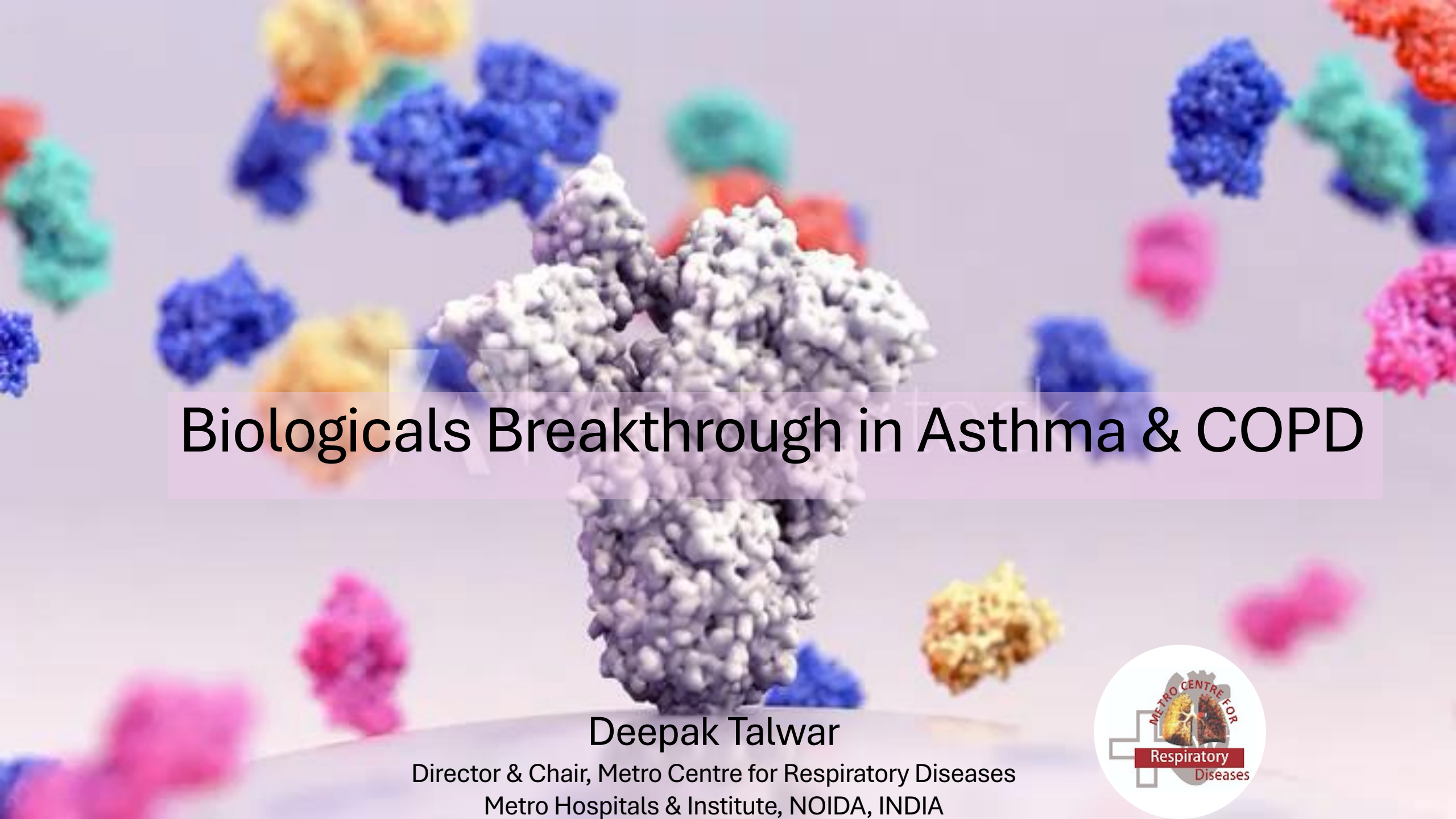


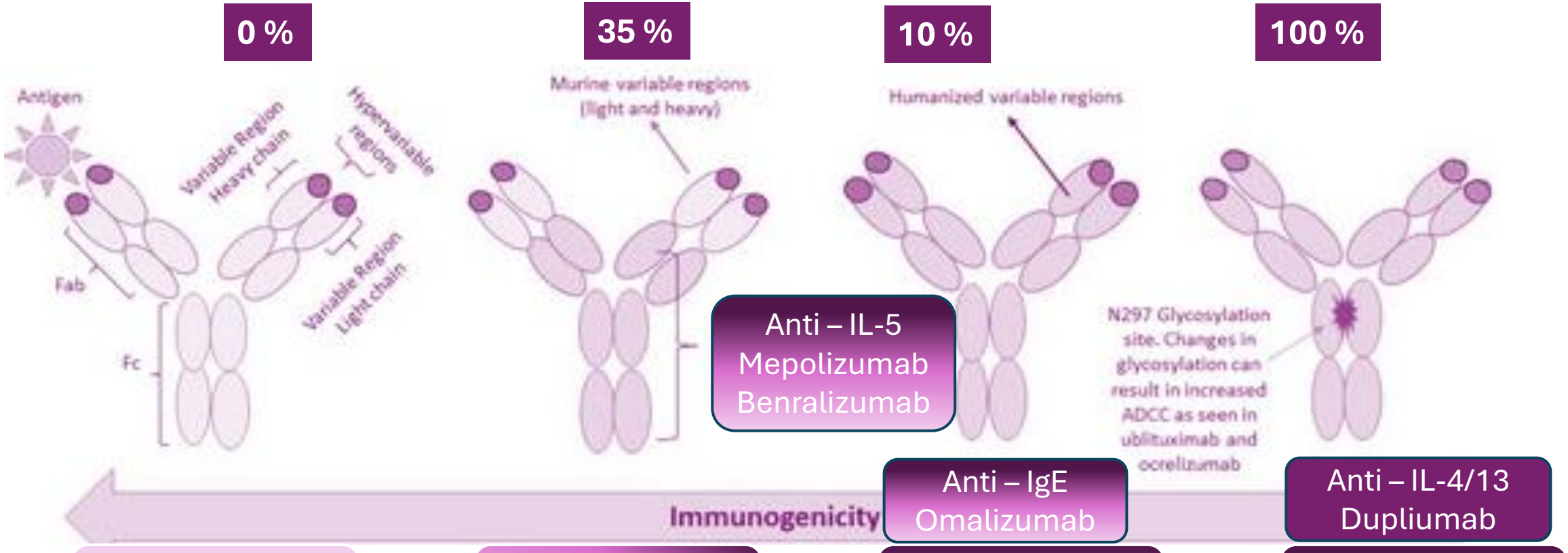
Biologicals Breakthrough in Asthma & COPD

