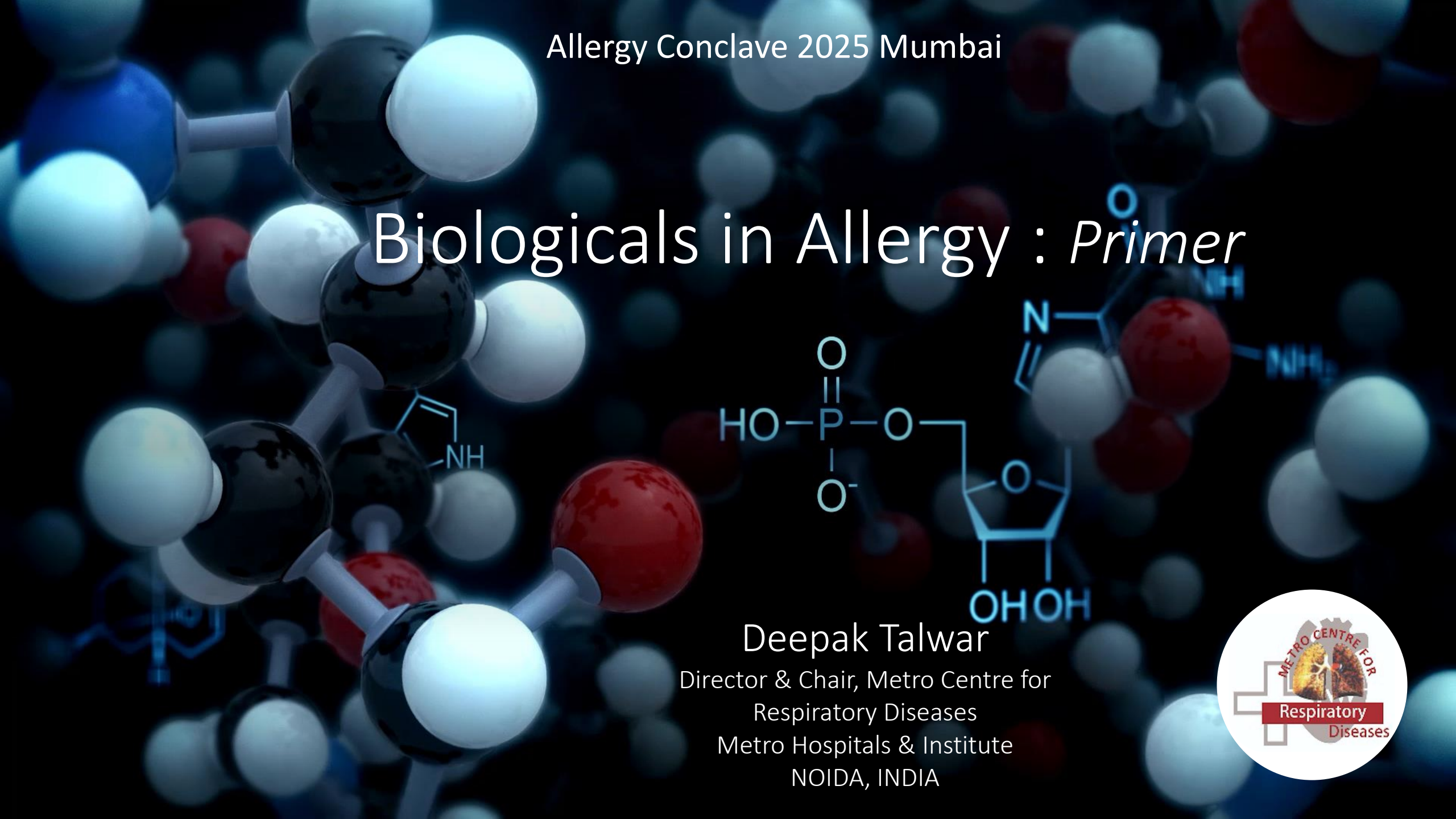
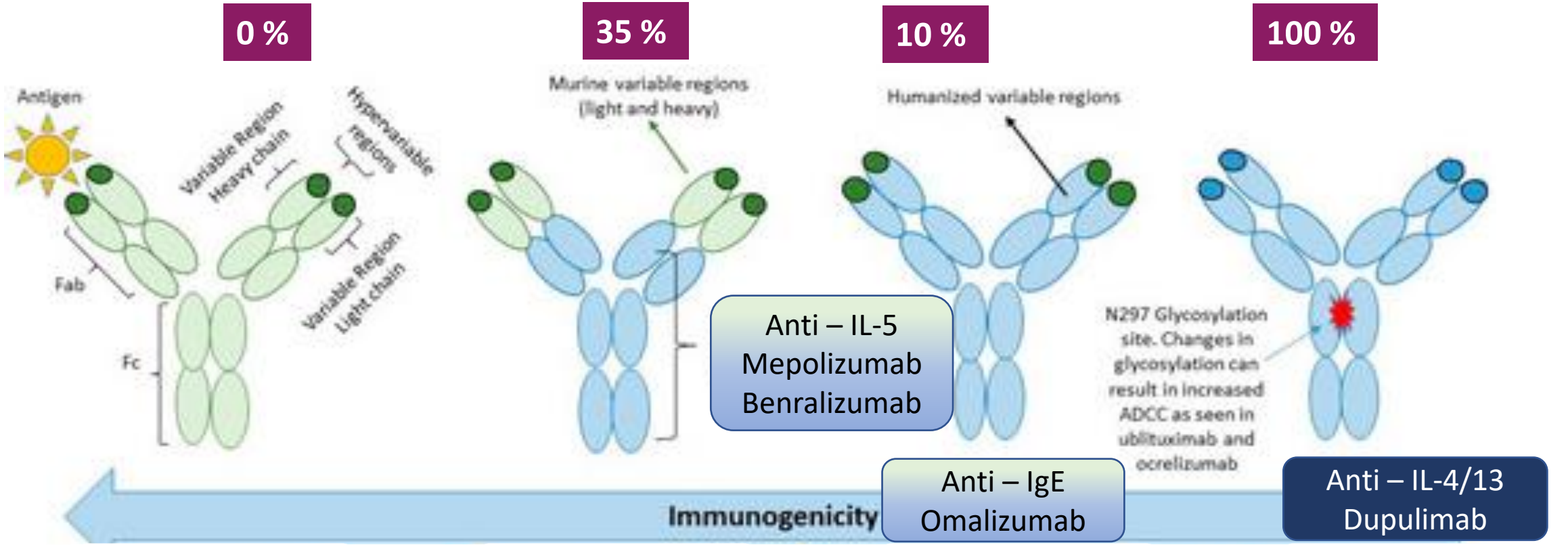
Allergy Conclave 2025 Mumbai

