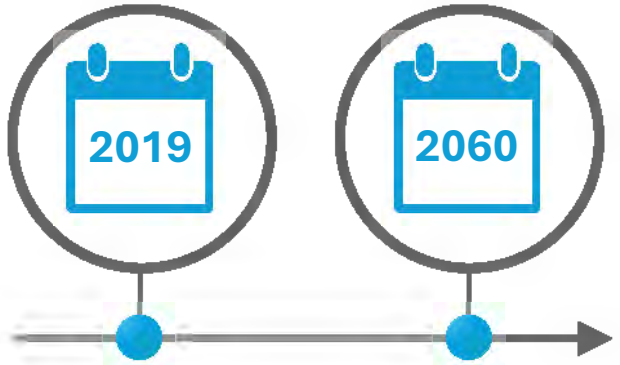
1.32 million
US ED Visits
and
536,000
US Hospitalizations in 2019[2]

$32.1 billion
Total US Economic Cost in 2010[3]

3rd leading
Cause of Death Globally[4]

>150,000
US Deaths Annually[5]

COPD-Related Deaths Are Expected to Increase Globally[1]



3.2 million

5.4 million

Chronic inflammation causes structural and functional changes that drive pathogenic processes[1-9]

Fibrosis and Airway Remodeling

- Narrowing of small airways
- Parenchyma deconstruction
- Increased air wall thickness
- Heightened bronchial tone

Barrier Dysfunction

- Increased permeability
- Goblet cell hyperplasia
- Ciliary cell reduction and dysfunction

Mucus Production

- Airway obstruction

Alveolar Membrane Breakdown

- Decreased gas exchange
- Hyperinflation

Clinical Consequences

- Persistent symptoms
- COPD exacerbations
- Progressive lung function decline
- Systemic effects

GOLD grades and severity of airflow obstruction in COPD (based on post-bronchodilator FEV1)

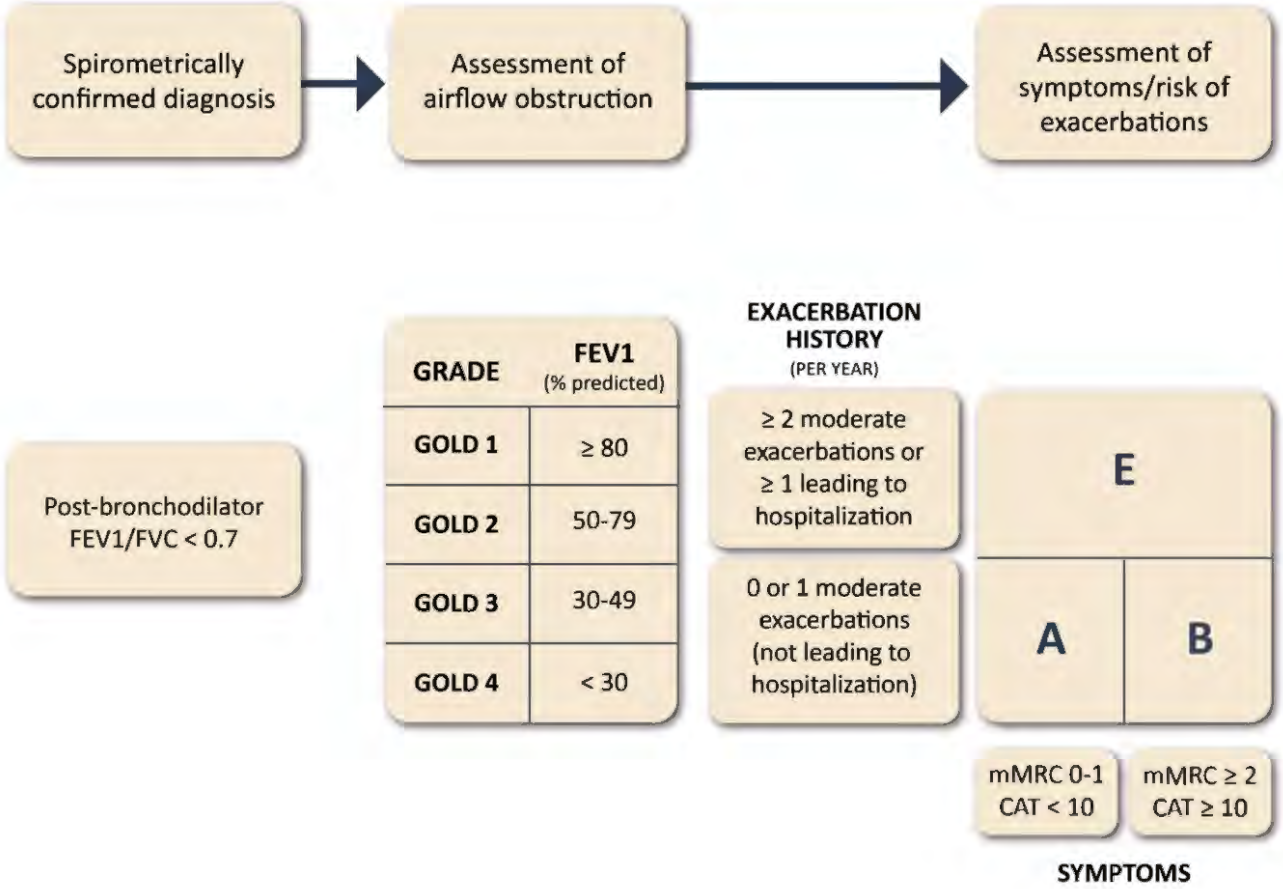
In COPD patients (FEV1/FVC < 0.7):

GOLD 1:	Mild	FEV1 ≥ 80% predicted
GOLD 2:	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3:	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4:	Very Severe	FEV1 < 30% predicted

Abbrevs: COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. https://goldcopd.org/2024-gold-report/. Updated 2024, Accessed April 25, 2024.

GOLD ABE Assessment Tool



Abbrevs: CAT™ , COPD Assessment Test™ ; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified Medical Research Council dyspnea questionnaire

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. https://goldcopd.org/2024-gold-report/. Updated 2024, Accessed April 25, 2024.

Assessment tools

CAT™ Assessment

Figure 2.9

For each item below, place a mark (x) in the box that best describes you currently.
Be sure to only select one response for each question.

EXAMPLE: I am very happy	0 X 2 3 4 5	I am very sad	Score
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

TOTAL SCORE: ☐

Modified MRC Dyspnea Scale

Figure 2.8

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

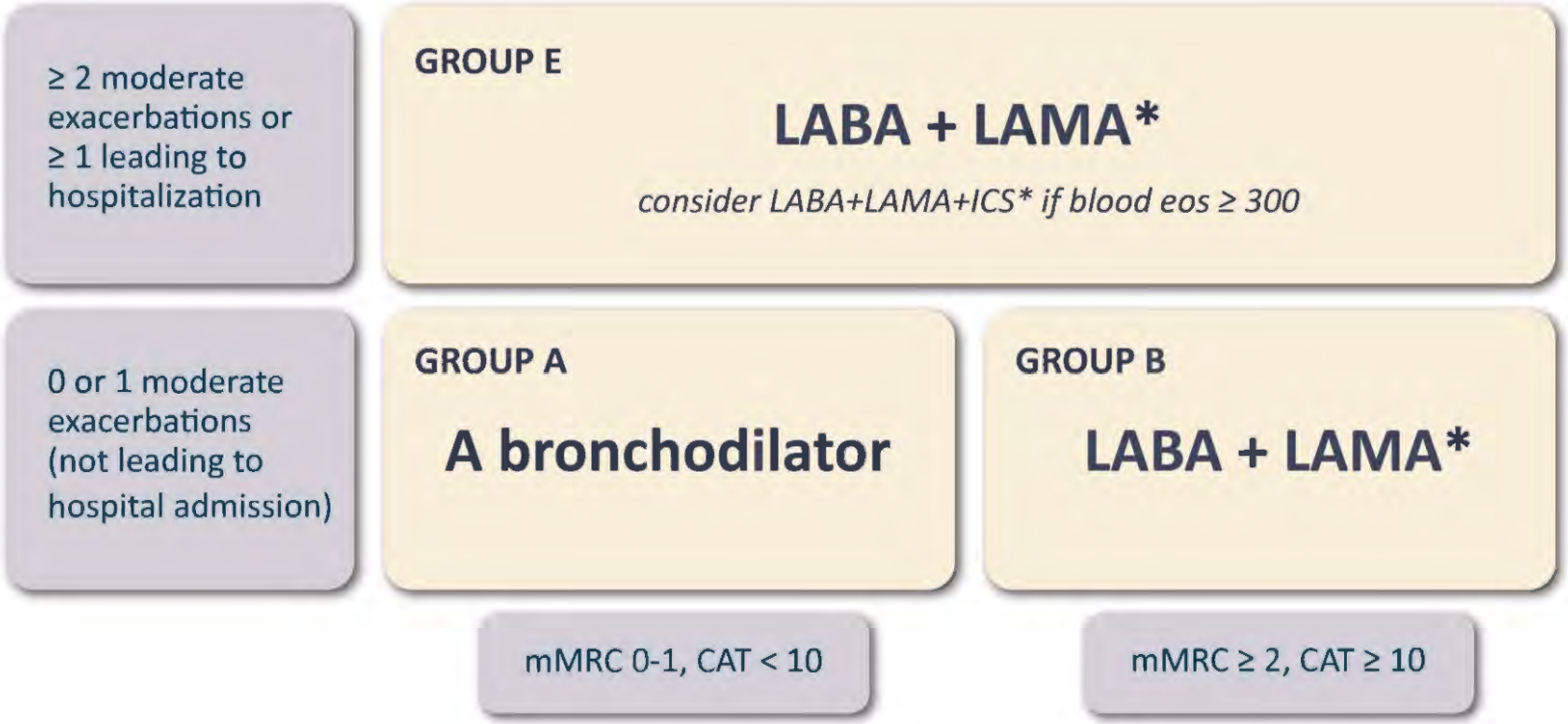
mMRC Grade 0	mMRC Grade 1	mMRC Grade 2	mMRC Grade 3	mMRC Grade 4
I only get breathless with strenuous exercise ☐	I get short of breath when hurrying on the level or walking up a slight hill ☐	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level ☐	I stop for breath after walking about 100 meters or after a few minutes on the level ☐	I am too breathless to leave the house or I am breathless when dressing or undressing ☐

Reference: ATS (1982) Am Rev Respir Dis. Nov;126(5):952-6.

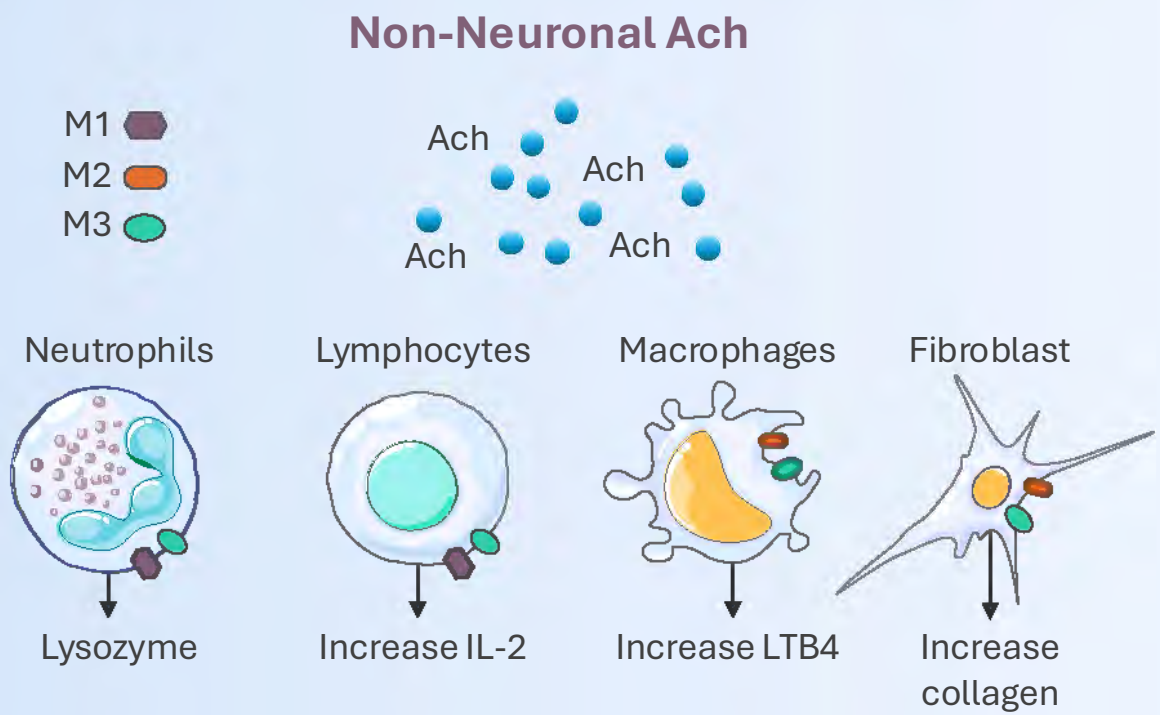
Abbrevs: CAT™, COPD Assessment Test™; MRC, Medical Research Council; mMRC, modified Medical Research Council dyspnea questionnaire

