

Latest Updates in Asthma :

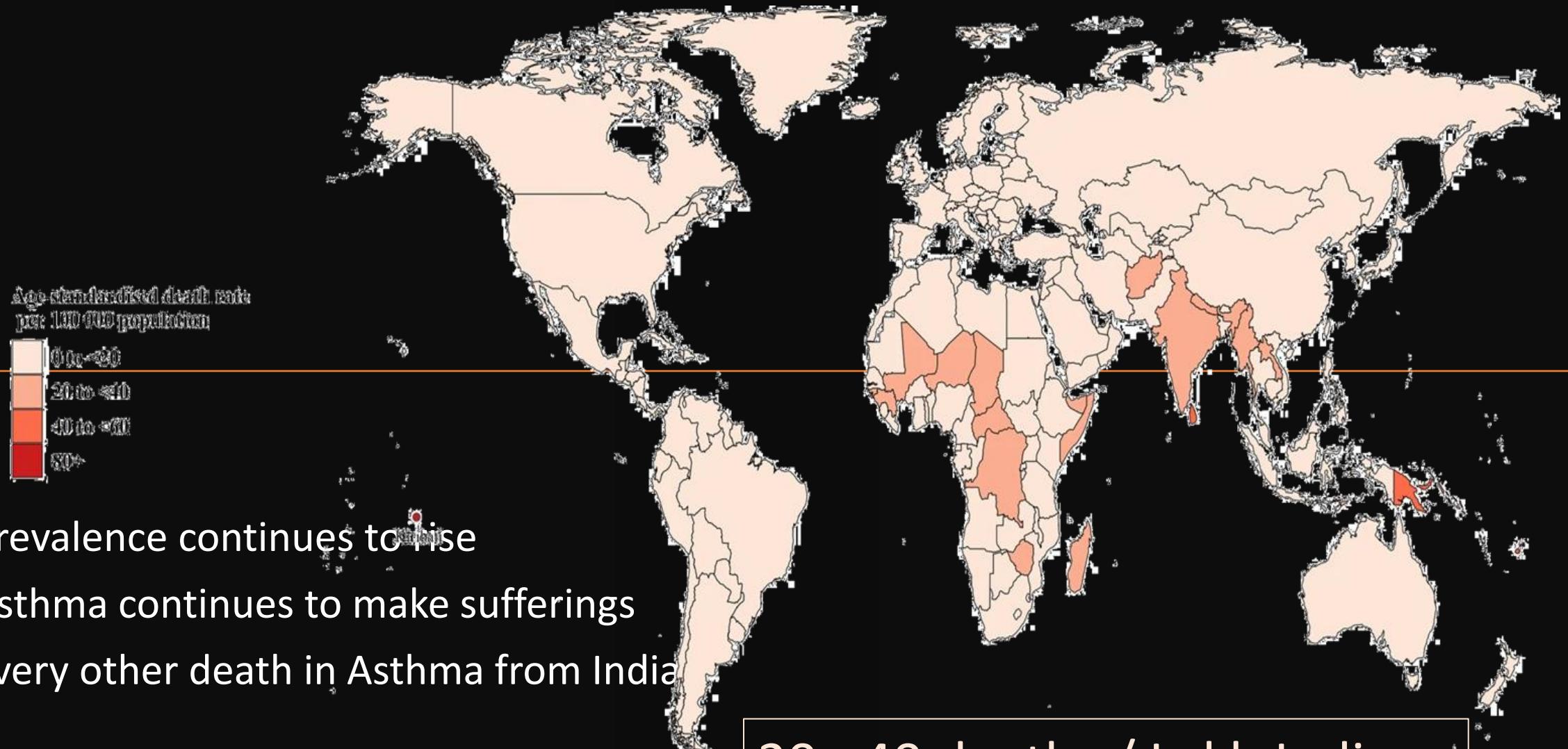
Biologics

Deepak Talwar

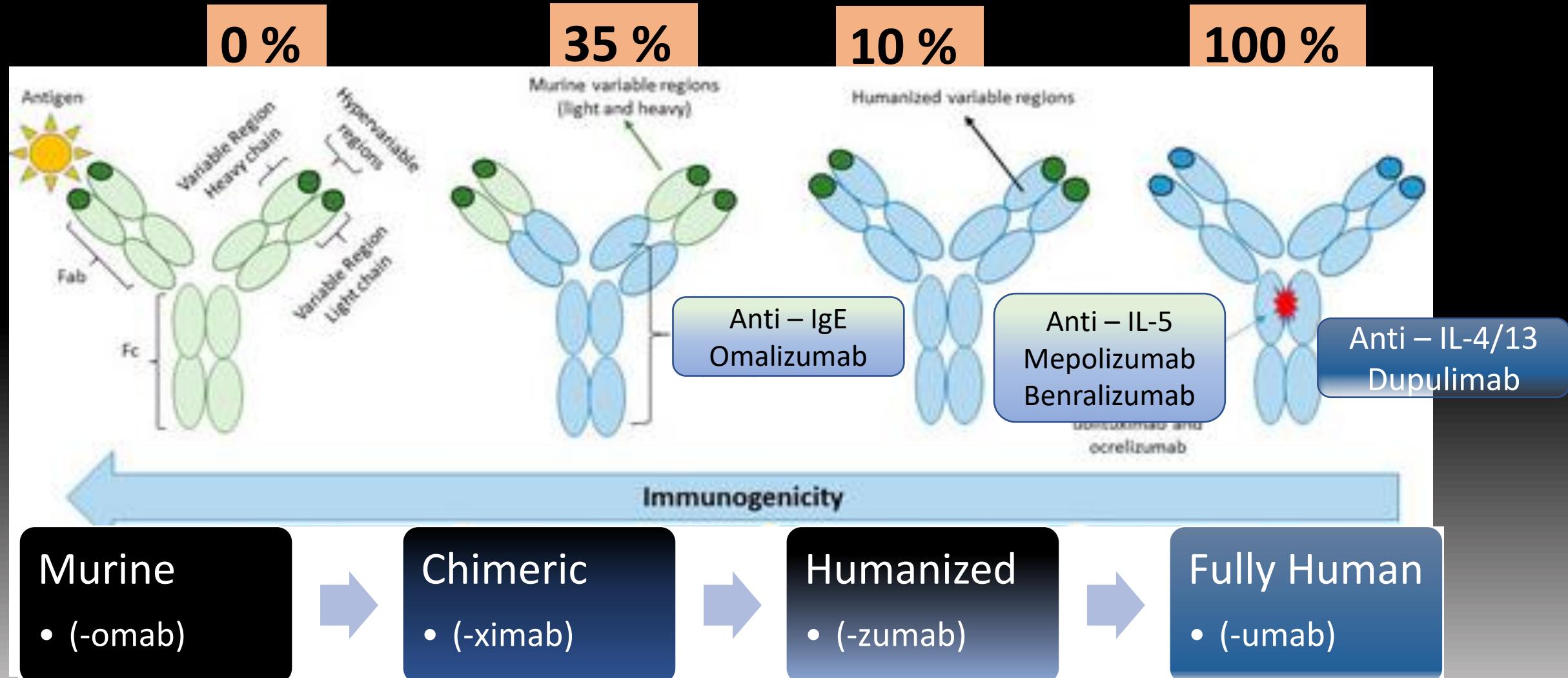
Director & Chair, Metro Centre for
Respiratory Diseases
Metro Hospitals & Institute
NOIDA, INDIA