Biologicals in Allergy : *Primer*



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

Biologicals : *Targeted Therapies*



Spectrum of Allergic Diseases & Role of Biologicals

Bronchial Asthma

Chronic Rhinosinusitis with Nasal Polyposis

Chronic Spontaneous Urticaria

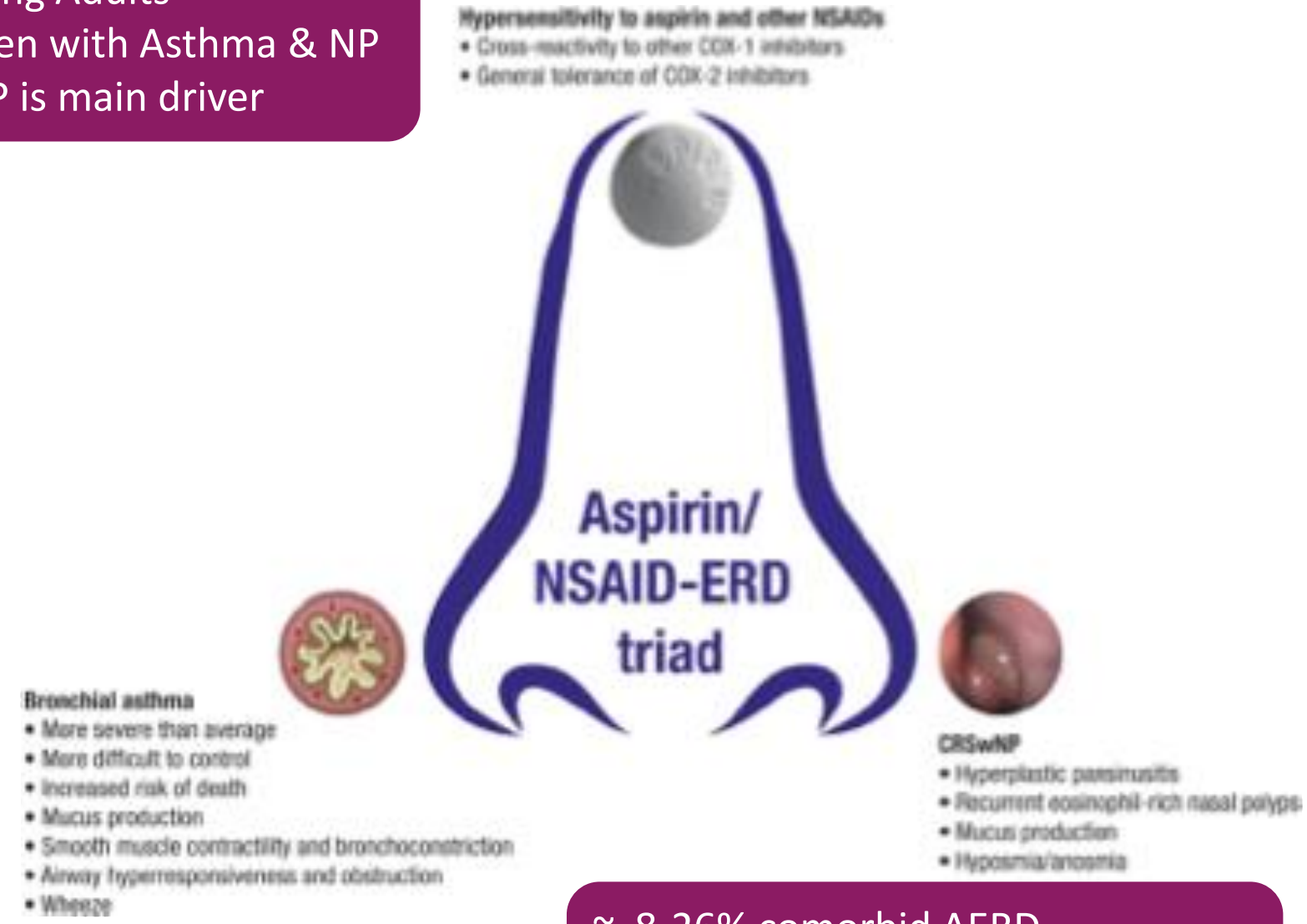
Atopic Dermatitis

Food Allergy

J Allergy Clin Immunol Pract 2021;9:1118-20.