Deepak Talwar

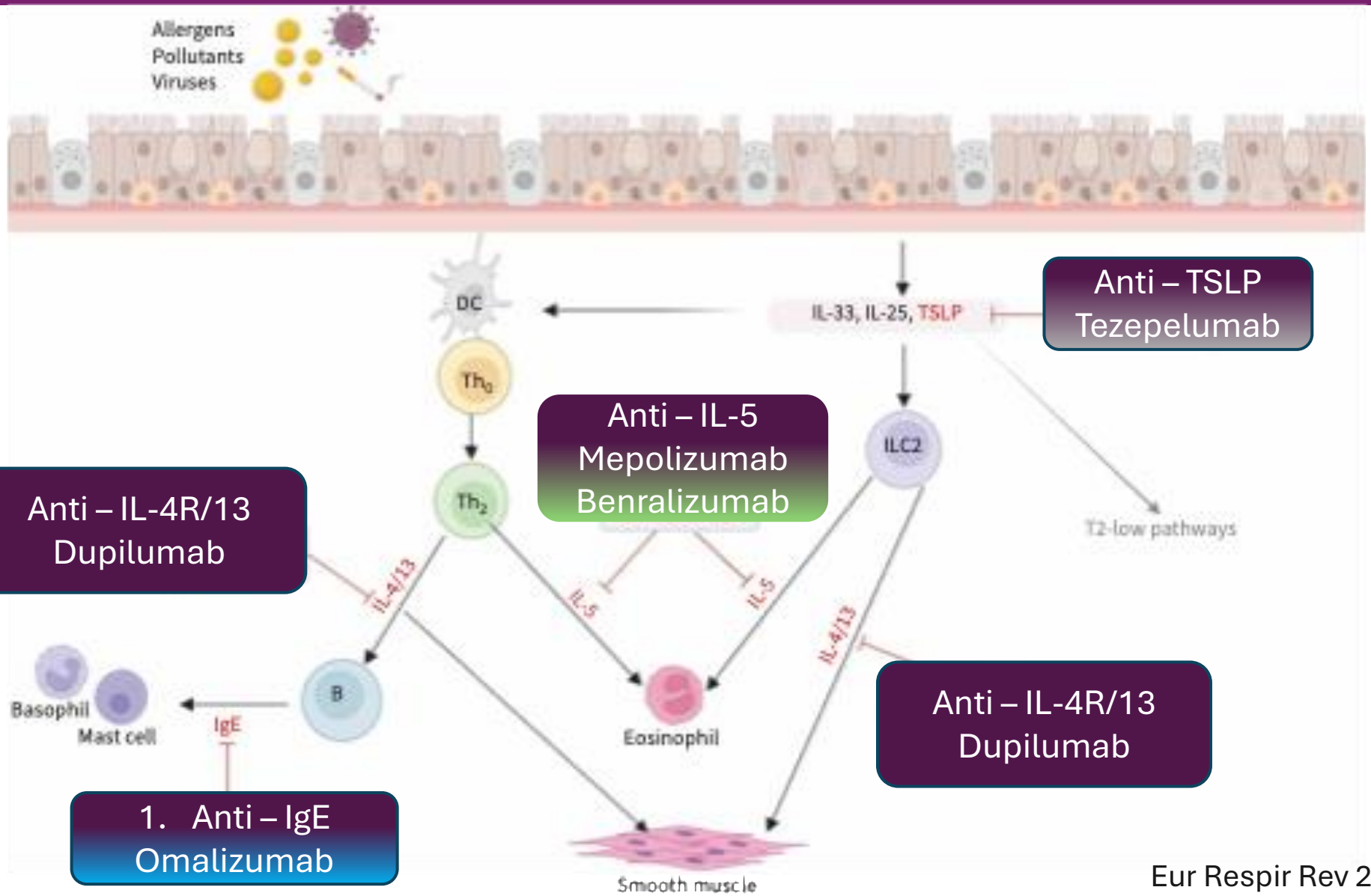
Director & Chair, Metro Centre for Respiratory Diseases

