PACS - OAD Symposium : Agra - 2025

Precision Medicine in Asthma (2025)

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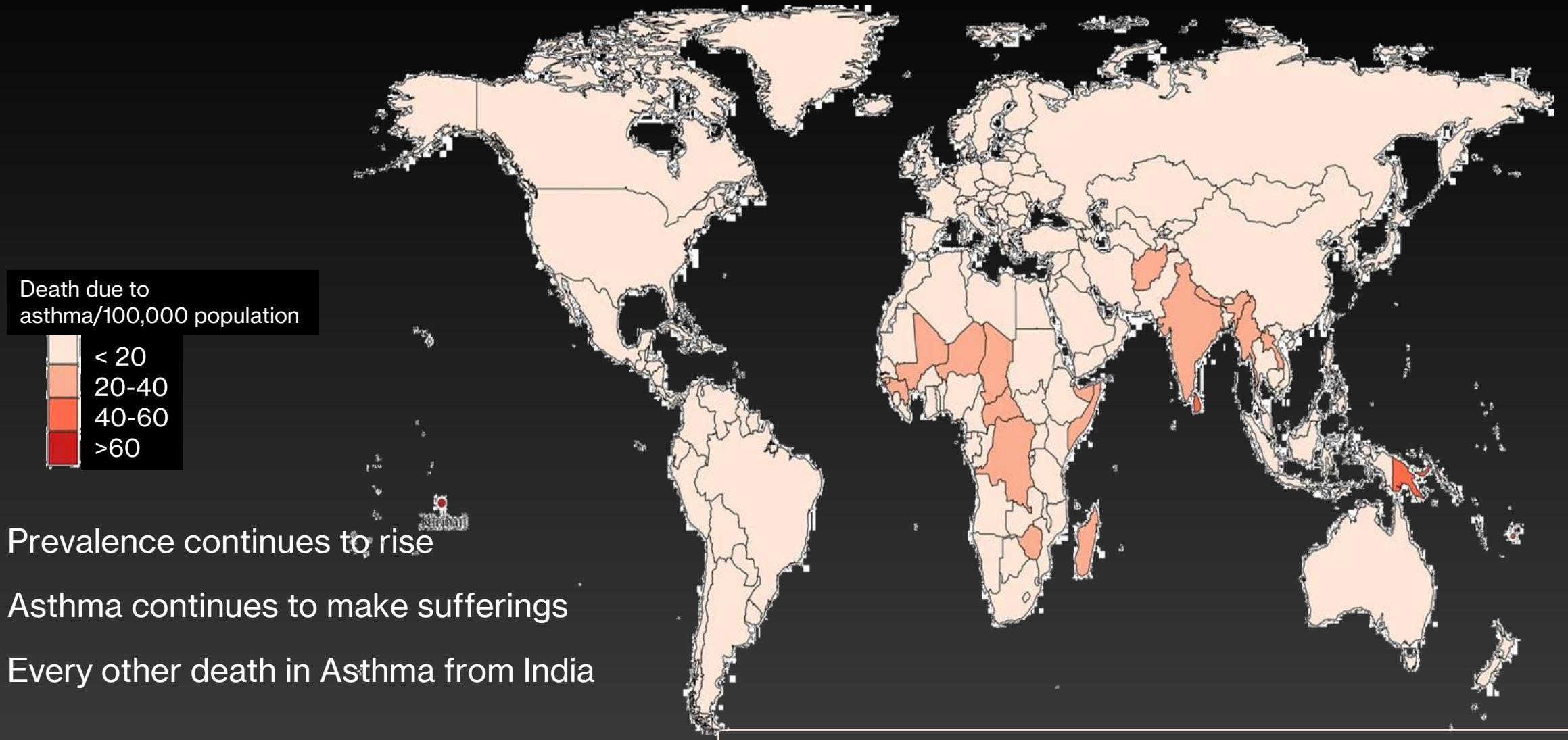
Death Continues to Haunt Asthma

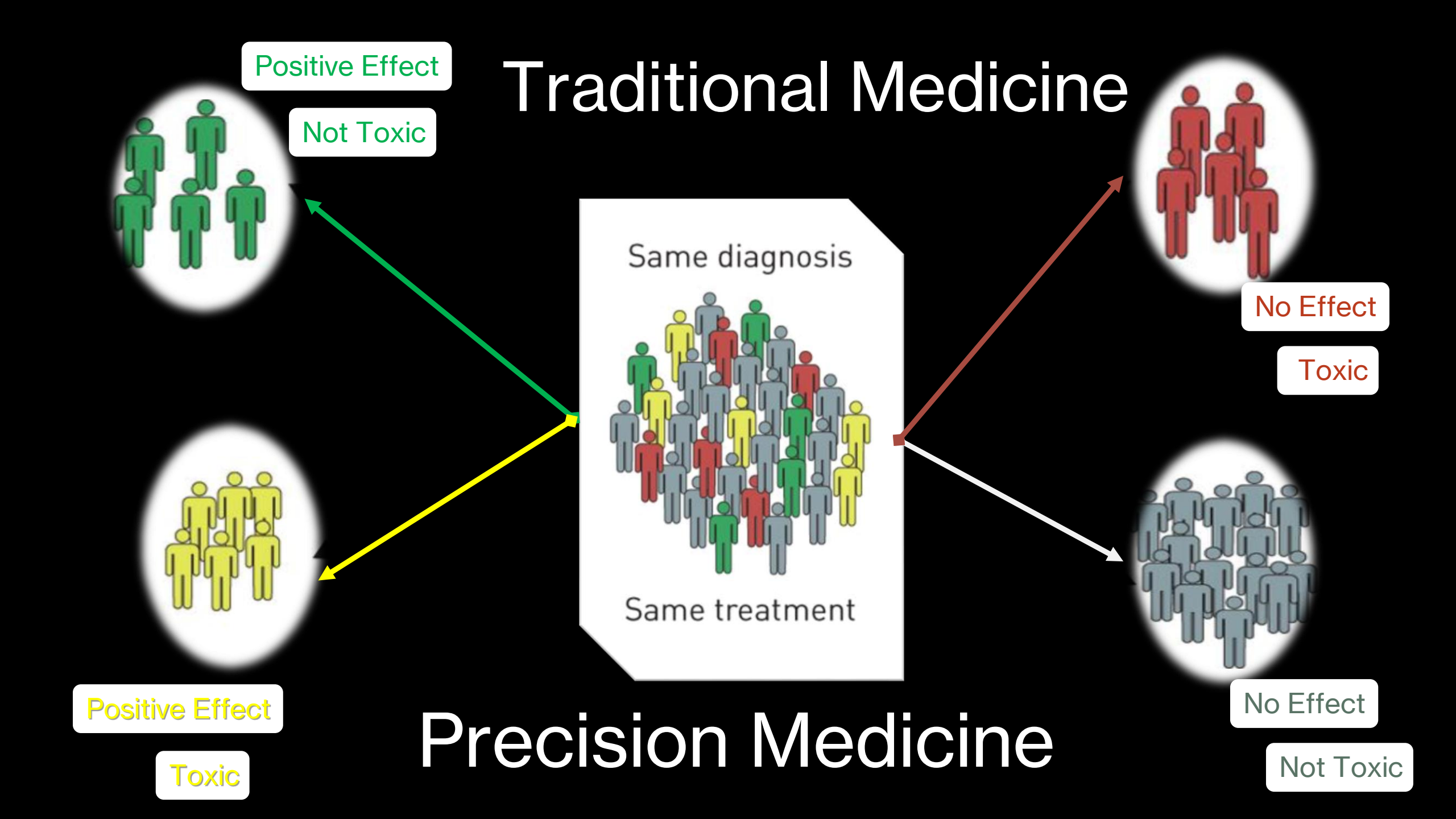


- Prevalence continues to rise
- Asthma continues to make sufferings
- Every other death in Asthma from India

