

# Advances In Asthma and COPD

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# Type 2 and Non Type 2 (Type 2 low) Asthma

## Type 2 Asthma

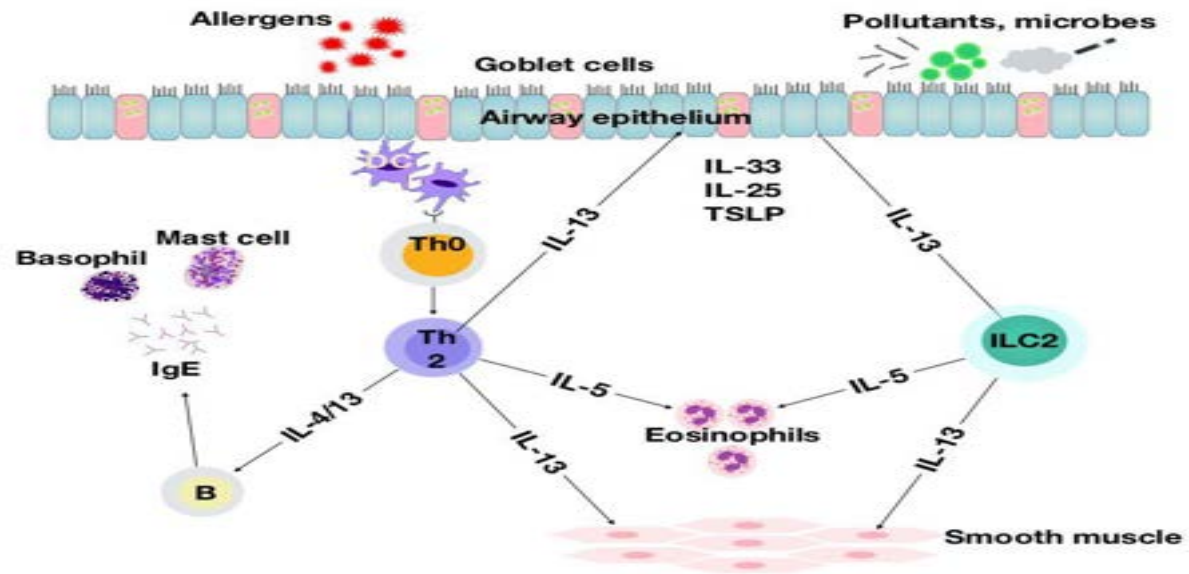
- Type 2 inflammation
- High eosinophil count
- Responsive to Inhaled corticosteroids
- Seasonal allergies

## Non Type 2 Asthma

- Non Type 2 inflammation
- High Neutrophil count
- Not responsive to inhaled corticosteroids

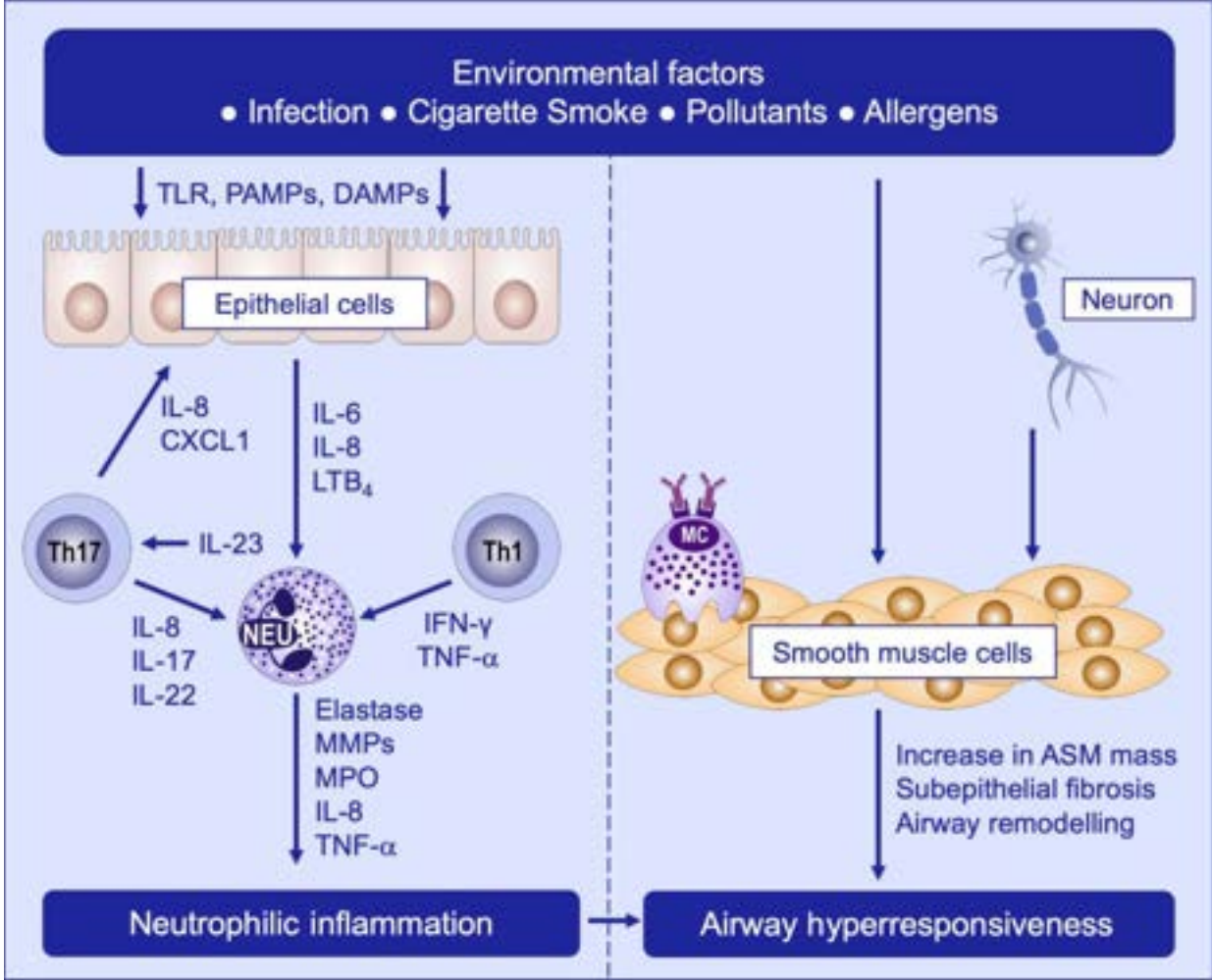
W Busse. European Respiratory Review 2022

# Type 2 Asthma Pathophysiology



Khurana S et al. Breathe June 2020

# Non Type 2 Pathophysiology



Sze & Nair. Allergy 2019

## Fractional Exhaled Nitric Oxide ( FeNO)

- NO- Regulates vascular and bronchial tone ( promotes dilation)
- Majority of NO in gas – derived from lower airways
- Clinical Use:
  - characterization: Type 2 or Non Type 2
  - selection and adjustment of therapy
- Fe NO > 50 ppb in adults, >35 ppb : eosinophilic inflammation