Chronic Rhinosinusitis with Nasal Polyposis

~ Young Adults
~ Often with Asthma & NP
~ TSLP is main driver

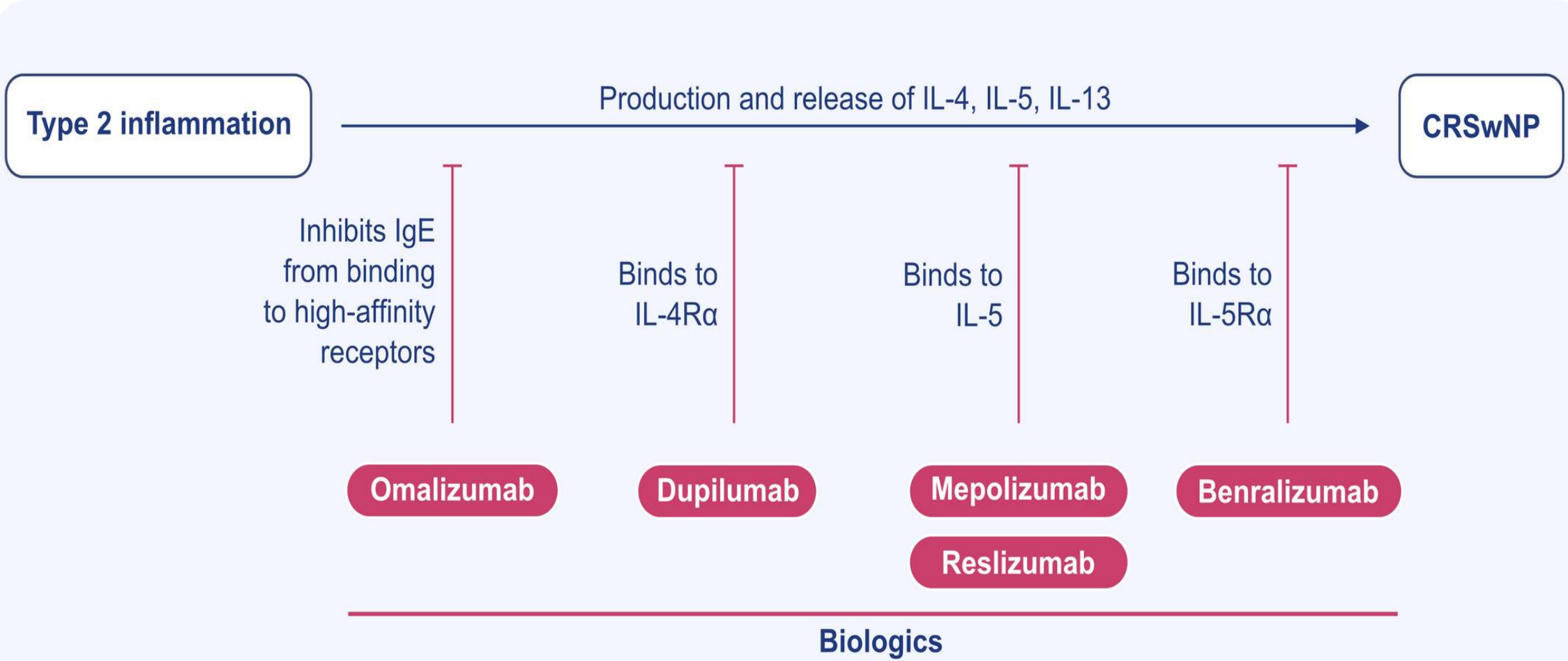


~ 67% associated Asthma
~ 60% Severe Asthma

~ 8-26% comorbid AERD
~ AERD in 7% Asthmatics
~ 90% CRSwNP and AERD severe NP

Allergy, Volume: 77, Issue: 12, Pages: 3593-3605, First published: 06 September 2022, DOI: (10.1111/all.15507)

