

PACS & Indore Chest Society- 2025

Latest Updates in Asthma :

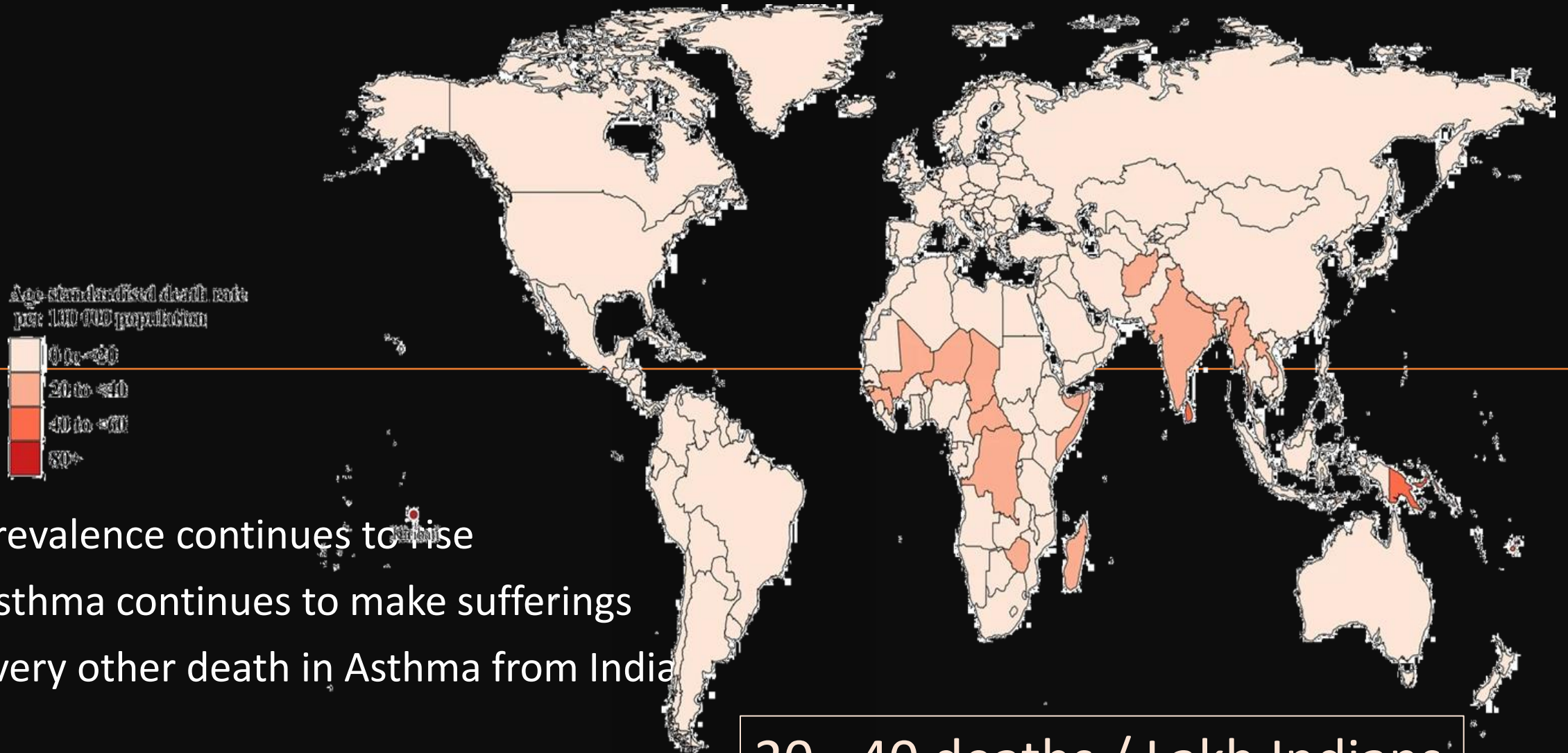
Biologicals

Deepak Talwar

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

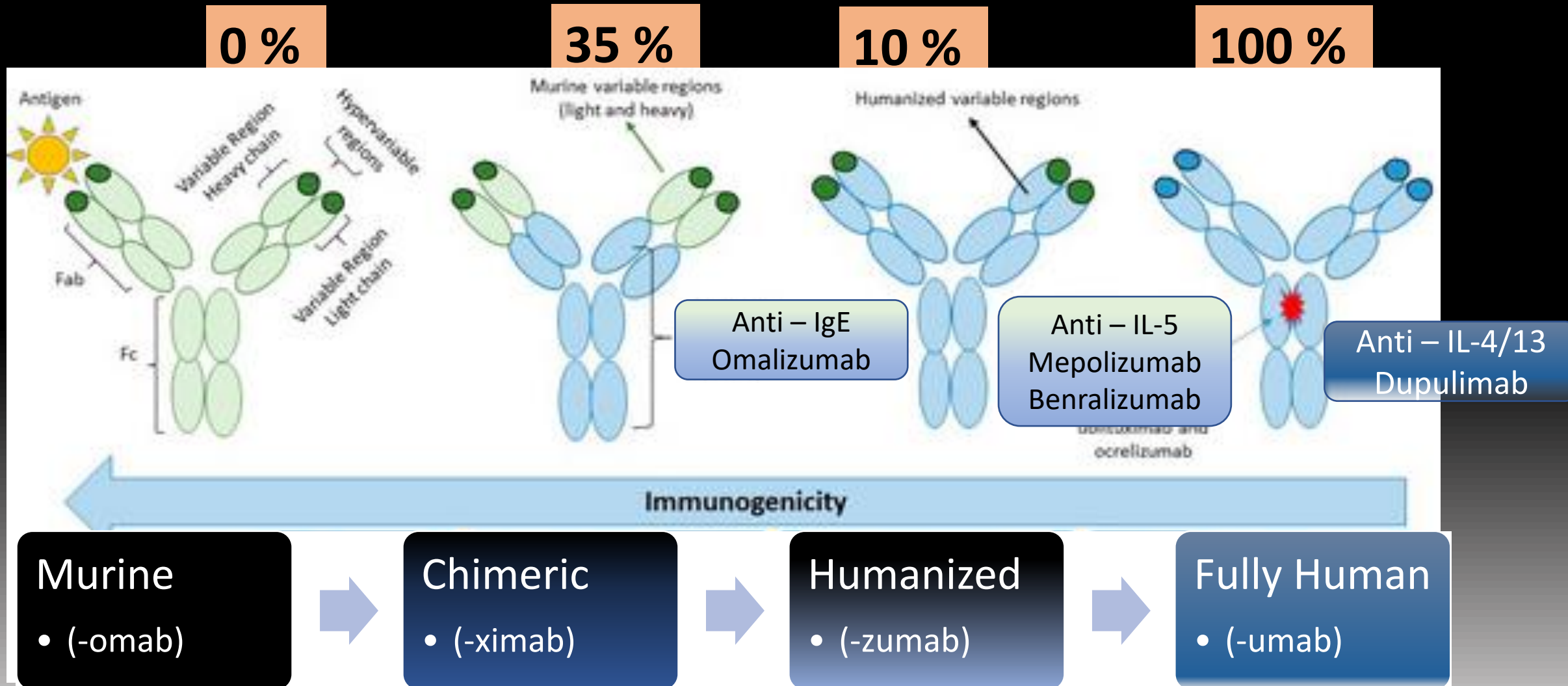


Death Continues to Haunt Asthma

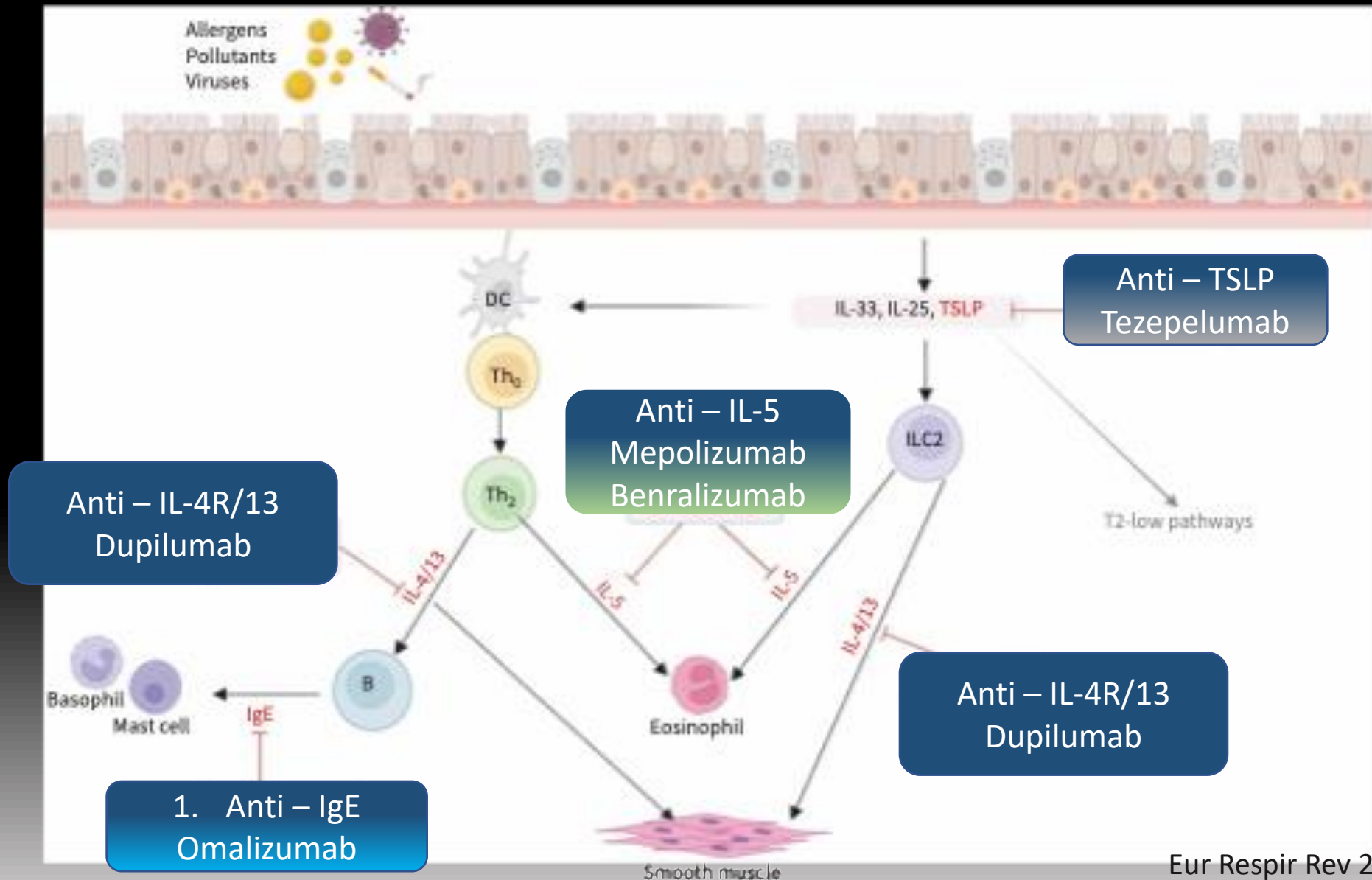


- Prevalence continues to rise
- Asthma continues to make sufferings
- Every other death in Asthma from India