Metro Hospitals & Institute, NOIDA, INDIA

Biologicals : *Targeted Therapies*

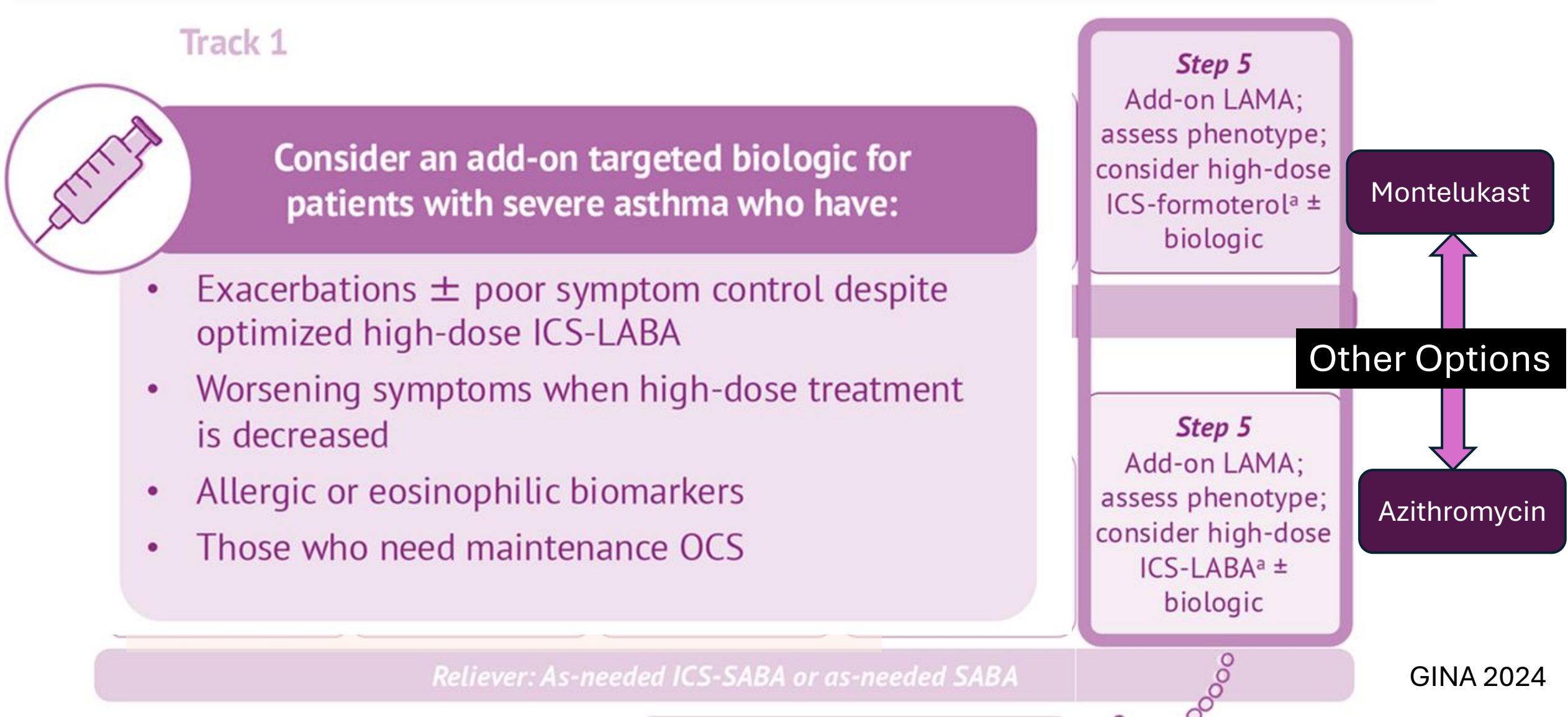


4 Biologicals for Airway Diseases



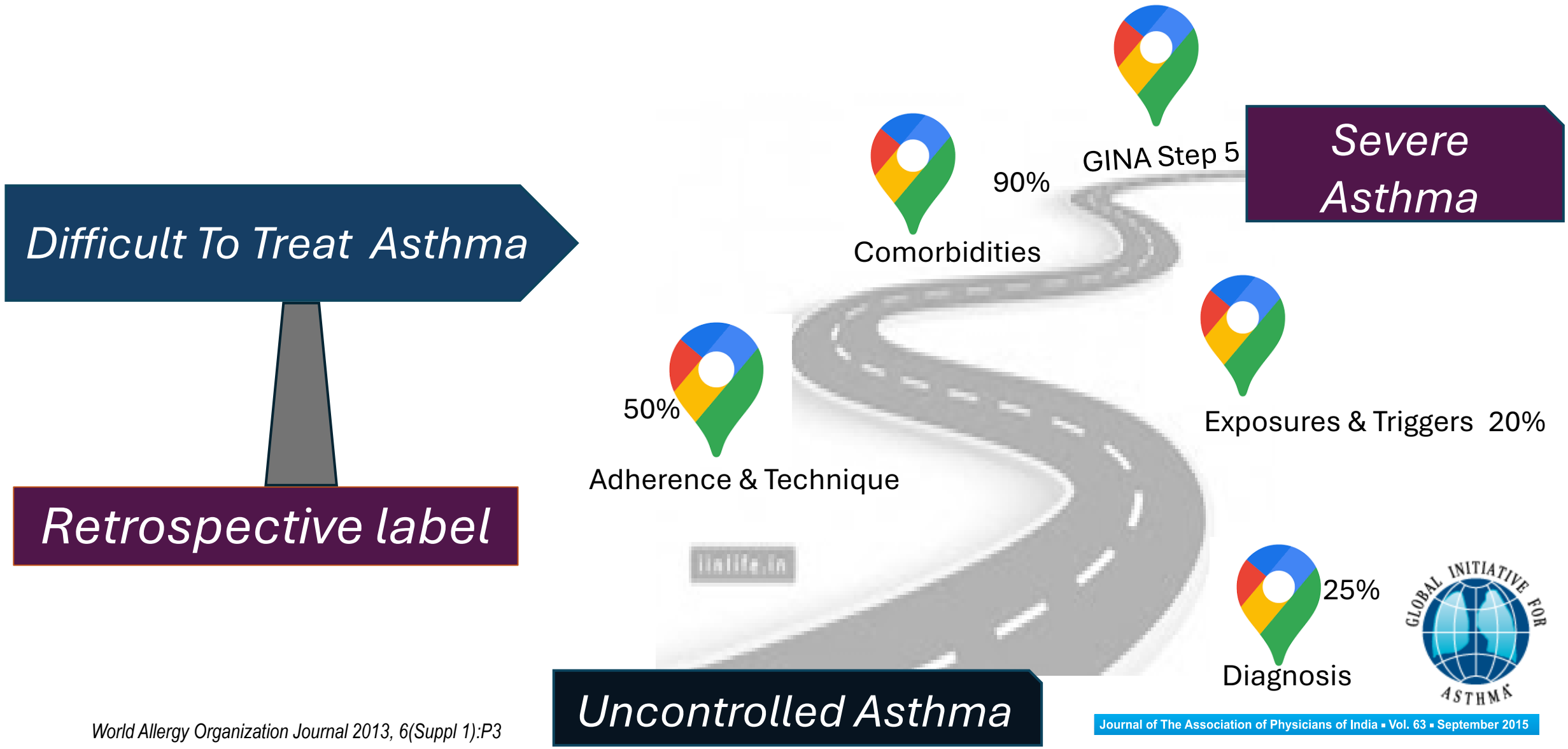
Eur Respir Rev 2025; 34: 240088

Biologicals in Asthma : *When to Use ?*



GINA 2024

Remember : All Uncontrolled Asthma is *NOT* Severe Asthma



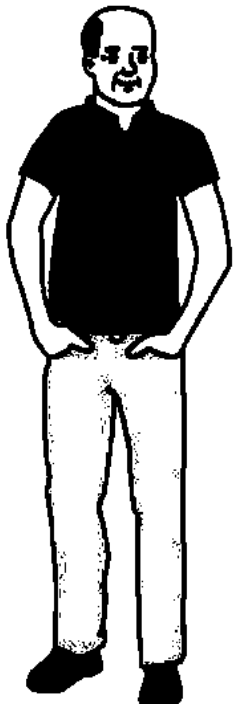
World Allergy Organization Journal 2013, 6(Suppl 1):P3

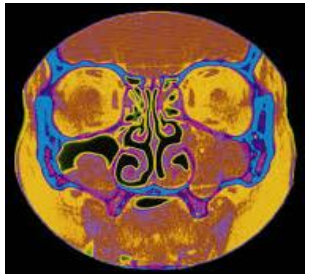
Which Severe Asthma Patients *Type 2 Inflammation*

Type 2 Severe Asthma : Atopic / Eosinophilic Phenotype

Type 2 Inflammation

- Age of onset of asthma: Childhood / Early adulthood
- Allergic comorbidities : Atopic dermatitis, AR, CSwNP, ABPA, EGA
- Oral steroids responsive





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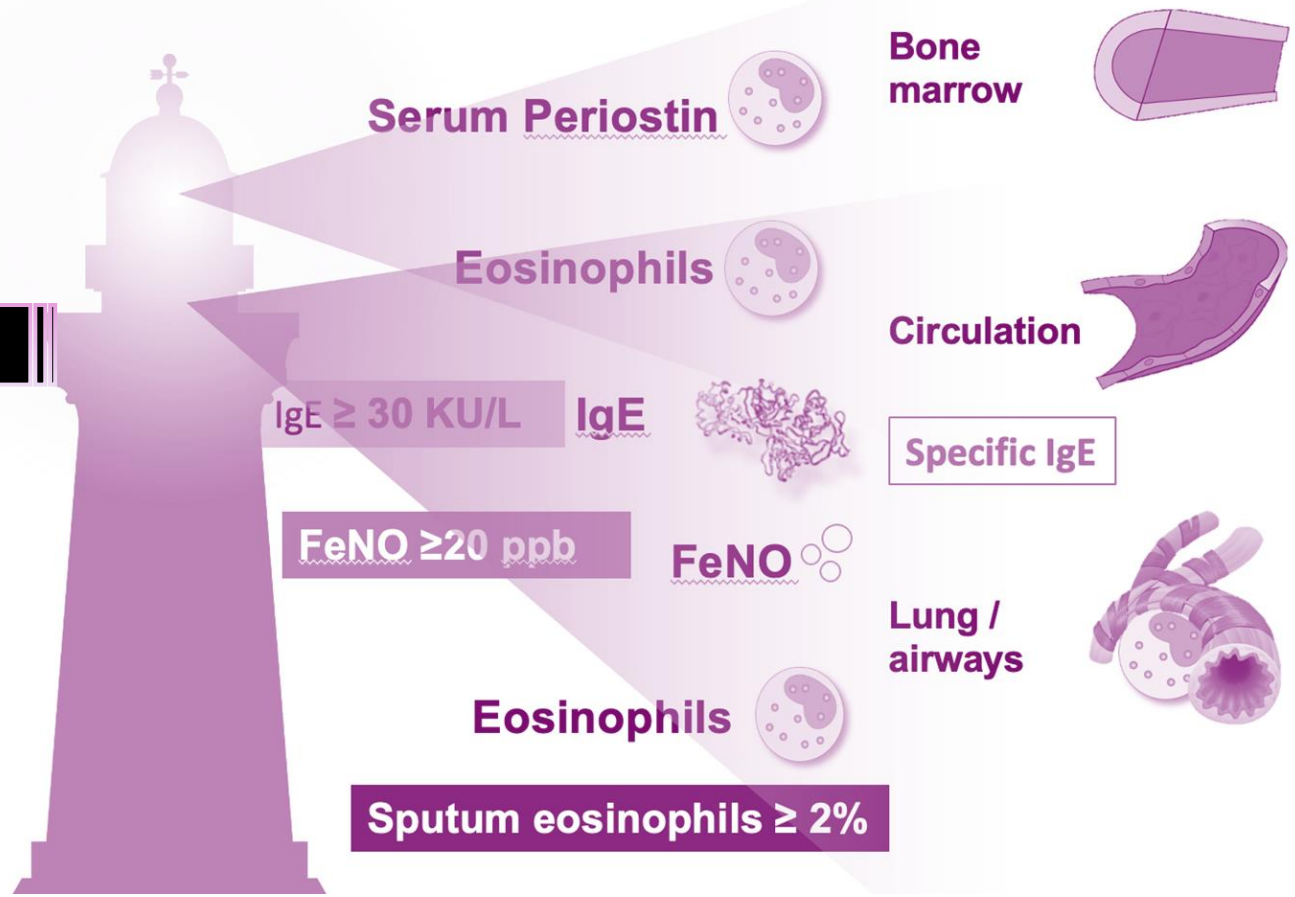
Identify T 2 High Asthma- *Biomarkers !*

Type 2 Inflammation*

- **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; Sidhu et al. Proc Natl Acad Sci USA 2010; 107:14170–14175; Suresh et al. Am J Respir Cell Mol Biol 2007; 37:97-104

Type 2 Severe Asthma India ~ 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

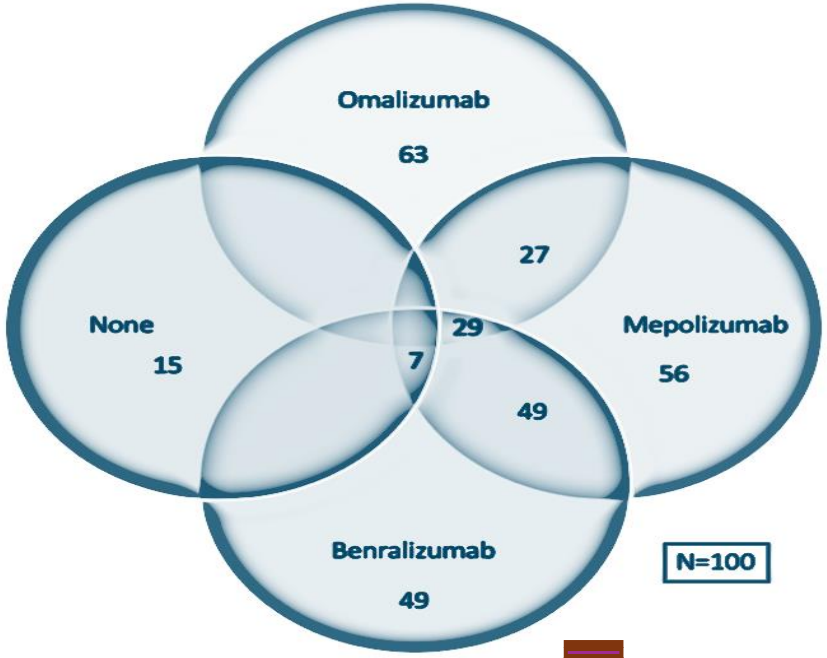
Deepak Talwar[1], Dhruv Talwar[2], Nitin Jain[3], Deepak Prajapat[4], Sourabh Pahuja[4]

[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

Single center, retrospective , observational study:

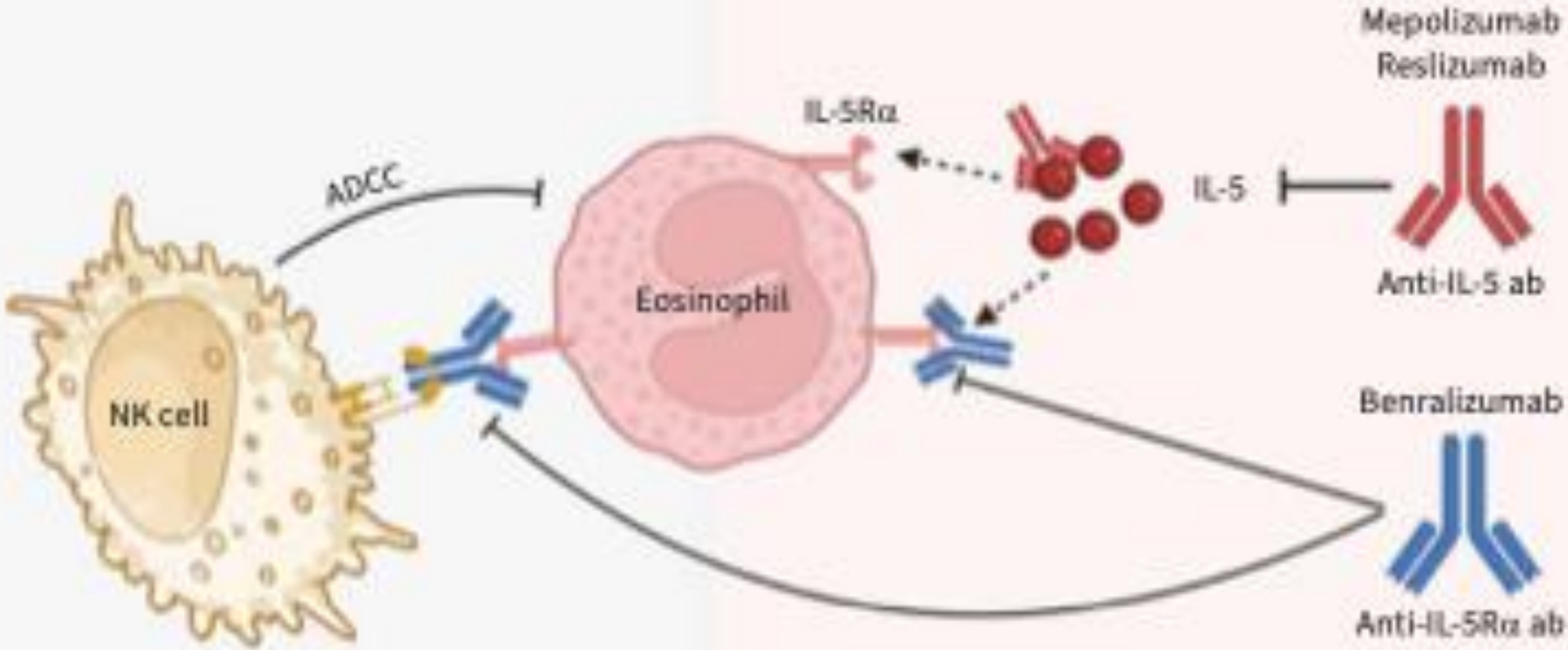
- 100 Adult severe asthmatics from SA Clinic
- Measurements :
  - Total/ Specific IgE
  - AEC
  - Skin prick tests
  - History of allergy,

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

Mepolizumab vs Benralizumab : *Both Anti-IL5 Mabs*



https://doi.org/10.1183/16000617.0088-2024

Remember : Match Expectations with 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 CRwNP	Childhood onset,, AEC ≥300, FeNo > 19.5, S Periostin >50 ng/ml, ↓FEV_1	Low mOCS, Later onset SA, ↓ BMI, AEC, ↑ Sputum Eos /AE	AEC, FEV_1<65%, mOCS, 'f' Exacerbations, AR

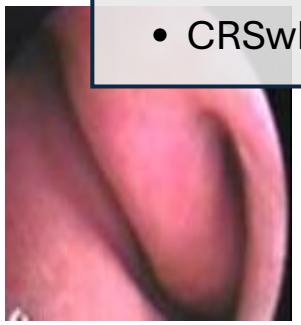
Choosing Biologicals in SA - 2025 !

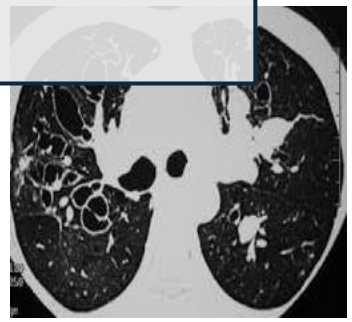
Omalizumab

Childhood Onset asthma

Comorbidities :

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



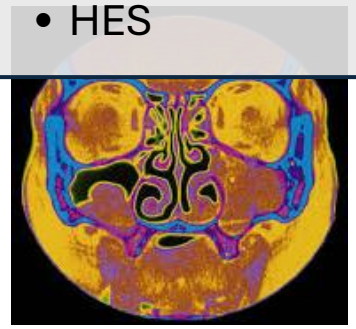
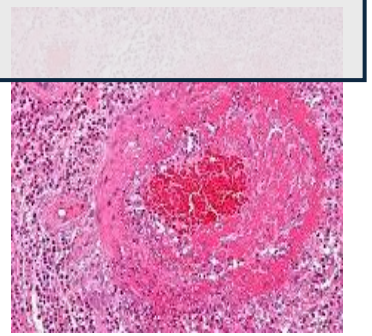


Mepolizumab

Late Onset asthma

Comorbidities :

- Chronic Sinusitis with NP
- EGPA
- HES

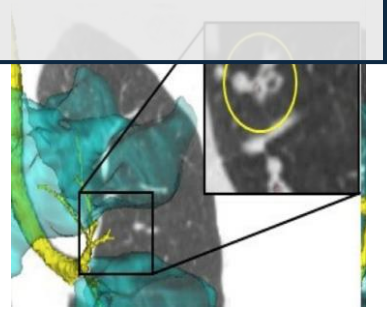



Benralizumab

Adult / Late Onset asthma

Comorbidities :

- Nasal Polyposis
- Airway Mucus
- HES / CEP

NO safety signal has come up with antibodies directed against IL-5 after up to 5 years administration for mepolizumab and > 2 years for Benralizumab

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 **Published:** April 28, 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 Last ***updated: 27 SEP 20***

Assessing Effectiveness of Biologicals : *FU@ 6 months*

Initial Trial for 4 months Minimum

Good /Response

Continue

No standard criteria for good response, but consi

- Symptom burden
- Exacerbations
- Treatment side effects
- Lung function
- Treatment intensity
- Patient satisfaction/concerns

Poor response

- Stop biologic
- Switch to a different biologic or T2-targeted therapy

Unclear response

- Extend trial to 6-12 mo

How to Treat Non-Type 2 SA - *GINA 2024* !

No Allergies

↓

Non-Type 2 Asthma?

- Check AEC - 3 times
- At least 1-2 weeks after stopping OCS
- Lowest possible dose of OCS