20 - 40 deaths / Lakh Indians / Year

Front. Public Health 10:1036674. doi: 10.3389/fpubh.2022.1036674

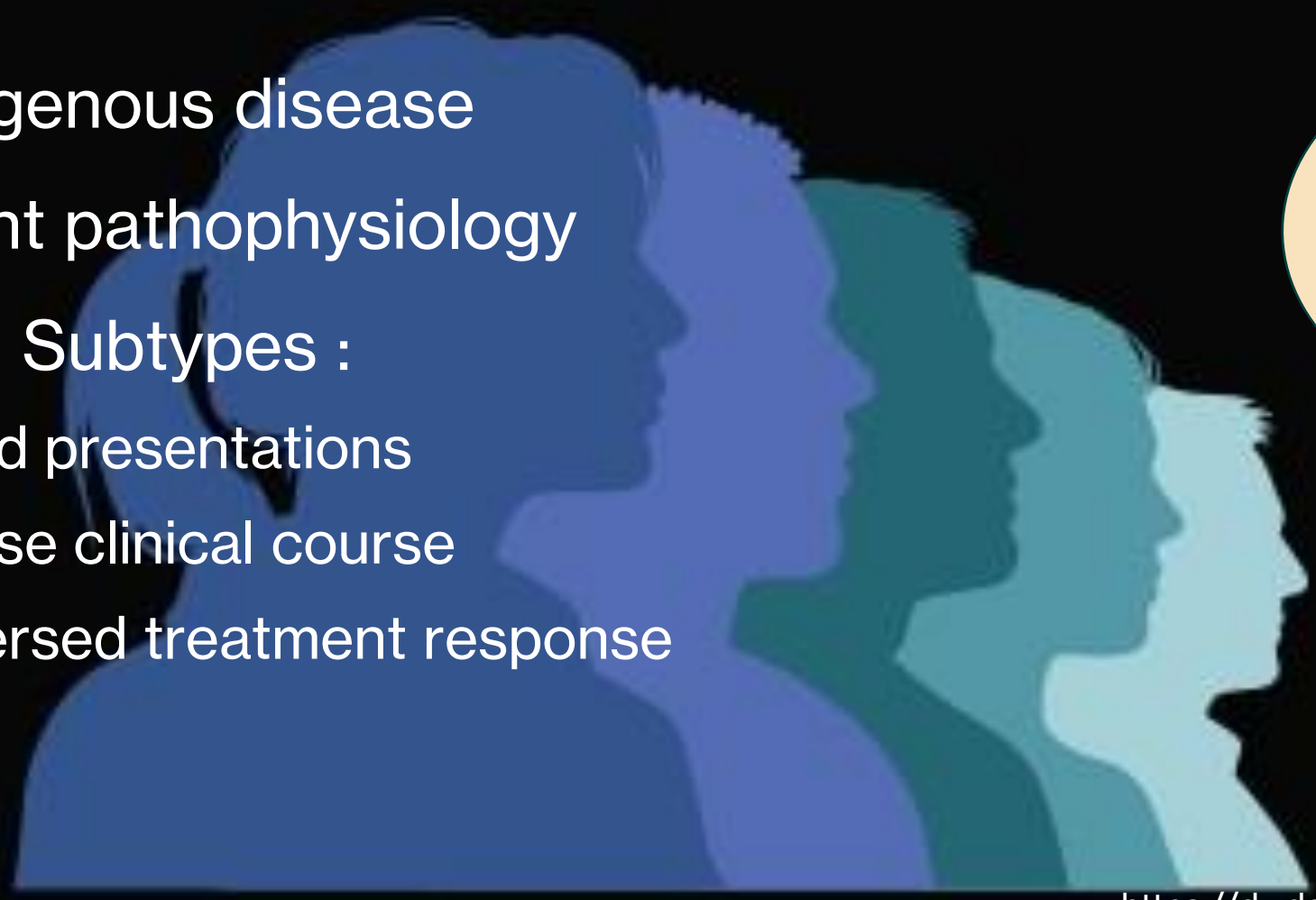
Traditional Medicine



Precision Medicine

Precision Medicine in Asthma : Why ?

- Heterogenous disease
- Different pathophysiology
- Several Subtypes :
  - Varied presentations
  - Diverse clinical course
  - Dispersed treatment response



Based on Treatable Traits

https://dx.doi.org/10.1016/j.intimp.2024.11218

Precision Medicine Based on Treatable Traits

‘Feature of an individual useful for predicting response to a particular treatment’

Trait

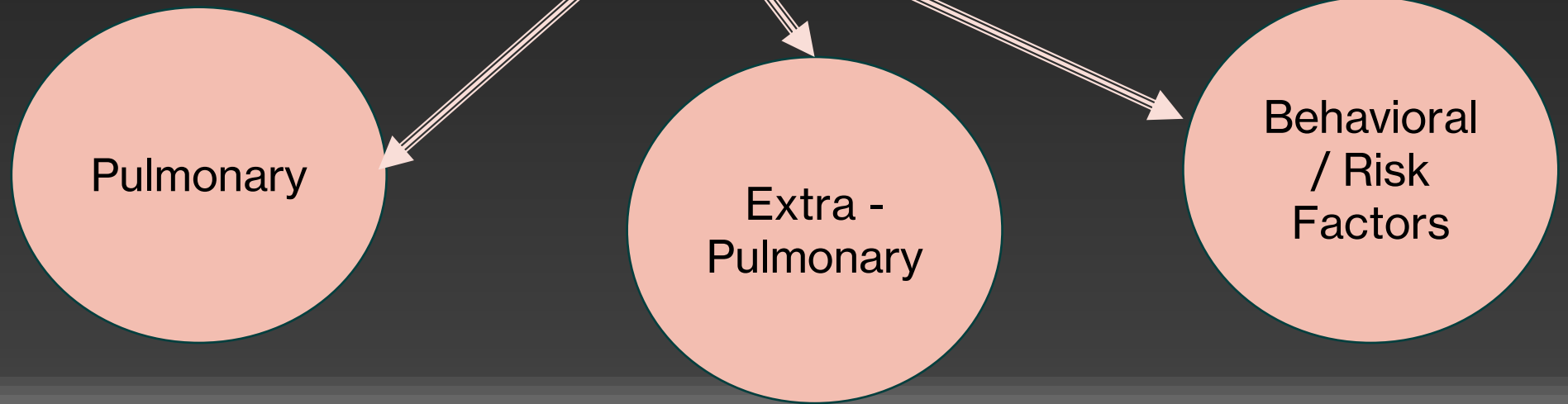
Treatable

e.g. Airflow limitation, High EOS, Non-adherence

Untreatable

e.g. Genetics, Structural changes, Age, Fibrosis

What it Needs to be a Treatable Trait ?