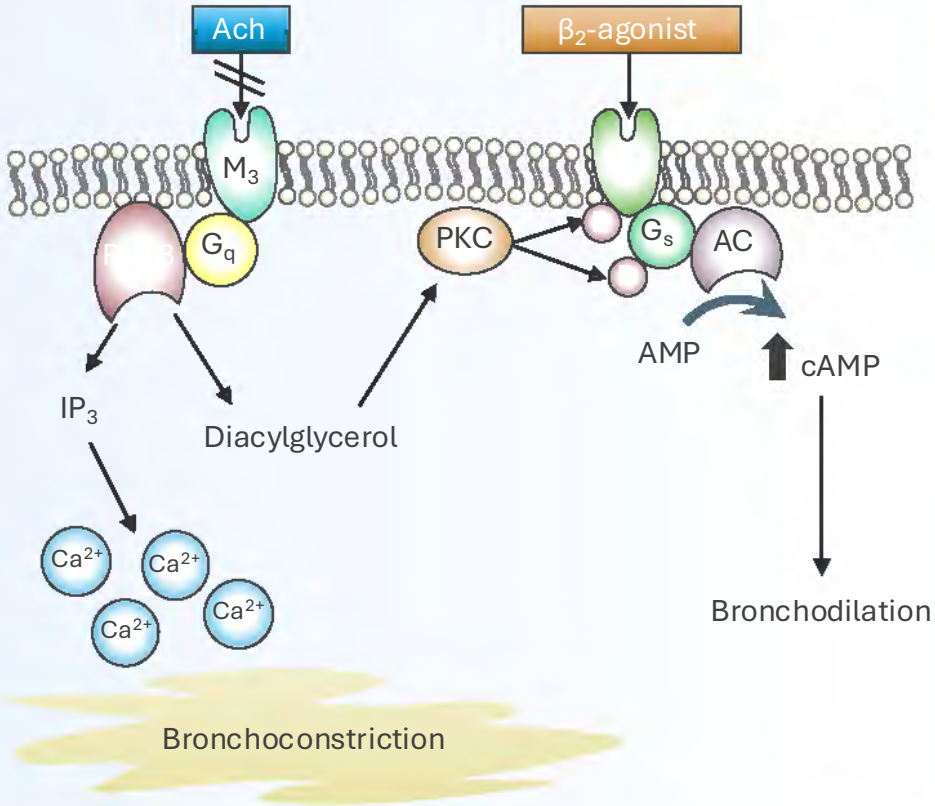
1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. https://goldcopd.org/2024-gold-report/. Updated 2024, Accessed April 25, 2024.

Initial Pharmacological Treatment



GOLD Therapy Mechanisms



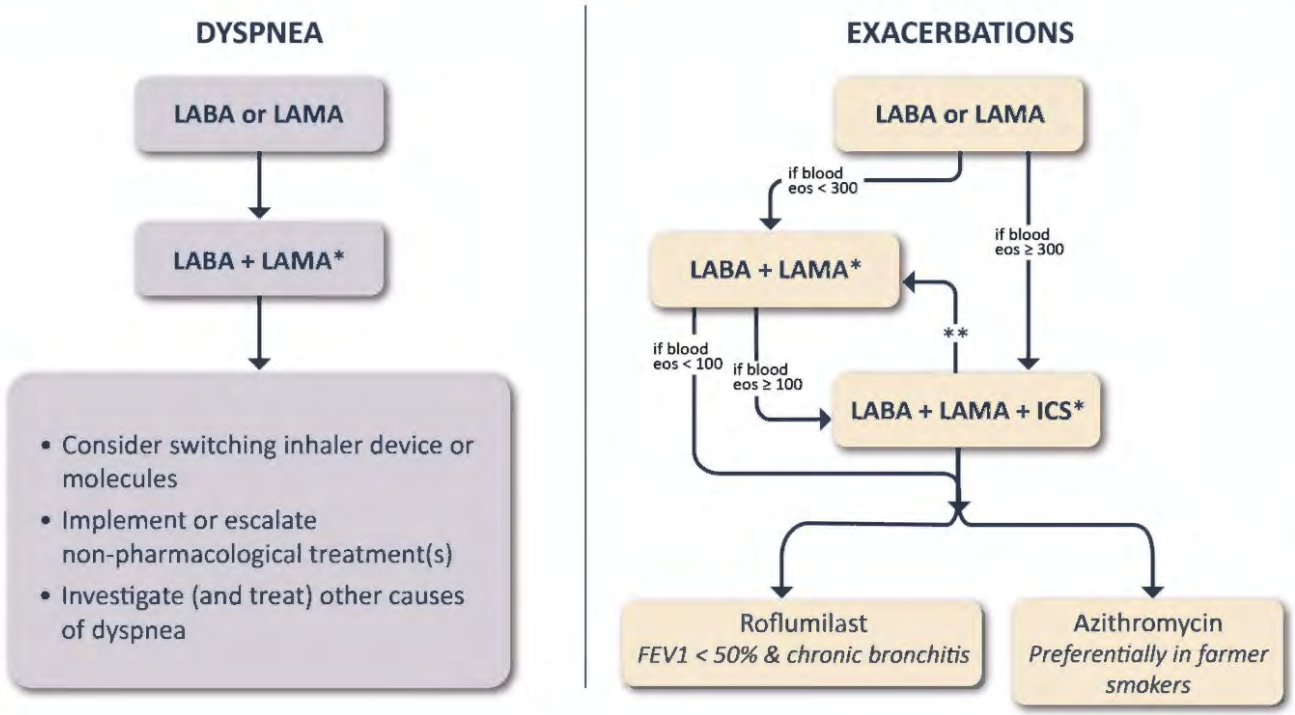


Abbrevs: Ach, acetylcholine; GOLD, Global Initiative for Chronic Obstructive Lung Disease; IL, interleukin

1. Bulkhi, A et al. *Drugs* (2016): 999-1013. doi:10.1007/s40265-016-0599-7

Follow-up Pharmacological Treatment[1]

- If response to initial treatment is appropriate, maintain it
- If NOT:
  - Check adherence, inhaler technique, and possible interfering comorbidities
    - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
  - Place patient in box corresponding to current treatment and follow indications
  - Assess response, adjust, and review
  - These recommendations do not depend on the ABE assessment at diagnosis



*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment.
**Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood EOS ≥300 cells/µl de-escalation is exacerbations refers to the number of exacerbations per year. Exacerbations refers to the number of exacerbations per year.
Abbrevs: EOS, eosinophils; FEV1, forced expiratory volume in one second; ICS, inhaled corticosteroids; LABA, long-acting beta agonist; LAMA, long-acting muscarinic antagonist.

Patient Case Discussion

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Jane

Interactive Patient Case Study

Case Details

68 y/o female seen for evaluation of COPD. No asthma as a child, no history of allergies. Smoke 1 PPD of cigarettes from age 25-60. Quit 8 years ago. Developed respiratory symptoms in her 50s was told she had COPD

Current Treatment Details

- Has flares frequently that require bursts of prednisone 3-4 times a year and antibiotics (usually azithromycin); she feels prednisone is her lifeline and takes 10-30 mg 1-2 times a week depending on how she feels
- She reports needing albuterol nebulizer a few times a week. For inhalers she is only using Albuterol. **She is on triple therapy but still suffering**

Lab/Test Results

PE: Good air entry; Scattered wheezing

Bloodwork: EOS 300 cells/ul | Radiology: PA/Lat CXR and unremarkable

	FVC %	FEV1 %	FEV1/FVC	FeNO (ppb)	TLC %	RV %	DLCO %
09/4/2013	41	71(%)	0.58				
4/4/2023	98	60	0.50	70	92	100	70

ACT, asthma control test; ANCA, Antineutrophil Cytoplasmic Antibodies; COPD, chronic obstructive pulmonary disease; CXR, chest xray; DLCO, diffusing lung capacity for carbon monoxide; EOS, eosinophil; FeNO, fractional exhaled nitric oxide; FEV1 (subscript 1), forced expiratory volume in 1 second; FVC, forced vital capacity; IgE, immunoglobulin E; ppb, parts per billion; PPD, packs per day; PA LAT, posterior anterior lateral; RV, residual volume; TLC, total lung capacity; y/o, year old

Type 2 Inflammation in COPD

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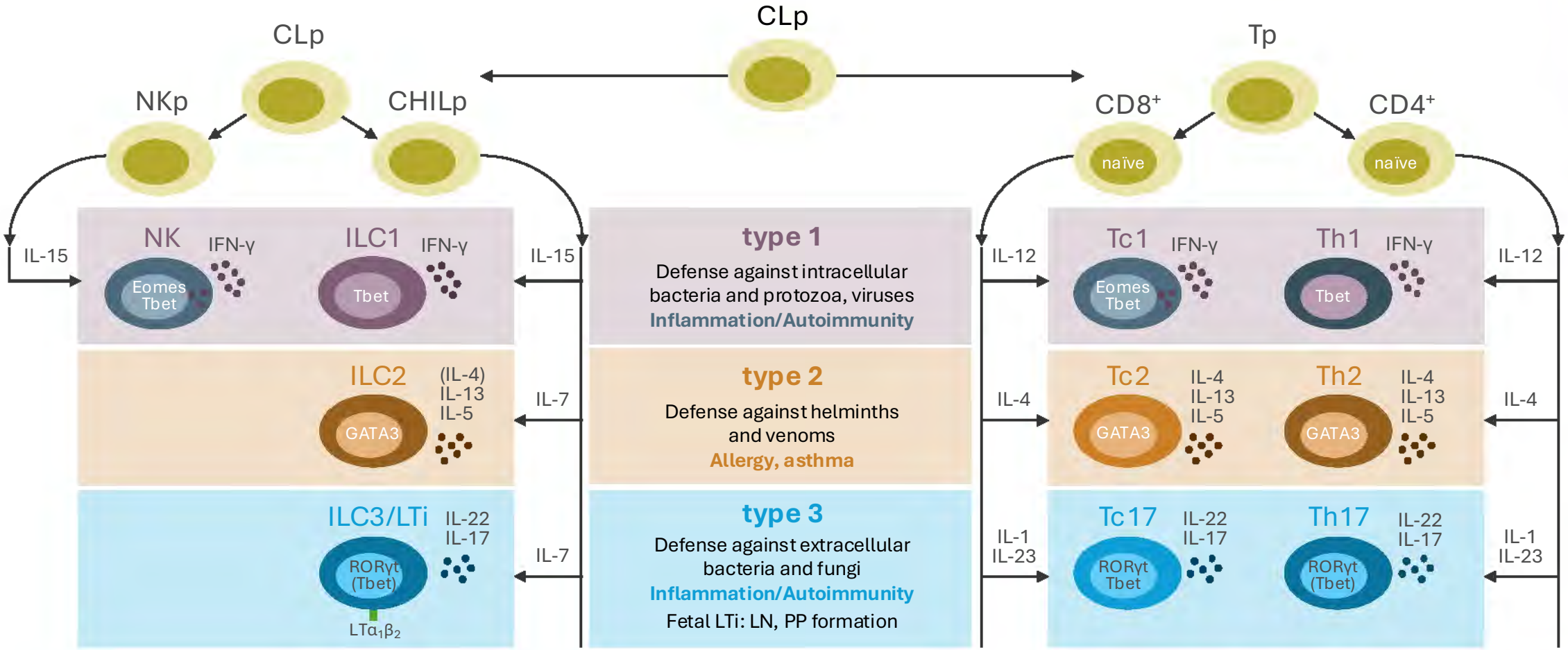
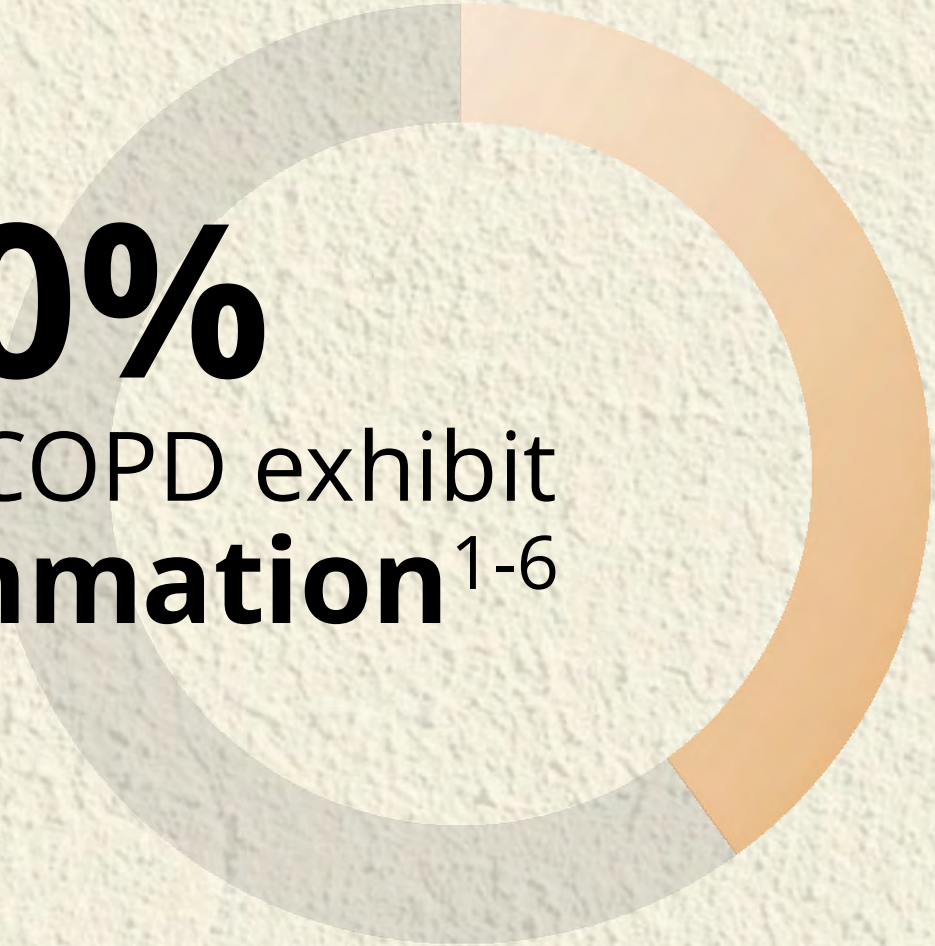
The innate and adaptive immune systems form three major kinds of cell-mediated effector immunity