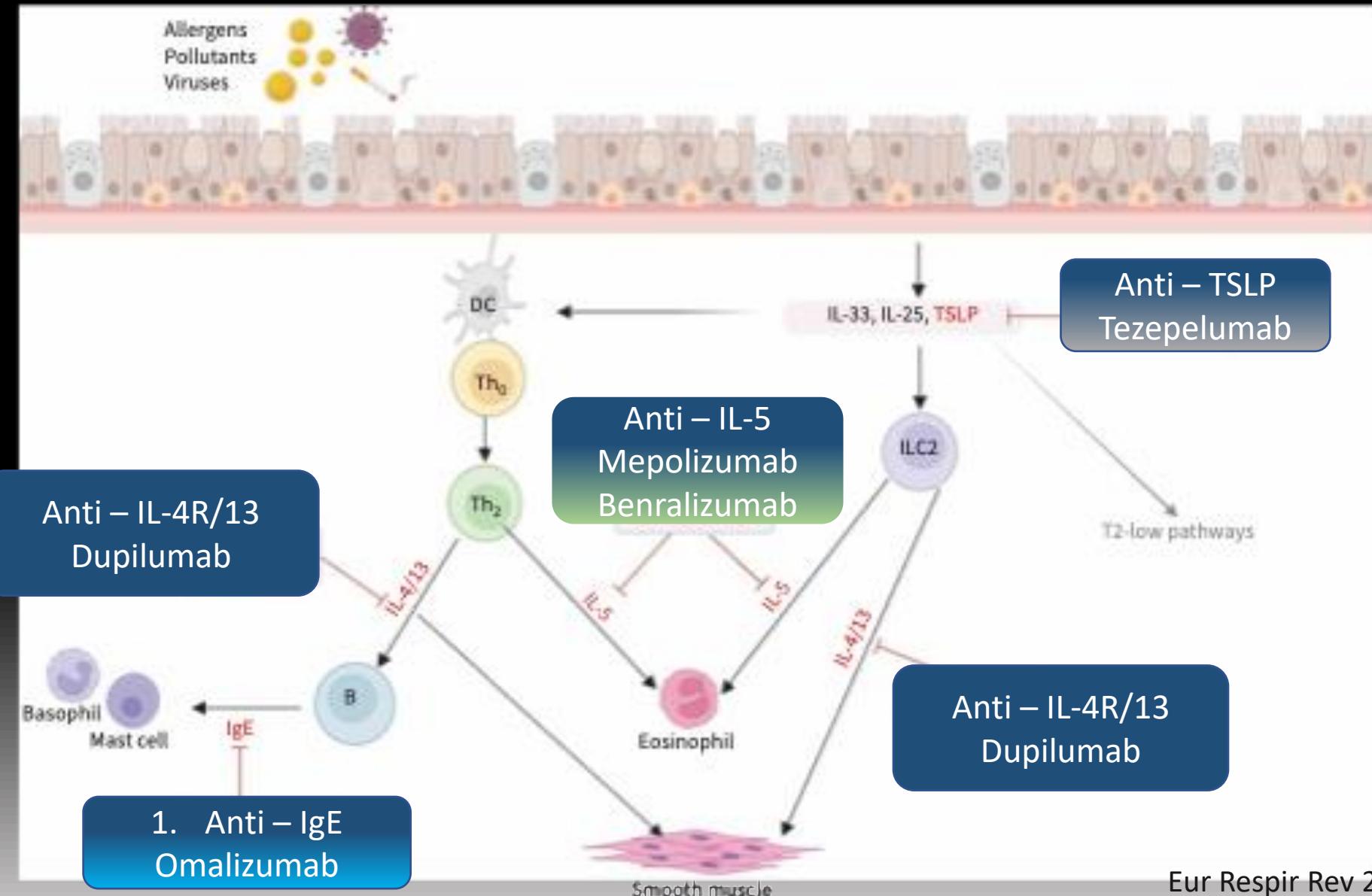
Death Continues to Haunt Asthma



Biologicals : *Targeted Therapies*



4 Biologicals for Airway Diseases



Why ???

NO to OCS !

- Oral steroids were used during the previous year by **89%** of patients
- On average, patients reported using oral steroids **10.5 times in a year.**

When ???