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

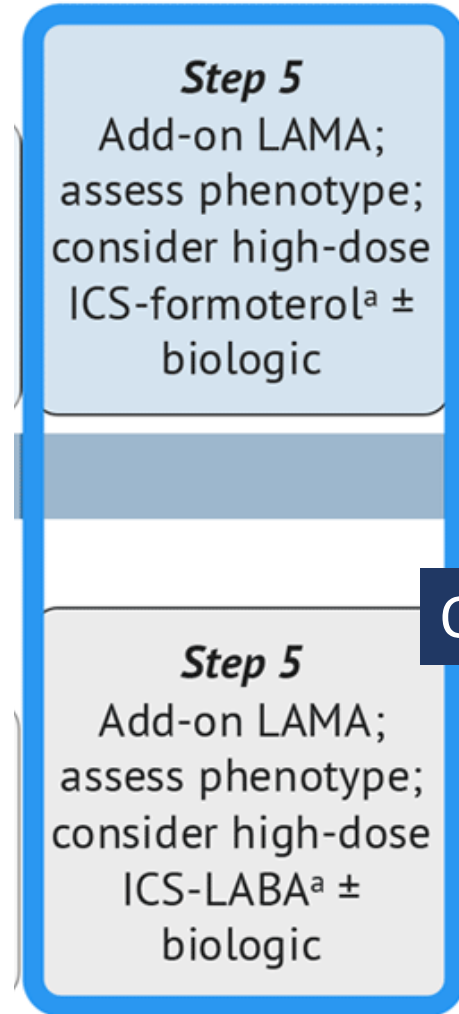
Track 1



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



Montelukast

Other Options

Azithromycin

Remember : All Uncontrolled Asthma is *NOT* Severe Asthma

Difficult To Treat Asthma

Retrospective label

Uncontrolled Asthma

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

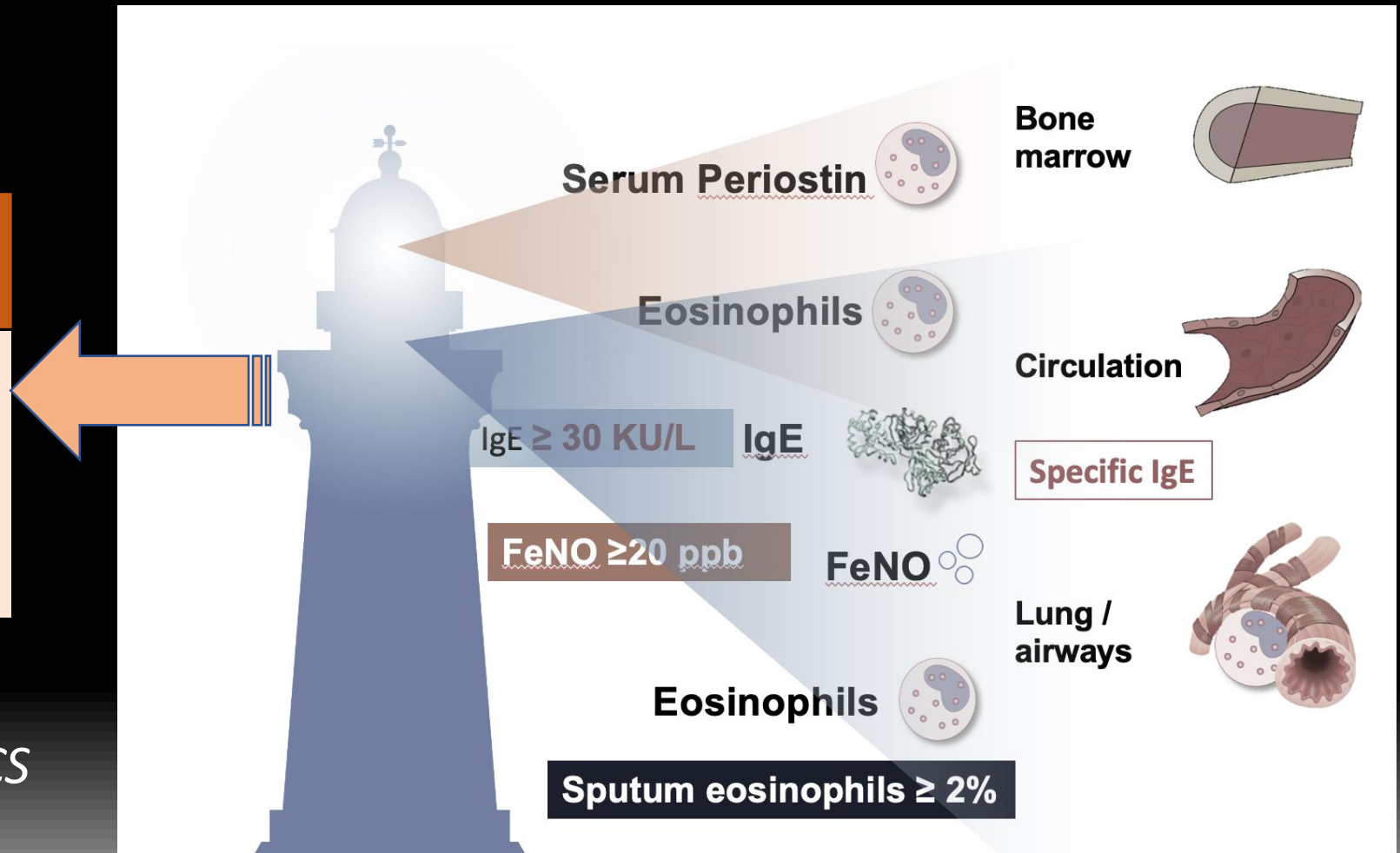


Identify T 2 Asthma- Biomarkers!

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

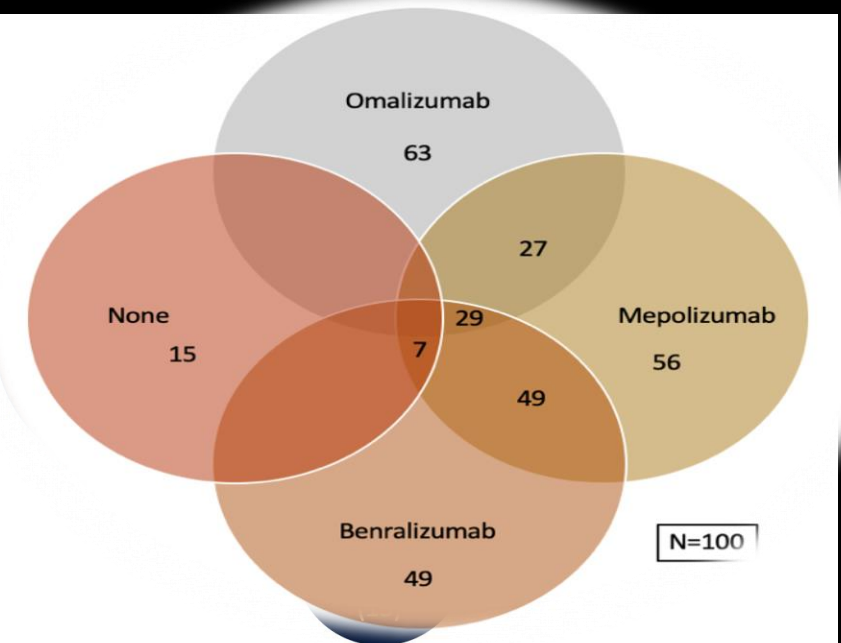
A retrospective observational study on pheno-endotypes of severe asthma among adults attending asthma clinic in a tertiary care centre in India

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,



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

T₂ Low asthma is only 15% at AEC cut off of 300 & 9% at @ AEC -150

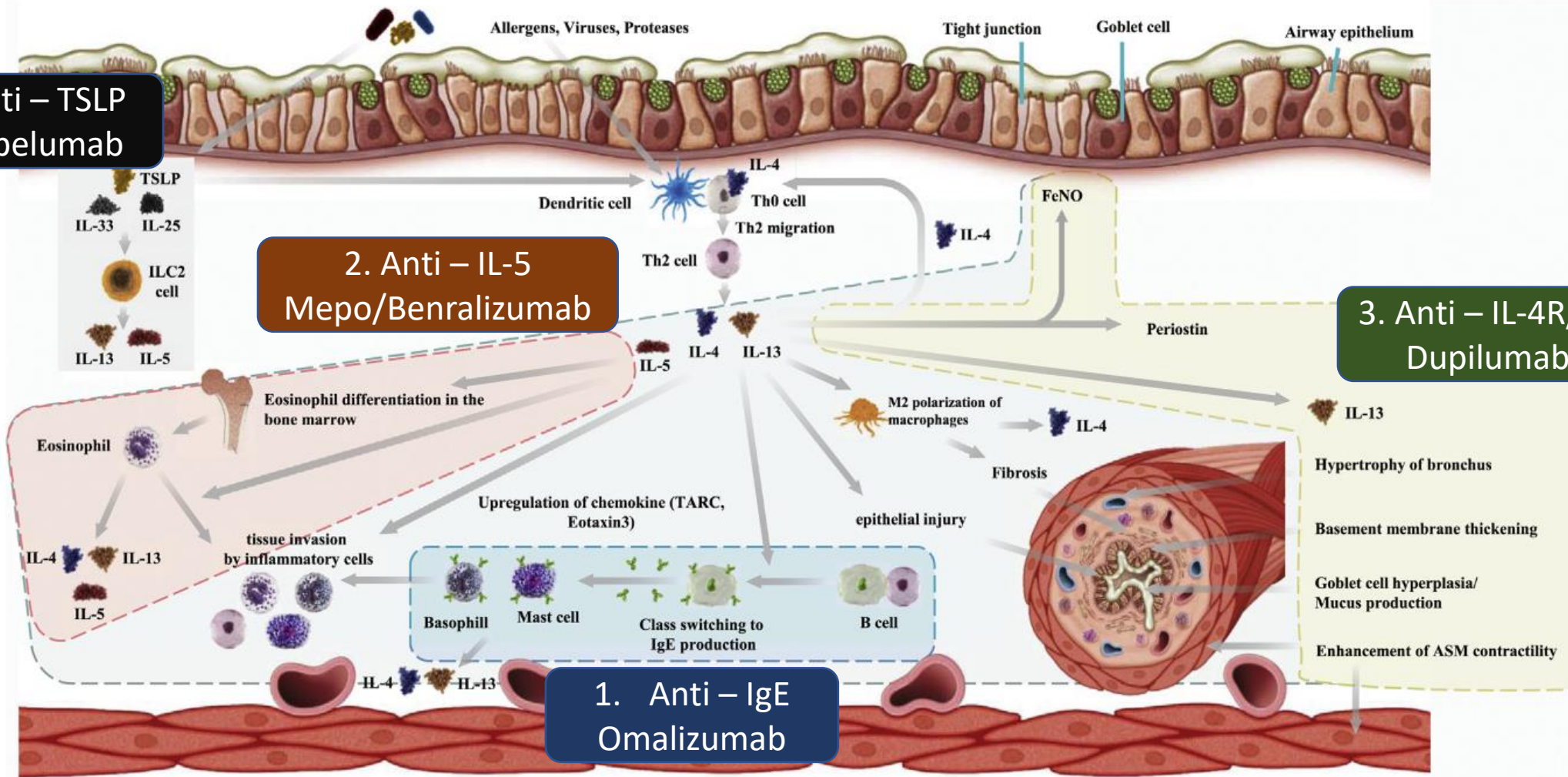
How ?? : Choose Appropriate Biologicals - *Drivers*