Treatable Traits in Asthma

Eosinophilic Airway Inflammation

Airflow Limitation (AL),

Exacerbations Prone

Mucus Hypersecretion

Dyspnoea

Neutrophilic airway inflammation

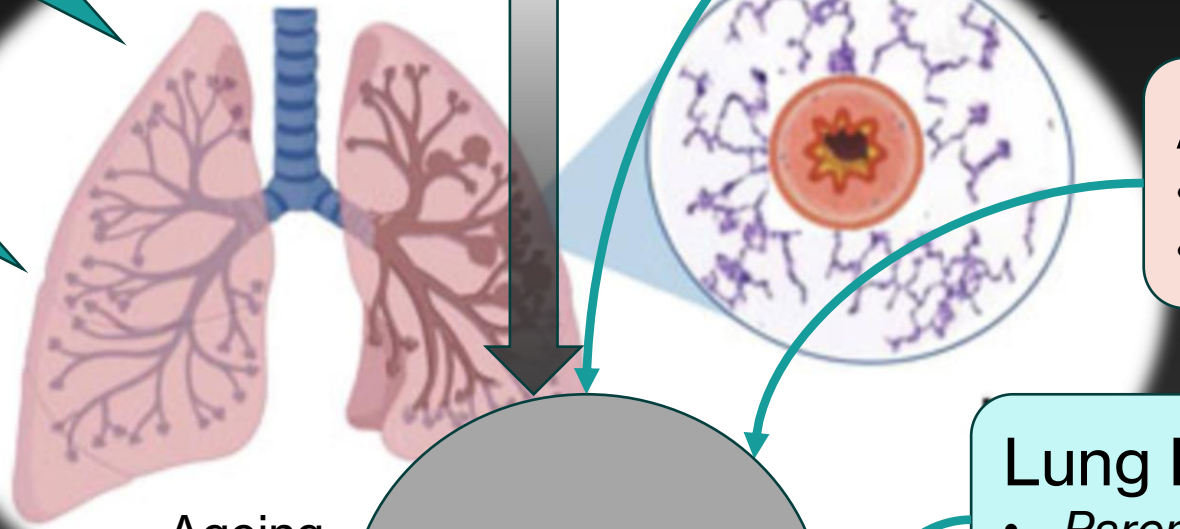
Small Airway Asthma

Airflow Limitation Trait : *? Treatable*

Long Standing Disease

Frequent Exacerbations

FEV_1 / FVC Ratio < 0.70



Ageing

Fixed Airway Obstruction

Inflammation :
- *Eosinophilic / Neutrophilic*
- *Proteolysis*

Airway Remodeling :
- *AW & BM Thickening*
- *Less Distensible Airways*

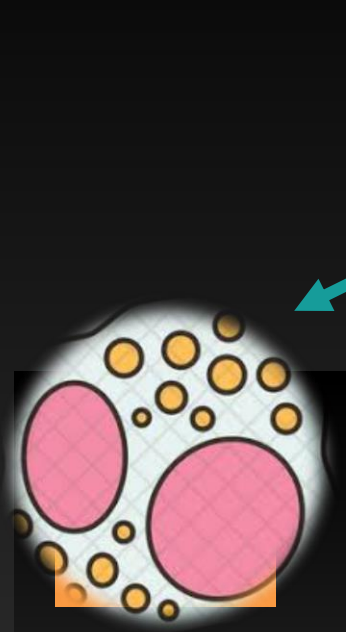
Lung Destruction :
- *Parenchymal Destruction*
- *Loss of alveolar attachments*

Potential Reversibility ?

Overtreatments ??

https://doi.org/10.3389/fphys.2022.898208

Exacerbation Prone Trait



Peripheral Eosinophilia :

> 200 /cmm

>400 /cmm for severe AE's

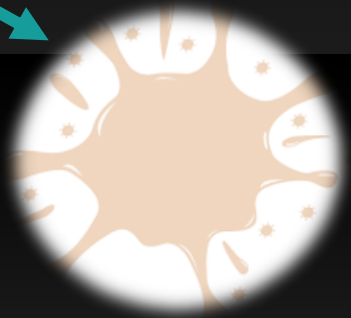
Any AEC > 300 /cmm

Fixed airflow limitation

Airway Remodeling

Parenchymal Destruction

Refractory to treatment



Mucus Dysfunction

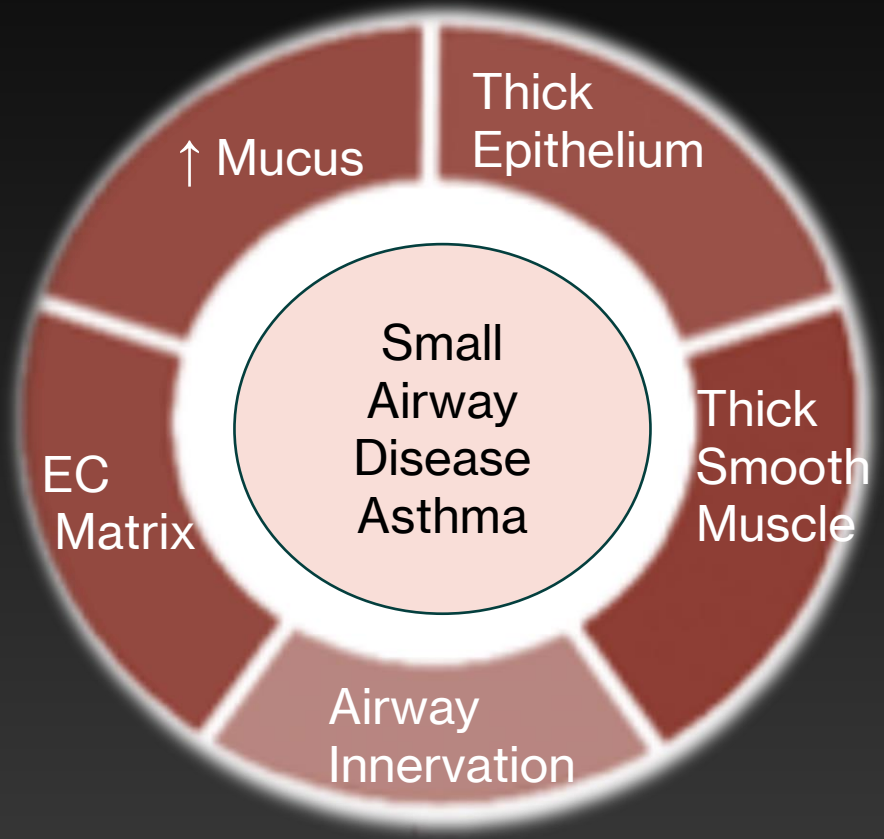
Worst Asthma Control

M3 receptors driven

Goblet cell Hyperplasia

Small Airway Disease Asthma

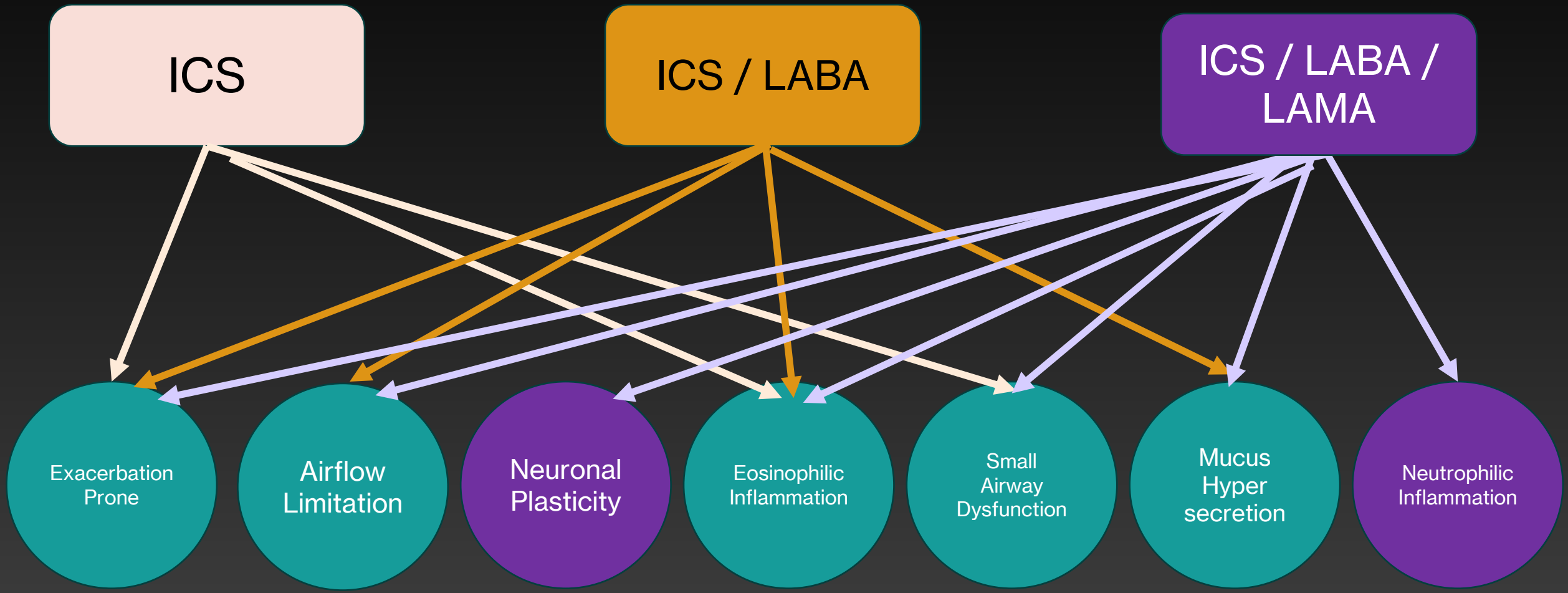
Extrafine Particle Inhaler



- SAD present in 50-60%
- Can occur without large airflow obstruction
- 27% of Severe Asthma had only SAD*
- Occurs all Asthma severities
- Associated with worst asthma control