Rationale for Biologicals : *Type 2 Inflammation*



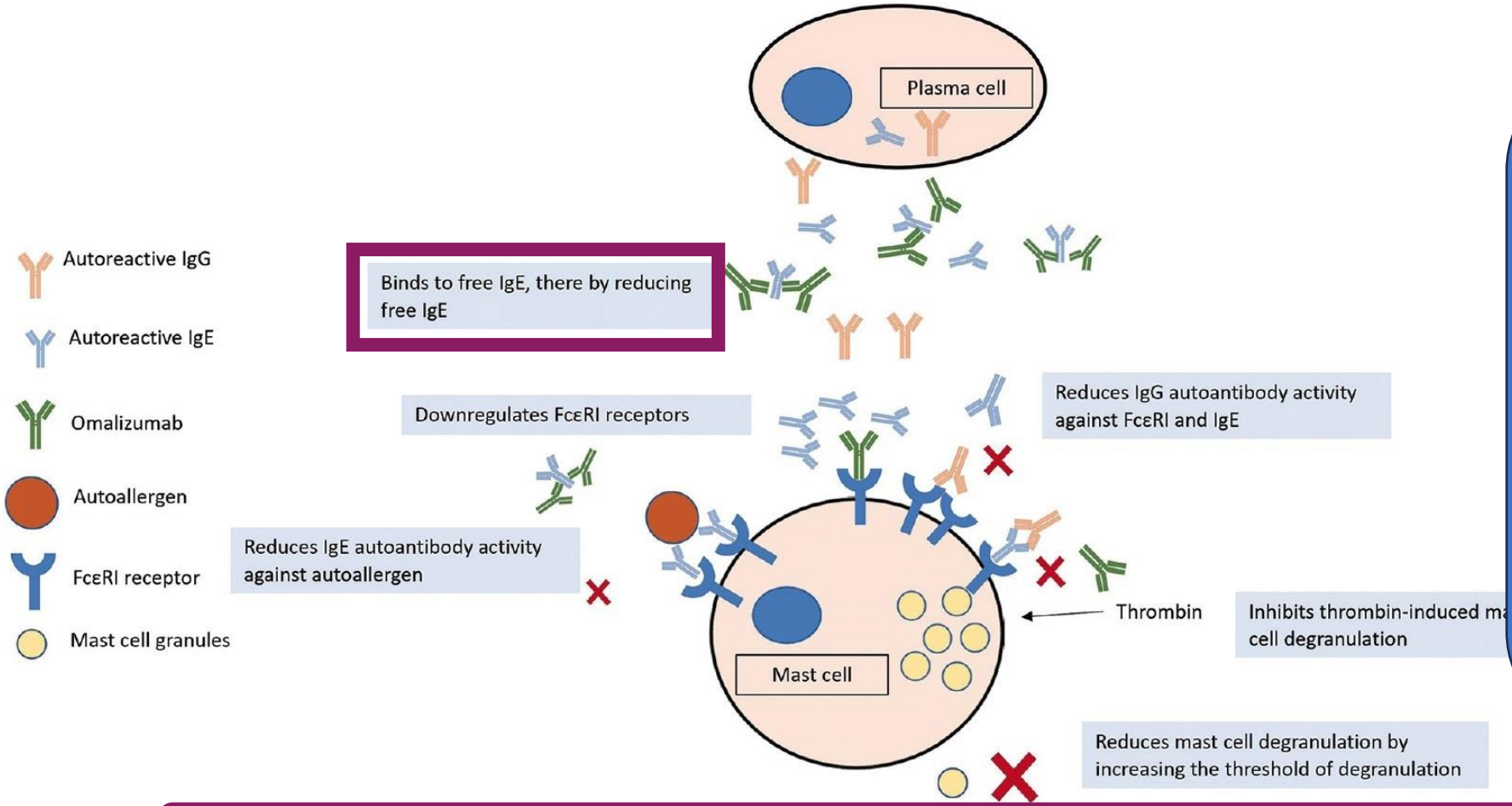
Allergy, Volume: 77, Issue: 12, Pages: 3593-3605, First published: 06 September 2022, DOI: (10.1111/all.15507)

From Bench to Bedside : Biologicals in CRSwNP

Biologicals	Clinical Trials	Results	Interpretation	Subgroup Inference
Omalizumab	POLYP 1 & POLYP 2 (Phase-III) Extension trial Sug group Analysis	Endoscopic, Clinical & and Patient-oriented Outcomes	Extension study showed full benefit after > 6 months of T/t	Benefits irrespective of Eosinophilia, Aspirin sensitivity or Asthma status (N-ERD improved)
Dupulimab	LIBERTY NP, SINUS 24 and SINUS 52	Improved nasal polyp, nasal congestion, smell	Improvement seen in 4-8 weeks, continued @52 weeks	Improvement irrespective of level of eosinophilia
Mepolizumab	SYNAPSE Phase 3 & 1 Prospective study	Improved nasal obstruction, ↓ need for sinus surgery	Need for OCS and AES decreased	Improvement irrespective of comorbid SA or N-ERD
Benralizumab	OSTRO, ANDHI and Post Hoc analysis	Improved nasal polyp and symptoms improved	Improved eosinophilic asthma and NP,	NP scores improve

Allergy. 2022;77:3593–3605.