4. Anti – TSLP Tezepelumab

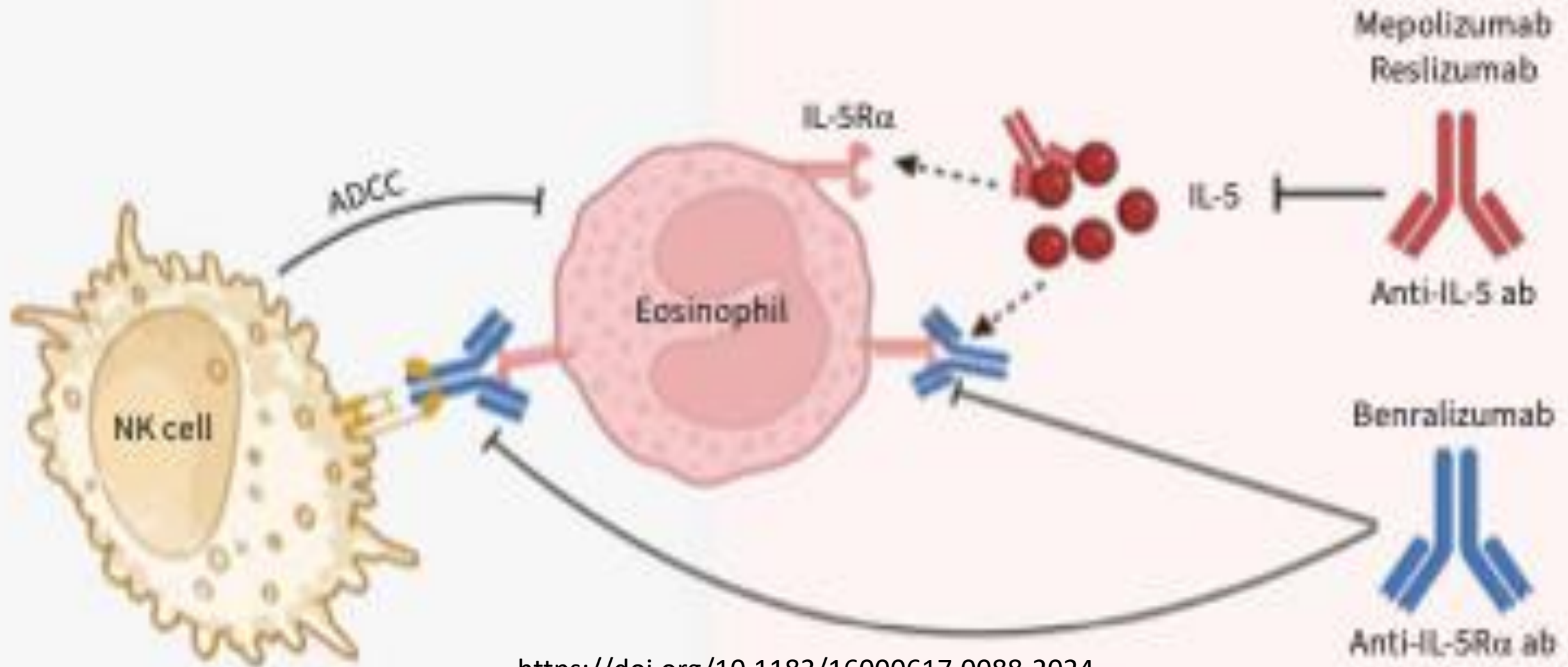
2. Anti – IL-5 Mepo/Benralizumab

3. Anti – IL-4R/13 Dupilumab

1. Anti – IgE Omalizumab



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 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

Biomarkers

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

Comorbidities :

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



Mepolizumab

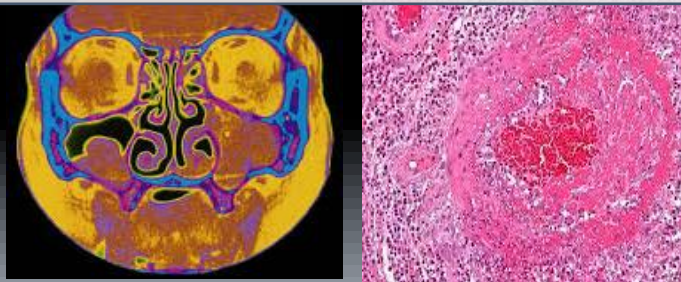
Late Onset asthma

Biomarkers :

- AEC, FeNO, Sputum Eosinophils

Comorbidities :

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



Benralizumab

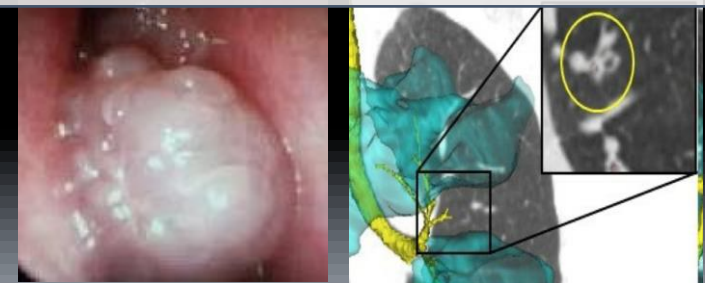
Adult / Late Onset asthma

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

ISSN: 2754-4761



F1000Research

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



Research Article

Open Access

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

Arjun Khanna^{1*}, 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]