## Adults & adolescents 12+ years

### Personalized asthma management:

Assess, Adjust, Review response

Symptoms  
Exacerbations  
Side-effects  
Lung function  
Patient satisfaction



Confirmation of diagnosis if necessary  
Symptom control & modifiable risk factors (including lung function)  
Comorbidities  
Inhaler technique & adherence  
Patient preferences and goals

Treatment of modifiable risk factors and comorbidities  
Non-pharmacological strategies  
Asthma medications (adjust down or up)  
Education & skills training

### Asthma medication options:

Adjust treatment up and down for individual patient needs

#### PREFERRED CONTROLLER

to prevent exacerbations and control symptoms

Other controller options

#### PREFERRED RELIEVER

Other reliever option

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
<b>PREFERRED CONTROLLER</b>	As-needed low dose ICS-formoterol *	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA Refer for phenotypic assessment ± add-on therapy, e.g. tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options	Low dose ICS taken whenever SABA is taken †	Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA is taken †	Medium dose ICS, or low dose ICS+LTRA ‡	High dose ICS, add-on tiotropium, or add-on LTRA ‡	Add low dose ICS, but consider side-effects
<b>PREFERRED RELIEVER</b>	As-needed low dose ICS-formoterol *		As-needed low dose ICS-formoterol for patients prescribed maintenance and reliever therapy ‡		
Other reliever option	As-needed short-acting β <sub>2</sub> -agonist (SABA)				

\* Data only with budesonide-formoterol (bud-form)

† Separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever only for patients prescribed bud-form or BDP-form maintenance and reliever therapy

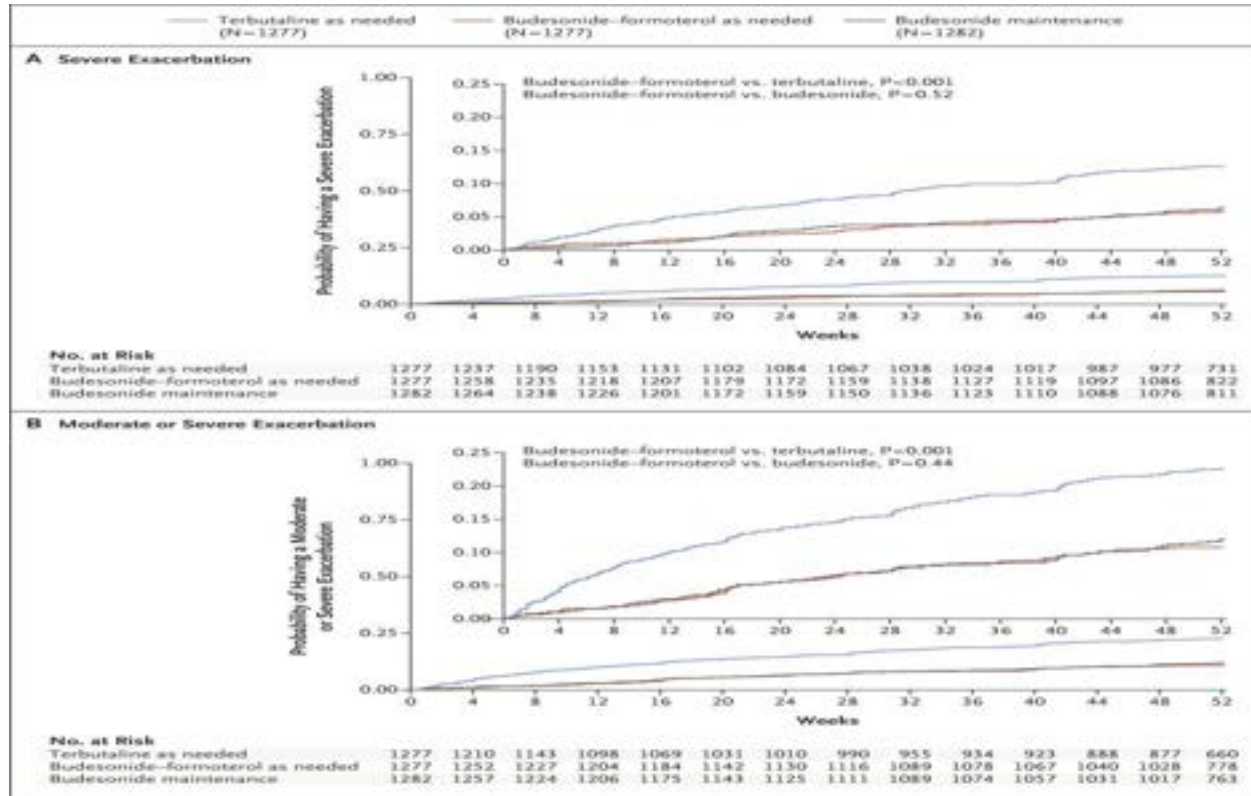
§ Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV<sub>1</sub> >70% predicted