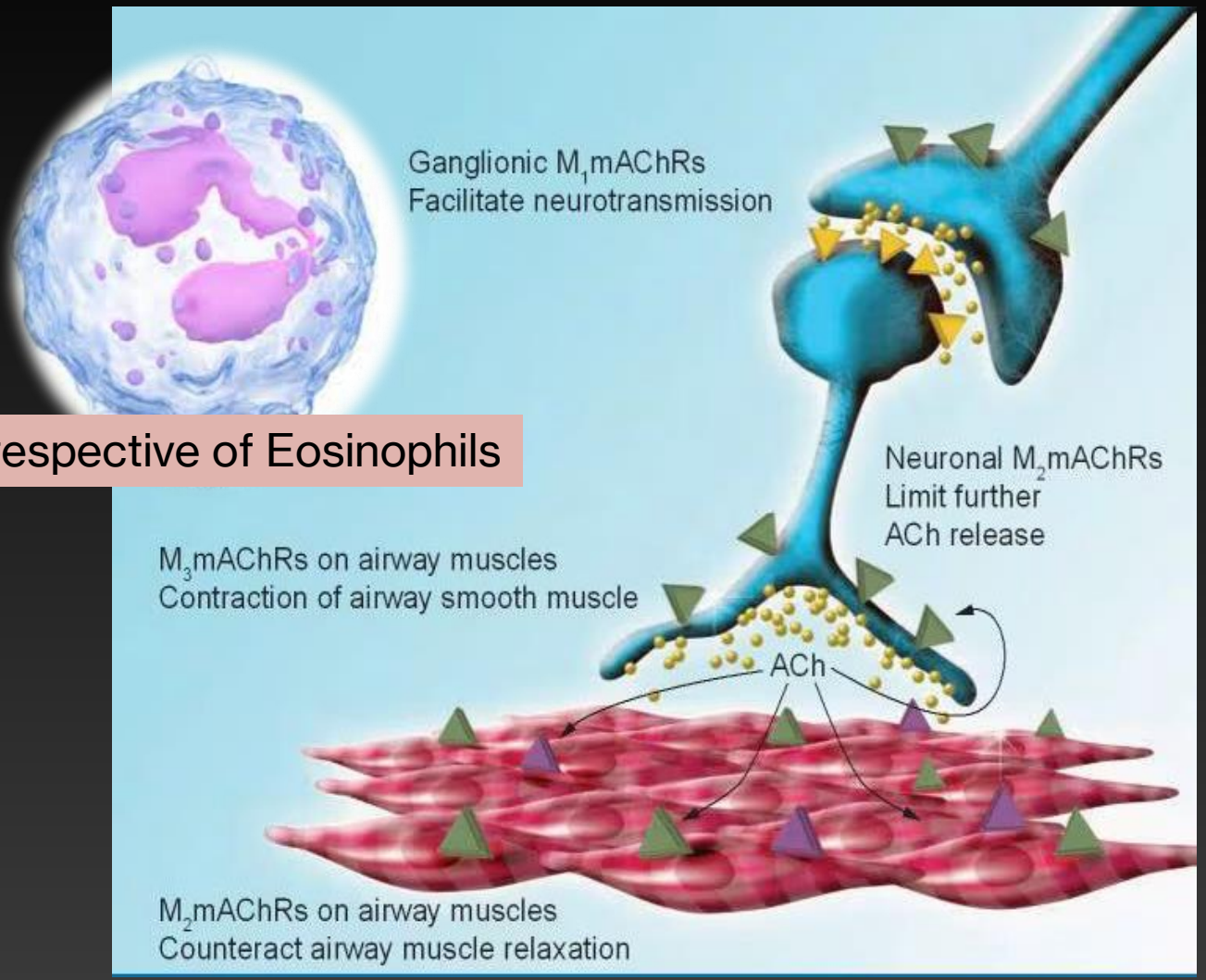
*Talwar D. Small airway involvement in severe asthma: Monaldi Arch Chest Dis doi:10.4081/monaldi.2024

Triple Therapy in Asthma & Treatable Treats

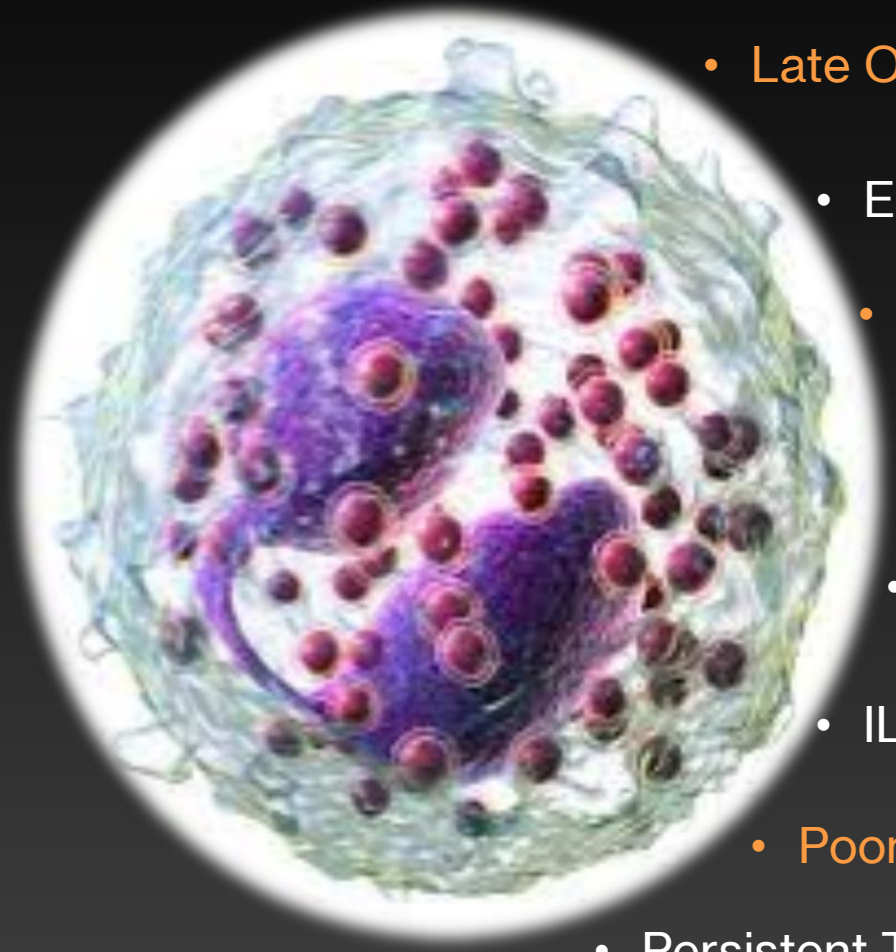


Role of LAMA in Asthma : Step 5 or 4 ?