CILp, common innate lymphoid precursor; CLp, common lymphoid precursor; eomes, eomesodermin; IFN, interferon; IL, interleukin; ILC, innate lymphoid cell; LN, lymph node; LT, lymphotoxin; LTi, lymphoid tissue inducer; NK, natural Killer; NKp, Natural killer progenitor PP, peyer patch; ROR, retinoic acid–related orphan receptor; Tc, Cytotoxic T; Th, T helper cell; Tp, T-cell progenitor.

1. Annunziato F et al. Delete title J All Clin Immunol. (it) 2015;



20-40%

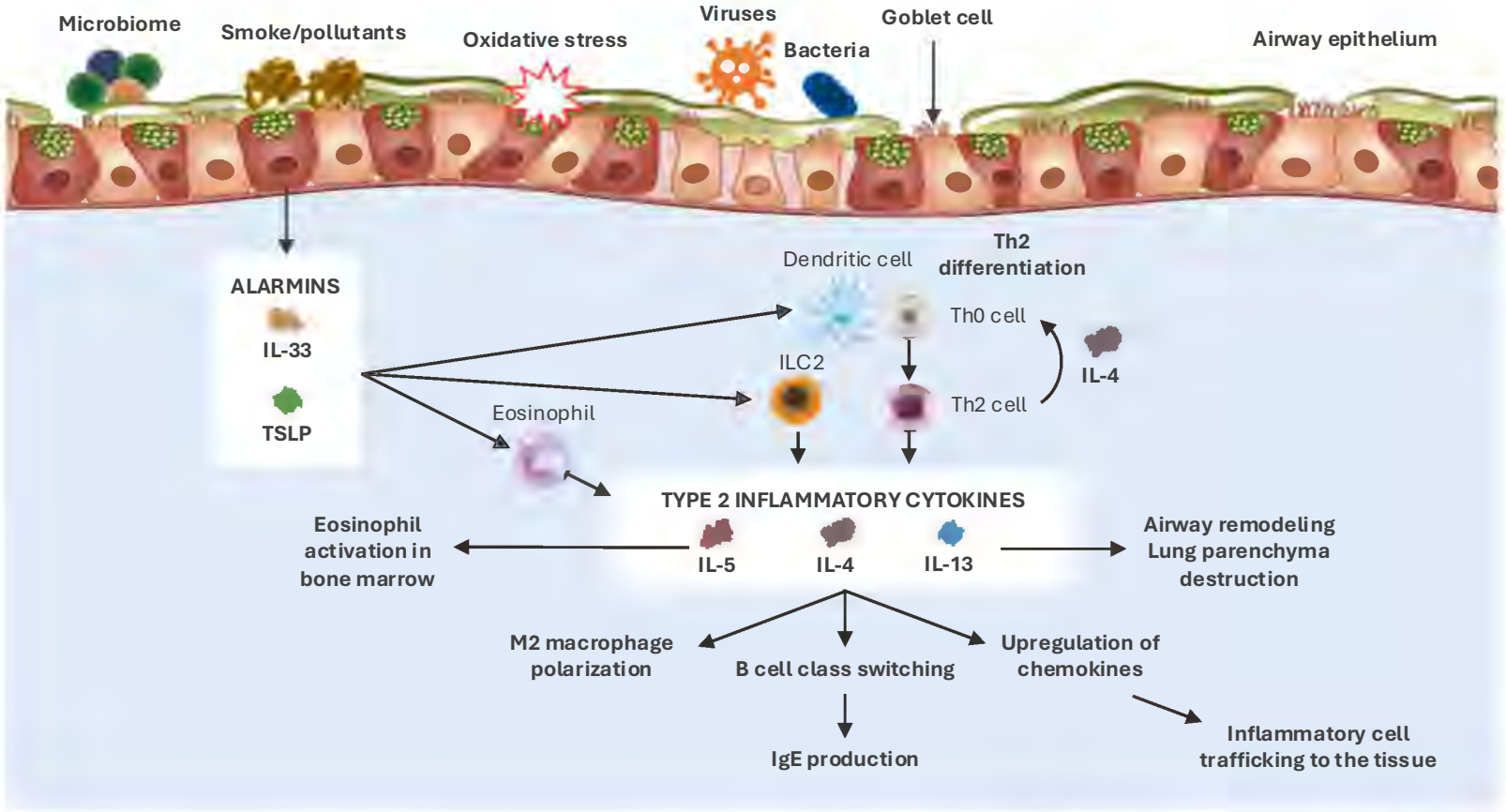
of patients with COPD exhibit

type 2 inflammation[1-6]

1. Rabe, KF. *Am J Resp Medicine* 2023;208(4) 395-405. doi:10.1164/rccm.202303-0455CI 2. Vedel-Krogh S et al. *Am J Respir Crit Care Med*. 2016;193(9):965-974. 3. Brightling C et al. *Eur Respir J*. 2019:54(2):1900651. 4. Bel EH et al. *Chest* : 2017;152(8):1278-1282. 5. Pizzichini, E et al. *Am J Resp Crit Care Med*. 1998;158(5 pt 1):1511-1517 doi:10.1164/ajrccm.158.5.9804028. 6. Saha, S et al. *Int J Chron Obstr Pulm Dis*. 2006;1:39-47. doi:10.2147/copd.2006.1.1.39

Type 2 Inflammation activates immune cells to promote eosinophil recruitment and IgE production

Blood eosinophil are a biomarker of type 2 inflammation[1]



COPD = chronic obstructive pulmonary disease

ILC2 = type 2 innate lymphoid cell

ST2 = suppression of tumorigenicity 2

Th = T-helper cell

TSLP = thymic stromal lymphopoietin

1. Rabe, Klaus F et al. “Targeting Type 2 Inflammation and Epithelial Alarmins in Chronic Obstructive Pulmonary Disease: A Biologics Outlook.” American journal of respiratory and critical care medicine vol. 208,4 (2023): 395-405. doi:10.1164/rccm.202303-0455CI

Type 2 cytokines IL-4, IL-13, and IL-5 have distinct and overlapping roles[1-7]

IL-4

- Th2 cell differentiation
- B-cell isotype switching and IgE production
- Mast cell and basophil degranulation
- Eosinophil recruitment and trafficking to tissue
- Epithelial/epidermal barrier dysfunction
- Tissue remodeling
- Smooth muscle proliferation, increased contractility, and hyperresponsiveness

IL-13

- Goblet cell hyperplasia
- Mucus production/ Mucociliary dysfunction
- Collagen deposition
- Fibrosis

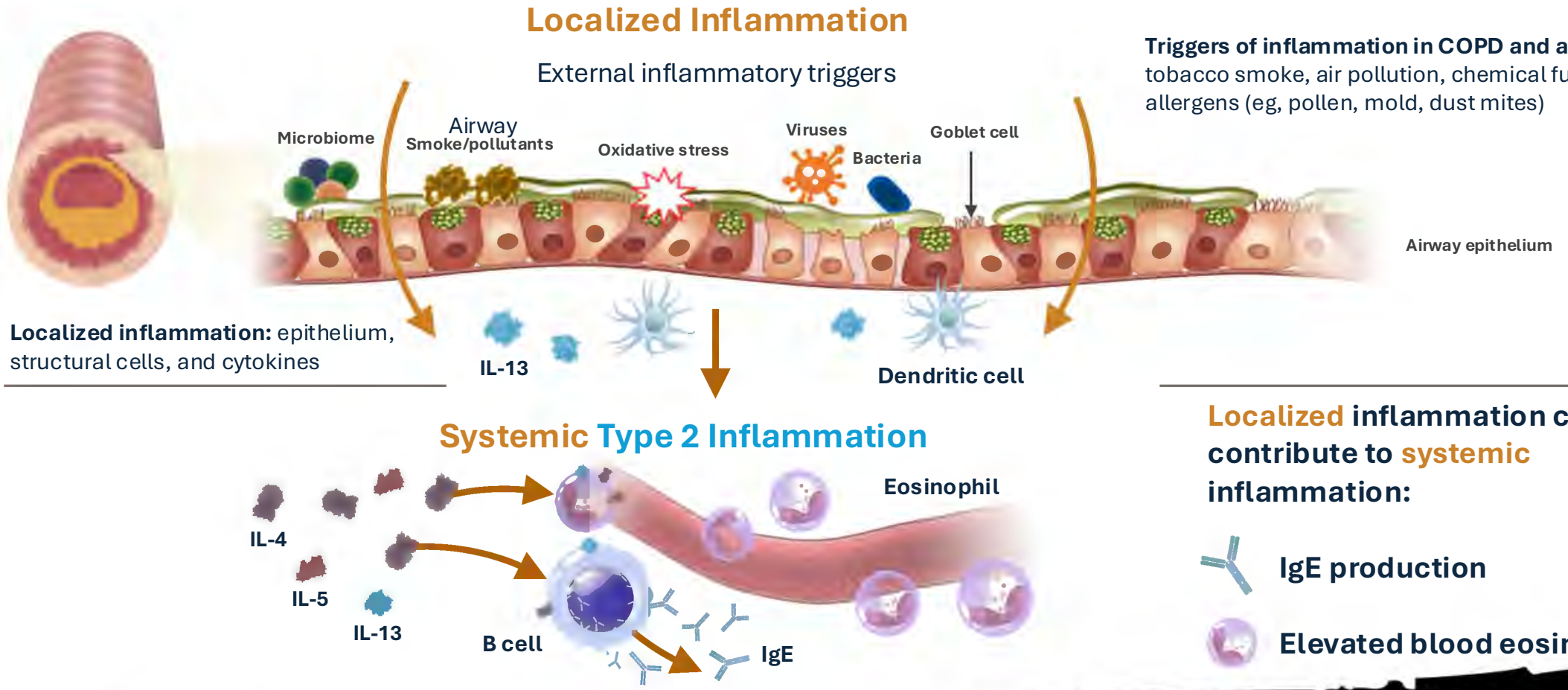
IL-5

- Eosinophil differentiation in bone marrow and survival in circulation

IL, interleukin; Th2, T helper cell 2.