2019 GINA report, global strategy for asthma management and prevention



## Formoterol/Budesonide vs SABA

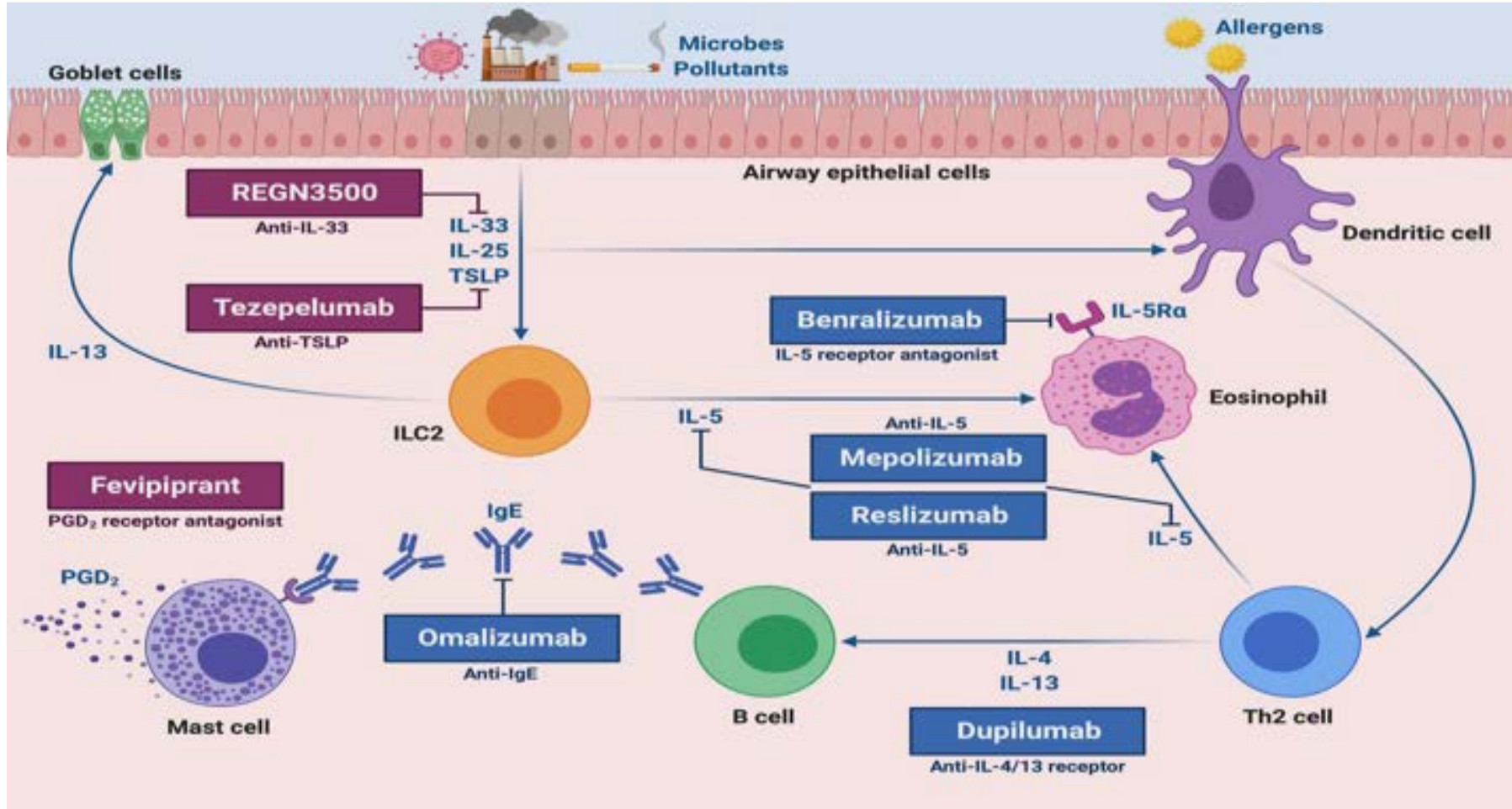
- As compared to SABA, severe exacerbation decreased by 60%
- Low steroid use.
- 4 studies- SYGMA 1 and 2, Novel START and PRACTICAL



Paul O'Byrne et al. NEJM 2018  
 Richard Beasley et al. NEJM 2019  
 Jo Hardy et al. Lancet 2019  
 Eric Bateman et al. NEJM 2018