Severe Asthma

Track 1



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

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

Reliever: As-needed ICS-SABA or as-needed SABA

Step 5

Add-on LAMA;
assess phenotype;
consider high-dose
ICS-formoterol^a ±
biologic

Montelukast

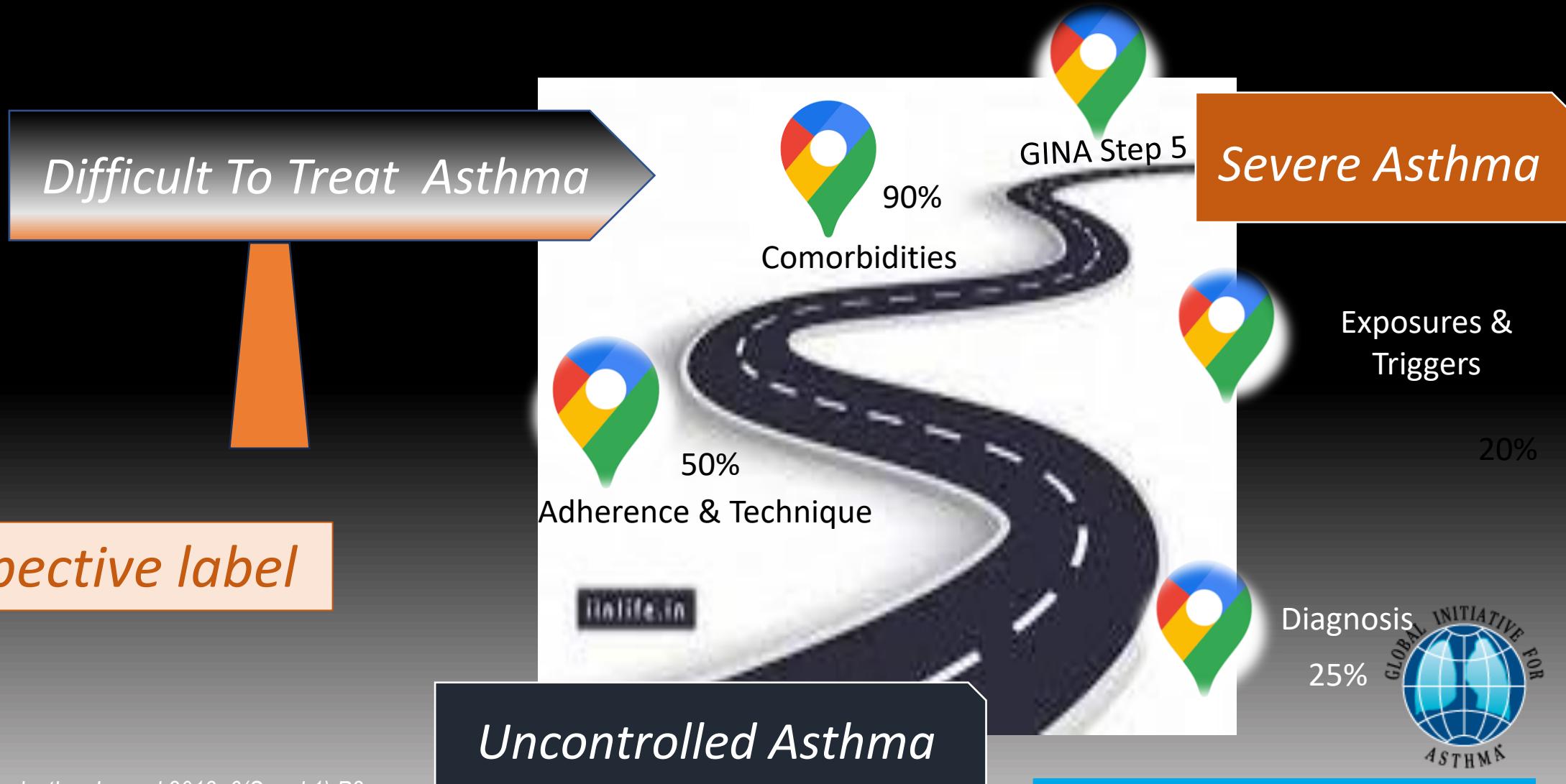
Step 5

Add-on LAMA;
assess phenotype;
consider high-dose
ICS-LABA^a ±
biologic

Other Options

Azithromycin

Remember : All Uncontrolled Asthma is *NOT* Severe Asthma



Which Severe Asthma : 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



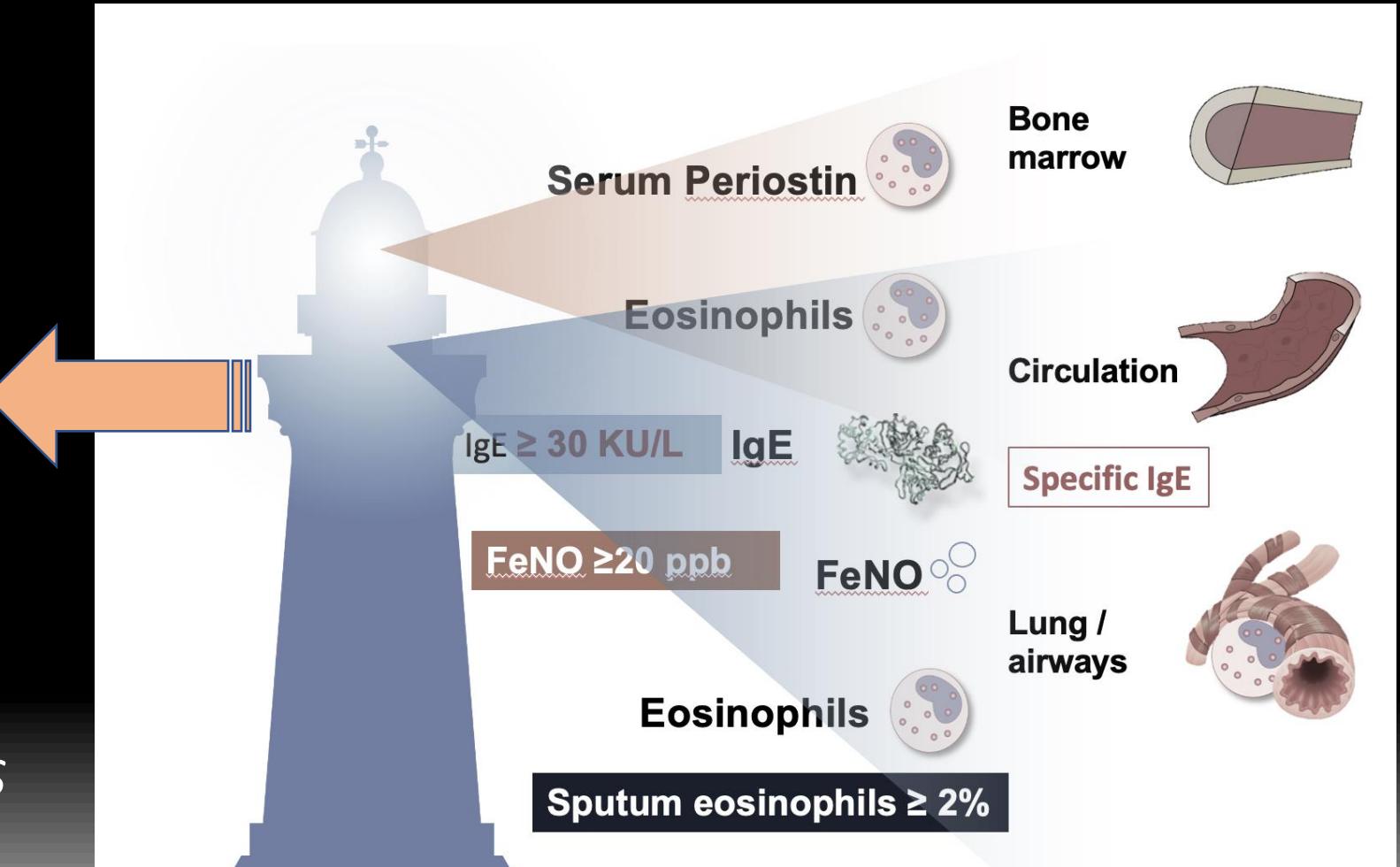
GINA 2023

Identify T 2 Asthma- Biomarkers!

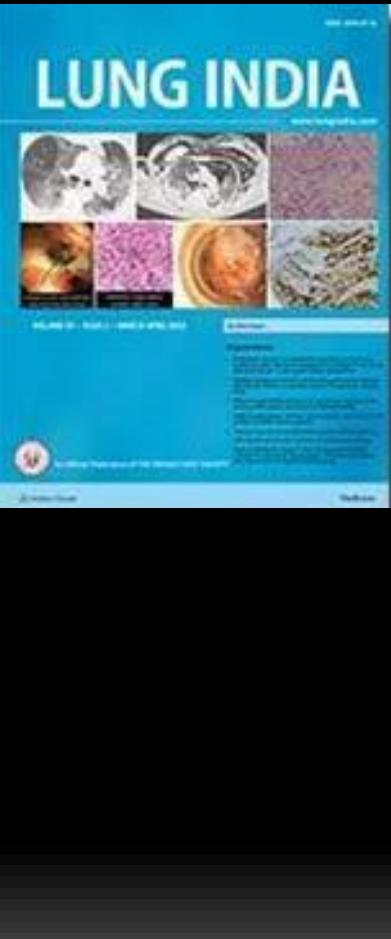
Type 2 Inflammation*

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

* Depends on dose of OCS & ICS



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

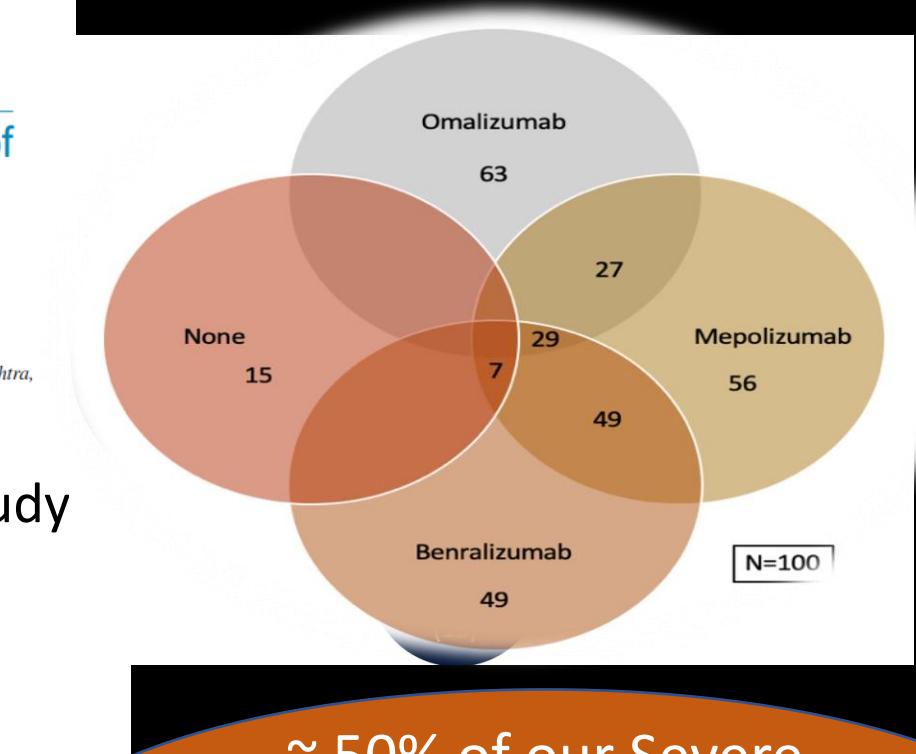
Deepak Talwar¹, Dhruv Talwar², Nitin Jain³, Deepak Prajapat⁴, Sourabh Pahuja⁴

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

Single center, retrospective , observational study

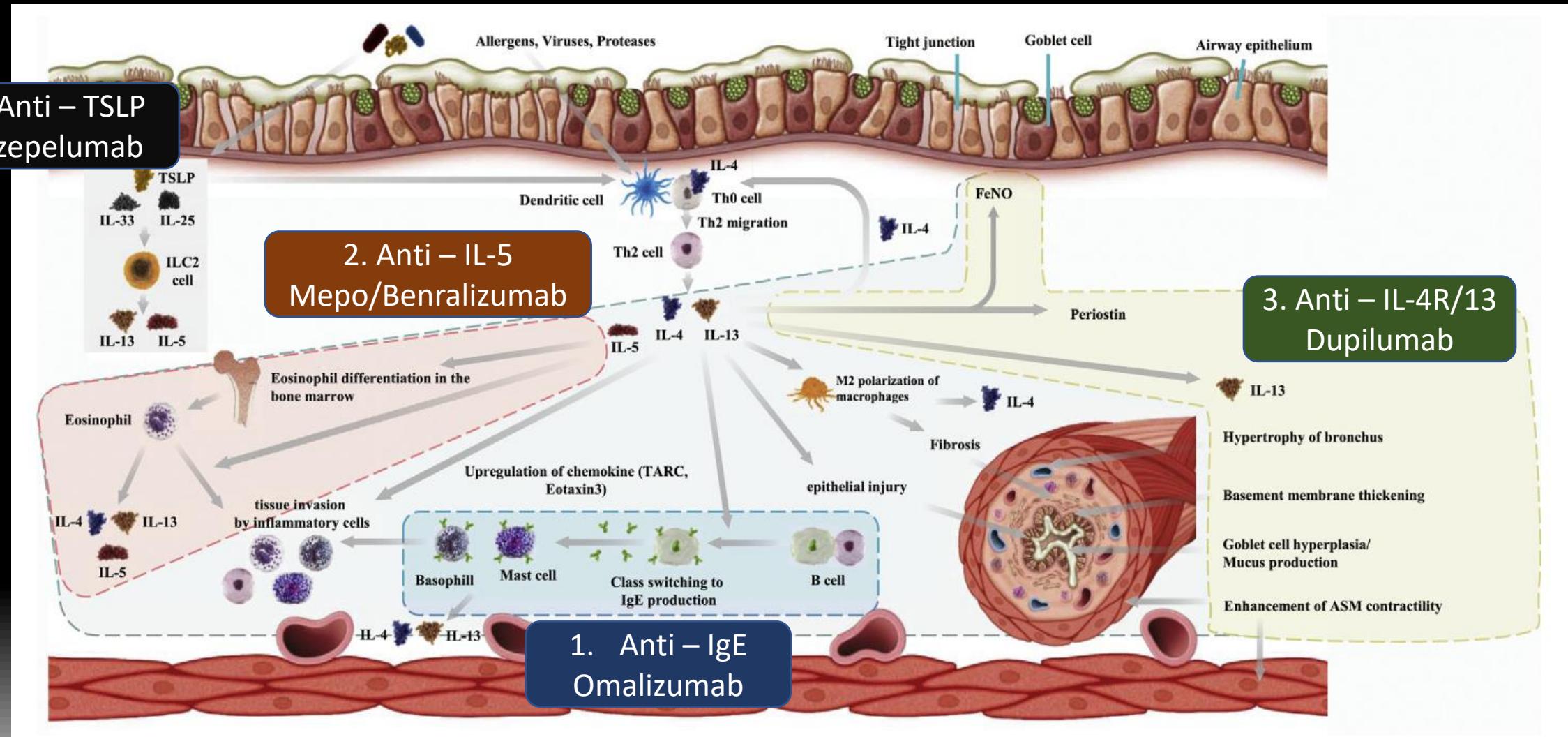
- 100 Adult severe asthmatics from SA Clinic
- Measurements :
 - Total/ Specific IgE
 - AEC
 - Skin prick tests
 - History of allergy,