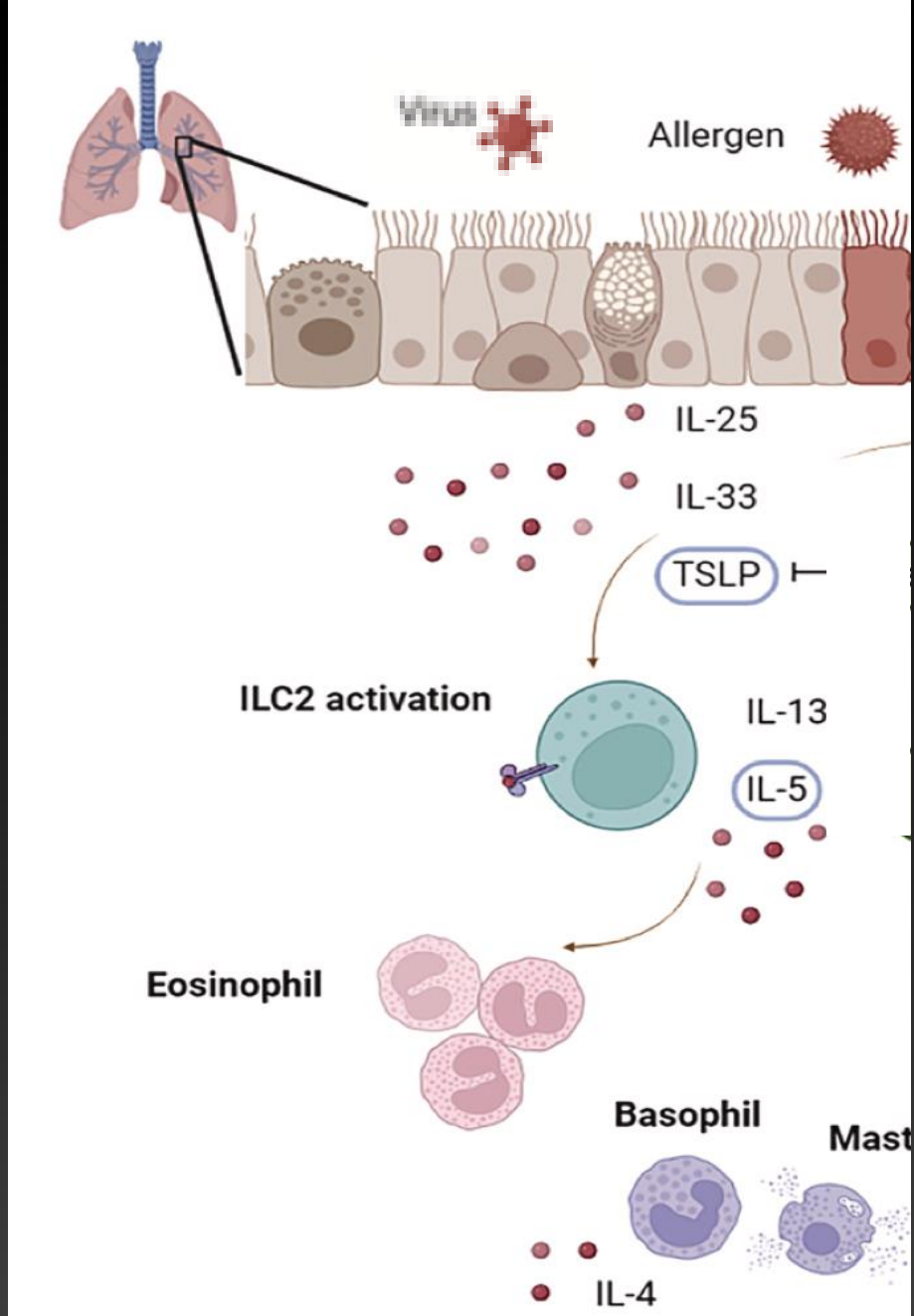
- Predictors of response :
  - Fixed airflow obstruction : Extrafine particle
  - Elderly
  - Current or former smokers
  - H/O Severe Exacerbations
  - H/O Moderate exacerbation in last year
  - Cholinergic plasticity
  - Women
  - Small airway disease
  - Mucus hypersecretion
  - Neutrophilic airway inflammation



Eosinophilic Airway inflammation



- Late Onset Adult Asthma
- Eosinophilic Inflammation
- Allergic Symptoms Minimal
- Irrelevant Elevated IgE
- ILC 2 Activation Mediated
- IL 5 /13 without T Cell Cascade
- Poor ICS Response
- Persistent T2 Inflammation - Biomarkers



https://doi.org/10.1016/j.intimp.2024.112189

Current & Future Position of SITT in Asthma

STEPS 1 – 2
As-needed-only low dose ICS-formoterol reliever

STEP 3
Low dose maintenance and reliever therapy (MART) with ICS formoterol

STEP 4
Medium dose maintenance and reliever therapy (MART) using low-dose ICS-formoterol

STEP 5
Refer for expert assessment, phenotyping, and add-on treatment for severe asthma

Exacerbations Prone
Small Airways Dysfunction

Airflow Limitation

SITT

Expected Outcomes

Better Asthma Control
Improve QoL
Slow decline in FEV1
Less hospitalizations

Respiratory Medicine 200 (2022) 106915

Severe Asthma Beyond Triple Therapy

Add Biological to Sever Asthma patient who is on Step 5 therapy and has ...

- Poor Asthma control
- Repeated Exacerbations
- Worsening on decreasing high intensity treatment
- On mOCS

+ Type 2 Inflammation

Step 5
Add-on LAMA; assess phenotype; consider high-dose ICS-formoterol[a] ± biologic