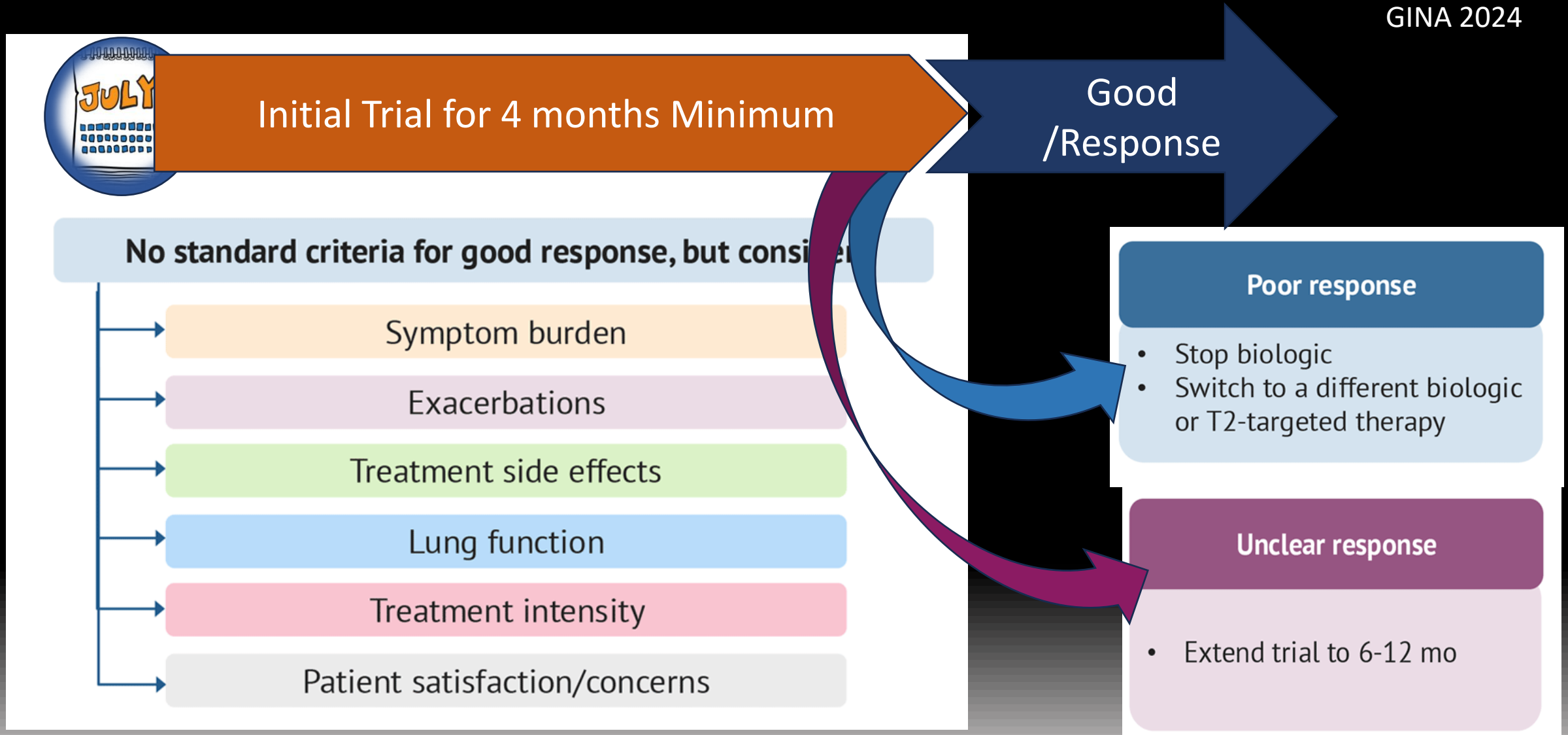
Deepak Talwar * ¹, Manoj Yadav², Nagarjuna Maturu³

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

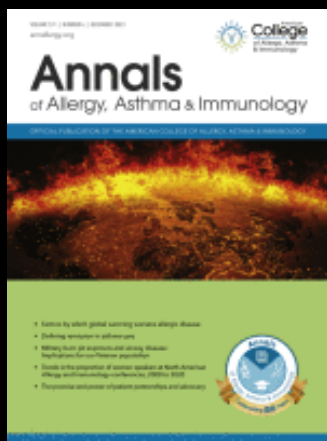
Fewer comorbidities

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

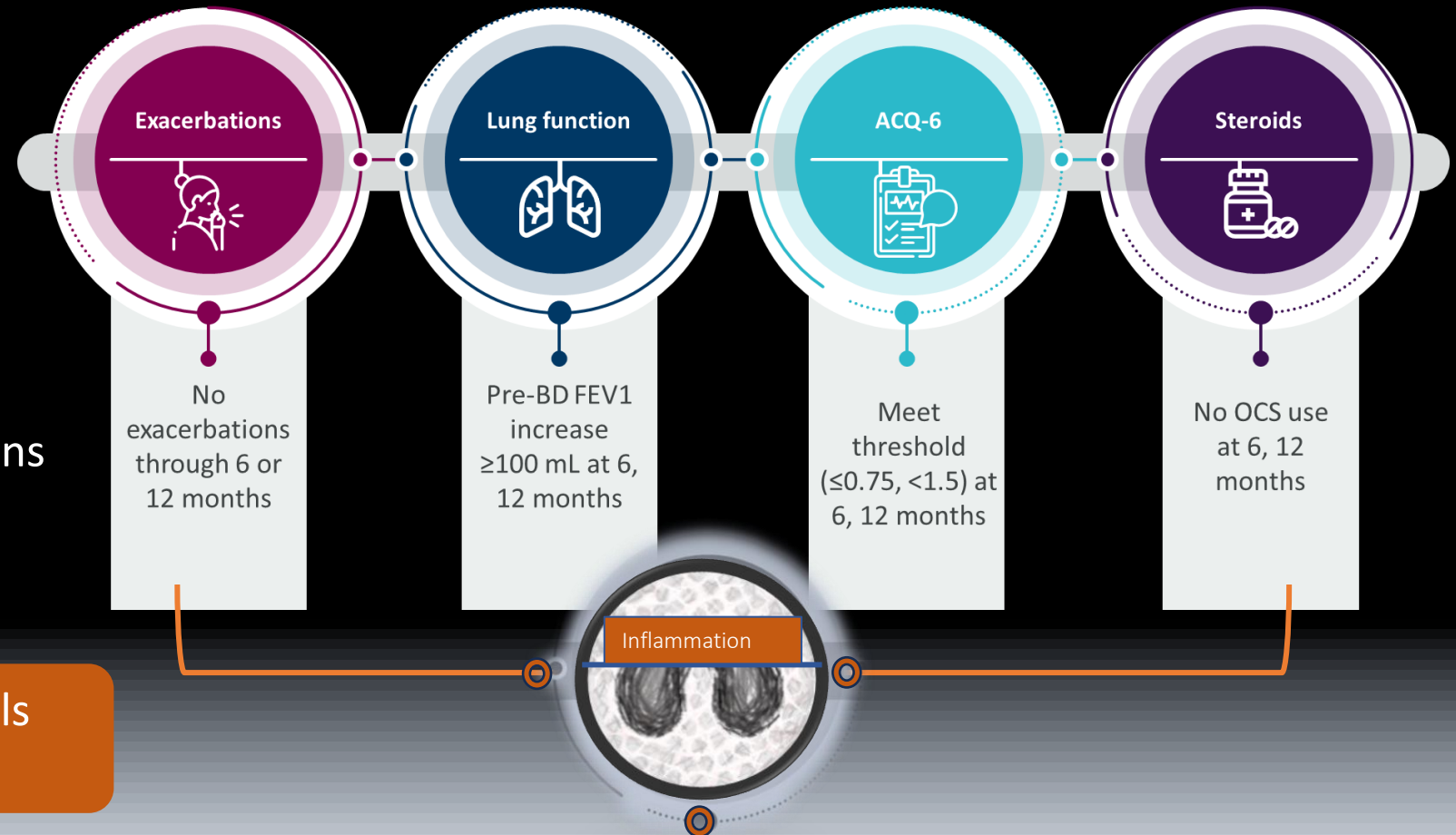




Clinical Remission :