Dupulimab

On Maintenance OCS

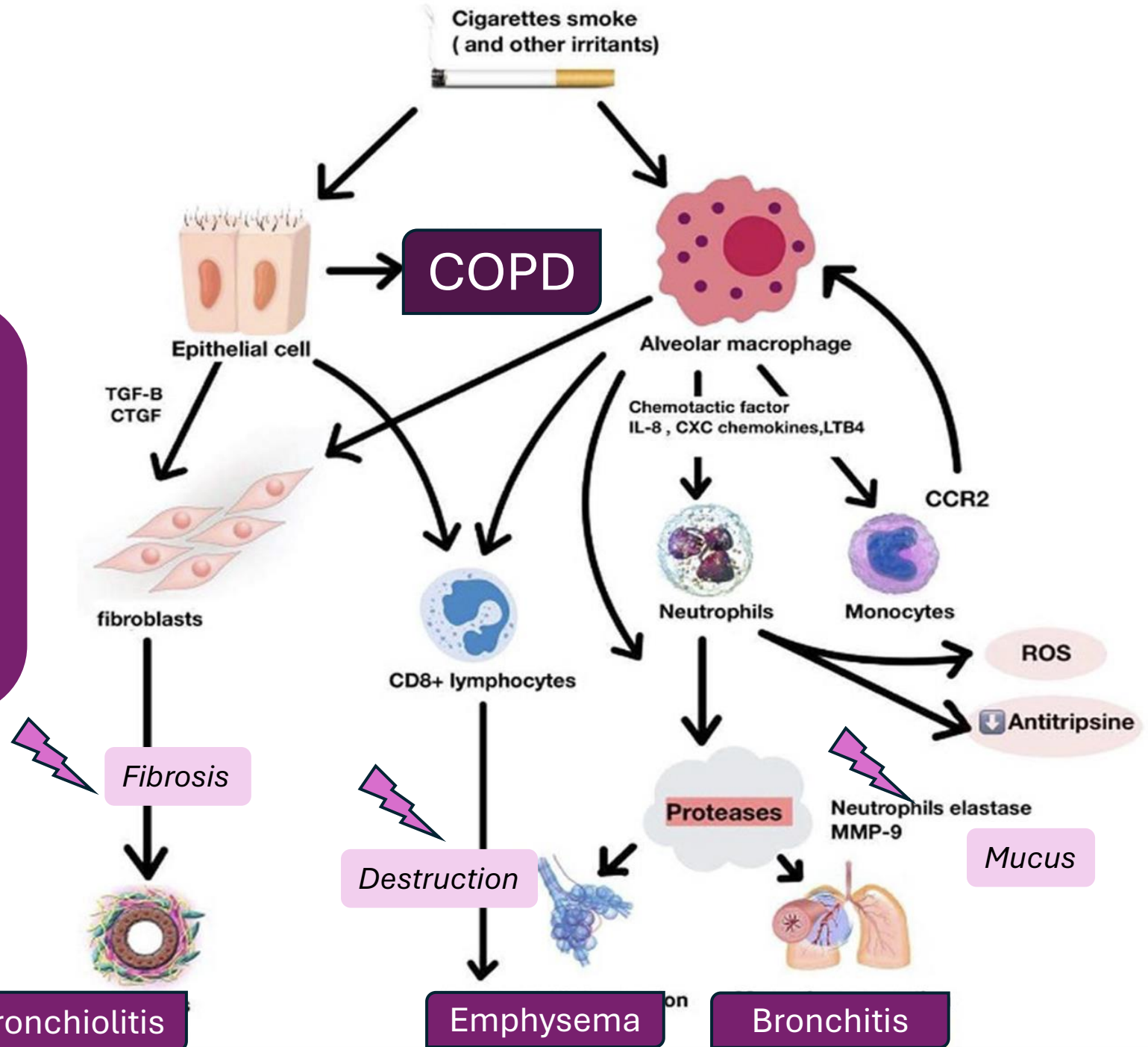
Consider

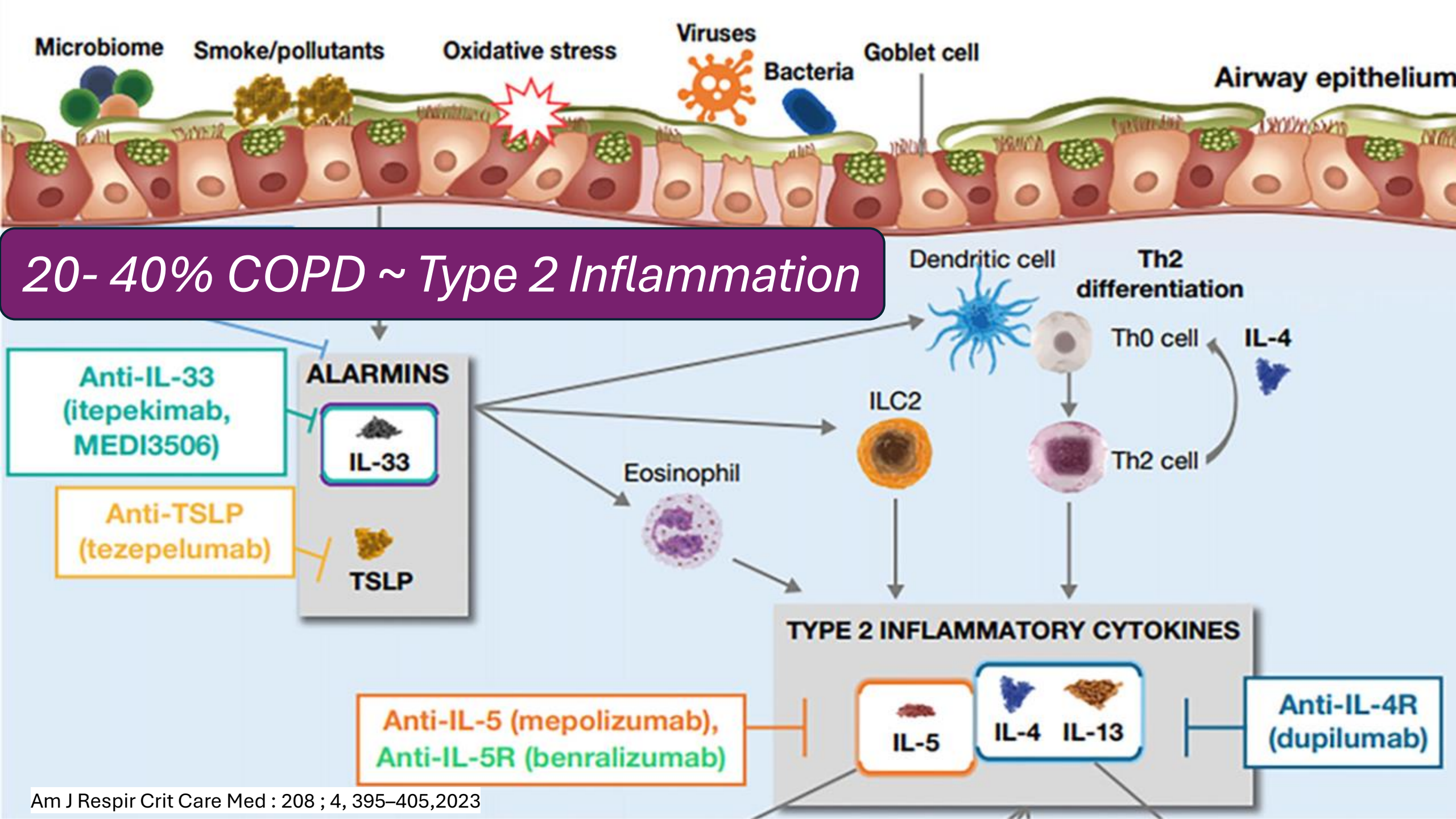
Tezepelumab

Not on Maintenance OCS

GINA 2024

COPD
'Different Biological Pathways'





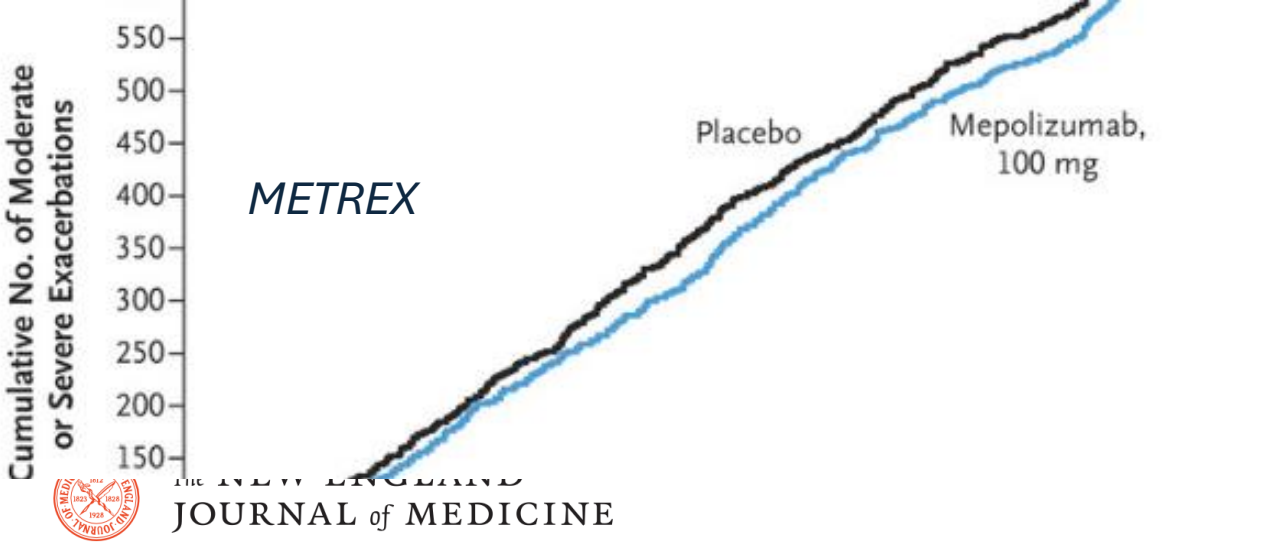
Am J Respir Crit Care Med : 208 ; 4, 395–405,2023