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

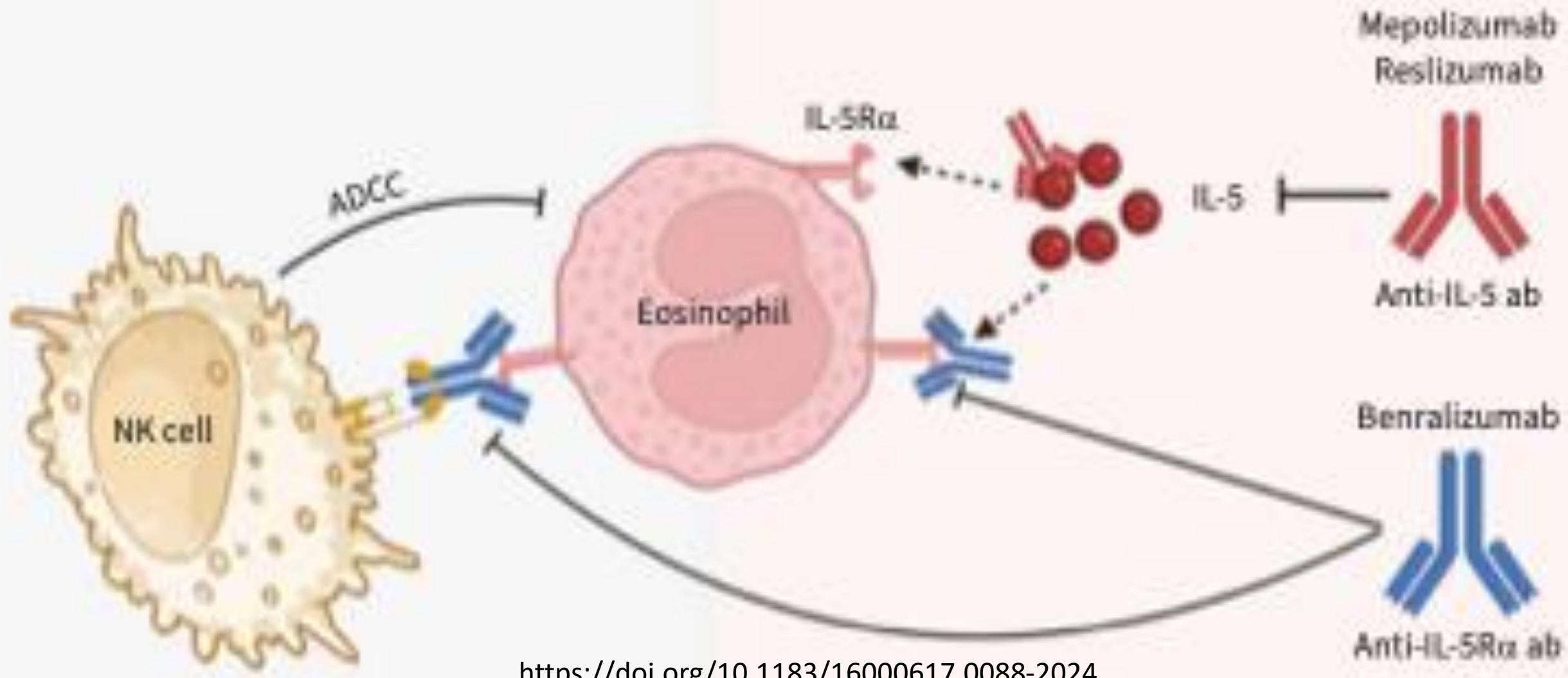


~ 50% of our Severe
Asthmatics were eligible
for both group of
biologics

How ?? : Choose Appropriate Biologicals - *Drivers*



Mepolizumab vs Benralizumab : Both Anti-IL5 Mabs



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 ng/ml, ↓FEV ₁	Low mOCS, Later onset SA, ↓ BMI, AEC, ↑ Sputum Eos /AE	AEC, FEV ₁ <65%, mOCS, 'f' Exacerbations, AR
CRwNP			

Choosing Biologicals in SA - 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

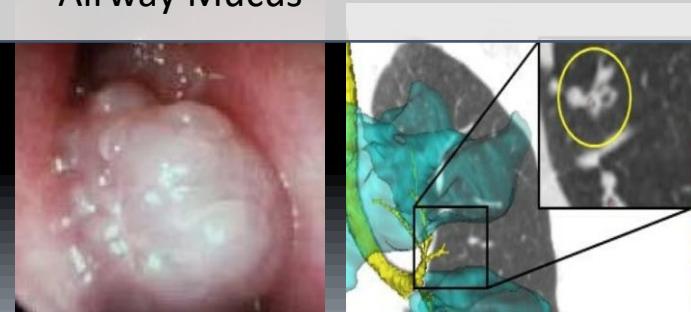
Adult / Late Onset asthma

Biomarkers :

- AEC, Sputum Eosinophils, FeNO

Comorbidities :

- Nasal Polyposis
- Airway Mucus



Patient Preferences : Cost, Reimbursement, Dosing

Biologicals in Severe Asthma- Indian Experience

Journal of Pulmonology Research & Reports

Research Article

ISSN: 2754-4761

F1000Research

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



Open Access

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

Arjun Khanna¹*, Deepak Talwar², Linija K Nair³

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.

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 Yadav², Nagarjuna Maturu³

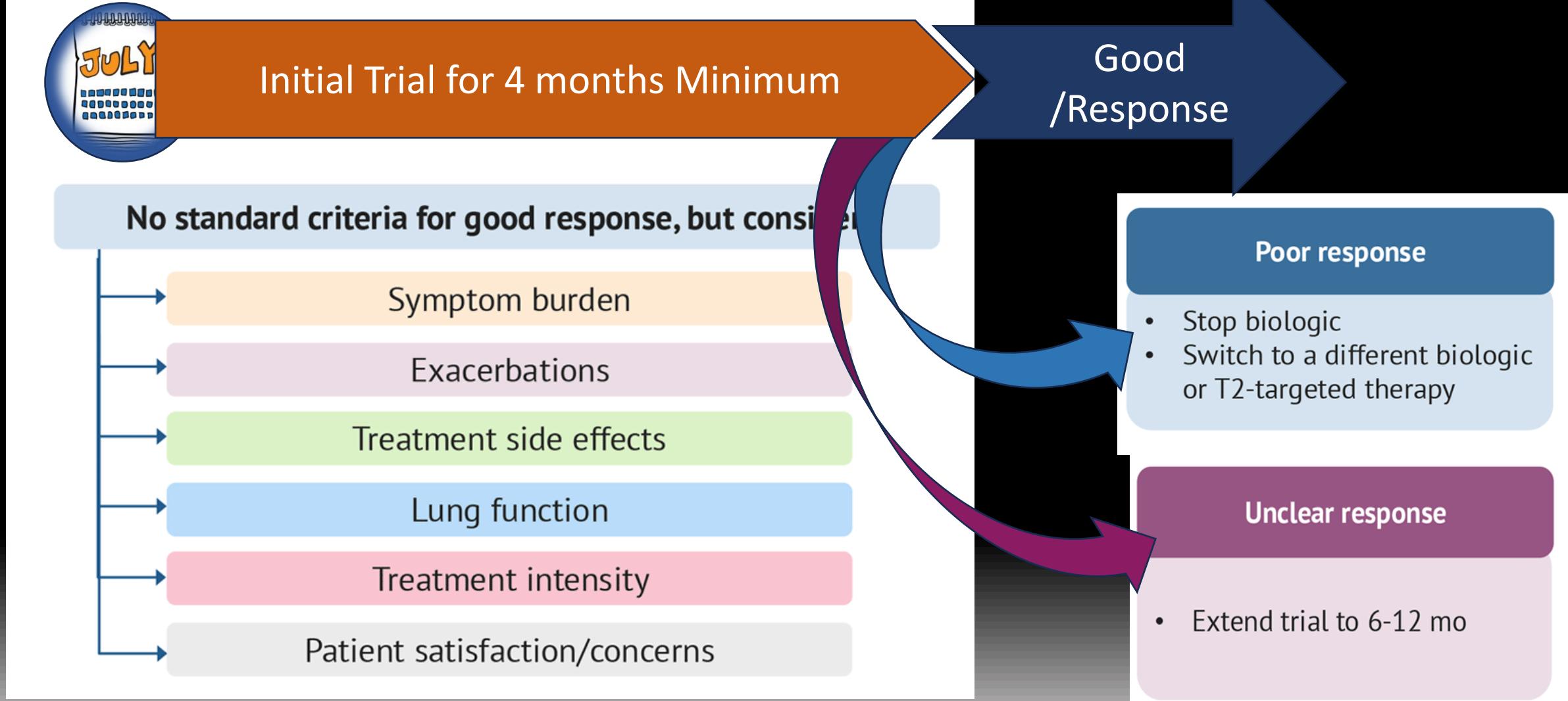
Conclusions:

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

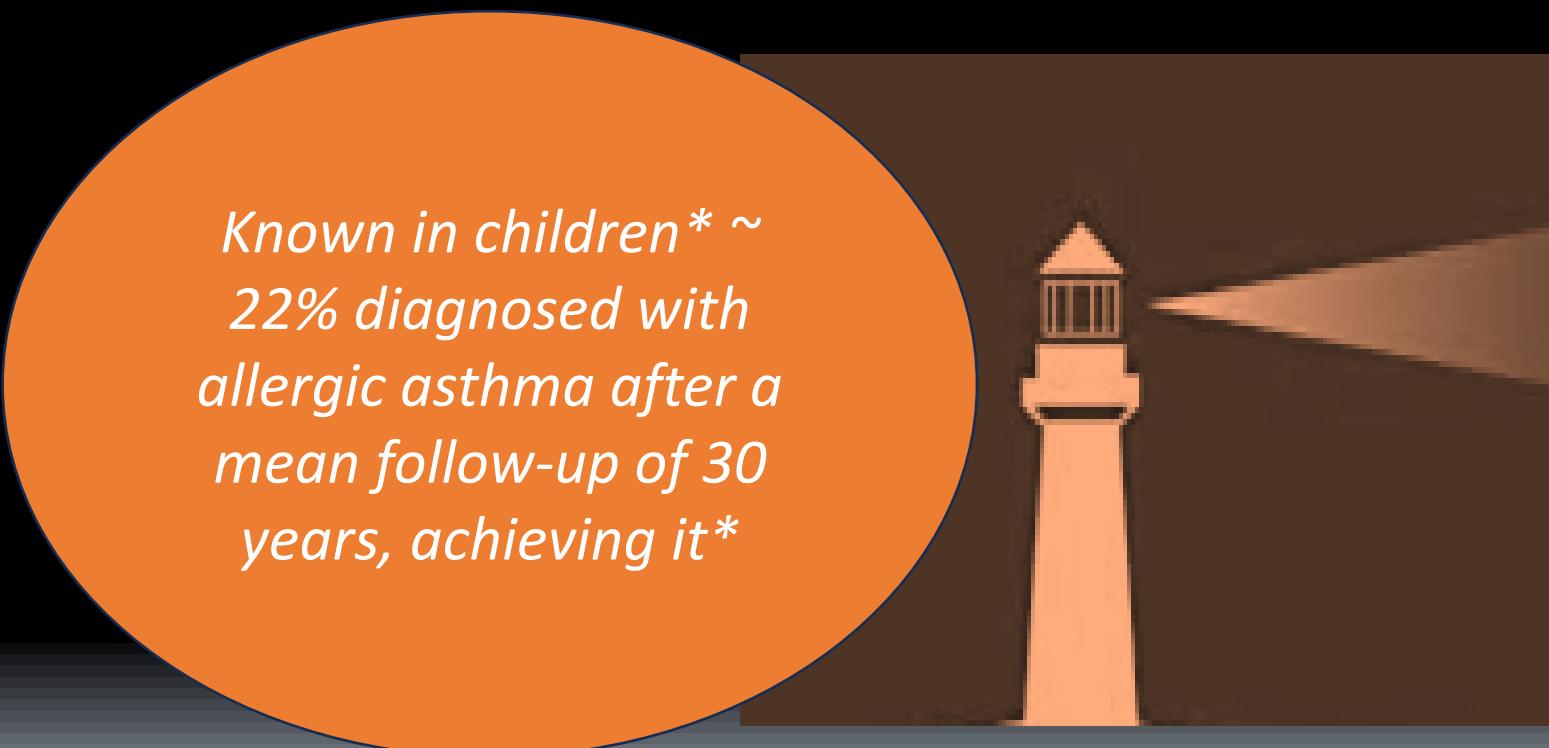


Assessing Effectiveness of Biologicals : FU@ 6 months

GINA 2024



Remission in Asthma : Cure ??



Known in children ~
22% diagnosed with
allergic asthma after a
mean follow-up of 30
years, achieving it**

Mild asthma

Better lung function

Better asthma control

Younger age

Early-onset

Shorter duration

Milder BHR

Fewer comorbidities

Never smoking

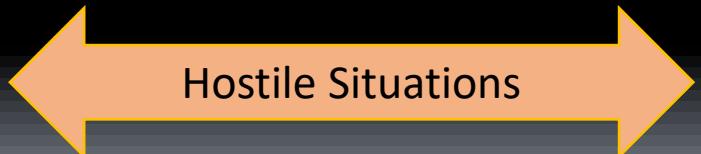
Remission in Severe Asthma : *New Concept*

- Complete or near complete disappearance of signs & symptoms of a disease e.g. cancer
- May last for months, years or rest of life
- Remission on / off treatment