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

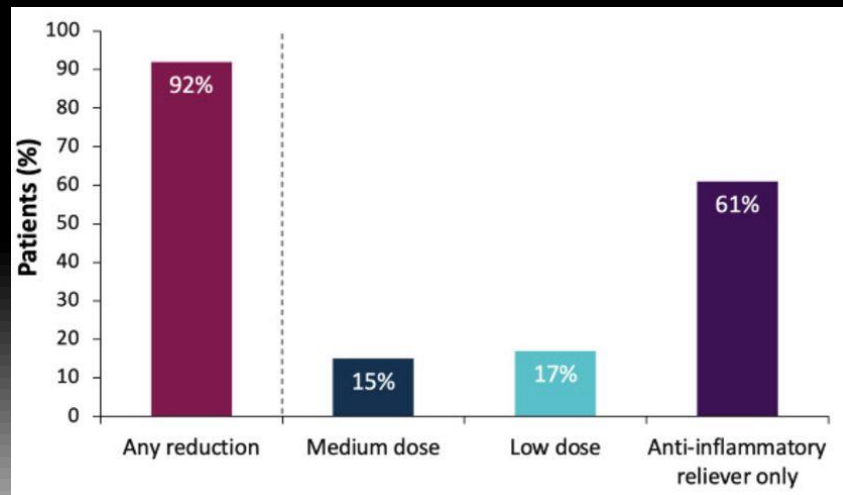
Clinical Remission in Asthma : *FACT* !

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 _{1pp} ≥ 80%	Post-BD FEV ₁ ≥ 80% <i>OR</i> 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 _{1pp} > 80% <i>OR</i> Pre-BD FEV ₁ > 20% from baseline; FEV1 > 95% of baseline**	Not included	Not included	Post-BD FEV _{1pp} ≥ 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%

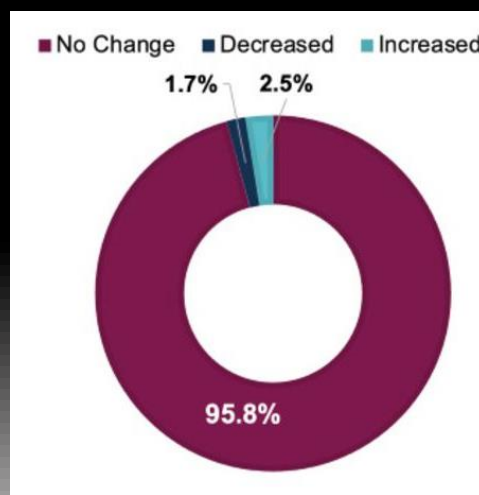
Can SA Patients Transform to Mild Asthma ?

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 Hjeltnes, Lynda Olinger, David Cohen, Andrew Menzies-Gow, Stephanie Korn, on behalf of the SHAMAL Investigators*



92% at 48 weeks had no AE



@ 48 weeks



Lancet 2024; 403: 271-81

When Biologicals Response Is Inadequate ?