Biologicals in COPD :
Anti IL-5 -Mepolizumab

METREX & METREO

3 More Ongoing Trials

SUMMER
MATINEE
&
COPD-HELP



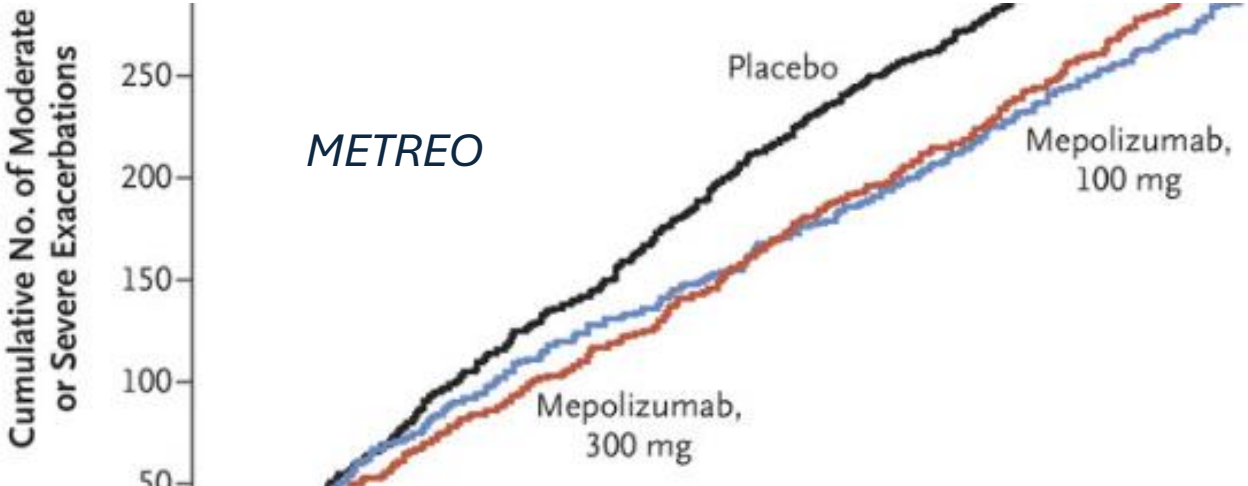
JOURNAL of MEDICINE

ORIGINAL ARTICLE

Mepolizumab for Eosinophilic Chronic Obstructive Pulmonary Disease

14-20% reduction

Authors: Ian D. Pavord, D.M., Pascal Chanez, M.D., Ph.D., Gerard J. Criner, M.D., Huib A.M. Kerstjens, M.D., Ph.D., Stephanie Korn, M.D., Ph.D., Njira Lugogo, M.D., Jean-Benoit Martinot, M.D., +7, and Frank C. Sciurba, M.D. Author Info & Affiliations



Benralizumab: *Anti IL - 5r Blocking Monoclonal antibody*

International Journal of Chronic Obstructive Pulmonary Disease Dovepress
open access to scientific and medical research
Open Access Full Text Article SHORT REPORT

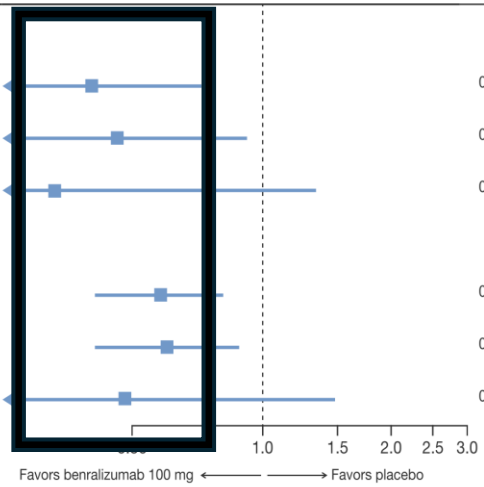
Benralizumab Prevents Recurrent Exacerbations in Patients with Chronic Obstructive Pulmonary Disease: A Post Hoc Analysis

Dave Singh[1], Gerard J Criner[2], Alvar Agusti[3], Mona Bafadhel[4], Johan Söderström[5], Gabriela Luporini Saraiva[6], Yue Song[6], Idlir Licaj[7], Maria Jison[6], Ubaldo J Martin[6], Ioannis Psallidas[8]

- Subgroup of COPD with:
  - ≥ 3 exacerbations on Triple therapy
  - Baseline AEC ≥ 300
- Benralizumab (100 mg/month) reduces risk of exacerbations @ 30- and 90-days post exacerbation (vulnerable period)

Exploratory post hoc analysis of the GALATHEA and TERRANOVA trials

	Exacerbation events		Crude rate		Rate ratio (95% CI)	*p* values
	Benralizumab	Placebo	Benralizumab	Placebo		
30 days						
Moderate/severe	14	62	1.67	4.55	0.40 (0.22, 0.72)	0.0022
Moderate	11	45	1.31	3.30	0.46 (0.24, 0.91)	0.0247
Severe	3	17	0.36	1.25	0.33 (0.08, 1.30)	0.1133
90 days						
Moderate/severe	48	127	1.93	3.74	0.58 (0.41, 0.81)	0.0017
Moderate	40	103	1.61	3.03	0.60 (0.41, 0.87)	0.0071
Severe	8	24	0.32	0.71	0.48 (0.16, 1.43)	0.1862



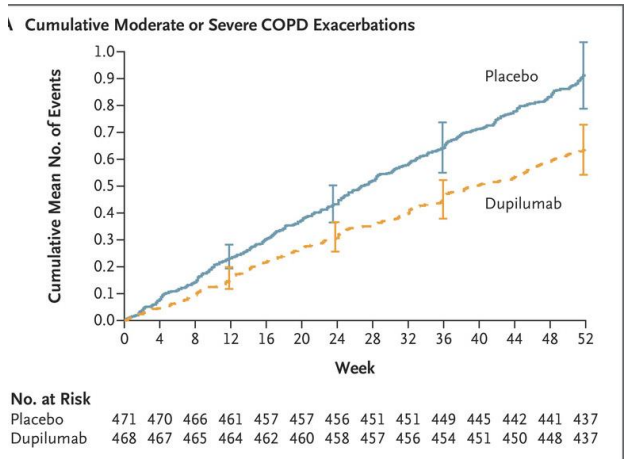
RESOLUTE - recruiting

International Journal of Chronic Obstructive Pulmonary Disease 2023:18

Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts

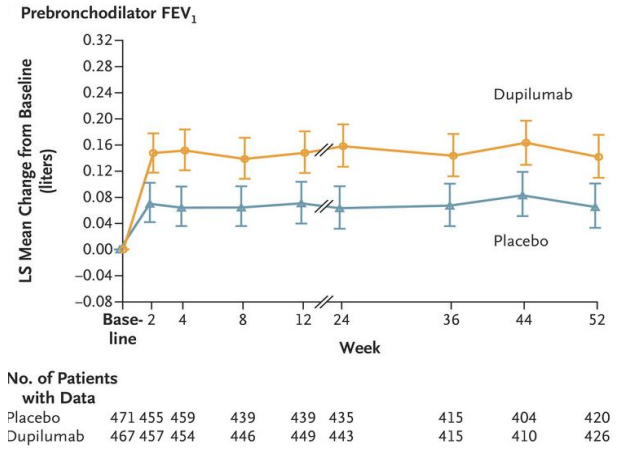
Surya P. Bhatt, M.D., M.S.P.H., Klaus F. Rabe, M.D., Ph.D., Nicola A. Hanania, M.D., Claus F. Vogelmeier, M.D., Jeremy Cole, M.D., Mona Bafadhel, M.D., Ph.D., Stephanie A. Christenson, M.D., Alberto Papi, M.D., Dave Singh, M.D., Elizabeth Laws, Ph.D., Leda P. Mannent, M.D., Naimish Patel, M.D., et al., for the BOREAS Investigators*

- Phase 3, double-blind, randomized trial
- COPD who had a blood eosinophil count of at least 300 per uml and an elevated exacerbation risk despite use of standard triple therapy
- Dupilumab (300 mg) or placebo subcutaneously once every 2 weeks



COPD with T2 inflammation (AEC ≥ 300) had fewer exacerbations, better lung function and QoL, and less severe respiratory symptoms