Relapse

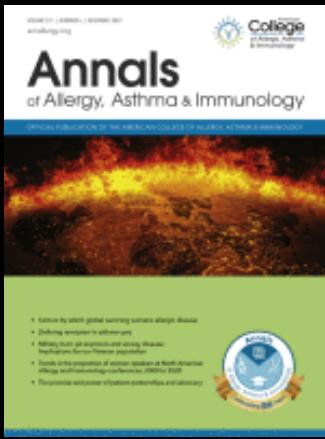
Return of disease
Activity



Flare

Worsening contr.
Exacerbati



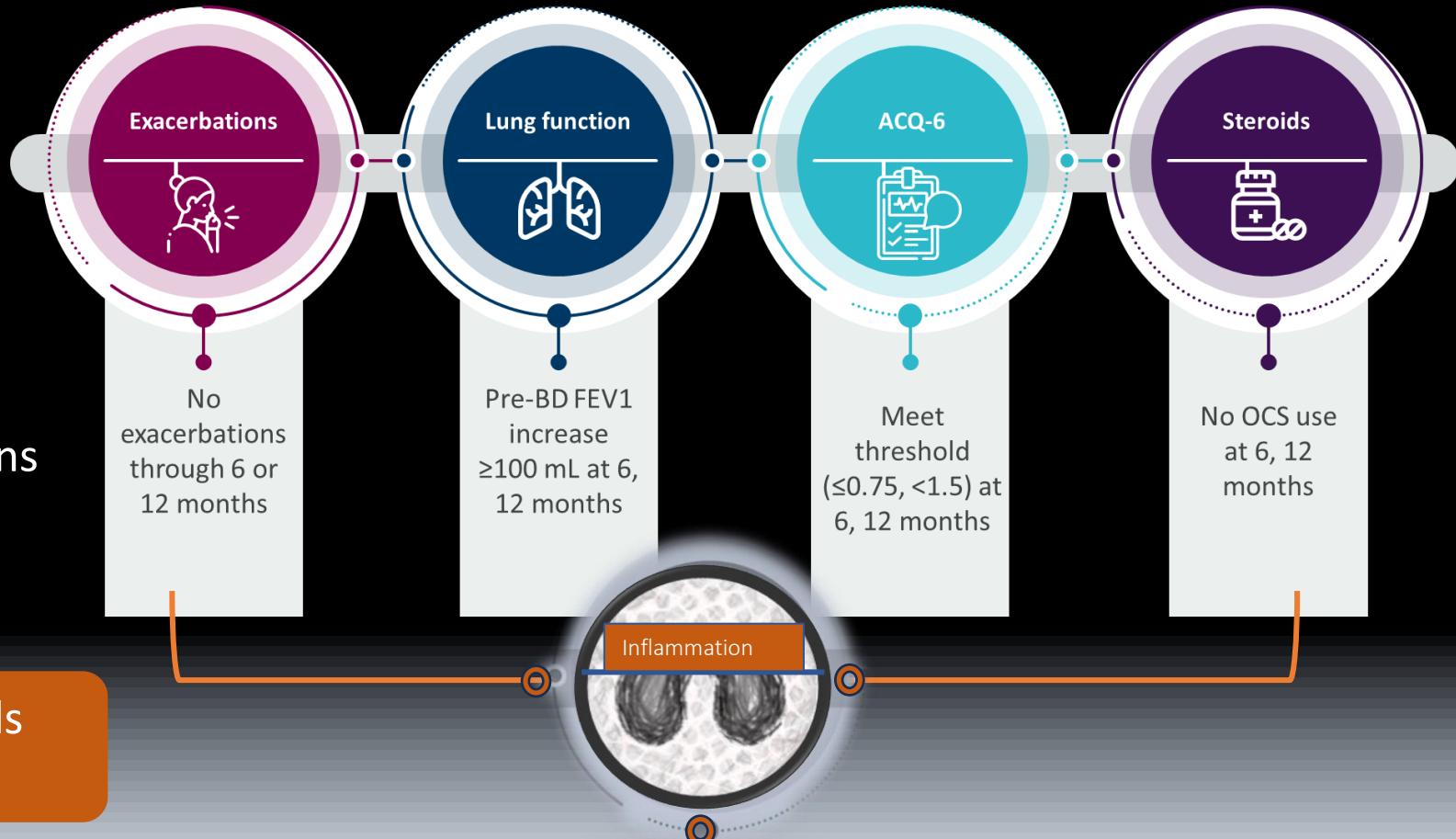


Clinical Remission :

Complete Remission on Treatment / Off Treatment

- No Exacerbations
- No OCS Use
- No Symptoms
- Stable / optimized Lung Functions
- Low Intensity controller T/t

- FeNO, AEC, Sputum eosinophils
- BHR



Clinical Remission in Asthma : FACT !

Criteria for Remission	Dupilumab	Benralizumab			Tezepelumab	Mepolizumab	Multiple Biologics		
	2021 ¹ QUEST Phase 3	2022 ² TRAVERSE OLE	2022 ³ SIROCCO/ CALIMA Phase 3	2022 ⁴ ANDHI Phase 3b	2023 ⁵ XALOC-1	2022 ^{6,7} NAVIGATOR Phase 3	2022 ⁸ REDES	2022 ⁹ CHRONICLE	2022 ¹⁰ Danish Registry
 Absence of symptoms ^{a,b} and	ACQ-5 < 1.5	ACQ-5 < 1.5	ACQ-6 < 1.5 ["] or ≤ 0.75	ACQ-6 < 1.5 ["] or ≤ 0.75	ACQ-5 < 1.5 or ACT ≥ 16	ACQ-6 ≤ 1.5 ^{a,b}	ACT ≥ 20	Majority ≥ (50%) ACT ≥ 20	ACQ ≤ 1.5
 Optimized/stabilized lung function and	Post-BD FEV ₁ pp ≥ 80% OR pre-BD FEV ₁ ≥ 100 mL	Post-BD FEV ₁ ≥ 80% OR pre-BD FEV ₁ ≥ 100 mL	Pre-BD FEV ₁ increase ≥ 100 mL	Pre-BD FEV ₁ increase ≥ 100 mL	Not included	Pre-BD FEV ₁ pp > 80% OR Pre-BD FEV ₁ > 20% from baseline; FEV1 > 95% of baseline ^{**}	Not included	Not included	Post-BD FEV ₁ pp ≥ 80%
 No exacerbations; no OCS ^c	✓	✓	✓	✓	✓	✓ ^d	✓	✓	✓
✓ Prevalence of clinical remission	31.7%	36.4%	26.3% ["]	28.7%	43%	14% [^] - 28.5% ^{**}	37%	35%	19%

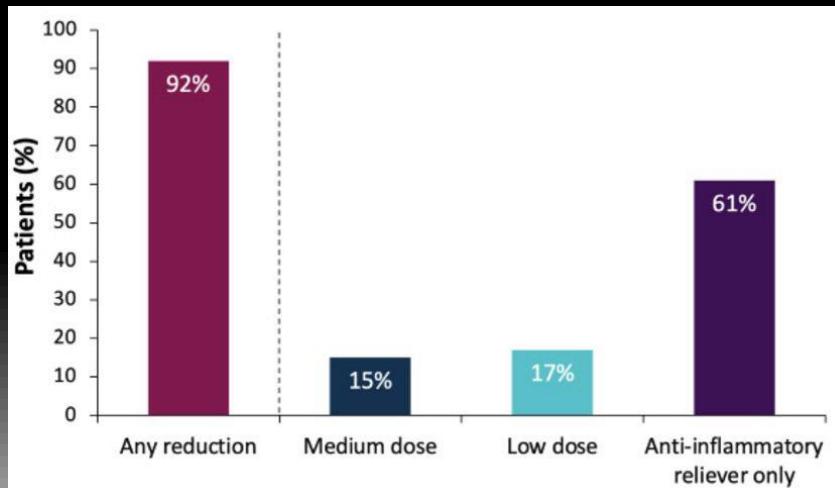
Can SA Patients Transform to Mild Asthma ?

Reduction of daily maintenance inhaled corticosteroids in patients with severe eosinophilic asthma treated with benralizumab (SHAMAL): a randomised, multicentre, open-label, phase 4 study

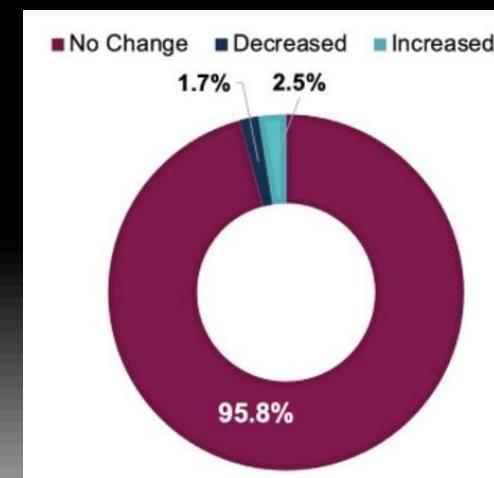
David J Jackson, Liam G Heaney, Marc Humbert, Brian D Kent, Anat Shavit, Lina Hiljemark, Lynda Olinger, David Cohen, Andrew Menzies-Gow, Stephanie Kam, on behalf of the SHAMAL Investigators*

Open Access

DOI: <https://doi.org/10.1136/lancet.2024.409.102181>



92% at 48 weeks had no AE



@ 48 weeks

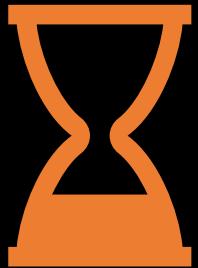
THE LANCET

"Parkinson's disease is the second most common neurodegenerative disease and is an important societal issue and global priority."

Volume 393, Issue 102181, 2024, Pages 1021-1031

DOI: <https://doi.org/10.1136/lancet.2024.409.102181>

When Biologicals Response Is Inadequate ?