Step 5
Add-on LAMA; assess phenotype; consider high-dose ICS-LABA[a] ± biologic

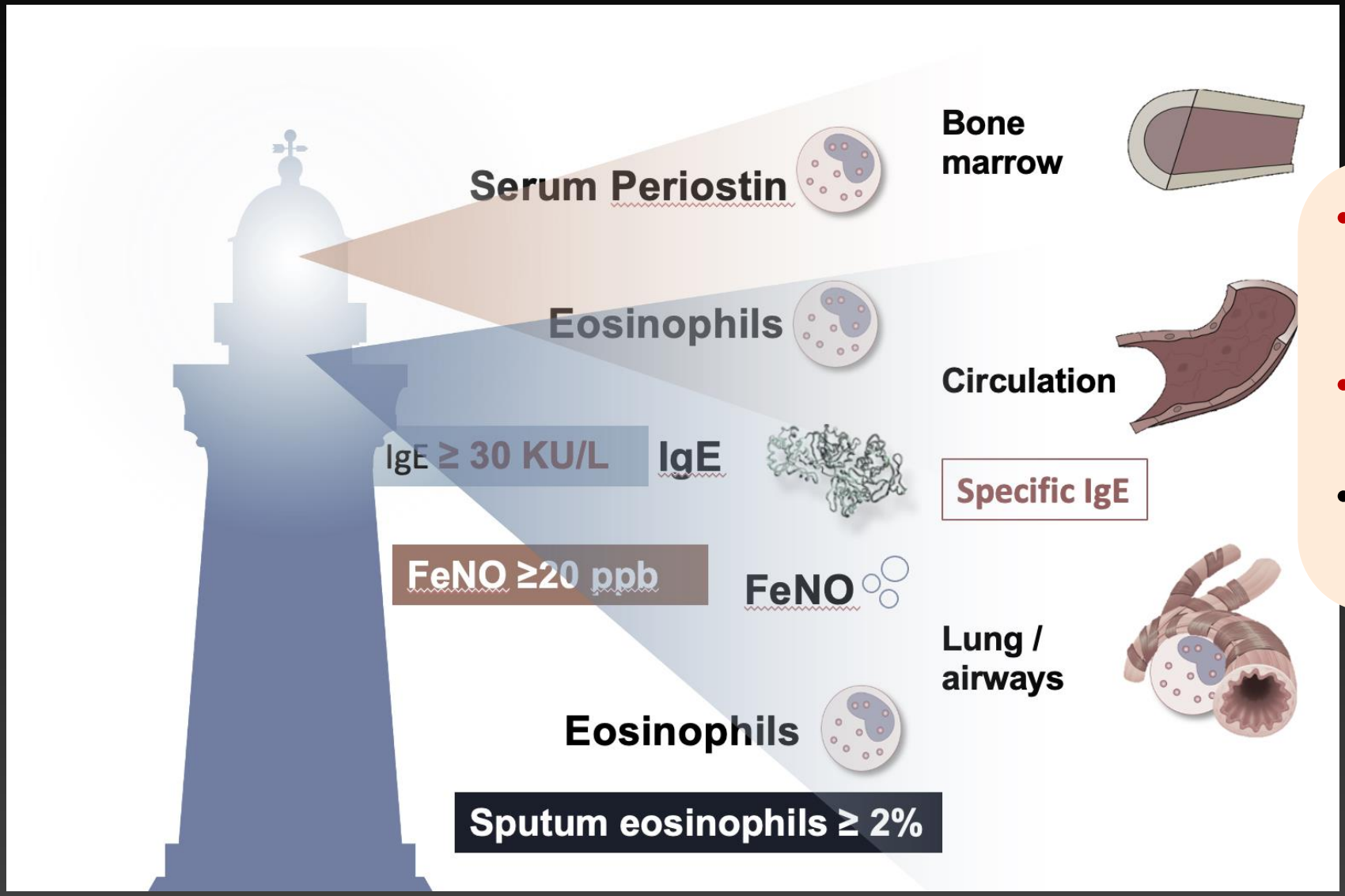
Montelukast

Other Options

Azithromycin

GINA 2024

Eosinophilic Airway Inflammation Trait : *Biomarkers*



- **Blood Eosinophils : ≥ 300 *** cells/uL
- **FeNO*: ≥20** ppb
- **Sputum Eosinophils : ≥ 2%**

** Depends on dose of OCS & ICS*

Scheerens et al. Clin Exp Allergy 2014; 44:38–46;

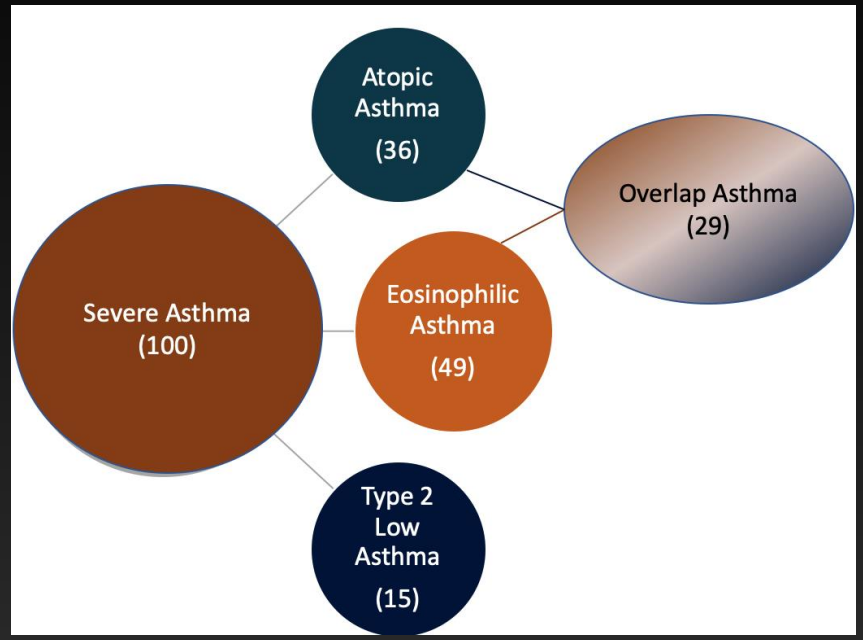
Type 2 Severe Asthma ~ 85 % : *Biologicals Eligible ~ 91%*

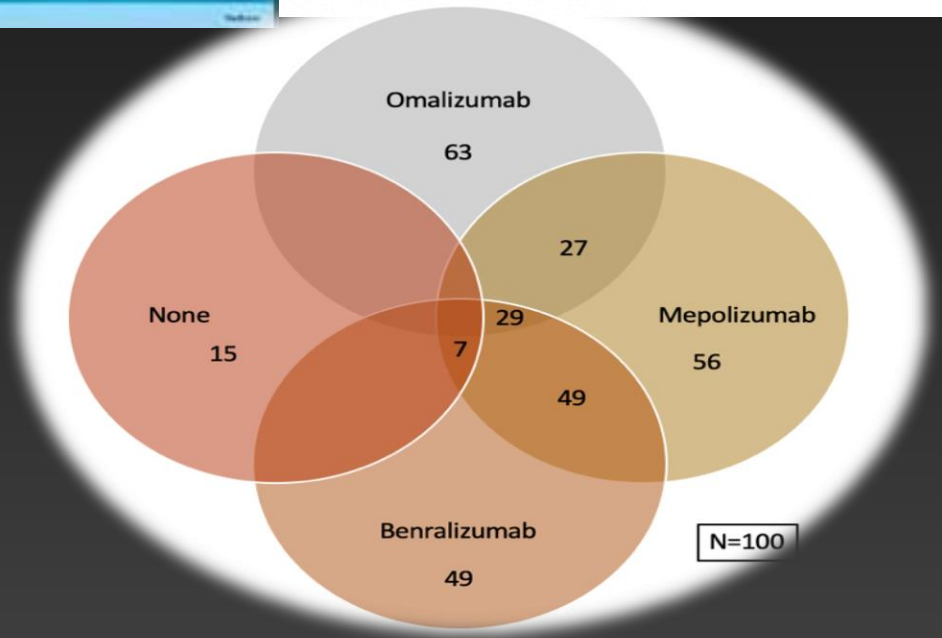
Original Article

A retrospective observational study on pheno-endotypes of severe asthma among adults attending asthma clinic in a tertiary care centre in India

Deepak Talwar[1], Dhruv Talwar[2], Nitin Jain[3], Deepak Prajapat[4], Sourabh Pahuja[4]

[1]Director and Chair, Metro Centre for Respiratory Diseases, Noida, Uttar Pradesh, India, [2]PGY III, JNMC Sawangi, Wardha, Maharashtra, India, [3]Senior Resident, Rajiv Gandhi Superspeciality Hospital, Tahirpur, New Delhi, India, [4]Consultant, Metro Centre for Respiratory Diseases, Noida, Uttar Pradesh, India