- 30% reduction in exacerbations
- 160 ml FEV_1



ATS 2024

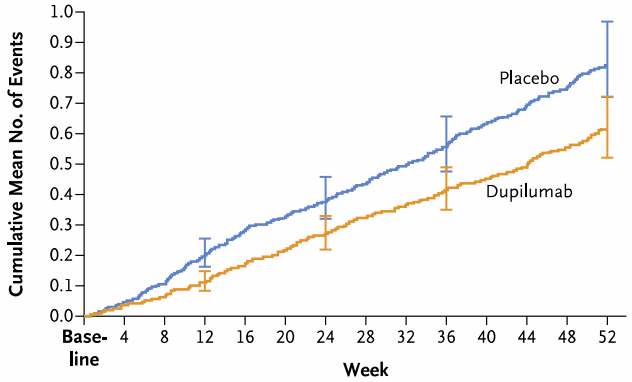
DUPIXENT's Symphony:
Raising the Curtain on the NOTUS COPD Trial

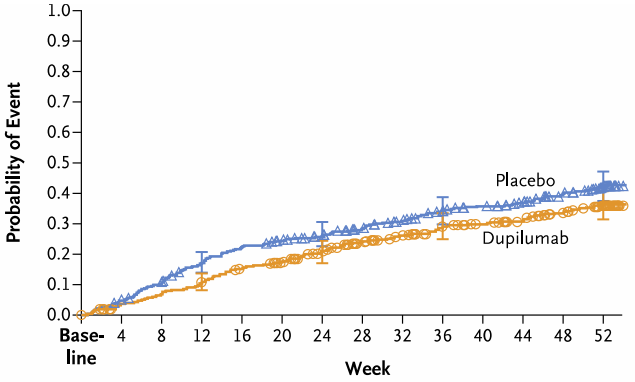
Read More

Dupilumab for COPD with Blood Eosinophil Evidence of Type 2 Inflammation

Authors: Surya P. Bhatt, M.D., M.S.P.H., Klaus F. Rabe, M.D., Ph.D., Nicola A. Hanania, M.D., Claus F. Vogelmeier, M.D., Mona Bafadhel, M.D., Ph.D., Stephanie A. Christenson, M.D., Alberto Papi, M.D. , +11 , for the NOTUS

NOTUS, Dupilumab reduced exacerbations by a magnitude never seen before with an investigational biologic in a phase 3 COPD clinical study



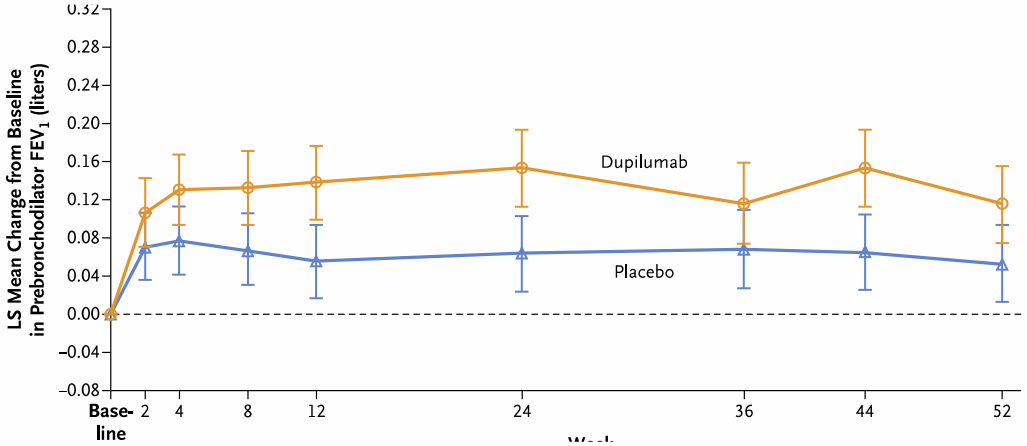


DOI: 10.1056/NEJMoa2401304

- 34% reduction in exacerbations
- 139 ml FEV_1
- ↑ Symptoms
- ↑ SGRQ

No Effect of

Age
Sex
Smoking
FEV1
Emphysema
Exacerbations



Biologicals in COPD: *Finally Wait is Over*

The NEW ENGLAND JOURNAL of MEDICINE

Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts

Surya P. Bhatt, M.D., M.S.P.H., Klaus F. Rabe, M.D., Ph.D., Nicola A. Hanania, M.D., Claus F. Vogelmeier, M.D., Jeremy Cole, M.D., Mona Bafadhel, M.D., Ph.D., Stephanie A. Christenson, M.D., Alberto Papi, M.D., Dave Singh, M.D., Elizabeth Laws, Ph.D., Leda P. Mannent, M.D., Naimish Patel, M.D., et al., for the BOREAS Investigators*

Published July 19, 2023 N Engl J Med 2023;389:274-275 D

EDITORIAL FREE PREVIEW

Biologics for COPD — Finally Here

Alvar Agusti, M.D., Ph.D.

Dupilumab for COPD with Blood Eosinophil Evidence of Type 2 Inflammation

Authors: Surya P. Bhatt, M.D., M.S.P.H., Klaus F. Rabe, M.D., Ph.D., Nicola A. Hanania, M.D., Claus F. Vogelmeier, M.D., Mona Bafadhel, M.D., Ph.D., Stephanie A. Christenson, M.D., Alberto Papi, M.D. , +11 , for the NOTUS

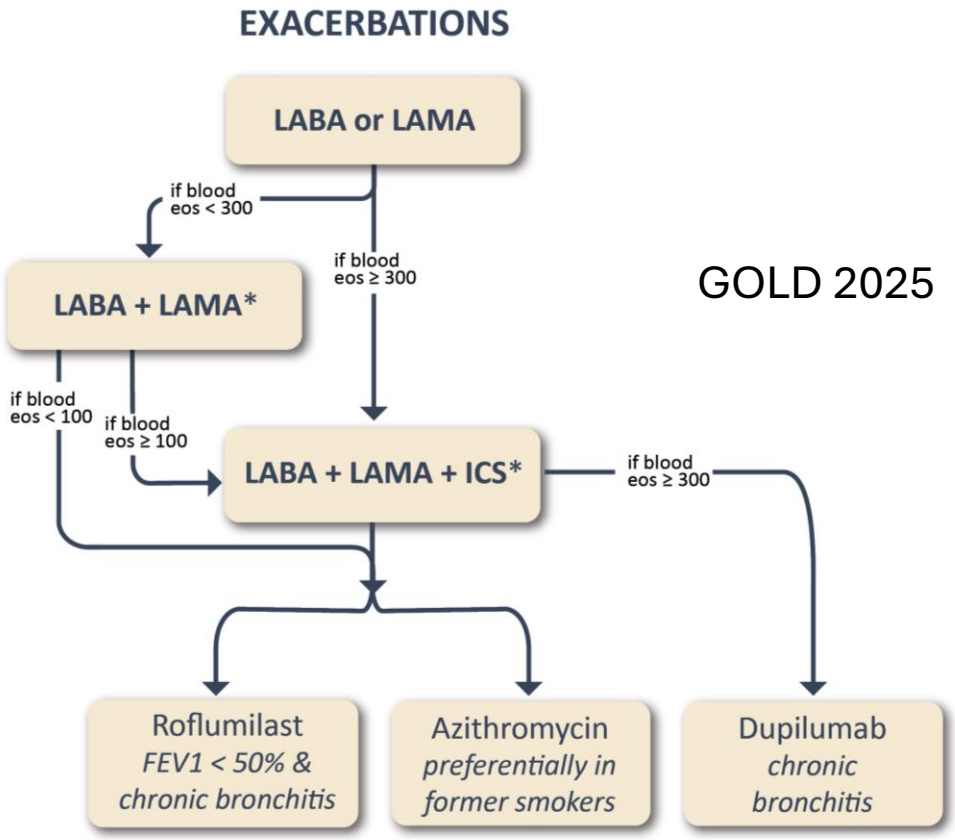
Published May 20, 2024 DOI: 10.1056/NEJMoa2401304

COPD with type 2 inflammation (AEC ≥ 300) on dupilumab had fewer exacerbations, better lung function and QoL, and less severe respiratory symptoms than those who received placebo

No Signal for Safety

Biologicals in COPD : Why & When ?