Early Failure : Baseline Fault

- Fewer exacerbations
- Low BEC
- mOCS use



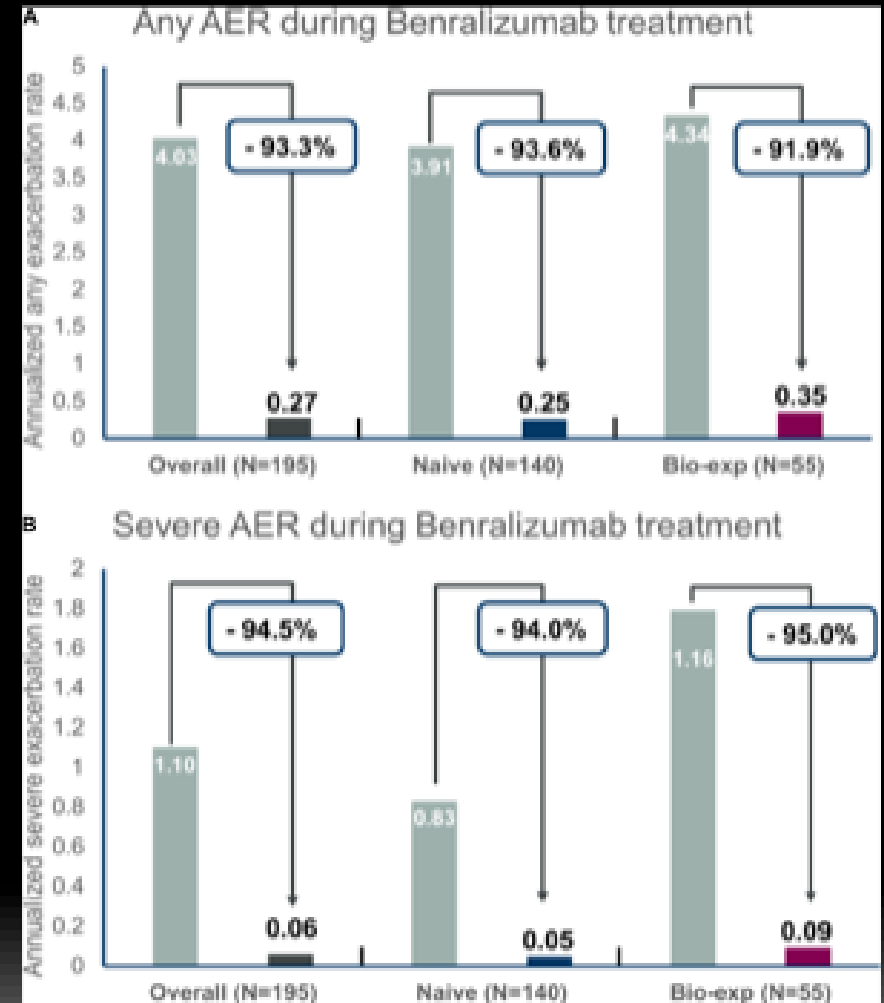
Late Failures : Resistance

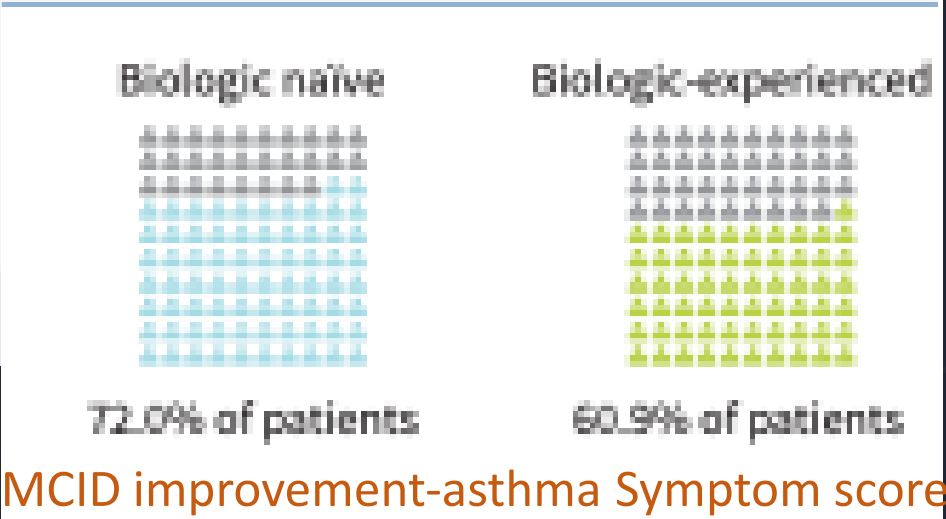
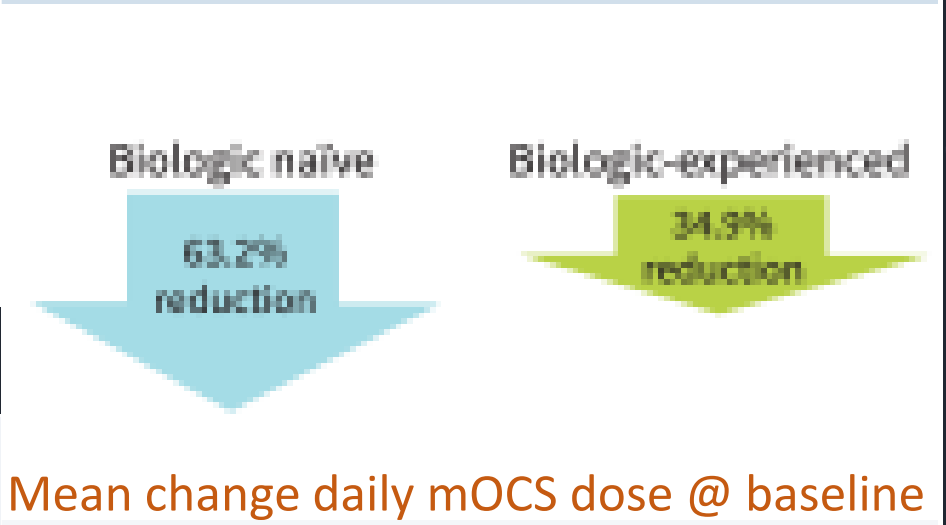
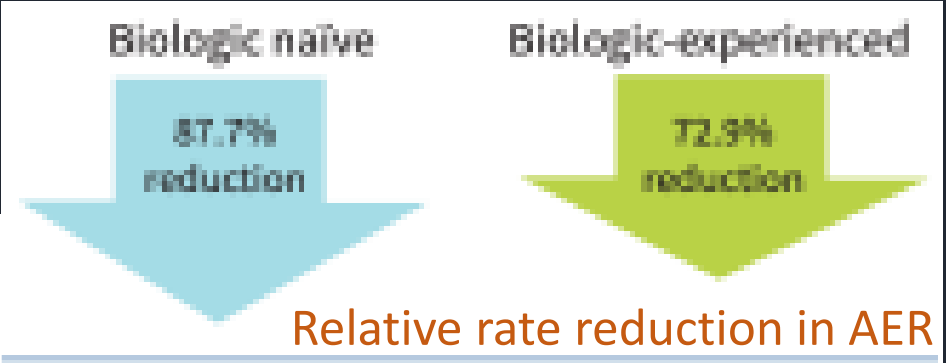
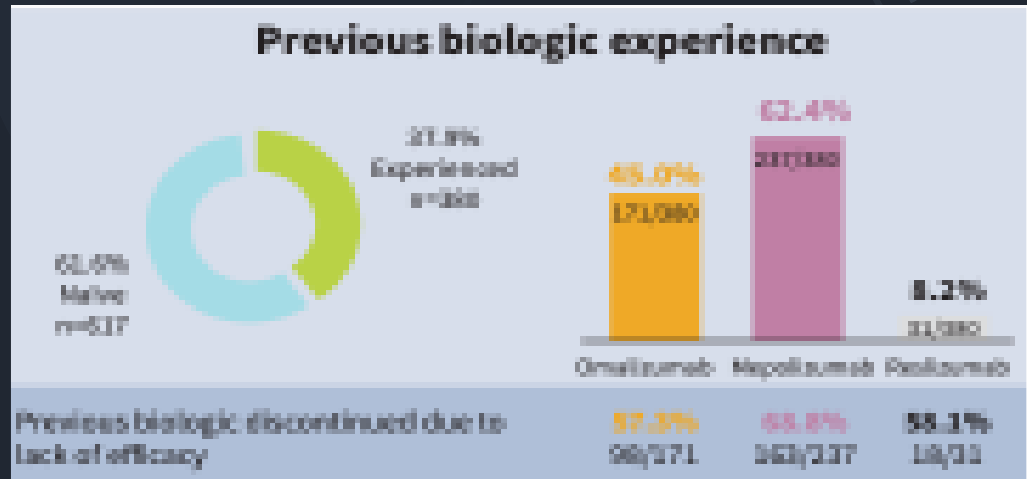