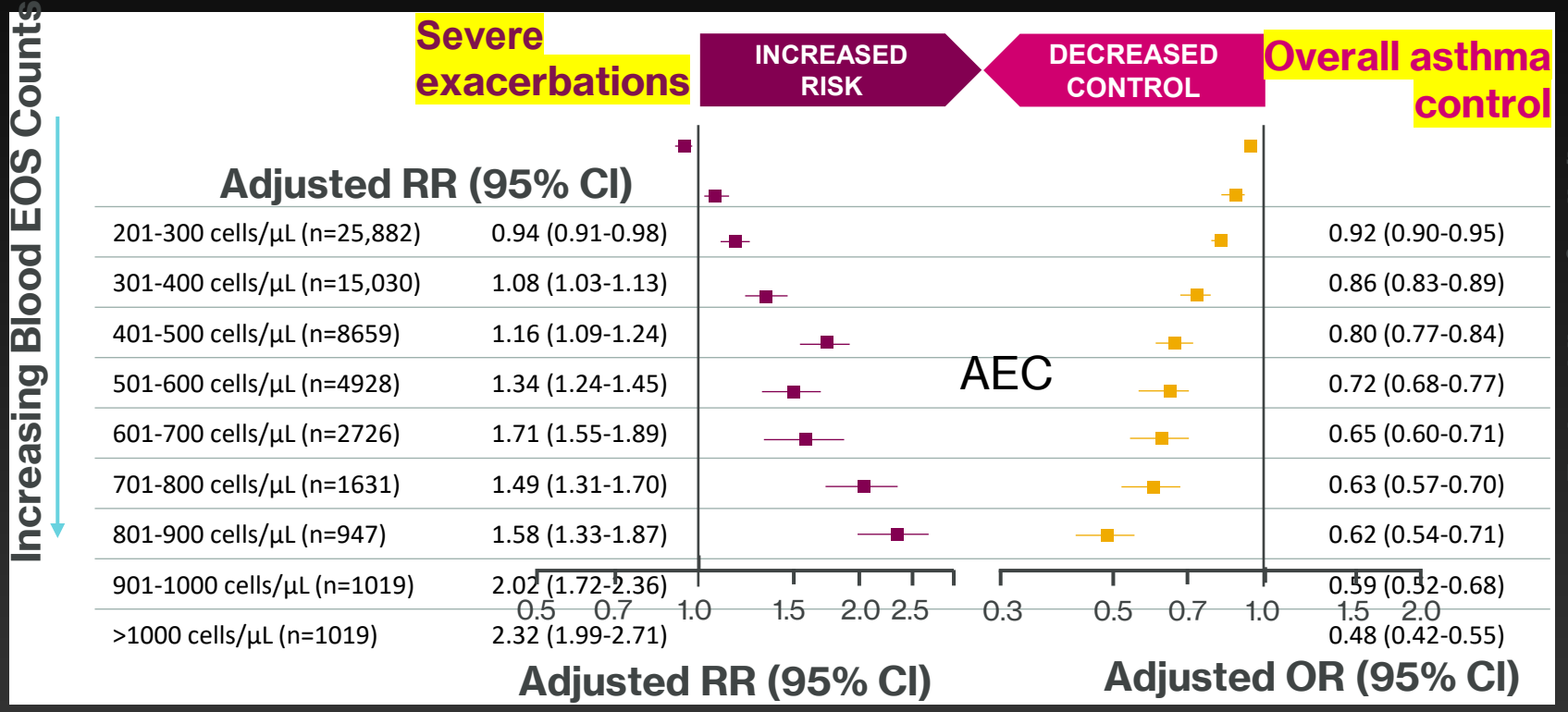


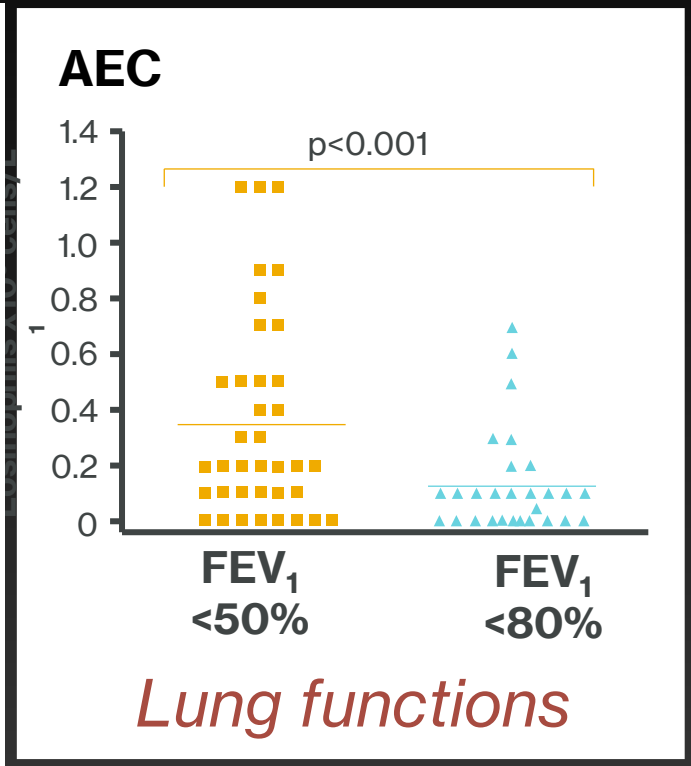
T_2 Low asthma is only 15% at AEC cut off of 300 & 9% at @ AEC -150

~ 50% of our Severe Asthmatics were eligible for both group of biologicals

Lung India 2022;39:393-400.

Elevated Blood Eosinophils is Most Important Biomarker



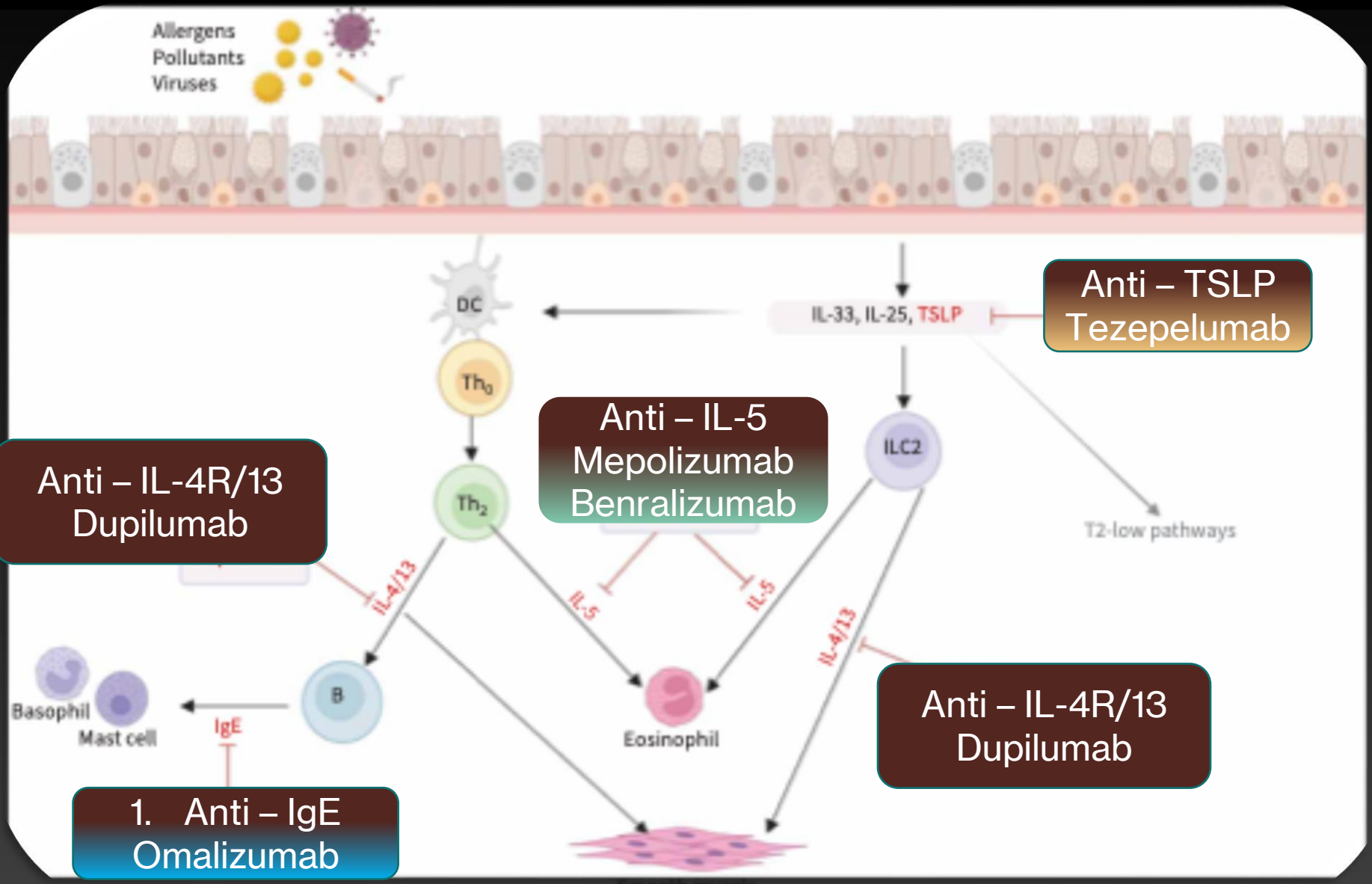


Frequent Exacerbations, Poorer Asthma Control & Lower Lung Function

EOS = eosinophil; FEV_1 = forced expiratory volume; OR = odds ratio; RR = relative risk.