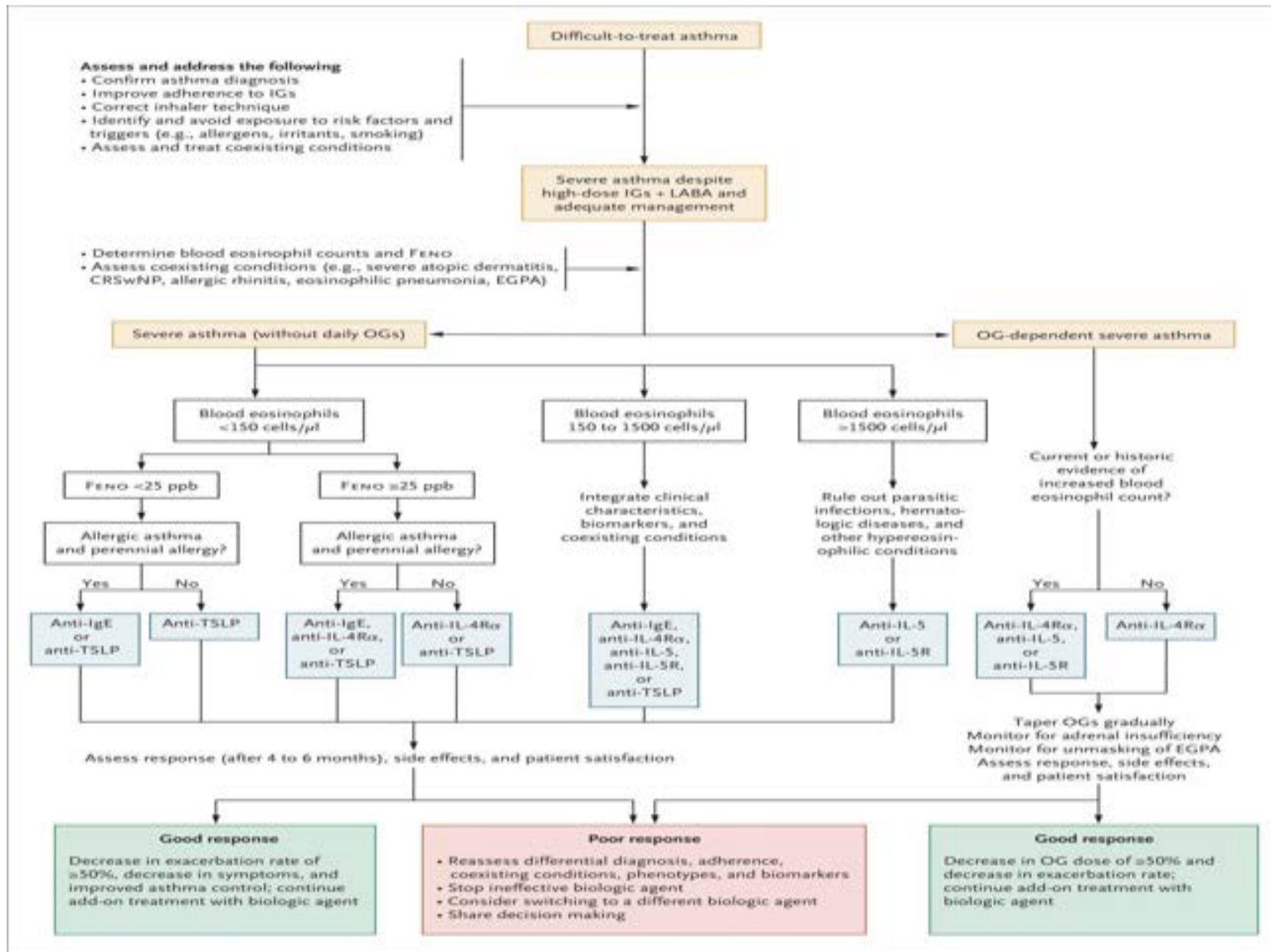


# Biologics for Severe asthma



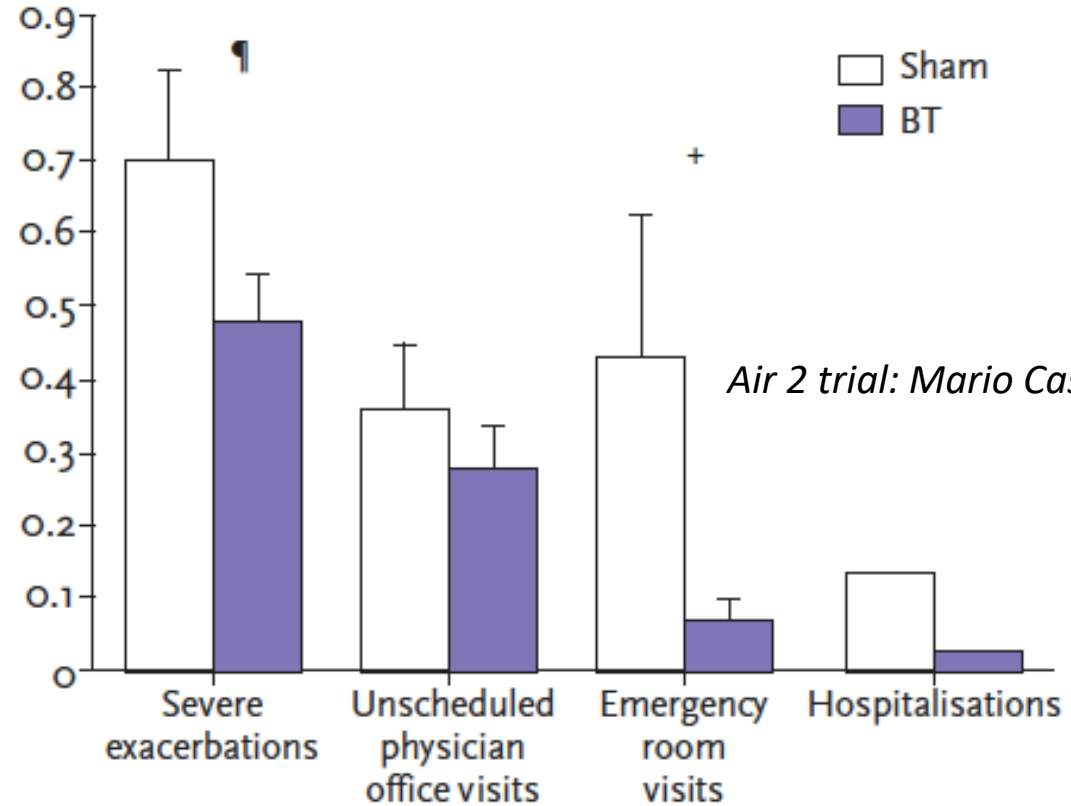
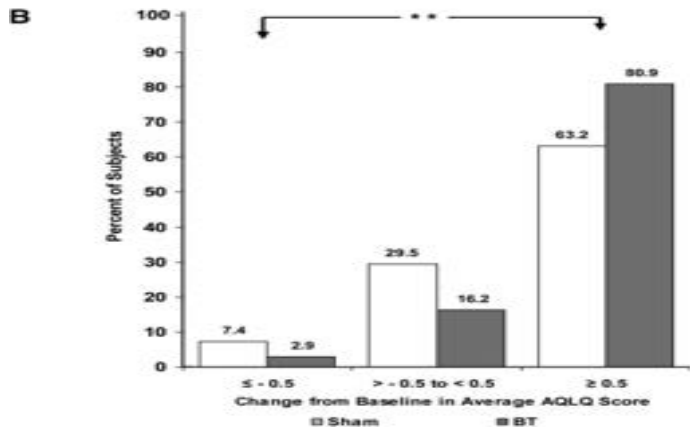
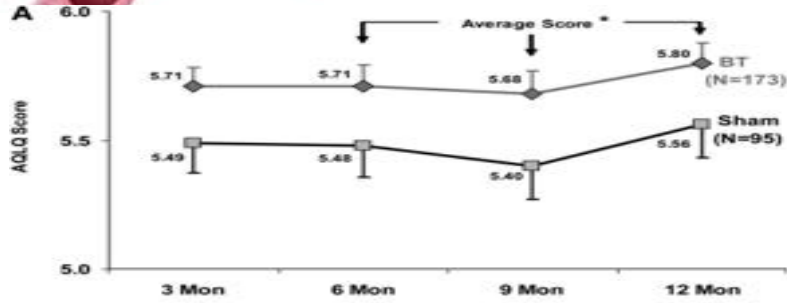
Nature Review Drug discovery

Drug	Mechanism	Route Setting
Omalizumab	Anti-IgE	Subcutaneous
Mepolizumab	Anti-IL5	Subcutaneous
Reslizumab	Anti-IL5	Intravenous
Benralizumab	Anti-IL5Ra	Subcutaneous
Dupilumab	Anti-IL4Ra	Subcutaneous
Tezepelumab	Anti-TSLP	Subcutaneous



Guy Brusselle MD and Gerald Koppelman MD NEJM 2022

# Bronchial Thermoplasty



10 yr BT data: Similar reduction for exacerbation at 10 yr as compared to 1 year.  
13% have developed bronchiectasis

*Rekha Chaudhuri MD et al. Lancet 2021*

# Advances In COPD

**Table 1. GOLD Staging**

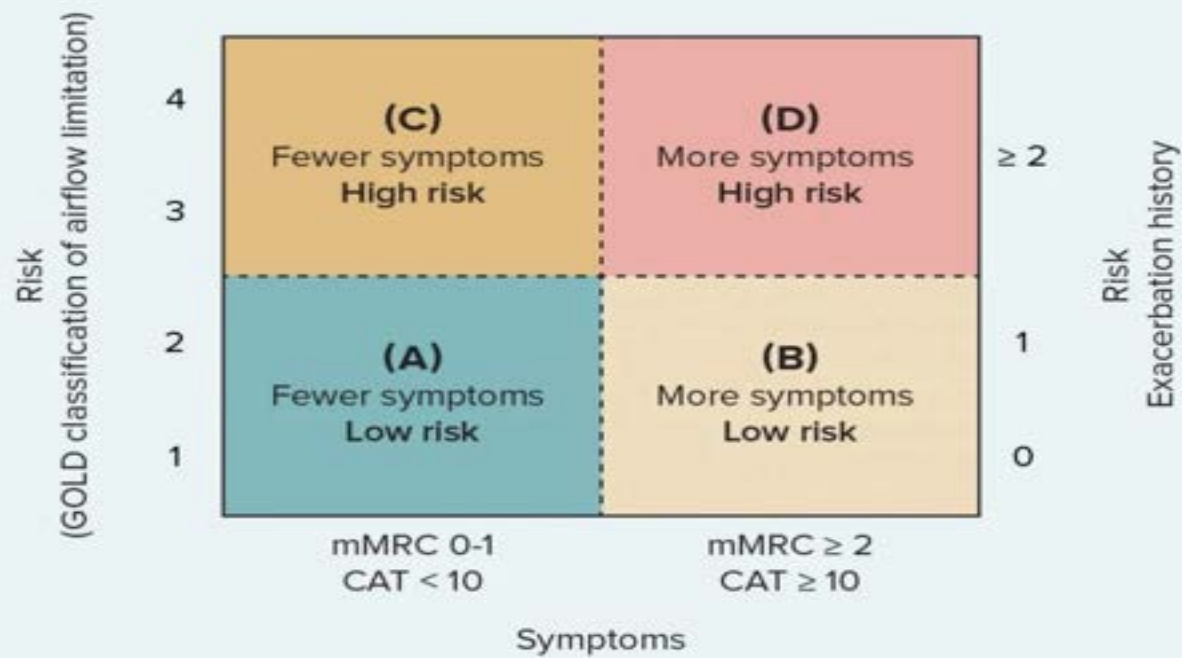
<b>GOLD Stage</b>	<b>COPD Severity</b>	<b>FEV<sub>1</sub>/FVC Ratio</b>	<b>FEV<sub>1</sub> Range<sup>a</sup></b>
I	Mild	<0.70	≥80% of normal
II	Moderate	<0.70	50%–79% of normal
III	Severe	<0.70	30%–49% of normal
IV	Very severe	<0.70	<30% of normal or <50% of normal with chronic respiratory failure present