Chronic Spontaneous Urticaria : Omalizumab

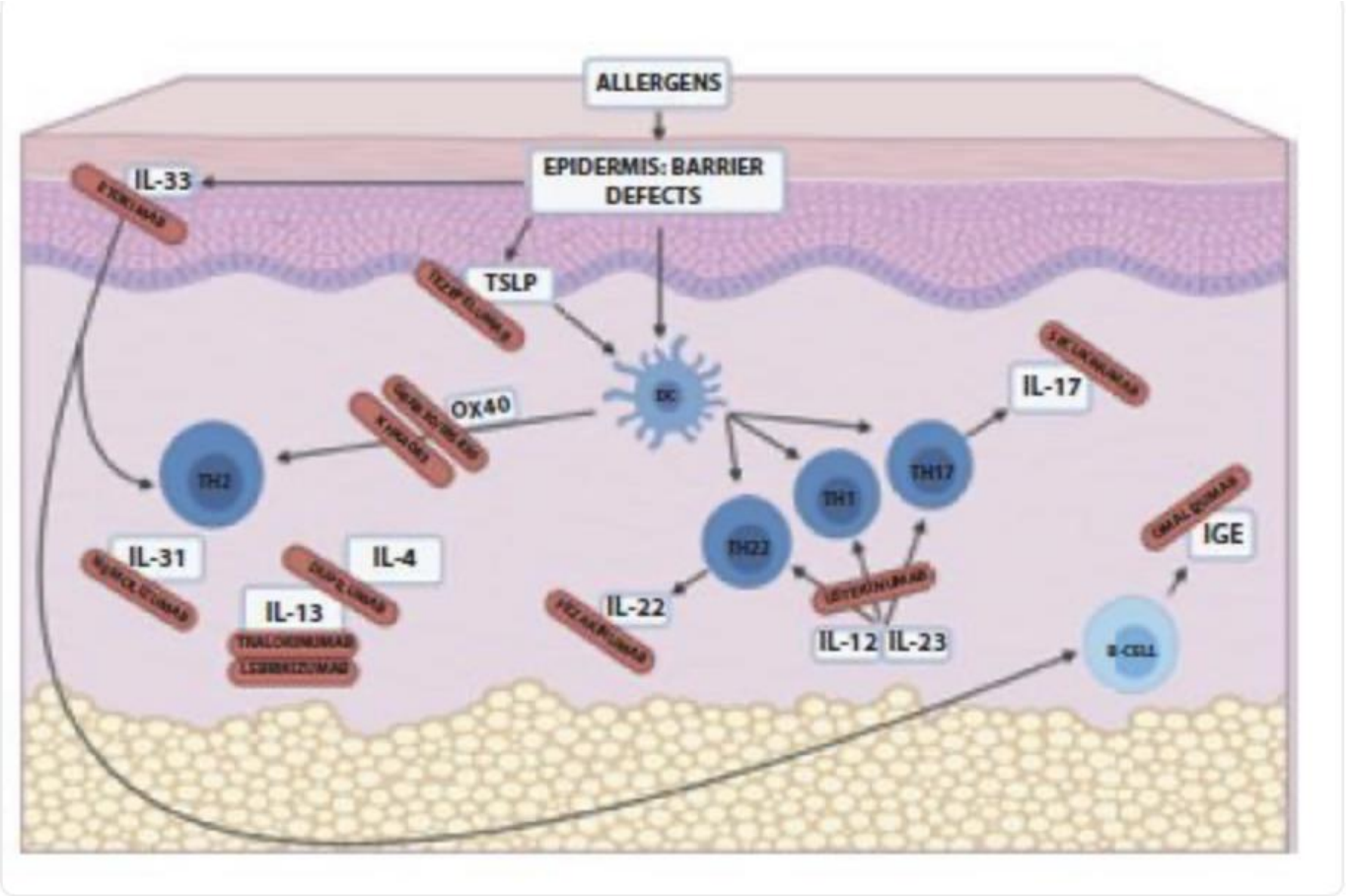


- 3 RCT's
- Each had 300+ patients of Anti-histamine Resistant CIU
- 75-300 mg Omalizumab/ month vs Placebo
- Omalizumab is safe and effective in AH R – CIU
- Start 300mg/month & up to 600 mg twice a month

complete and Partial response rates of 72.2% and 17.8%, respectively

Mustari, Indian Dermatology Online Journal 14(1):p 9-20, Jan–Feb 2023.

Atopic Dermatitis : Biologicals - Dupulimab



- Most common inflammatory skin disorder
- Affects people of all ages and ethnicities
- Typical age-dependent clinical features
- Substantial individual suffering
- Huge economic impact

Schneider S. Dermatol Pract Concept. 2021 1;11(4)