1. Gandhi NA et al. *Nat Rev Drug Discov*. 2016;15:35-50. **2.** Robinson D et al. *Clin Exp Allergy*. 2017;47:161-175. **3.** Corren J. *Curr Allergy Asthma Rep*. 2013;13:415-420. **4.** Manson ML et al. *J Allergy Clin Immunol*. 2020;145:808-817. **5.** Stott B et al. *J Allergy Clin Immunol*. 2013;132:446-454. **6.** Gutzmer R et al. *J Allergy Clin Immunol*. 2009;23:619-625. **7.** George L et al. *Allergy*. 2020;75(2):370-380.

Localized type 2 inflammation may contribute to systemic inflammation[1-5]



Triggers of inflammation in COPD and asthma: tobacco smoke, air pollution, chemical fumes, allergens (eg, pollen, mold, dust mites)

Localized inflammation: epithelium, structural cells, and cytokines

Localized inflammation can contribute to systemic inflammation:

- IgE production
- Elevated blood eosinophils

“There is evidence that on average blood eosinophil counts are higher in COPD patients”

“Higher blood eosinophil counts in COPD patients are associated with increased lung eosinophil numbers and the presence of higher levels of markers of type-2 inflammation in the airways” - GOLD Report 2024

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. https://goldcopd.org/2024-gold-report/. Updated 2024, Accessed April 25, 2024.

Patients with elevated type 2 inflammatory biomarkers may have an increased risk of exacerbation[1]

Signs of Systemic Inflammation

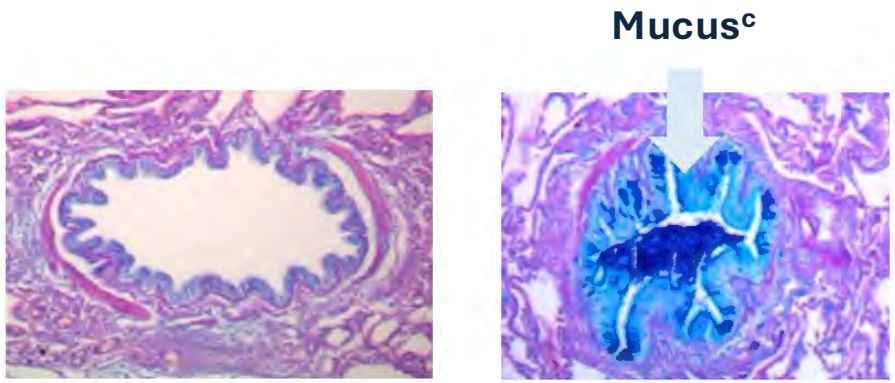
Elevated blood EOS are associated with:

1.76x

greater risk for a severe exacerbation[3,a]

more-impaired lung function[4,b]

Histologic Signs of Localized Inflammation

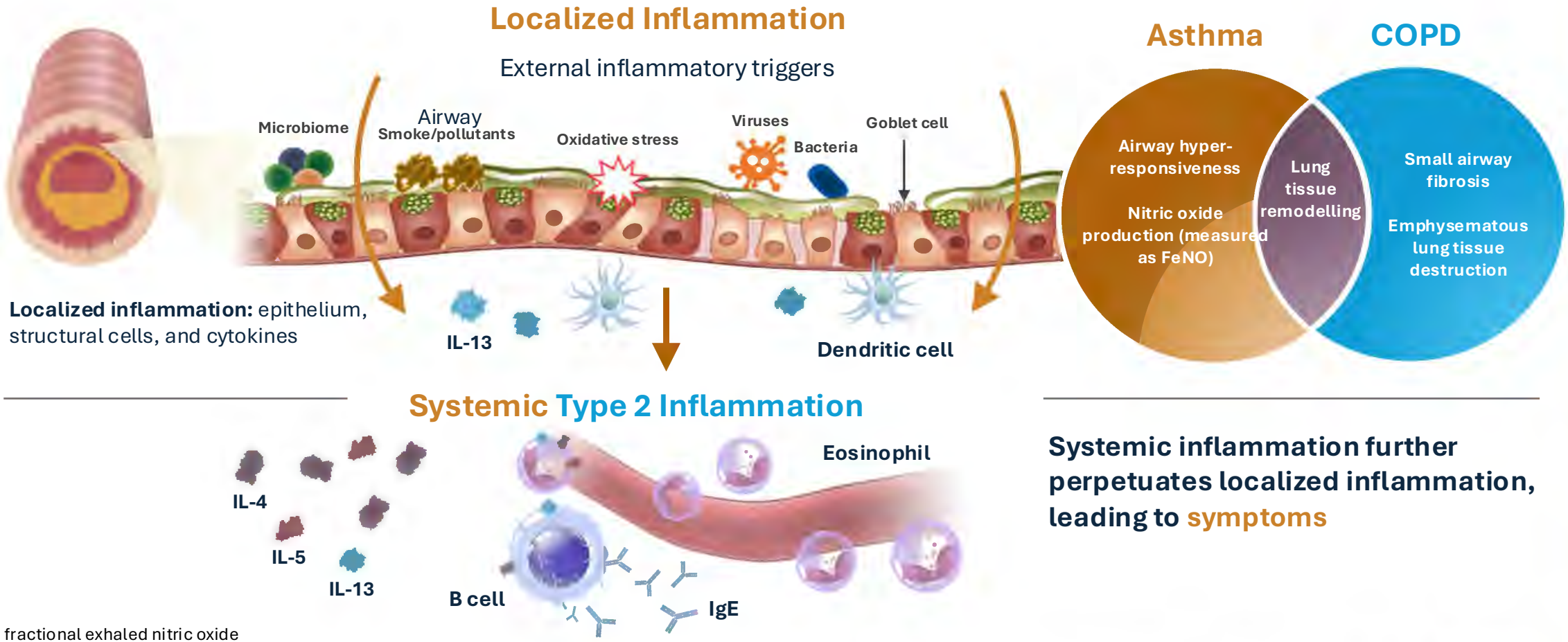


Control **COPD[2]**

[a]Eosinophilic COPD was defined as blood EOS ≥340 cells/µL. A severe exacerbation was defined as a hospitalization due to COPD. Exacerbations had to be a minimum of 4 weeks apart to be considered separate exacerbations; [b]in a cohort of patients with EOS ≥200 cells/µL. [c]Alcian blue PAS staining of mucus in airway epithelial cells.
PAS, periodic acid-Schiff.

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. https://goldcopd.org/2023-gold-report-2/. Updated 2023. Accessed June 22, 2023. **2.** Fritzsching B et al. *Am J Respir Crit Care Med*. 2015;191(8):902-913. **3.** Vedel-Krogh S et al. *Am J Respir Crit Care Med*. 2016;193(9):965-974. **4.** George L et al. *Allergy*. 2020;75(2):370-380.

Systemic type 2 inflammation can perpetuate localized inflammation[1-5]

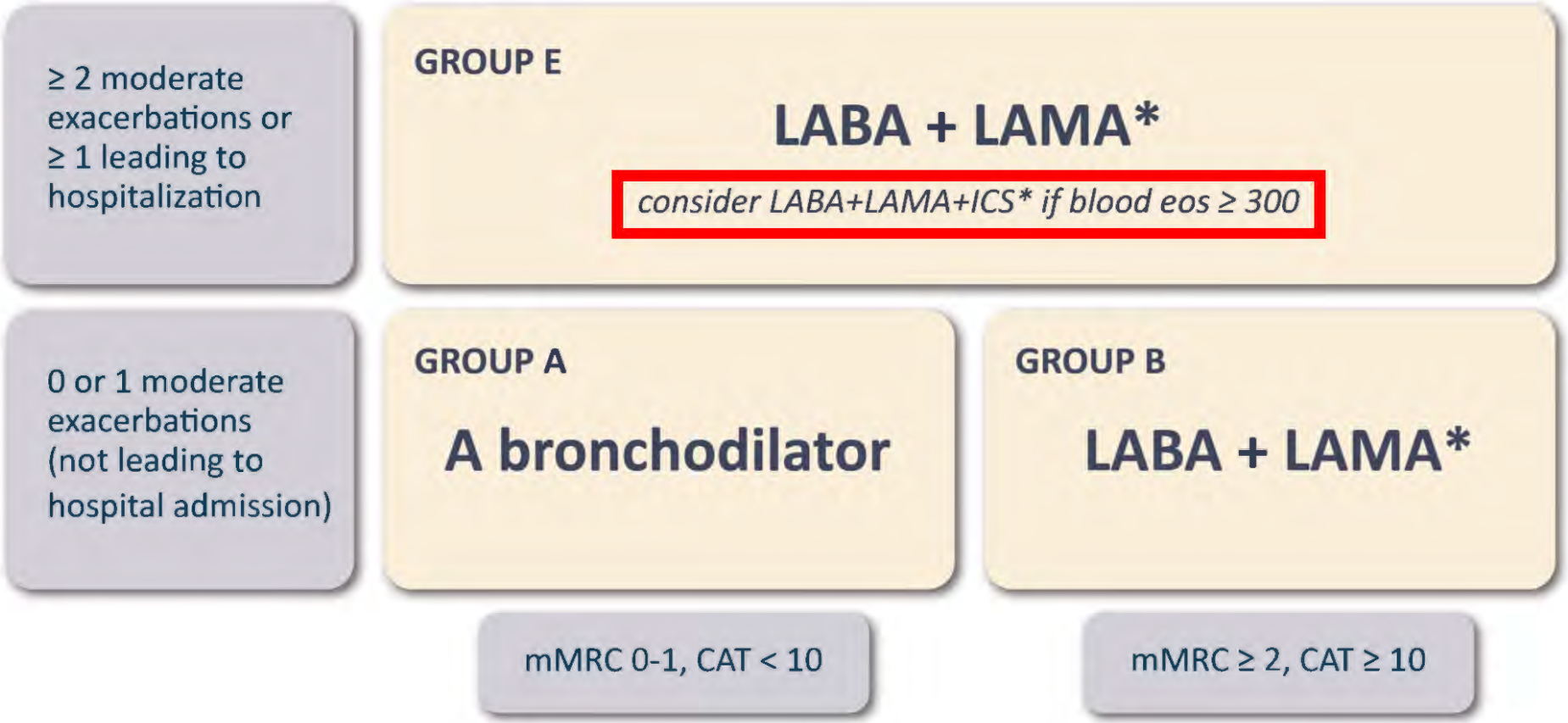


Systemic inflammation further perpetuates localized inflammation, leading to symptoms

FeNO, fractional exhaled nitric oxide

1. Schleimer RP, Berdnikovs S. *J Allergy Clin Immunol*. 2017;139(6):1752-1761. **2.** Gandhi NA et al. *Nat Rev Drug Discov*. 2016;15:35-50. **3.** Higham A et al. *Allergy*. 2021;76(6):1861-1864. **4.** Kume H et al. *Front Pharmacol*. 2019;10:765. **5.** Aghapour M et al. *Am J Respir Cell Mol Biol*. 2018;58(2):157-169.

The GOLD Report



*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
Abbrevs: CAT™, COPD Assessment Test™; EOS, eosinophils; ICS, inhaled corticosteroids; LABA, long-acting beta agonist; LAMA, long-acting muscarinic antagonist; mMRC, modified Medical R

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. https://goldcopd.org/2024-gold-report/. Updated 2024, Accessed April 25, 2024.