COPD=chronic obstructive pulmonary disease; FEV<sub>1</sub>=forced expiratory volume in 1 s; FVC=forced vital capacity; GOLD=Global initiative for chronic Obstructive Lung Disease

<sup>a</sup>As recorded in electronic health records, which did not specify pre- or post-bronchodilator.

2022 Global Initiative for Chronic Obstructive Lung Disease

## GOLD criteria for severity of AIRFLOW OBSTRUCTION IN COPD



healthline

2022 Global Initiative for Chronic Obstructive Lung Disease



## MODIFIED MRC DYSPNEA SCALE<sup>a</sup>

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

mMRC Grade 0.	I only get breathless with strenuous exercise.	<input type="checkbox"/>
mMRC Grade 1.	I get short of breath when hurrying on the level or walking up a slight hill.	<input type="checkbox"/>
mMRC Grade 2.	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.	<input type="checkbox"/>
mMRC Grade 3.	I stop for breath after walking about 100 meters or after a few minutes on the level.	<input type="checkbox"/>
mMRC Grade 4.	I am too breathless to leave the house or I am breathless when dressing or undressing.	<input type="checkbox"/>

<sup>a</sup> Fletcher CM. BMJ 1960; 2: 1662.

## CAT™ ASSESSMENT

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.

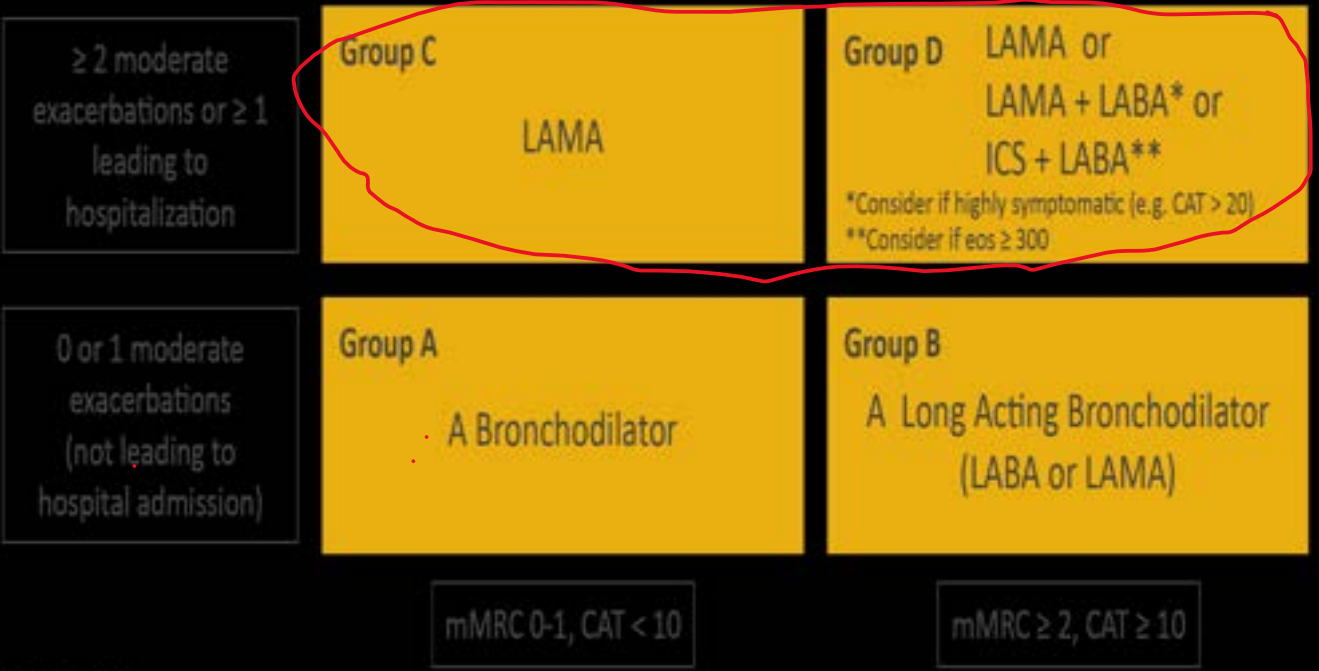
EXAMPLE: I am very happy	0	1	2	3	4	5	I am very sad	SCORE
	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>		
I never cough	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>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

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

TOTAL SCORE:



# INITIAL PHARMACOLOGICAL TREATMENT



2022 Global Initiative for Chronic Obstructive Lung Disease

FIGURE 4.2



# MANAGEMENT CYCLE

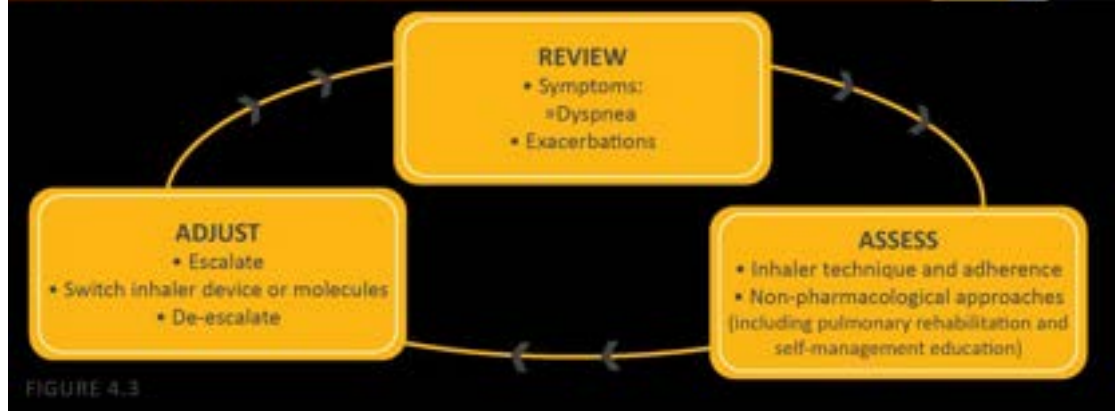


FIGURE 4.3

# Treatment of COPD

Long acting Beta agents(LABA) and Long acting muscaranic agents( LAMA)

Both agents – improve quality of life, exacerbations and pulmonary functions

Combination therapy> monotherapy: Lung function, exacerbation and quality of life.