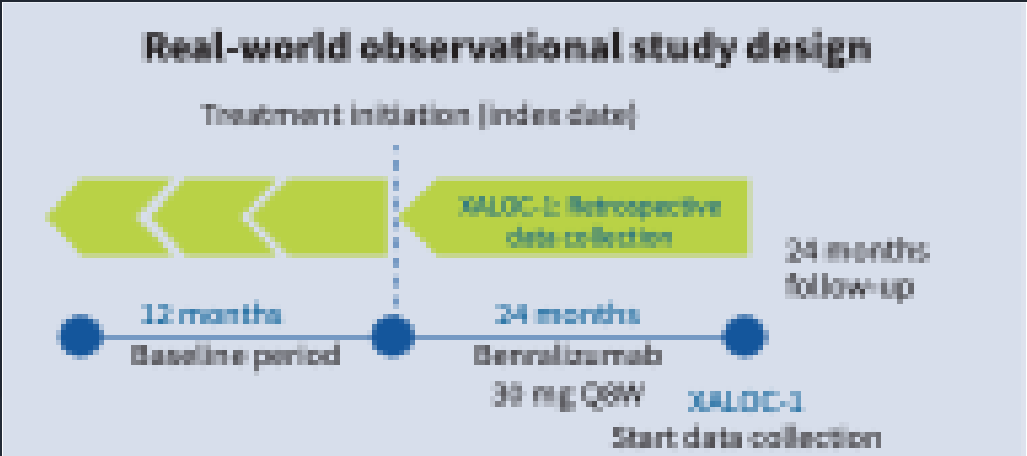
- Airway Eosinophilia
- Neutralizing Ab to MAB's
- Comorbidities

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





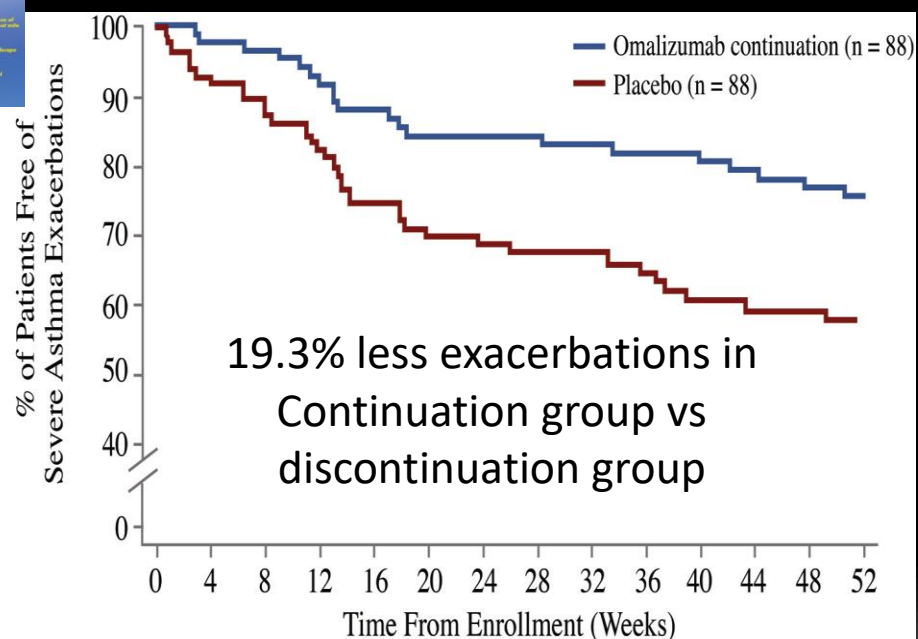
Results of Switching Biologicals

XALOC 1 Program

Can Biologicals be Stopped ?