Severe COPD and Exacerbations

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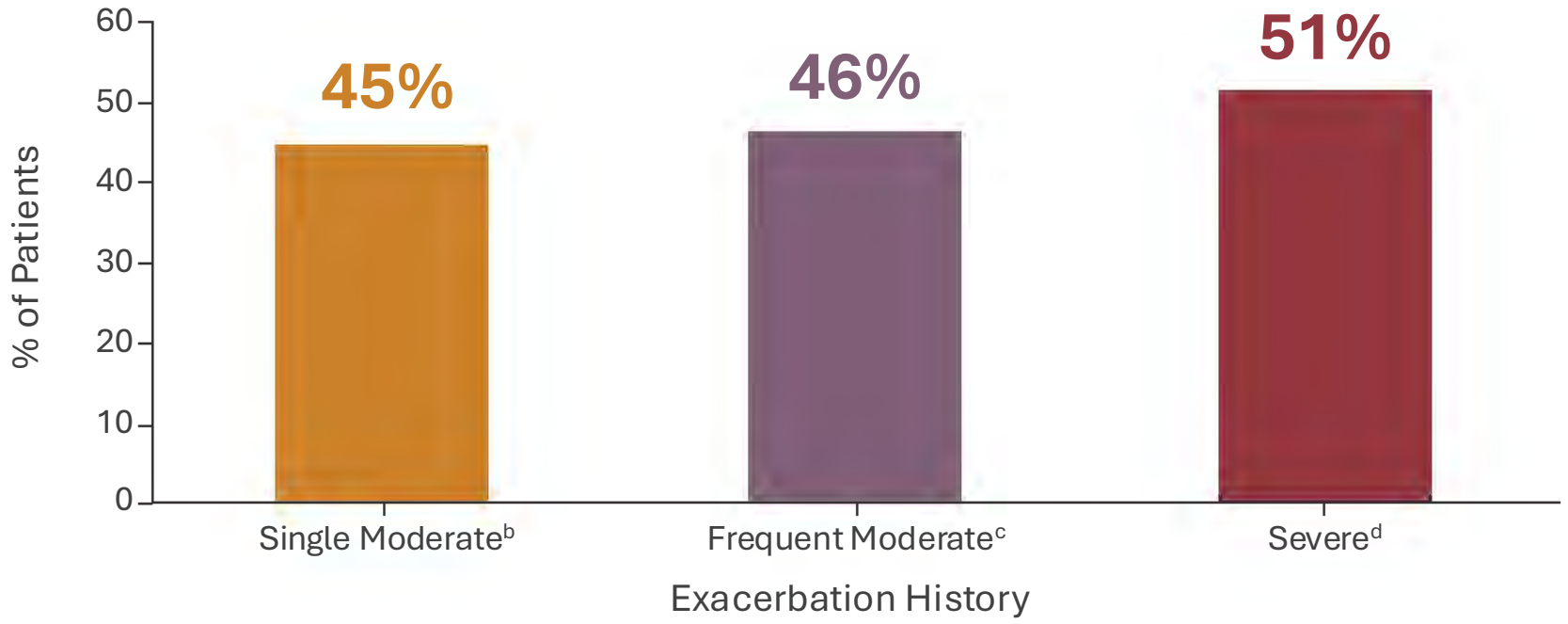
Many patients continue to experience exacerbations despite maximal inhaled therapy[1]

Subgroup Analysis of a Phase 3 Trial[a]



[a]52-week, randomized, double-blind, phase 3 trial that assessed the efficacy and safety of fluticasone furoate/umeclidinium/vilanterol triple therapy versus fluticasone furoate/vilanterol or umecidinium vilenterol in patients aged ≥40 years with symptomatic COPD and a history of exacerbations. [b]Single moderate exacerbation history was defined as 1 moderate/no severe exacerbation in the prior year. [c]Frequent moderate exacerbation history was defined as ≥2 moderate/no severe exacerbations in the prior year. [d]Severe exacerbation history was defined as ≥1 severe/any moderate exacerbation in the prior year.

1. Halpin, David M G et al. "The effect of exacerbation history on outcomes in the IMPACT trial." The European respiratory jo urnal vol. 55,5 1901921. 21 May. 2020, doi:10.1183/13993003.01921-2019

COPD exacerbations have serious implications on patient quality of life [1,2]

1 in 5 patients

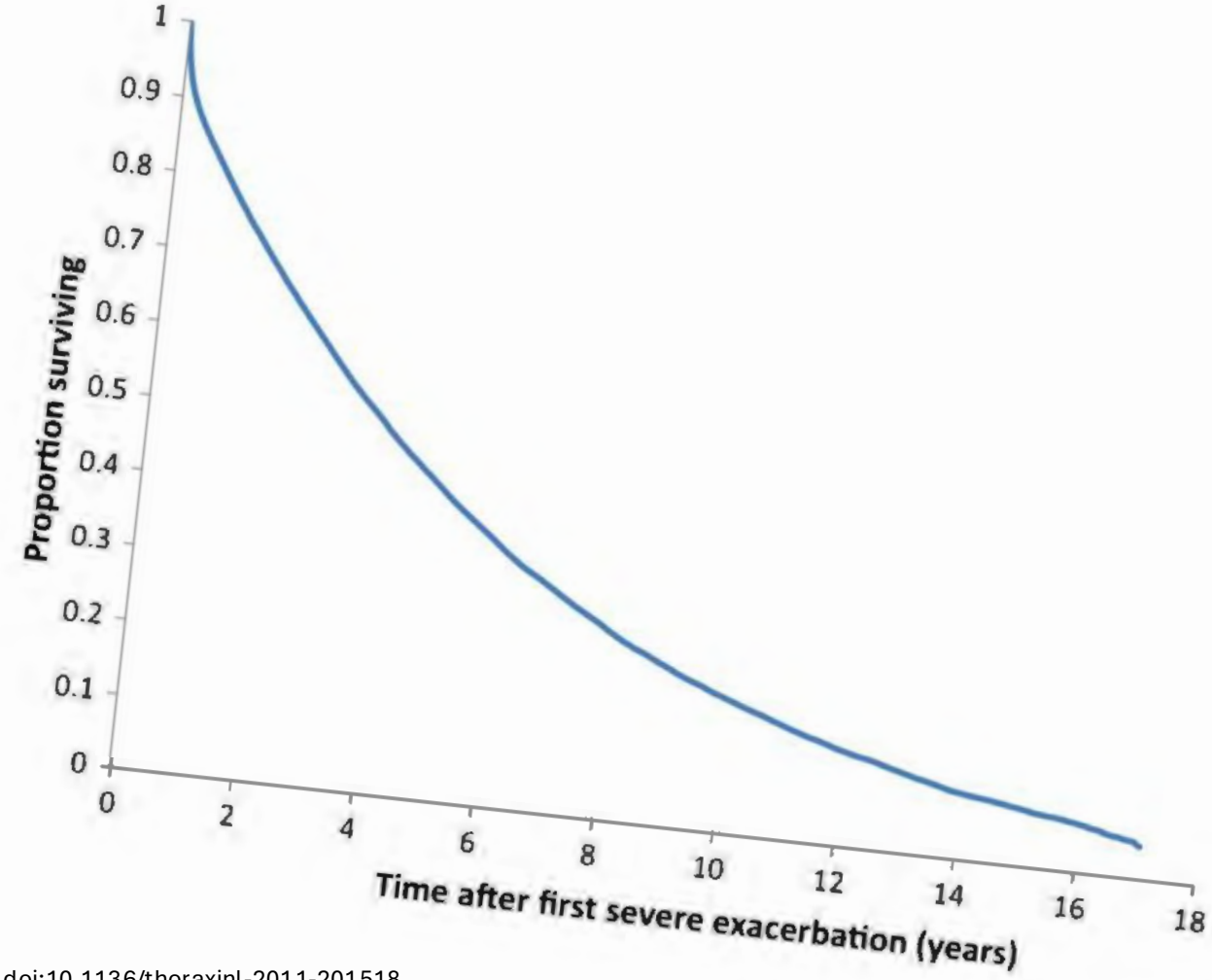
With a severe exacerbation are re-hospitalized within **30 days**[4]

~25% of patients

Fail to restore lung function within **5 weeks** of an exacerbation[3]

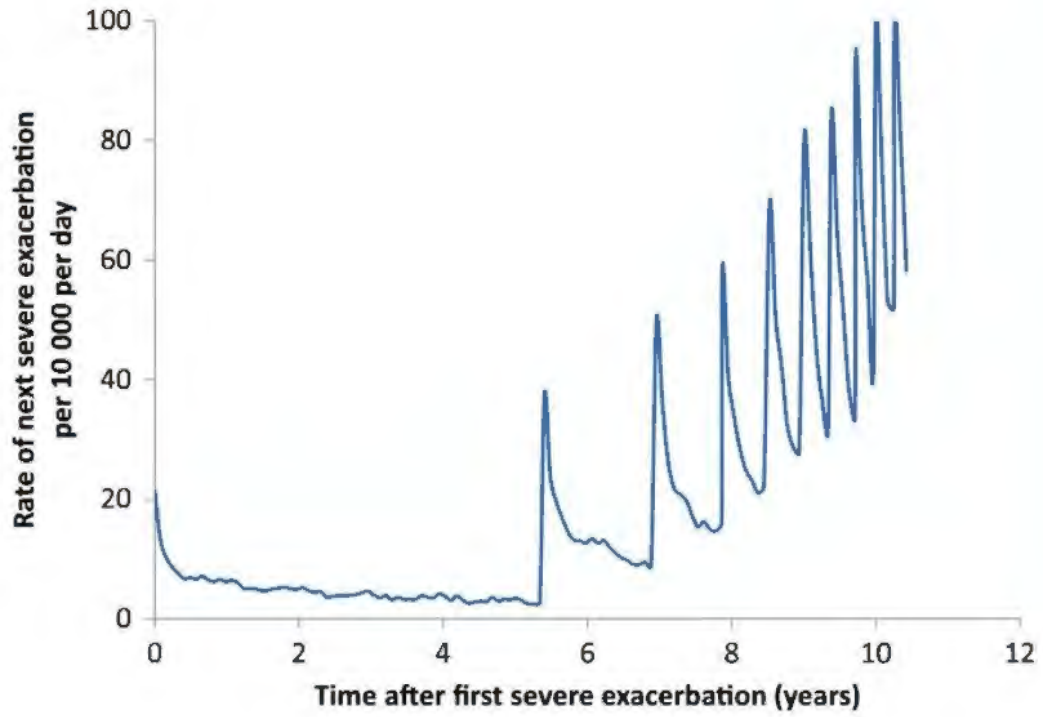
50% of patients died less than 4 years after their first hospitalization for COPD[5,a]

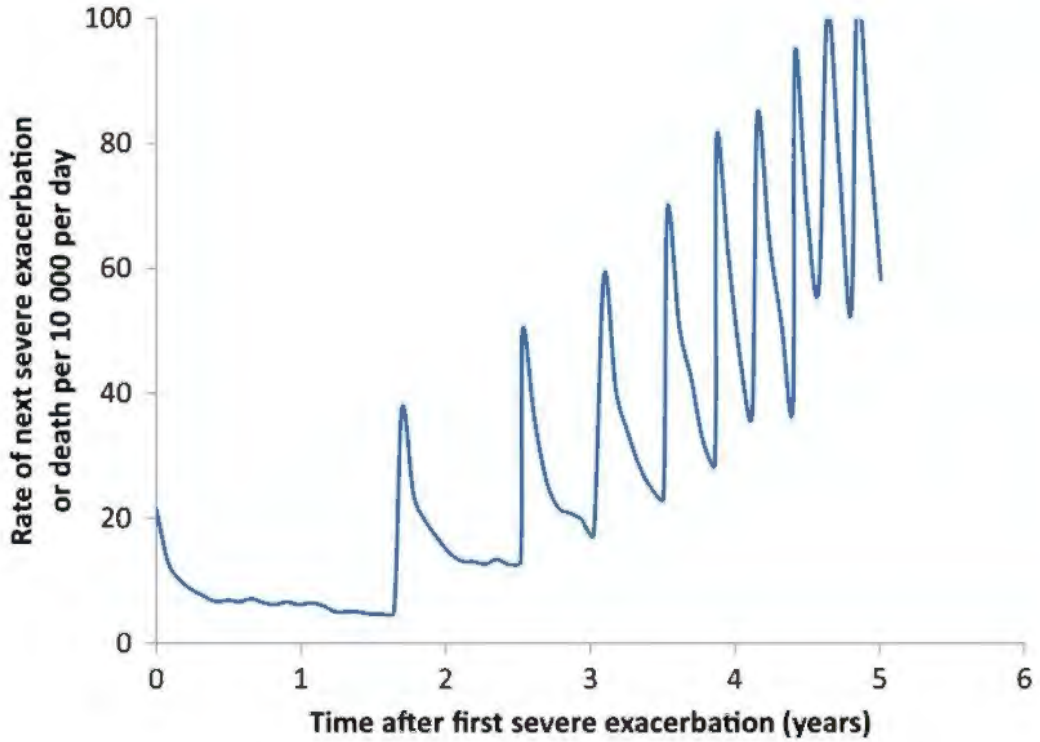
The risk of mortality continuously increases after each exacerbation[1]



1. Suissa, S et al. Thorax 2012;67(11):957-963. doi:10.1136/thoraxjnl-2011-201518

The risk of severe exacerbation increases after each exacerbation[1]