Dupilumab in Atopic Dermatitis

The NEW ENGLAND JOURNAL of MEDICINE

SPECIALTIES TOPICS MULTIMEDIA CURRENT ISSUE LEARNING/CME AUTHOR CENTER PUBLICATIONS

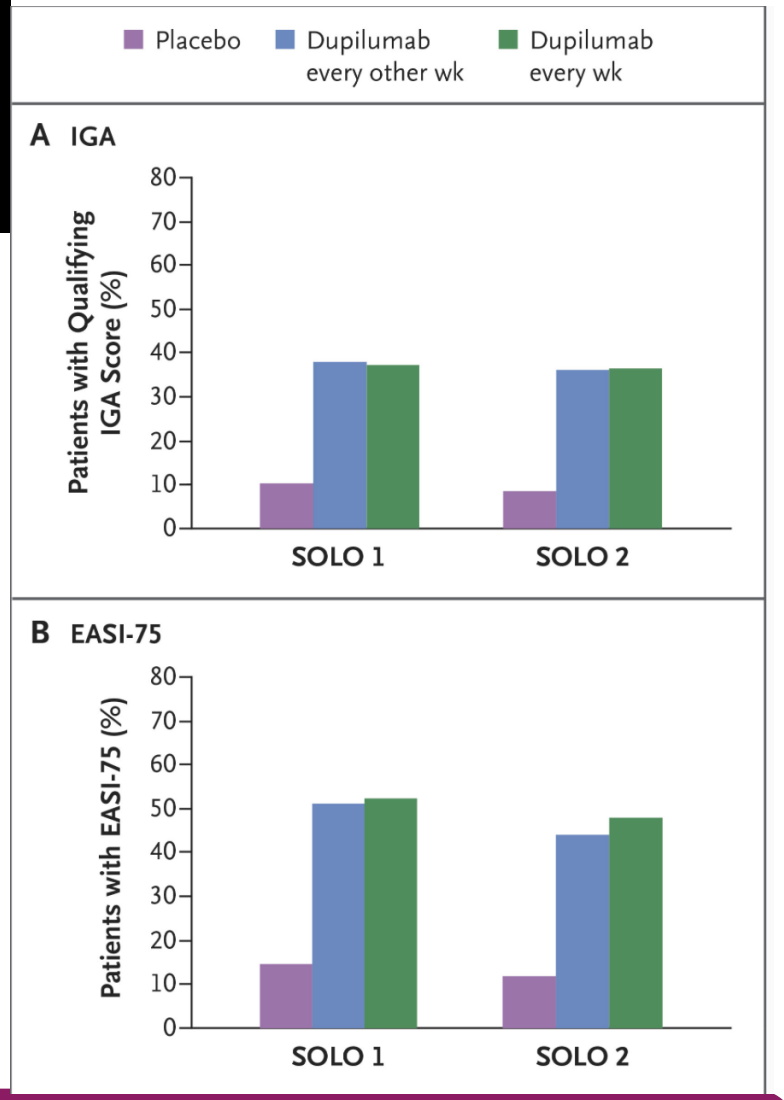
ORIGINAL ARTICLE

Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis

Authors: Eric L. Simpson, M.D., Thomas Bieber, M.D., Ph.D., Emma Guttman-Yassky, M.D., Ph.D., Lisa A. Beck, M.D., Andrew Blauvelt, M.D., Michael J. Cork, M.B., Ph.D., Jonathan I. Silverberg, M.D., Ph.D., M.P.H., +18, for the SOLO 1 and SOLO 2 Investigators* Author Info & Affiliations

Published December 15, 2016 | N Engl J Med 2016;375:2335-2348 | DOI: 10.1056/NEJMoa1610020

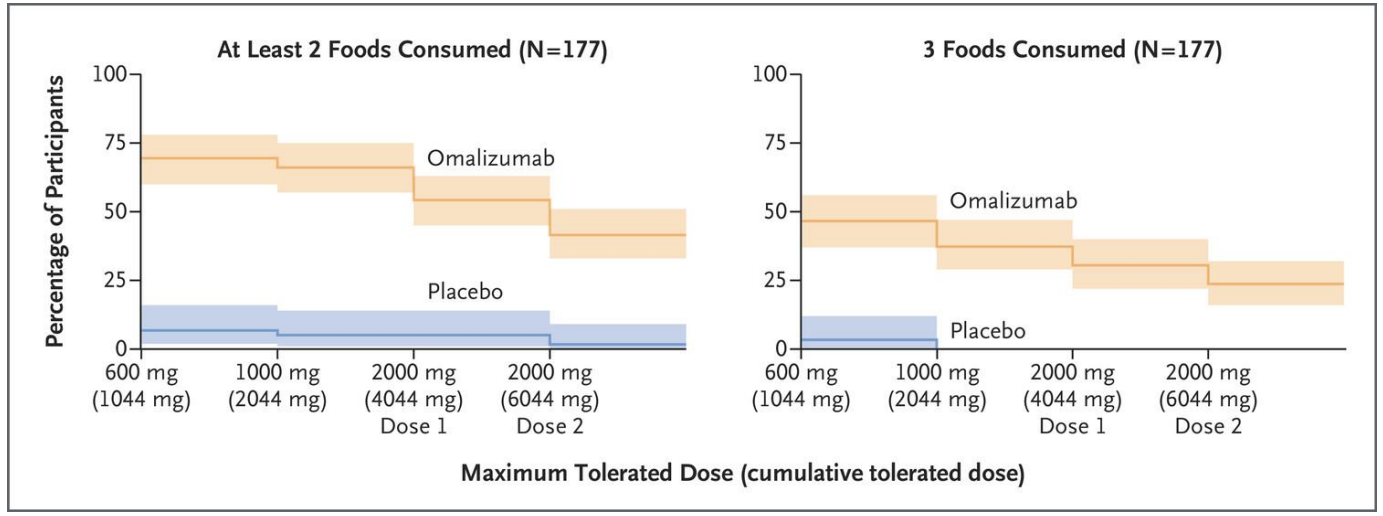
VOL. 375 NO. 24 | Copyright © 2016



In two phase 3 trials of identical design involving patients with atopic dermatitis, dupilumab improved the signs and symptoms of atopic dermatitis, including pruritus, symptoms of anxiety and depression, and quality of life, as compared with placebo

Food Allergy & Biologicals

- 462 patients randomized trial
- Age 1 year – 55 years
- Multiple Food Allergies
- Omalizumab vs Oral immunotherapy



N Engl J Med 2024;390:889-899

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Omalizumab for the Treatment of Multiple Food Allergies

Wood RA et al. DOI: 10.1056/NEJMoa2312382

CLINICAL PROBLEM

Food allergy affects up to 8% of children and 10% of adults in the United States, and a large percentage of people with food allergies are allergic to multiple foods. Because management has relied on food avoidance and emergency treatment in cases of accidental exposure, quality of life is affected. Omalizumab, a monoclonal anti-IgE antibody, holds promise as a monotherapy for people with multiple food allergies.

CLINICAL TRIAL

Design: A phase 3, multicenter, double-blind, randomized, placebo-controlled trial assessed the efficacy and safety of omalizumab for patients with multiple food allergies, including peanut allergy.