Early Failure : Baseline Fault

- Fewer exacerbations
- Low BEC
- mOCS use

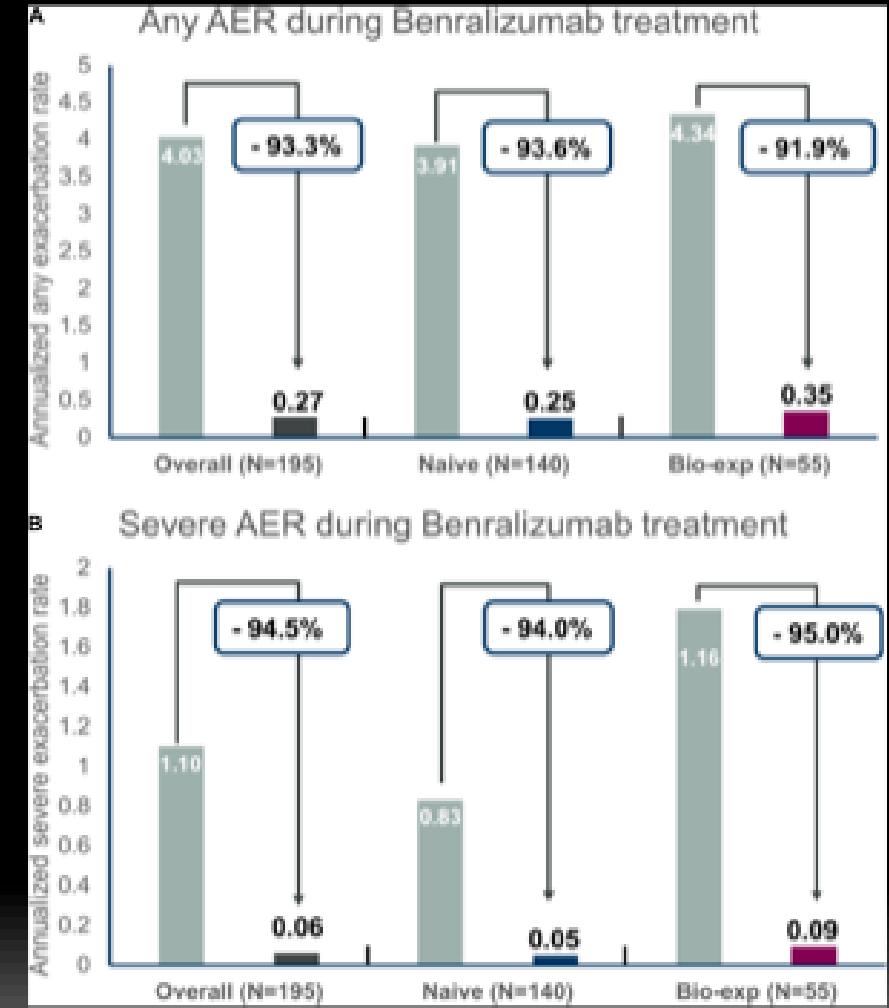
Late Failures : Resistance

- Airway Eosinophilia
- Neutralizing Ab to MAB's
- Comorbidities

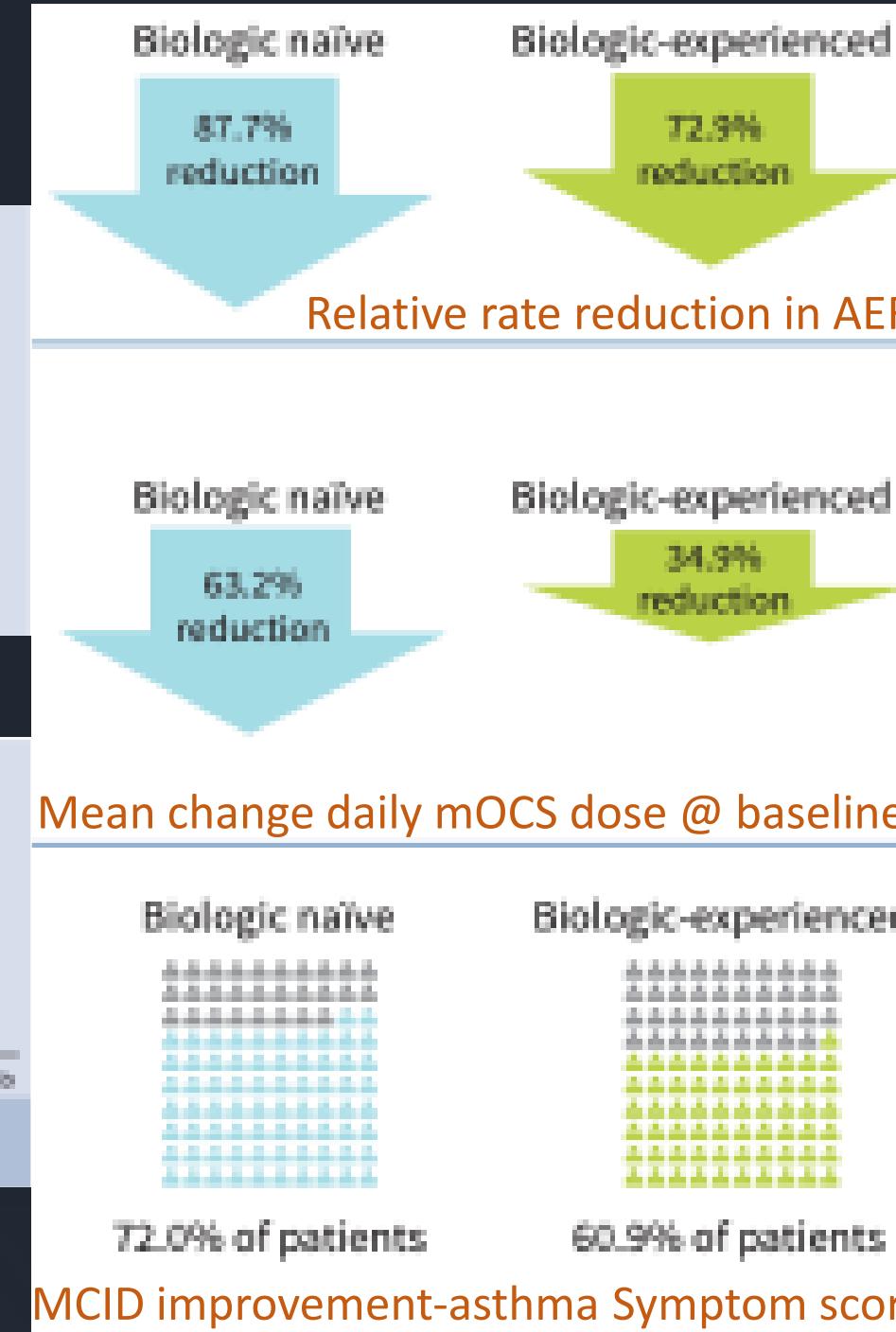
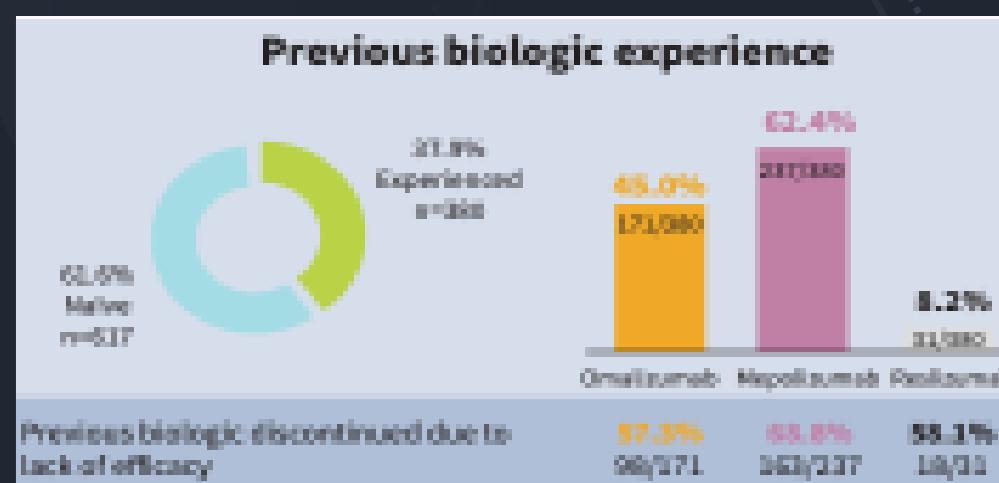
20% refractory to biologicals @ 1 year

Failure : Can We Switch Biologicals ?

- 58 previously exposed to Omalizumab / Mepolizumab or Omalizumab + Mepolizumab patients with inadequate response switched to Benralizumab
- Suboptimal Control
 - Patients switched to Benralizumab improved if they were more atopic
 - Benralizumab improved overall asthma control in switched patients