1. Suissa, S et al. *Thorax* 2012;67(11);957-963. doi:10.1136/thoraxjnl-2011-201518

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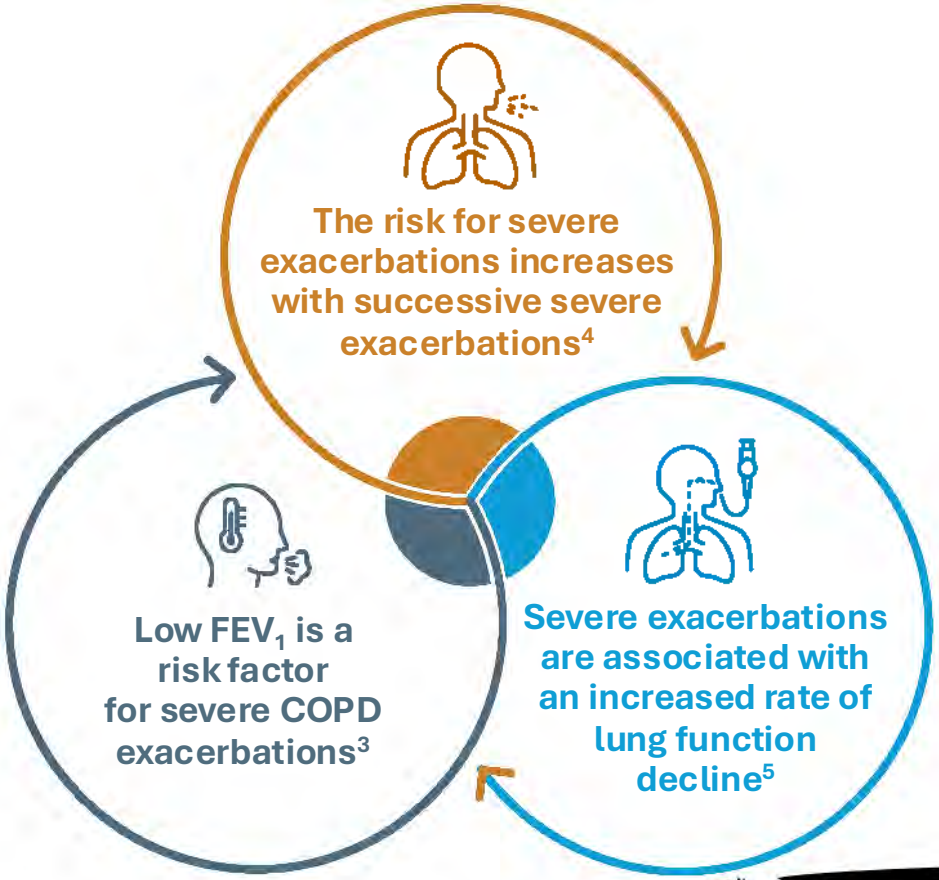
Exacerbations are associated with progressive irreversible lung damage[1,2]

Cycle of Exacerbations and Lung Function Decline

Triggers of acute exacerbations[1,4]

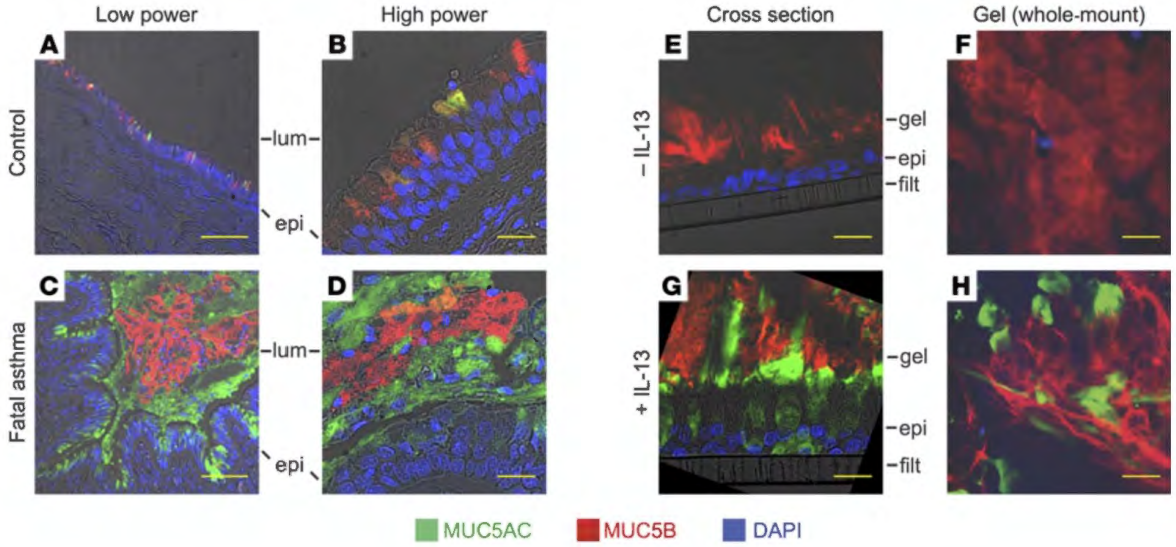
- Respiratory infections
- Pollution (eg, smoke, CO, ozone, PM, SO_2)
- Allergens
- Prior exacerbations



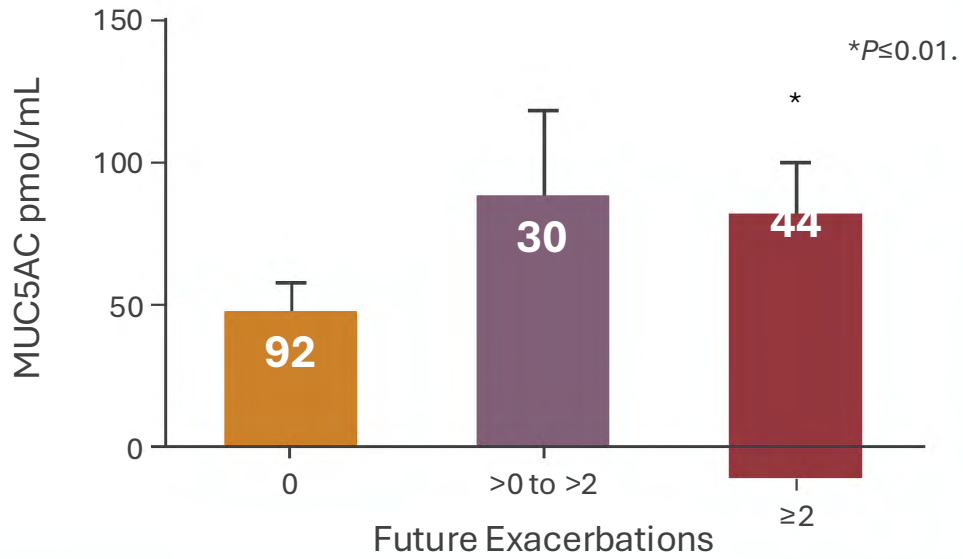
Increased risk of hospitalization and death

MUC5AC has been associated with increased exacerbations[1-3]

Mucin staining in airways[1]



Association between MUC5AC concentration and total future exacerbations[2]



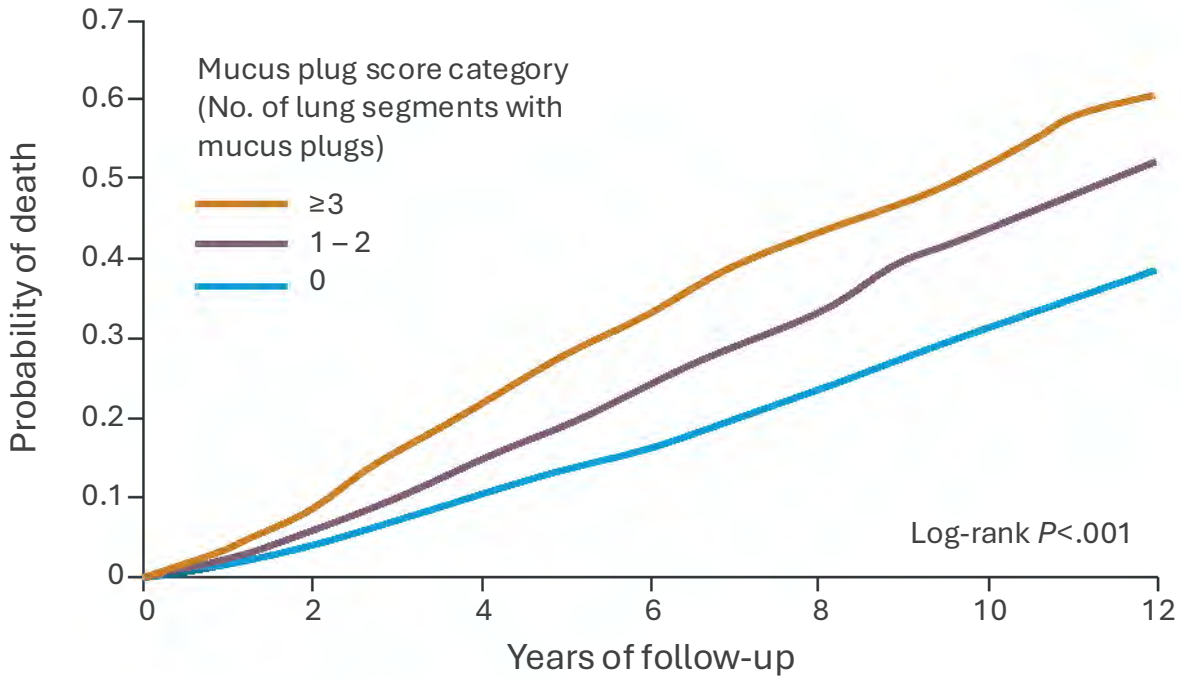
"Sputum **MUC5AC has been associated more specifically with increased exacerbation frequency, increased symptoms, and greater lung function decline.**[3]" - GOLD Report 2024

Abbrev: GOLD, Global Initiative for Chronic Obstructive Lung Disease; IL, interleukin.

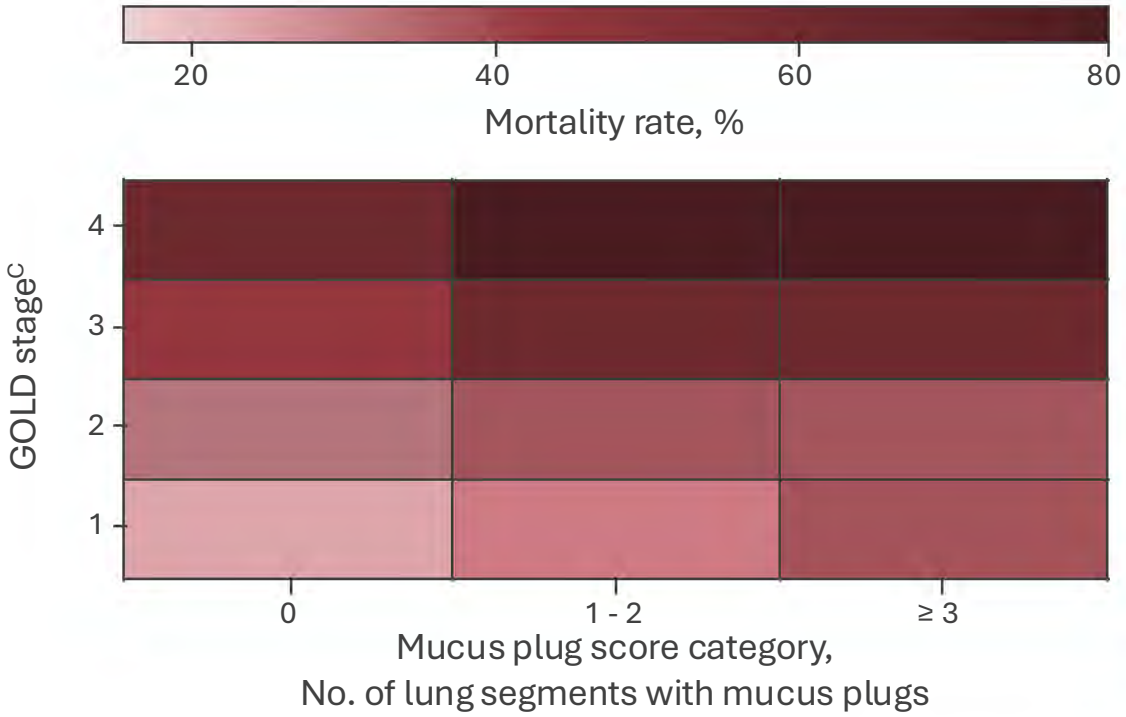
1. Bonser, LR et al. *J Clin Inv*. 2016;126(6):2367-2371. doi:10.1172/JCI84910. 2. Radicioni, G et al. *Lancet*. 2021;9(11)1241-1254 doi:10.1016/S2213-2600(21)00079-5. 3. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. https://goldcopd.org/2024-gold-report/. Updated 2024, Accessed April 25, 2024.