Intervention: 177 children and adolescents 1 to 17 years of age who were allergic to peanuts (i.e., had food challenge reactivity to ≤100 mg of peanut protein) and at least two other protocol-specified foods (food challenge reactivity to ≤300 mg of cashew, egg, milk, walnut, wheat, or hazelnut) were assigned, in a 2:1 ratio, to receive subcutaneous omalizumab or placebo every 2 to 4 weeks for 16 to 20 weeks, after which the food challenges were repeated. The primary end point was consumption of a single dose of ≥600 mg of peanut protein without dose-limiting symptoms.

RESULTS

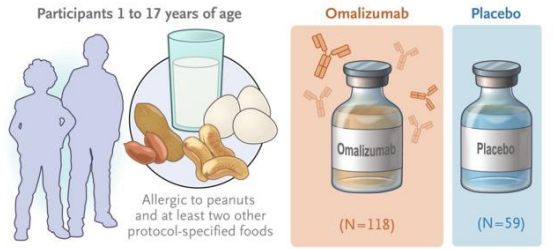
Efficacy: The percentage of participants who were able to consume ≥600 mg of peanut protein without dose-limiting symptoms was nearly 10 times higher in the omalizumab group than in the placebo group. Key secondary end points (the consumption of cashew, egg, or milk at prespecified threshold doses) also favored omalizumab.

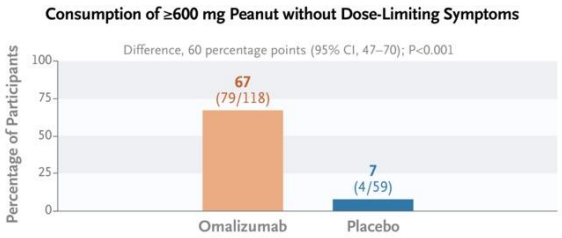
Safety: The incidence of adverse events was similar in the two groups.

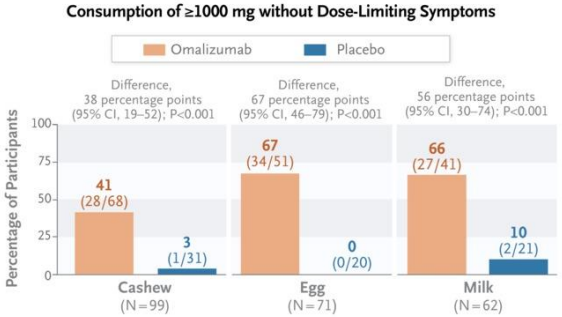
LIMITATIONS AND REMAINING QUESTIONS

- The cohort comprised mostly non-Hispanic and White children, which limits the generalizability of the findings.
- Patients with high baseline IgE levels were excluded.