# Factors to consider adding Inhaled Corticosteroids

## Strong Support

- History of hospitalization for COPD Exacerbation
- $\geq 2$  COPD exacerbations/year
- Concomitant asthma
- Eosinophil count  $>300/\mu\text{L}$

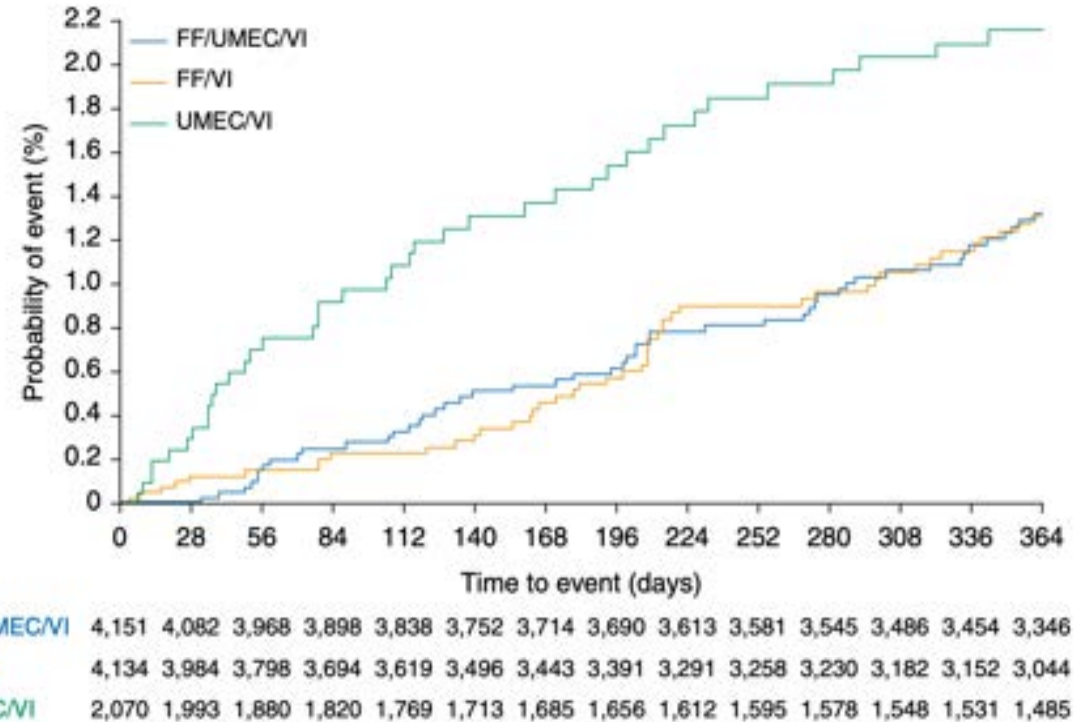
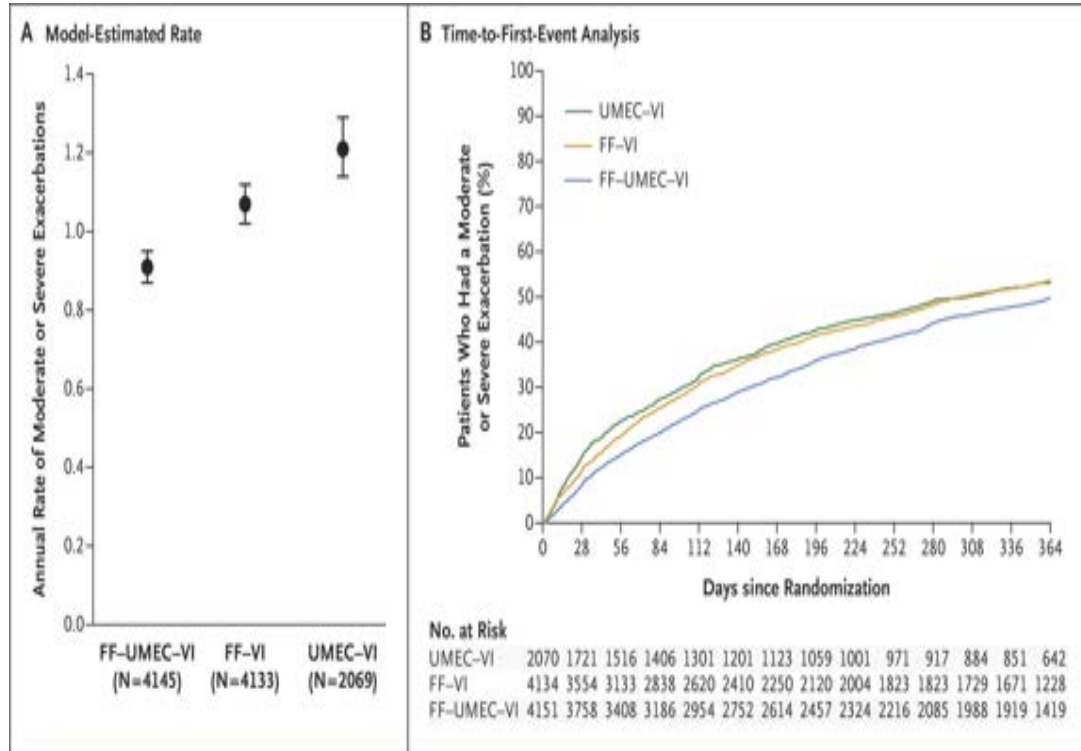
## Against Usage

- History of Pneumonias
- Eosinophil count  $<100/\mu\text{L}$
- H/O mycobacterial infection