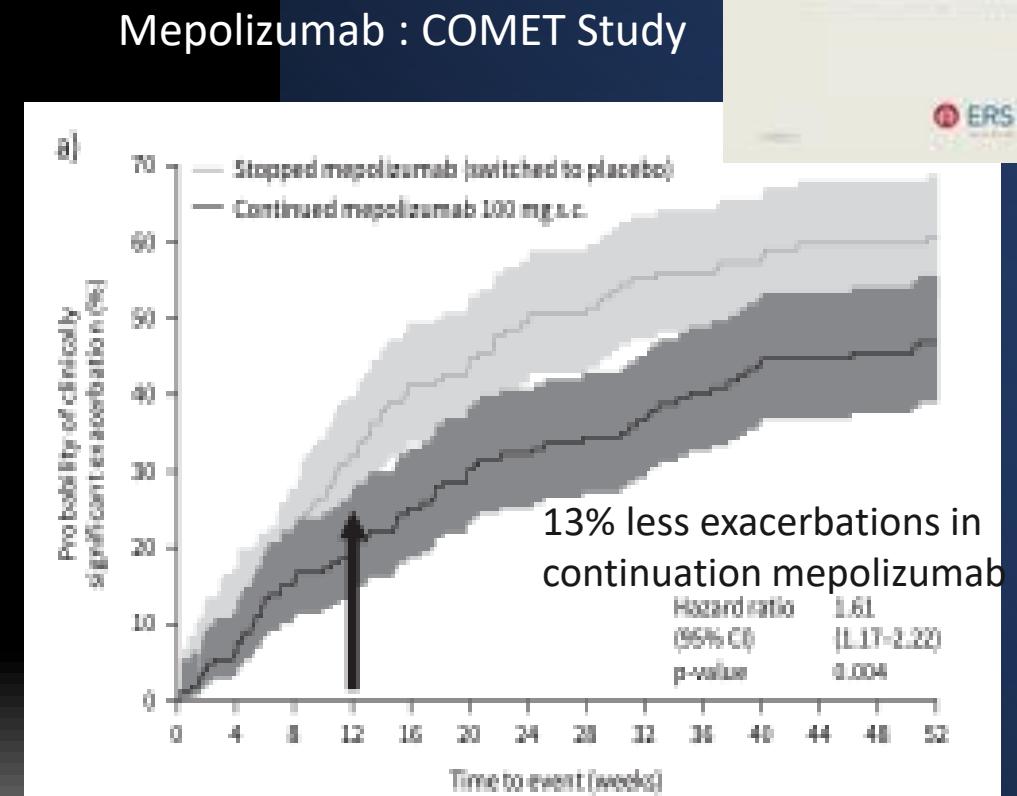
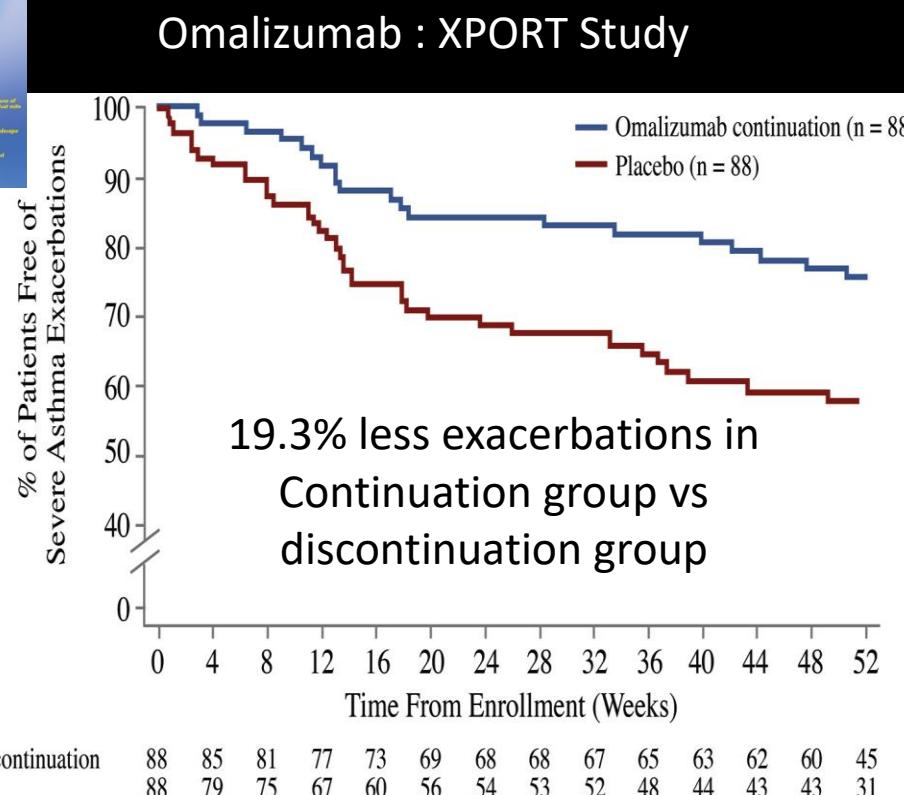
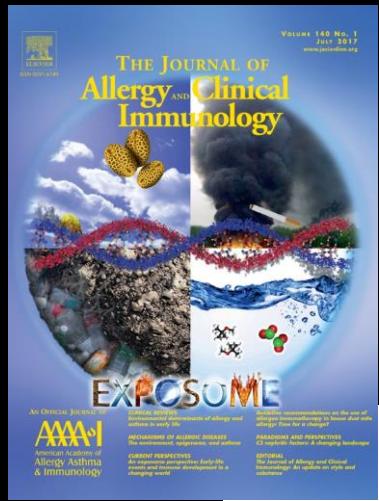


Results of Switching Biologicals

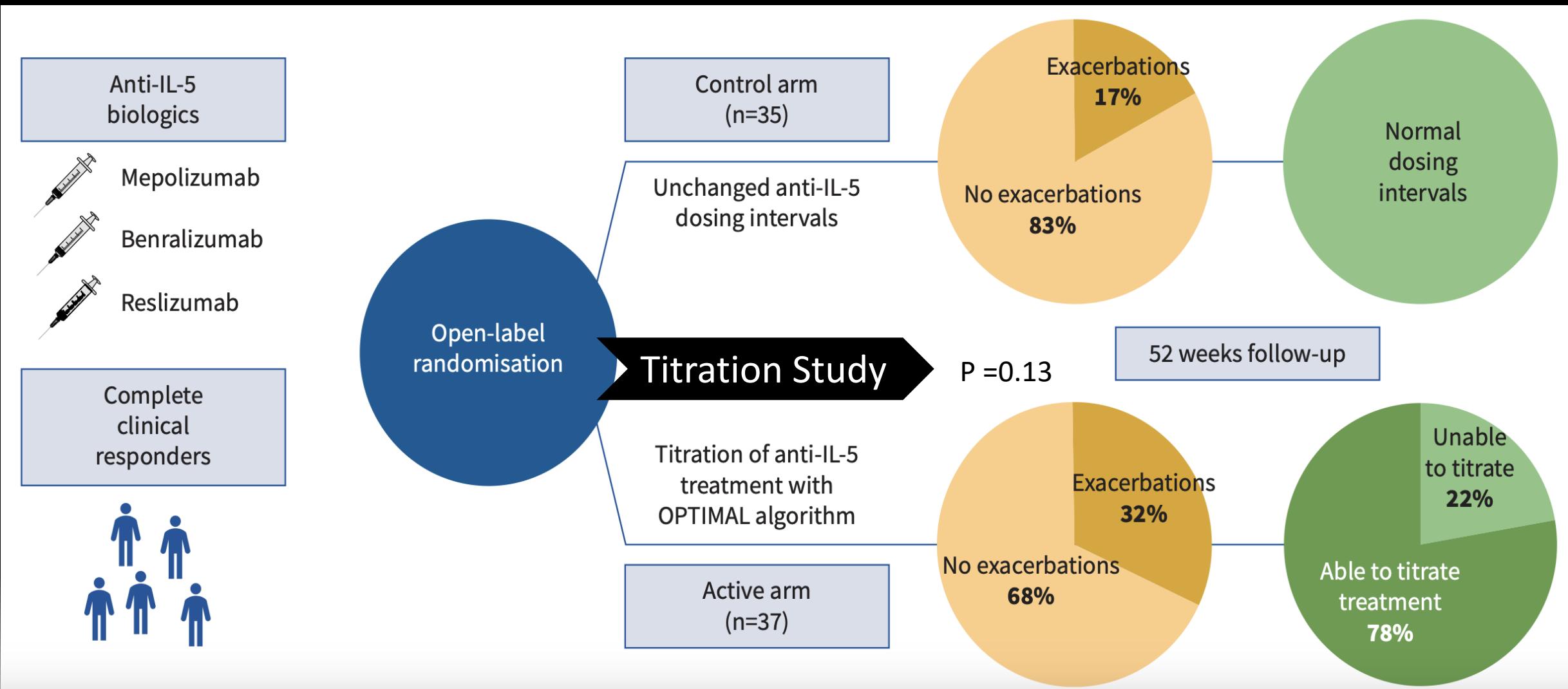


XALOC 1 Program

Can Biologicals be Stopped ?



How to Stop Biologicals ? *OPTIMAL Study*



Biologicals In Asthma : Conclusions

Why

Zero OCS Use

When :

Uncontrolled Asthmatics on GINA Step 5

Which :

Type 2 Severe Asthma (Biomarkers)

How :

Match comorbidities & Expectations

When to stop :

Space / Abrupt



Dr Deepak Talwar

Director & Chair MCRD



Dr Kanishka Kumar Singh

Senior Consultant



Dr Deepak Prajapat

Senior Consultant



Dr Rahul Khera

Consultant



BLOCK YOUR DATE 15TH 16TH 17TH
AUGUST 2025

Thank You