1. Price D et al. *Lancet Respir Med*. 2015;3:849-858; 2. Bumbacea D et al. *Eur Respir J.* 2004;24:122-128.

Biologicals for T2 Eosinophilic Inflammation



Eur Respir Rev 2025; 34: 240088

Realistic Expectations - *Matching Research*

SA Outcomes	Omalizumab	Mepolizumab	Benralizumab
Reduction in Exacerbations	25% reduction	~ 50 %	40 -70 %
Reduction in maintenance OCS	50% dose reduction in those at 15 mg/day baseline	50% dose reduction 2-6 months↓	50 - 80%
FEV_1	2.1%	100 ml	**100 -160 ml @ 4 weeks**
QoL	SGRQ Asthma diaries	ACQ5 + 0.4 SGRQ +7 points	ACQ < 0.5 SGRQ +8.1 points
Real World Data	Reduction in AE in 42% vs 63 % & 28% vs 48% @ baseline	**Reduction in AE ~ 50%** Reduction in mOCS ~ 50%	**All improved with 70% exacerbation free** @2years
Predictors for Response	Childhood onset,, AEC ≥300, FeNo > 19.5, S Periostin >50	Low mOCS, Later onset SA, ↓ BMI, AEC,	AEC, FEV_1<65%, mOCS, 'f' Exacerbations, AR

Choosing Biologicals in Severe Asthma - 2025 !

Omalizumab

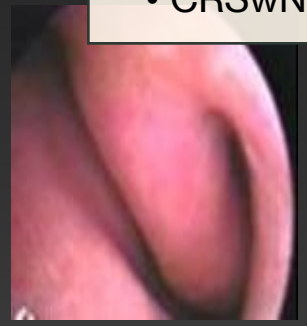
Childhood Onset asthma

Biomarkers

- Serum IgE, BMI, SPT/Specific IgE, FeNO

Comorbidities :

- Allergic rhinitis
- Chronic idiopathic urticaria
- Food Allergy
- CRSwNP



Mepolizumab

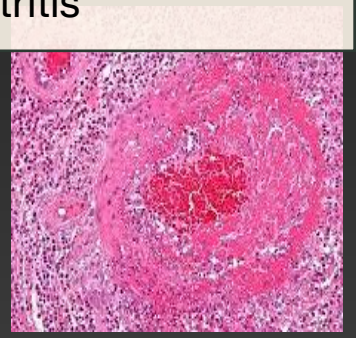
Late Onset asthma

Biomarkers :

- AEC, FeNO, Sputum Eosinophils

Comorbidities :

- Chronic Sinusitis with NP
- EGPA
- HES
- Eosinophilic Gastritis

Benralizumab

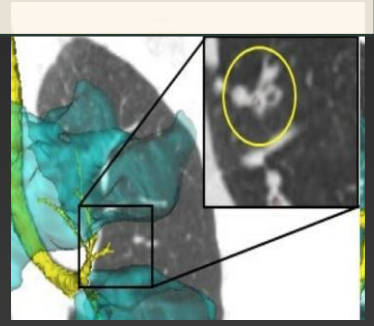
Adult / Late Onset asthma

Biomarkers :

- AEC, Sputum Eosinophils, FeNO

Comorbidities :

- Nasal Polyposis
- Airway Mucus
- EGPA

Patient Preferences : Cost, Reimbursement, Dosing

Indirect Comparison Between Mepolizumab vs Benralizumab on Asthma Exacerbations & mOCS Use

	Asthma Exacerbation Rate Reduction	% Patients with Zero Exacerbations in Asthma
Mepolizumab	Dream : - 48% Mensa : - 53% Musca : - 58% Sirius : - 32%	Cosmos : 52% Columbia : 33%
Benralizumab	SIRROCO : -51% Andhi : - 59% Zonda : - 70% Ponente ; -62% Bora : -82% Meltemi: - 96%	Bora : 74% Meltemi : 87% @ 5 years Zonda : -77% Ponente : 74%

Multiple Publications .

Biologicals in Severe Asthma– *Indian Experience*

ISSN: 2754-4761

Journal of Pulmonology Research & Reports

SCIENTIFIC Research and Community

Research Article Open Access

Efficacy & Safety of Omalizumab in Indian Adult Patients with Severe Allergic Asthma: A Retrospective Observational Study

Arjun Khanna[1]*, Deepak Talwar[2], Linija K Nair[3]

Conclusions:

Omalizumab led to improved asthma control, lung function, and QoL and allowed a reduction in the dosage of medications for asthma. The improvement was observed irrespective of age and biomarker levels.

J Pulmonol Res Rep, 5(2): 4-6 2023

F1000Research F1000Research 2023, 12:1225 Last updated: 27 SEP 2023

Check for updates

CLINICAL PRACTICE ARTICLE

An early Indian experience with benralizumab - A compendium on severe asthma cases: a case series [version 1; peer review: awaiting peer review]

Deepak Talwar * [1], Manoj Yadav[2], Nagarjuna Maturu[3]

Conclusions:

In all cases, management with Benralizumab resulted in optimal clinical and functional improvement, a decline in systemic steroid use, and improved QoL.

F1000 Research 2023, 12:1225

Precision Medicine Asthma

Extra- Pulmonary

Pulmonary

Behavioral

Obesity
AF Limitation
Eosinophils
Infection
Cough
Mucus
A/CRF
Smoking
Occupation
Pollution
Poor Preceiver
Technique
Adherence
Anxiety / depression
ILO
CRSwNP
GERD
CVD
Skin / Food Allergy
OSA

Pavord et al. J Allergy Clin Immuno lPract, 2023

Extra- Pulmonary Treatable Traits in Asthma

Trait	Diagnostic Criteria	Choice of Treatment
Cachexia / Obesity 	BMI	Diet & Physical activity
Deconditioning 	CPET	Exercise , Pulmonary Rehabilitation
OSA 	PSG	PAP , weight loss if Obese
CVS Comorbidity 	EKG, ECHO, BNP	ACEi, Bets blockers, Diuretics
GERD 	UGIE, Esophageal PH monitor	PPI , H_2 blockers
Chronic Rhino-sinusitis 	Clinical, Imaging	Intra-nasal steroids
Vocal cord Dysfunction 	FOL, Dynamic MRI	Speech Therapy
Psychiatric Disorders 	Questionnaires, Psychiatric Exam	CBT, Pharmacotherapy

Behavioral / Risk Factors-Treatable Traits in Asthma

Trait	Diagnostic Criteria	Choice of Treatment
Smoking & Exposures 	Exhaled CO, Urinary Cotinine	Cessation Support, NRT, Pharmacotherapy, Avoidance
Exposures to allergens, 	RAST, SPT AQI	Avoidance, Desensitization
Poor Perceiver 	Mismatch : Objective vs Subjective findings	Reassurance, Breathing Exercises
Side Effects of Drugs 	Monitored withdrawal	Therapeutic Optimization
Inhaler's Polypharmacy	Multiple devices	Device Rationalization
Technique & Adherence 	Observation	Education, Simpler to use devices, easy regimens
Family Support 	Observation	Family therapy

Conclusions:

Asthma is heterogenous disease with poor outcomes even today
Shifting strategy from ‘One Size Fits All” to Precision medicine is needed
Precision medicine is based on identifying ‘Treatable Traits’ and address them
Most important treatable traits in asthma are: Eosinophils, AL, AE, can occur at any GINA Step
SITT addresses these traits in many asthmatics
Uncontrolled eosinophilia is targeted with Biologicals
Biologicals either target IgE or Eosinophil mediated uncontrolled inflammation
Extra-pulmonary Traits are responsible for most of difficult asthma
Behavioral traits also need to be addressed before using biologicals

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Dr Kanishka Kumar Singh

Senior Consultant

Dr Deepak Prajapat

Senior Consultant

Dr Rahul Khera

Consultant

Thank You

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