## Favors Usage

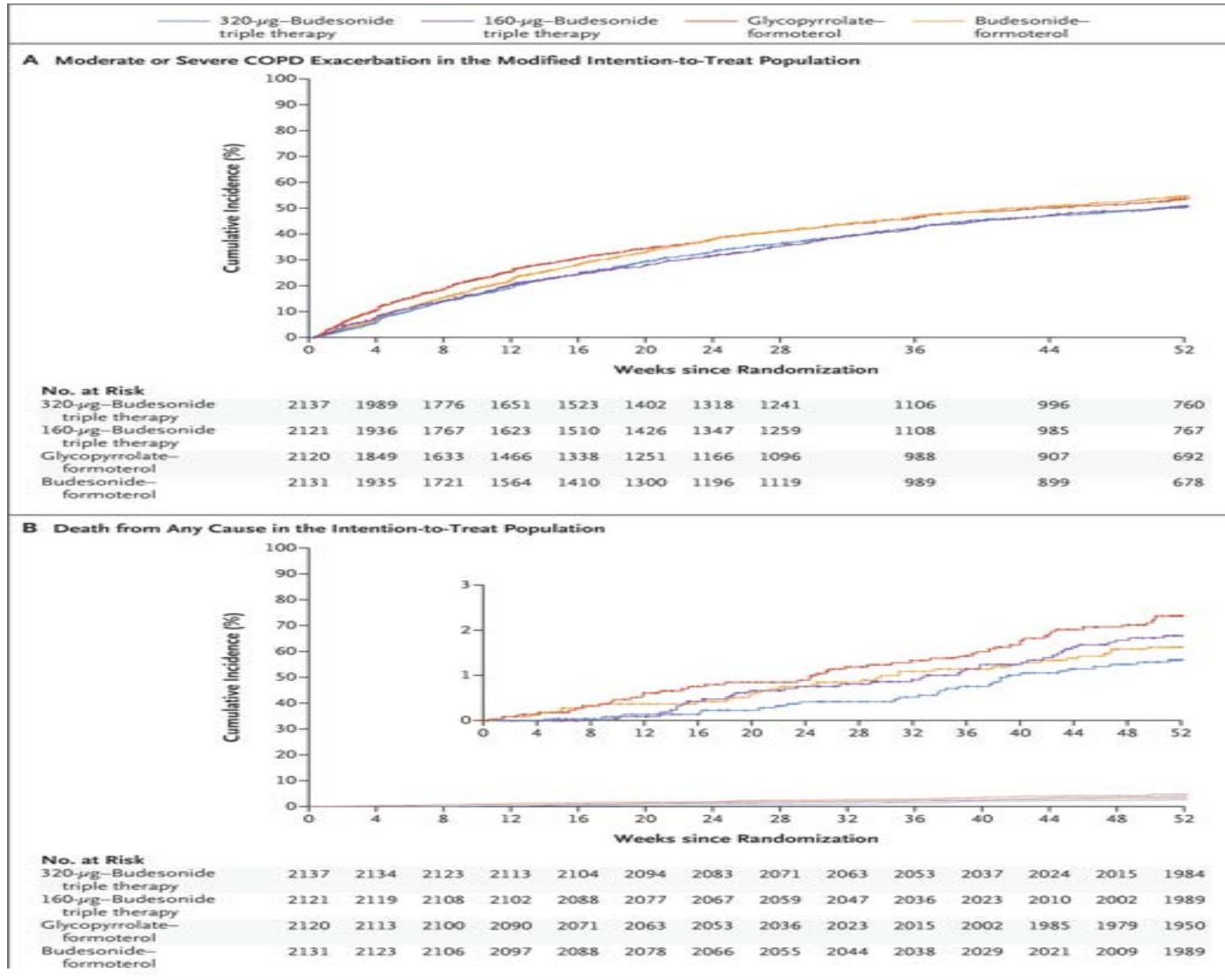
- Eosinophil count 100- 300/ $\mu\text{L}$
- 1 exacerbation moderate per year

# IMPACT Trial



David Lipson MD et al. NEJM 2018

# ETHOS Trial



Claus Rabe MD et al. NEJM 2020

# Bronchoscopic Lung Reduction Endobronchial Valve

- One way valve
- Severe Emphysema with hyperinflation.
- Severe symptoms in spite of medical therapy.



Zephyr



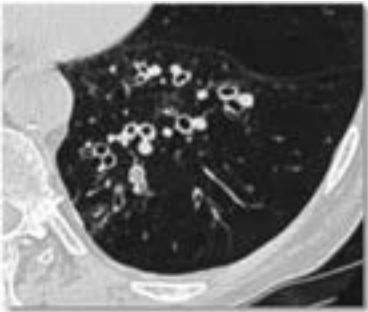
Spiration

Major Complication:  
Pneumothorax- upto 72 hrs.

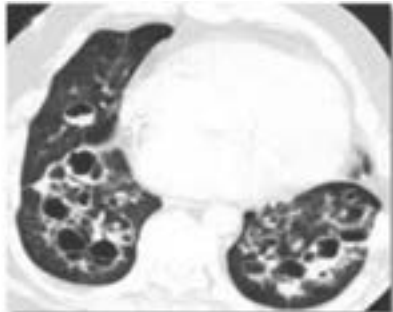


# Patient Selection

- Severe Symptoms: CAT score >10, mMRC >2
- Six minute walk 100-450 m.
- Post bronchodilator FEV/FVC <70%, FEV1 15-50%
- Post bronchodilator RV >175% of predicted and RI/TLC >55%- Looking for Hyperinflation



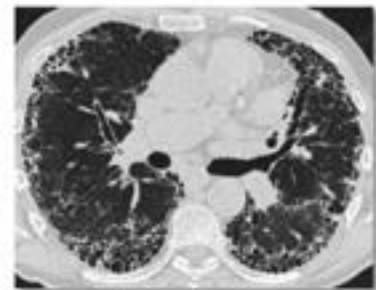
Airway disease



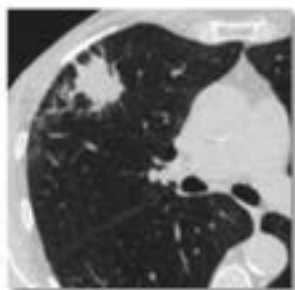
Bronchiectasis



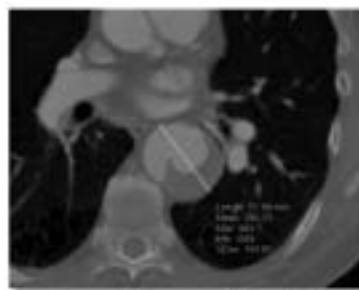
Paraseptal Emphysema



Fibrosis



Suspicious nodule



Accidental findings

## Not a Candidate:

- $\text{paCO}_2 >60$ ,  $\text{PaO}_2 <45$  on RA
- CHF, EF <40%
- Pulmonary hypertension, RVSP >50 mmHg
- Previous Lobectomy, lung transplant or LVR surgery
- Frequent infectious exacerbation or symptomatic bronchiectasis
- DLCO <20% or >60% of predicted