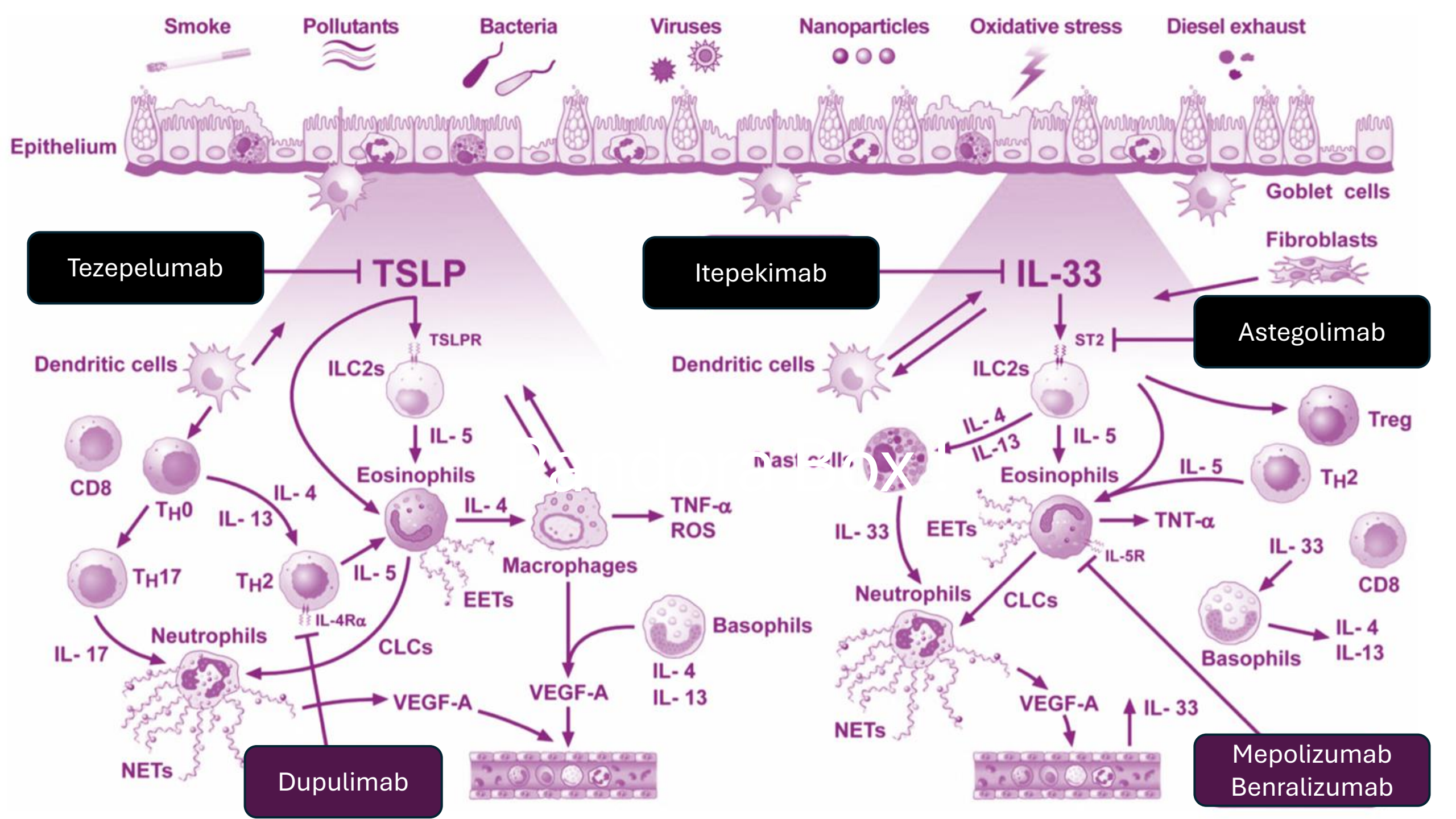
- ~ 67% exacerbate on SITT
- ~ 50% exacerbated despite add on Roflumilast/ Macrolides
- Type 2 inflammation in COPD:
  - ↑ Future risk of exacerbations in 'f' exacerbators
  - Some with both COPD & Asthma (ACO)
- *~ 40% exacerbations in COPD are eosinophilic*



GOLD 2025

Treatable trait : Eosinophilic COPD

European Journal of Internal Medicine 2024.05.011


Smoke
Pollutants
Bacteria
Viruses
Nanoparticles
Oxidative stress
Diesel exhaust
Epithelium
Goblet cells
Fibroblasts
Tezepelumab
TSLP
Itepekimab
IL-33
Astegolimab
ST2
TSLPR
Dendritic cells
ILC2s
IL- 5
Eosinophils
IL- 4
IL- 13
CD8
TH0
TH17
TH2
IL-4Rα
IL- 5
IL- 4
TNF-α
ROS
Macrophages
EETs
Basophils
IL- 4
IL- 13
Neutrophils
IL- 17
CLCs
VEGF-A
NETs
Dupulimab
IL- 4
IL-13
Treg
TH2
IL- 5
IL- 33
EETs
TNT-α
IL-5R
CD8
Basophils
IL- 4
IL-13
NETs
VEGF-A
IL- 33
Mepolizumab
Benralizumab

Treatable Trait in Airway Disease : *Precision Medicine*

Treat to Target in OAD's

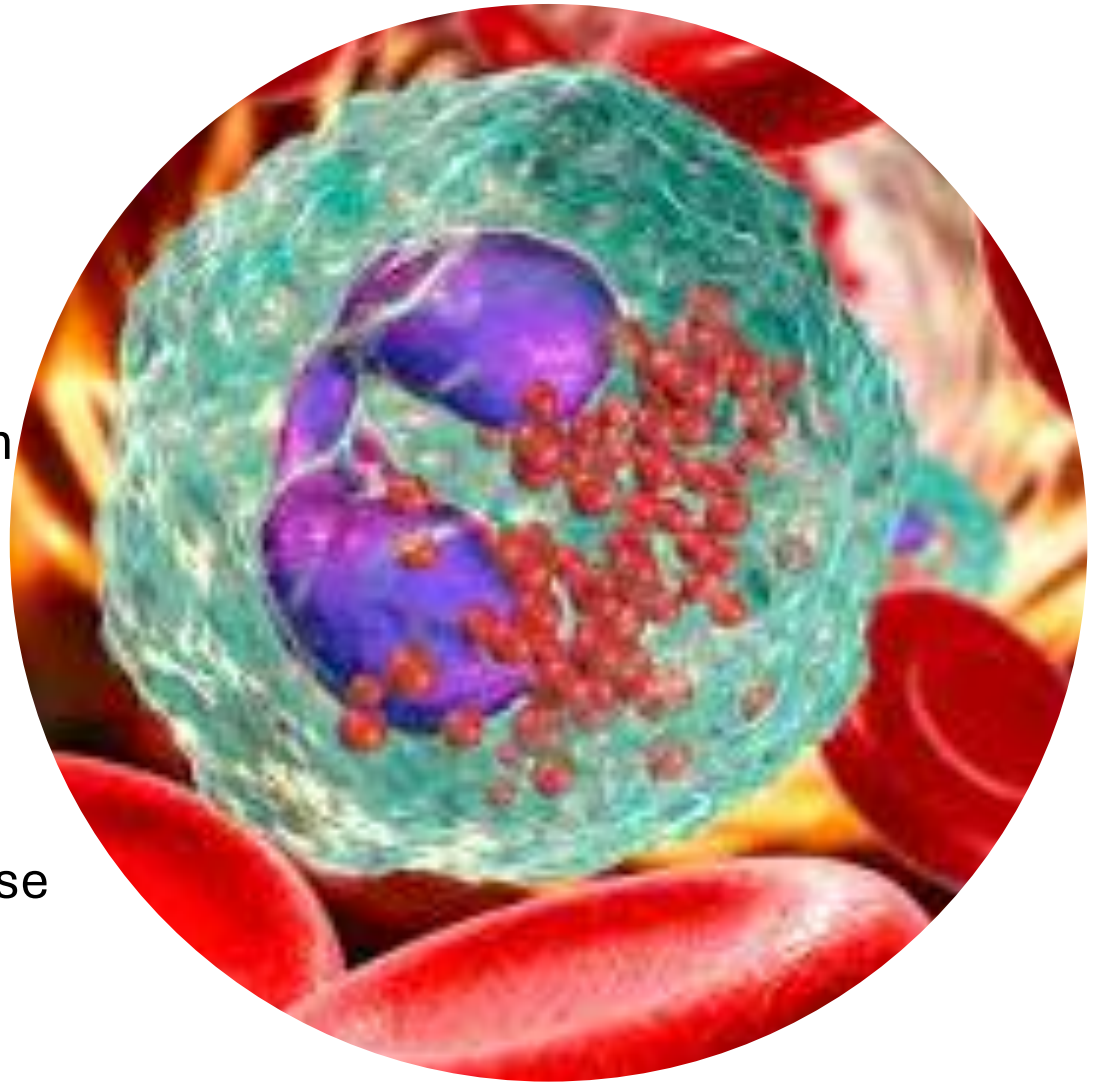
Asthma or COPD

Type 2 Inflammation

On Triple therapy

Poor disease control

Improve disease outcomes



Dr Deepak Talwar

Director & Chair MCRD

Dr Kanishka Kumar Singh

Senior Consultant

Dr Deepak Prajapat

Senior Consultant

Dr Rahul Khera

Consultant

Thank You

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