Mucus causing airway obstruction is associated with higher all-cause mortality

Unadjusted probability of death by mucus plug score[a]



All-cause mortality by GOLD stage and mucus plug score[b]



[a]Plot included 4188 participants with COPD, and was adjusted for age, sex, race and ethnicity, body mass index, smoking status, pack-years of smoking, post-BD FEV1, and computed tomography measures of emphysema and airway wall thickness. [b]Mortality rate was calculated as the number of participants who died divided by the number of participants (GOLD and mucus plug score category) x 100.
[C]GOLD stages were defined as 1 (mild, n=78B), FEV, pp 280: 2 (moderate, n=1887), FEV, pp 250 to <80; 3 (severe, n=1127), FEV, pp 230 to <50; and 4 (very severe, n=583), FEV1 pp <30.
Abbrevs: COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

1. Diaz, AA et al. *JAMA*. 2023;329(21):1832-1839. doi:10.1001/jama.2023.2065

Advanced Therapies in Development for Severe COPD

Black People Like Me 2024

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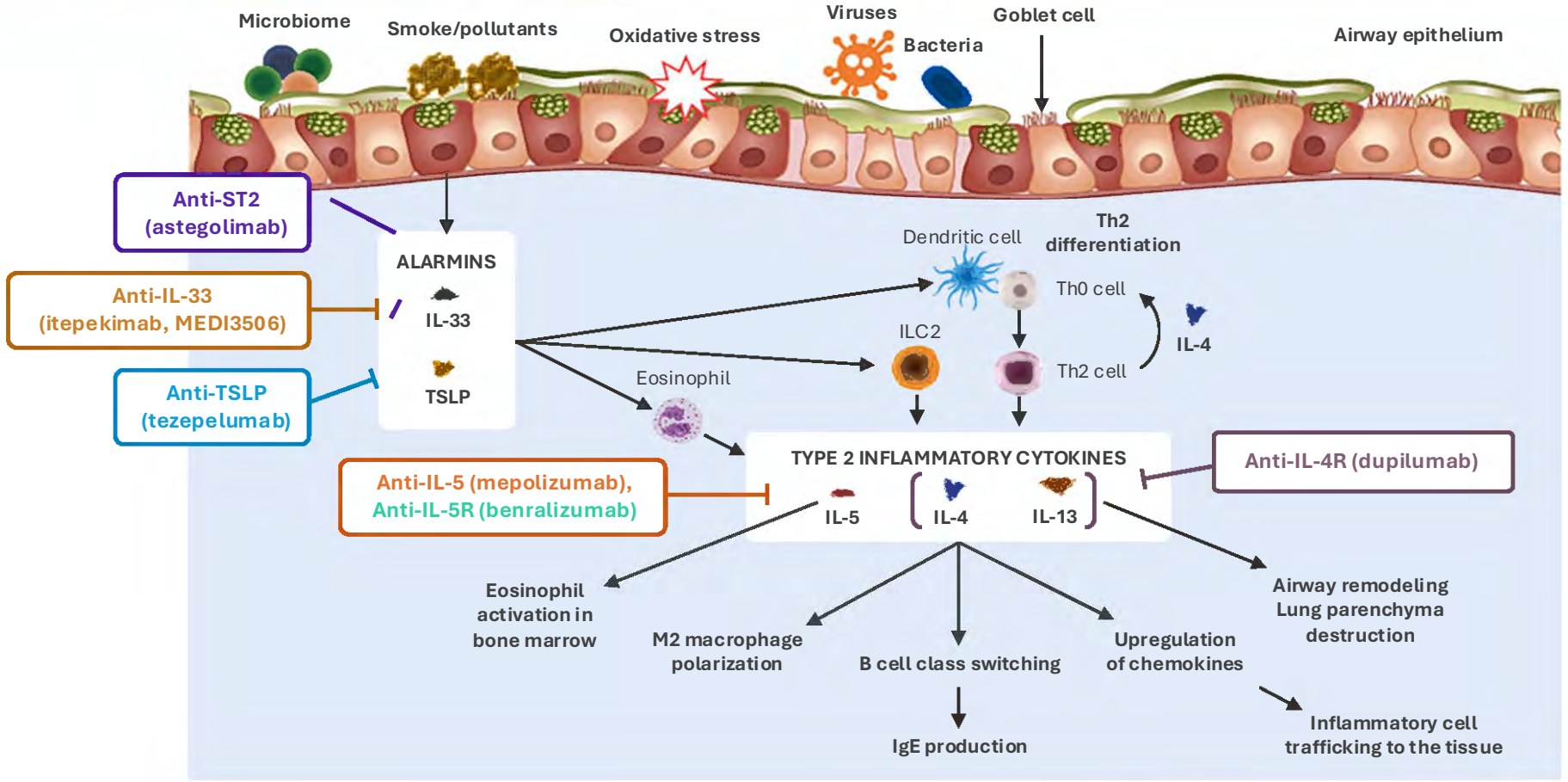
Biologics in development for type 2 inflammation



IL, interleukin; ILC2,type 2 innate lymphoid cell; ST2,suppression of tumorigenicity 2; Th,T-helper cell; TSLP,thymic stromal lymphopoietin

1. Rabe, KF et al. *Am J Resp Crit Care Med*. 2023;208(4):395-405. doi:10.1164/rccm.202303-0455CI

Target	Inhibitor	Study	Asthma Exclusion	Blood EOS	Primary Endpoint/Results
IL-5	Mepolizumab, 100 mg Q4W	Ph3 METREX Completed	Excluded patients with current asthma in current/former smokers and history of asthma in nonsmokers	No cutoff; stratification by blood eosinophil	Aannual rate of moderate or severe exacerbations **Results**: Reduced exacerbations in those with highest baseline blood eosinophils
	Mepolizumab, 100 mg Q4W, 300 mg Q4W	Ph3 METREO Completed	Excluded patients with current asthma in current/former smokers and history of asthma in nonsmokers	≥150 cells/µl at screening or ≥300 cells/µl in past year	Annual rate of moderate or severe exacerbations **Results**: Primary and secondary endpoint results were not significant
	Mepolizumab, 100 mg Q4W	Ph3 MATINEE Estimated primary completion: August 2024	Excluded patients with current diagnosis or history of asthma	≥300 cells/µl at screening and documented historical ≥150/µl within 12 mo to 1 mo before screening or visit 1	Annualized rate of moderate* or severe† exacerbations
IL-5Rα	Benralizumab, 30 mg Q4W/Q8W, 100 mg Q4W/Q8W	Ph3 GALATHEA Completed	Excluded patients with asthma as a primary or main diagnosis according to GINA guidelines or other	Stratification by blood eosinophils; cap for blood eosinophil counts	Annualized COPD exacerbation Rate ratio in patients with baseline blood eosinophil counts >220 cells/µl **Results**: No reduction in annualized exacerbation rate ratios vs. placebo
	Benralizumab, 10 mg Q4W/Q8W, 30 mg Q4W/Q8W, 100 mg Q4W/Q8W	Ph3 TERRANOVA Completed	Excluded patients with asthma as a primary diagnosis according to GINA guidelines or other	Stratification by blood eosinophils; cap for blood eosinophil counts	Annualized COPD exacerbation Rate ratio in patients with baseline blood eosinophil counts >220 cells/µl **Results**: No reduction in annualized exacerbation rate ratios vs. placebo
	Benralizumab, 100 mg Q4W (first three doses) and Q8W	Ph3 RESOLUTE Estimated primary completion: August 2025	Excluded patients with current diagnosis or history of asthma or asthma/COPD overlap, excluding resolved childhood asthma	≥300 cells/µl at screening and documented historical ≥150/µl within 52 wk of enrollment	Annualized rate of moderate* or severe† exacerbations
IL-4Rα	Dupilumab, Q2W	Ph3 BOREAS Completed	Excluded patients with current diagnosis or history of asthma	≥300 cells/µl at visit 1	Annualized rate of moderate* or severe† exacerbations **Results**: Significant 30% reduction in moderate or severe exacerbations vs placebo
	Dupilumab, Q2W	Ph3 NOTUS Completed	Excluded patients with current diagnosis or history of asthma	≥300 cells/µl at visit 1	Annualized rate of moderate* or severe† exacerbations **Results:** Significant reduction in moderate or severe acute exacerbations by 30% compared to placebo

Target	Inhibitor	Study	Asthma Exclusion	Blood EOS	Primary Endpoint/Results
IL-33	Itepekimab, Q2W	Ph2 Completed	Excluded patients with asthma	No cutoff	Annualized rate of moderate to severe acute exacerbations of chronic obstructive pulmonary disease **Results**: **Reduced exacerbations and improved lung function in subgroup of former smokers**
	Itepekimab, Q2W, Q4W in former smokers	Ph3 AERIFY-1 Estimated primary completion: June 2025	Excluded patients with current diagnosis or history of asthma	No cutoff	Annualized rate of acute moderate* or severe† exacerbations
	Itepekimab, Q2W in current and former smokers, Q4W in former smokers	Ph3 AERIFY-2 Estimated primary completion: May 2025	Excluded patients with current diagnosis or history of asthma	No cutoff	Annualized rate of acute moderate* or severe† exacerbations in former smokers
	Tozarakimab, NR	Ph2 FRONTIER-4 Estimated primary completion: Study results delayed	Excluded patients with asthma	No cutoff	Change from baseline to Week 12 in prebronchodilator FEV1
ST-2 (IL-33R)	Astegolimab, 490 mg Q4W	Ph2a COPD-ST2OP Completed	Excluded patients with known respiratory disorders other than COPD	No cutoff	Frequency of moderate to severe exacerbations **Results: No reduction in exacerbation rates in the ITT population**
	Astegolimab, Q2W or Q4W, dose NR	Ph2b Estimated primary completion: February 2025	Excluded patients with asthma	No cutoff	Annualized rate of moderate and severe COPD exacerbations
TSLP	Tezepelumab, Q4W, dose NR	Ph2 COURSE Completed	Excluded patients with asthma	No cutoff	Moderate or severe COPD exacerbation rate ratio (tezepelumab vs. placebo) Results: **Nonsignificant 17% reduction in annualized rate of moderate or severe exacerbations**