# Radiological Assessment

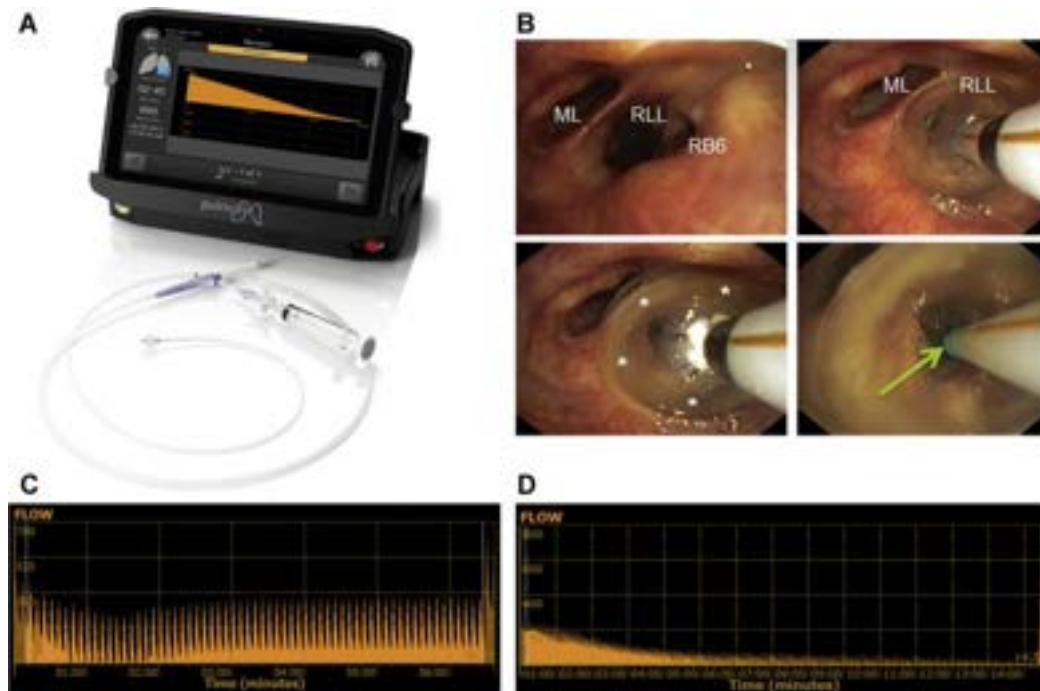
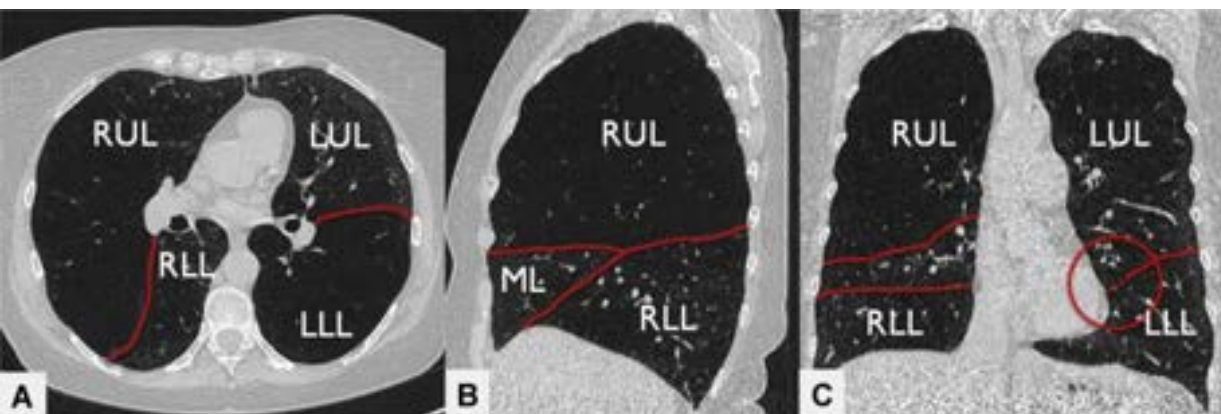
-Quantitative analysis of HRCT

Fissure Integrity:

->95%: No Chartis assessment

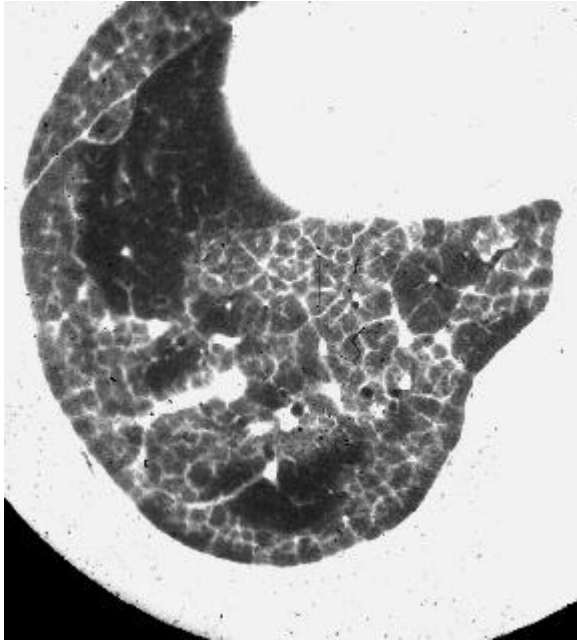
-<80%: Not a candidate- significant Collateral ventilation

-80-95% Chartis measurement

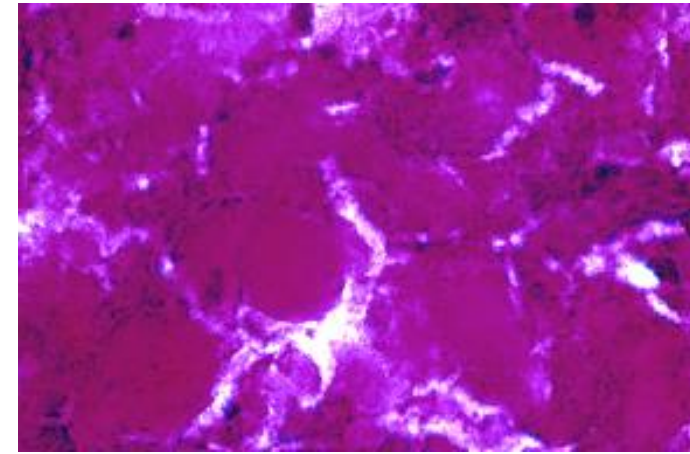


# Whole Lung Lavage

Only indication is Pulmonary Alveolar Proteinosis



Crazy Paving



PAS stain of BAL fluid in pulmonary alveolar proteinosis

# Whole Lung Lavage

- Double lumen ET Tube- ventilate one lung and lavage one lung at a time
- Lavage with 15-20 L of normal saline. Serial aliquots of 1-1.5 L
- Usually One lung at a time.
- With Inhaled GM- CSF, these patients are well controlled now.



**THANK YOU**