Omalizumab : XPORT Study

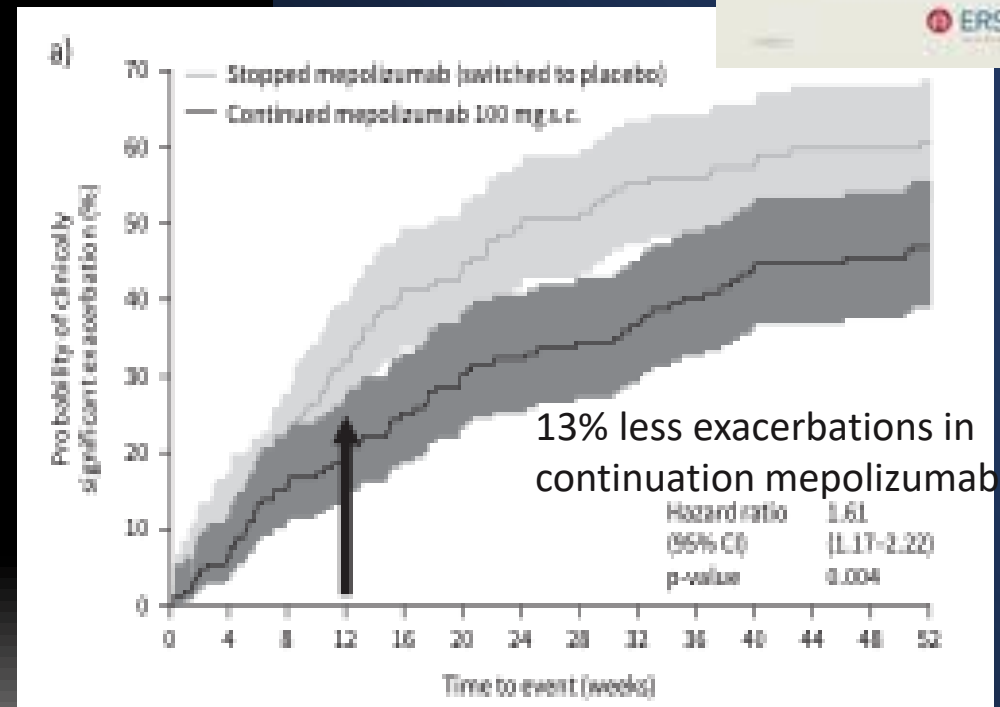


No. at risk	0	4	8	12	16	20	24	28	32	36	40	44	48	52
Omalizumab continuation	88	85	81	77	73	69	68	68	67	65	63	62	60	45
Placebo	88	79	75	67	60	56	54	53	52	48	44	43	43	31

J Allergy Clin Immunol. 2017 Jul;140(1):162-169.

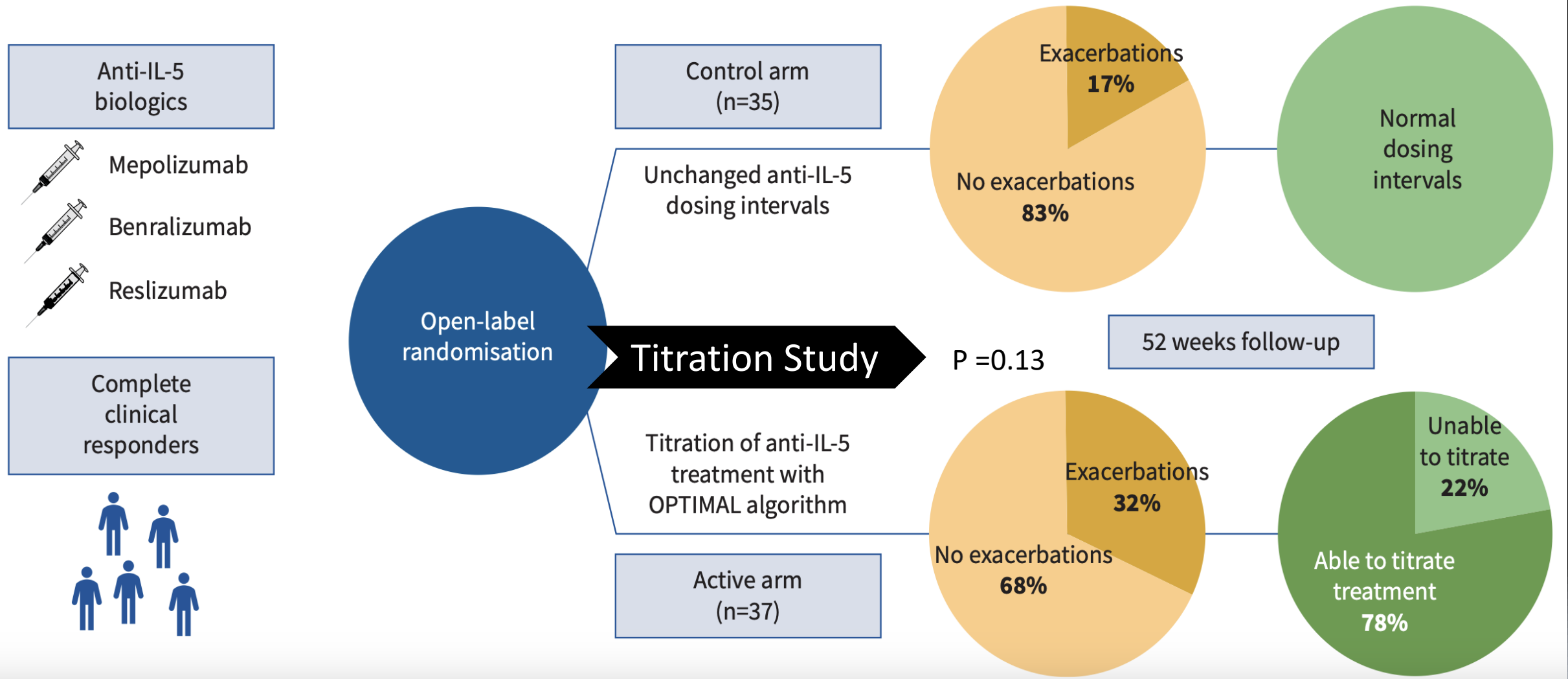


Mepolizumab : COMET Study



Eur Respir J 2022; 59: 2100396

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 Khara

Consultant



Thank You