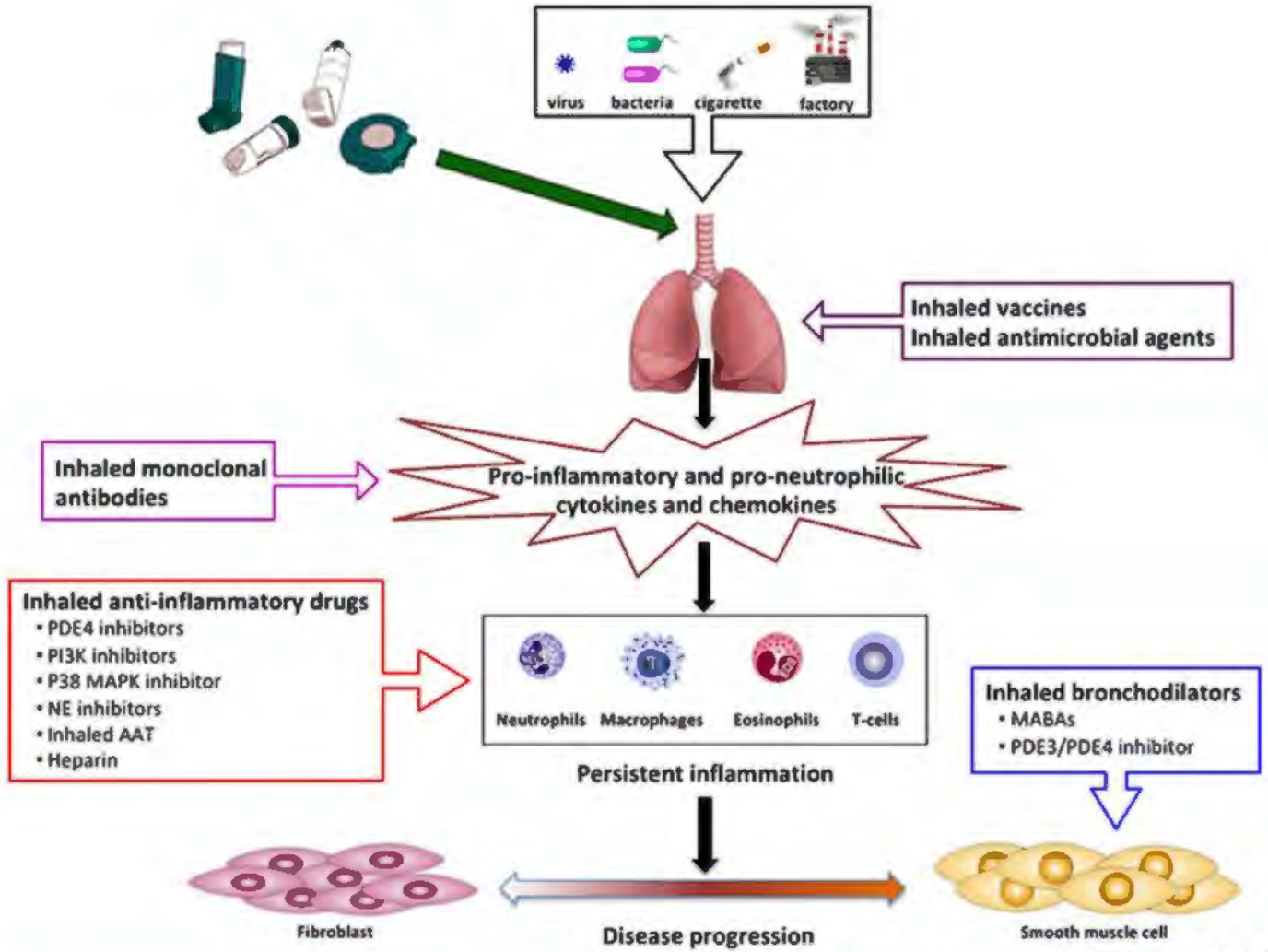
Definition of abbreviations: AERIFY-1 = Study to Assess the Efficacy, Safety, and Tolerability of SAR440340/REGN3500/Itepekimab in Chronic Obstructive Pulmonary Disease; AERIFY-2 = Study to Assess the Efficacy, Safety, and Tolerability of SAR440340/REGN3500/Itepekimab in Chronic Obstructive Pulmonary Disease; BOREAS = Pivotal Study to Assess the Efficacy, Safety and Tolerability of Dupilumab in Patients With Moderate-to-Severe COPD with Type 2 Inflammation; COPD = chronic obstructive pulmonary disease; COPD-ST2OP = Anti-ST2 (MSTT1041A) in COPD; COURSE = Tezepelumab COPD Exacerbation Study; FRONTIER-4 = A Phase II, Randomized, Double-Blind, Placebo-controlled Study to Assess MEDI3506 in Participants with COPD and Chronic Bronchitis; GALATHEA = Benralizumab Efficacy in Moderate to Very Severe Chronic Obstructive Pulmonary Disease with Exacerbation History; GINA = Global Initiative for Asthma; ITT = intention-to-treat; MATINEE = Mepolizumab as Add-On Treatment in Participants with COPD Characterized by Frequent Exacerbations and Eosinophil Level; METREO = Efficacy and Safety of Mepolizumab as an Add-On Treatment in Chronic Obstructive Pulmonary Disease; METREX = Study to Evaluate Efficacy and Safety of Mepolizumab for Frequently Exacerbating Chronic Obstructive Pulmonary Disease Patients; NOTUS = Pivotal Study to Assess the Efficacy, Safety and Tolerability of Dupilumab in Patients with Moderate to Severe COPD with Type 2 Inflammation; NR = not reported; Ph = phase; Q2W = every 2 weeks; Q4W = every 4 weeks; Q8W = every 8 weeks; RESOLUTE = Efficacy and Safety of Benralizumab in Moderate to Very Severe Chronic Obstructive Pulmonary Disease With a History of Frequent Exacerbations; TERRANOVA = Efficacy and Safety of Benralizumab in Moderate to Very Severe Chronic Obstructive Pulmonary Disease with Exacerbation History; TSLP = thymic stromal lymphopoietin.

*Acute worsening of respiratory symptoms that requires systemic corticosteroids and/or antibiotics.

†Acute exacerbations of COPD that require hospitalization

...202303-0455CI, 2. Bhatt, Surya P et al. "Dupilumab for COPD with Type 2 Inflammation Indicated ... of medicine vol. 389,3 (2023): 205-214. doi:10.1056/NEJMoa2303951

Inhaled therapies in development for COPD



Abbreviations: AAT, COPD, chronic obstructive pulmonary disease; MABA MAPK NE

1. Cazzola, M. 2024 *Curr Res Pharm Drug Disc* 2022;3:100092. doi:10.

How would you treat Jane?

Jane

Interactive Patient Case Study

Case Details

68 y/o female seen for evaluation of COPD. No asthma as a child, no history of allergies. Smoke 1 PPD of cigarettes from age 25-60. Quit 8 years ago. Developed respiratory symptoms in her 50s was told she had COPD

Current Treatment Details

- Has flares frequently that require bursts of prednisone 3-4 times a year and antibiotics (usually azithromycin); she feels prednisone is her lifeline and takes 10-30 mg 1-2 times a week depending on how she feels
- She reports needing albuterol nebulizer a few times a week. For inhalers she is only using Albuterol. **She is on triple therapy but still suffering**

Lab/Test Results

PE: Good air entry; Scattered wheezing

Bloodwork: EOS 300 cells/ul | Radiology: PA/Lat CXR and unremarkable

	FVC %	FEV1 %	FEV1/FVC	FeNO (ppb)	TLC %	RV %	DLCO %
09/4/2013	41	71(%)	0.58				
4/4/2023	98	60	0.50	70	92	100	70

ACT, asthma control test; ANCA, Antineutrophil Cytoplasmic Antibodies; COPD, chronic obstructive pulmonary disease; CXR, chest xray; DLCO, diffusing lung capacity for carbon monoxide; EOS, eosinophil; FeNO, fractional exhaled nitric oxide; FEV1 (subscript 1), forced expiratory volume in 1 second; FVC, forced vital capacity; IgE, immunoglobulin E; ppb, parts per billion; PPD, packs per day; PA LAT, posterior anterior lateral; RV, residual volume; TLC, total lung capacity; y/o , year old

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Jane’s response to dupilumab

Jane

Interactive Patient Case Study

Case Details

68 y/o female seen for evaluation of COPD. No asthma as a child, no history of allergies. Smoke 1 PPD of cigarettes from age 25-60. Quit 8 years ago. Developed respiratory symptoms in her 50s was told she had COPD

Updated Treatment

- Patient started dupilumab 300 mg q2w. No problem with injections
- Exercise tolerance improved. Patient able to stop prednisone completely. No flares in 12 months
- Stopped using controller medication-- uses only albuterol PRN

Updated Lab/Test Results

	FVC %	FEV1 %	FEV1/FVC	FeNO (ppb)	TLC %	RV %	DLCO %
09/4/2013	41	71(%)	0.58				
4/4/2023	98	60	0.50	70	92	100	70
4/2/2024 post-dupilumab	**93**	**77**	**0.65**	**30**			

COPD, chronic obstructive pulmonary disease; DLCO, diffusing lung capacity for carbon monoxide; FeNO, fractional exhaled nitric oxide; FEV1 (subscript 1), forced expiratory volume in 1 second; FVC, forced vital capacity; ppb, parts per billion; PPD, packs per day; PRN, as needed; q2w, every 2 weeks; RV, residual volume; TLC, total lung capacity; y/o, year old.

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Dupilumab may be the first biologic approved for use in uncontrolled COPD patients

Dupilumab displayed positive results in uncontrolled patients from the BOREAS trial

Study Design

Assess safety and efficacy in

939 patients

aged 40-80

with **moderate to severe COPD** and evidence of **type 2 inflammation**;

current and former smoker, uncontrolled disease with maximal standard of care inhaled therapies

Primary Endpoint Results

30% reduction in moderate or severe exacerbations

compared with placebo (rate ratio, 0.70; 95% CI, 0.58 to 0.86; P<0.001)

Annualized rate of moderate or severe exacerbations of COPD was

0.78
(95% CI, 0.64 - 0.93)
in the dupilumab group

and

1.10
(95% CI, 0.93 - 1. 30)
in the placebo group

Safety findings were consistent with known safety profile

Bhatt, Surya P et al. "Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts." The New England journal of medicine vol. 389,3 (2023): 205-214. doi:10.1056/NEJMoa2303951

Dupilumab may be the first biologic approved for use in uncontrolled COPD patients

Dupilumab displayed positive results in uncontrolled patients from the NOTUS trial

Study Design

Assess safety and efficacy in

935 patients

aged 40-85

with **moderate to severe COPD** and evidence of **type 2 inflammation**;

current and former smoker, uncontrolled disease with maximal standard of care inhaled therapies

Primary Endpoint Results

34% reduction in moderate or severe exacerbations

compared with placebo (rate ratio, 0.66; 95% CI, 0.54 to 0.82; P<0.001)

Annualized rate of moderate or severe exacerbations of COPD was

0.86
(95% CI, 0.70 - 1.06)
in the dupilumab group

and

1.30
(95% CI, 1.05 - 1.60)
in the placebo group

Safety findings were consistent with known safety profile

Bhatt, Surya P et al. “Dupilumab for COPD with Type 2 Inflammation.” The New England journal of medicine vol. 390,24 (2024): 2274-2283. doi:10.1056/NEJMoa2401304

Ensifentrine is the first inhaled product with a novel mechanism for maintenance treatment for COPD

Ensifentrine displayed positive results in patients from the ENHANCE-1 trial

Study Design

Assess safety and efficacy in

763 patients
aged 40-80
With **COPD**

current and former smoker,
either on no maintenance therapy or on stable LAMA or LABA therapy

Rates of adverse events were similar between the two groups

Primary Endpoint Results

Ensifentrine treatment resulted in **significant improvement** from baseline in Week 12 average FEV_1 $AUC_{0\text{-}12\,h}$ vs. placebo (87 mL; 95% CI, 55 to 119; P<0.001)

LS mean change from baseline

61 ml
(95% CI, 25 to 97)
in the ensifentrine group

and

-26 ml
(95% CI, -64 to 13)
in the placebo group

Secondary Endpoint Results

36% reduction in moderate or severe exacerbations over 24 weeks compared with placebo (rate ratio, 0.64; 95% CI, 0.40 to 1.00; P=0.05)

Anzueto, Antonio et al. "Ensifentrine, a Novel Phosphodiesterase 3 and 4 Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease: Randomized, Double-Blind, Placebo-controlled, Multicenter Phase III Trials (the ENHANCE Trials)." The American Journal of Respiratory and Critical Care Medicine vol. 208,4 (2023), doi:10.1164/rccm.202306-0944OC

Ensifentrine is the first inhaled product with a novel mechanism for maintenance treatment for COPD

Ensifentrine displayed positive results in patients from the ENHANCE-2 trial

Study Design

Assess safety and efficacy in

790 patients aged 40-80

With **COPD**

current and former smoker, either on no maintenance therapy or on stable LAMA or LABA therapy

Primary Endpoint Results

Ensifentrine treatment resulted in **significant improvement** from baseline in Week 12 average FEV_1 $AUC_{0\text{-}12\,h}$ vs. placebo (94 mL; 95% CI, 65 to 124; P<0.001)

LS mean change from baseline

48 ml (95% CI, 30 to 66) in the ensifentrine group

and

-46 ml (95% CI, -70 to -13) in the placebo group

Rates of adverse events were similar between the two groups

Secondary Endpoint Results

43% reduction in moderate or severe exacerbations compared to placebo (rate ratio, 0.57; 95% CI, 0.38 to 0.87; P=0.009)

Anzueto, Antonio et al. "Ensifentrine, a Novel Phosphodiesterase 3 and 4 Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease: Randomized, Double-Blind, Placebo-controlled, Multicenter Phase III Trials (the ENHANCE Trials)." The American Journal of Respiratory and Critical Care Medicine vol. 208,4 (2023), doi:10.1164/rccm.202306-0944OC

Patient Story

Presented by:
Misako Bonner

Black People Like Me 2024

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Questions & Answers Session

Black People Like Me 2024

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Closing Remarks & Thank You!