Links: Full Article | NEJM Quick Take | Editorial



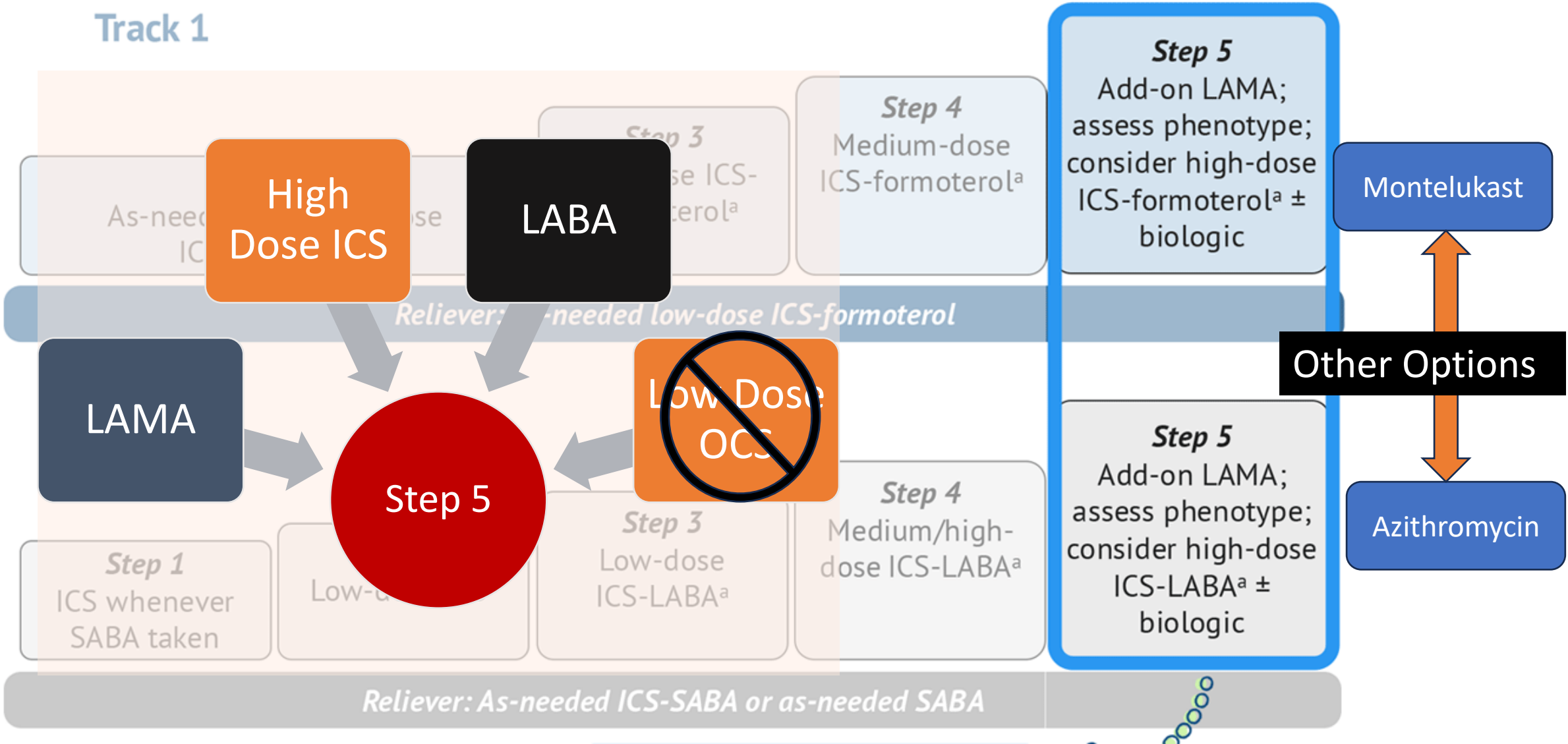




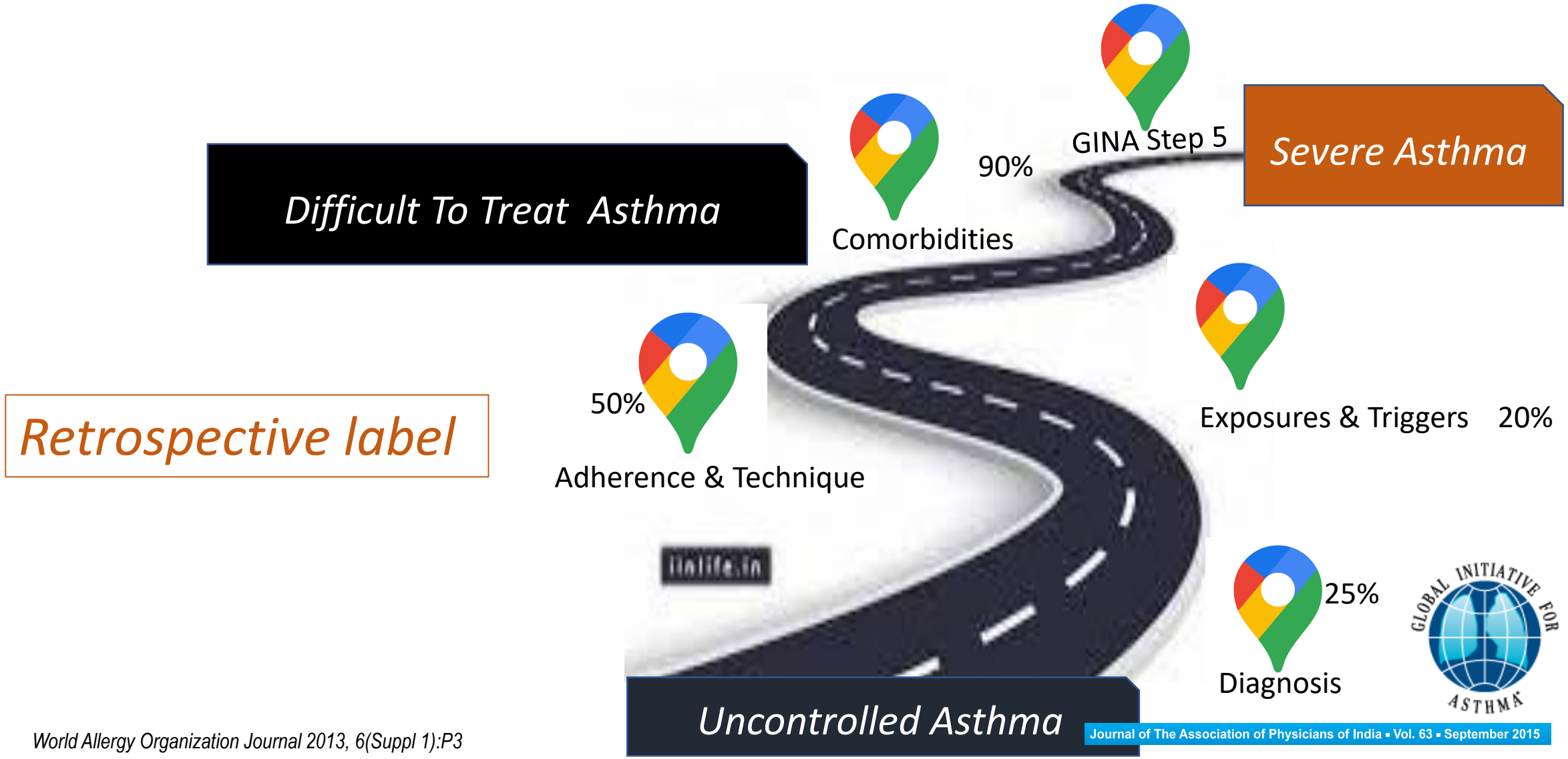
CONCLUSIONS

In children as young as 1 year of age with multiple food allergies, including peanut allergy, omalizumab was superior to placebo in increasing the reaction threshold for peanut and other common food allergens.

Severe Asthma and Biologicals



All Uncontrolled Asthma is *NOT* Severe Asthma # Biologicals



Retrospective label

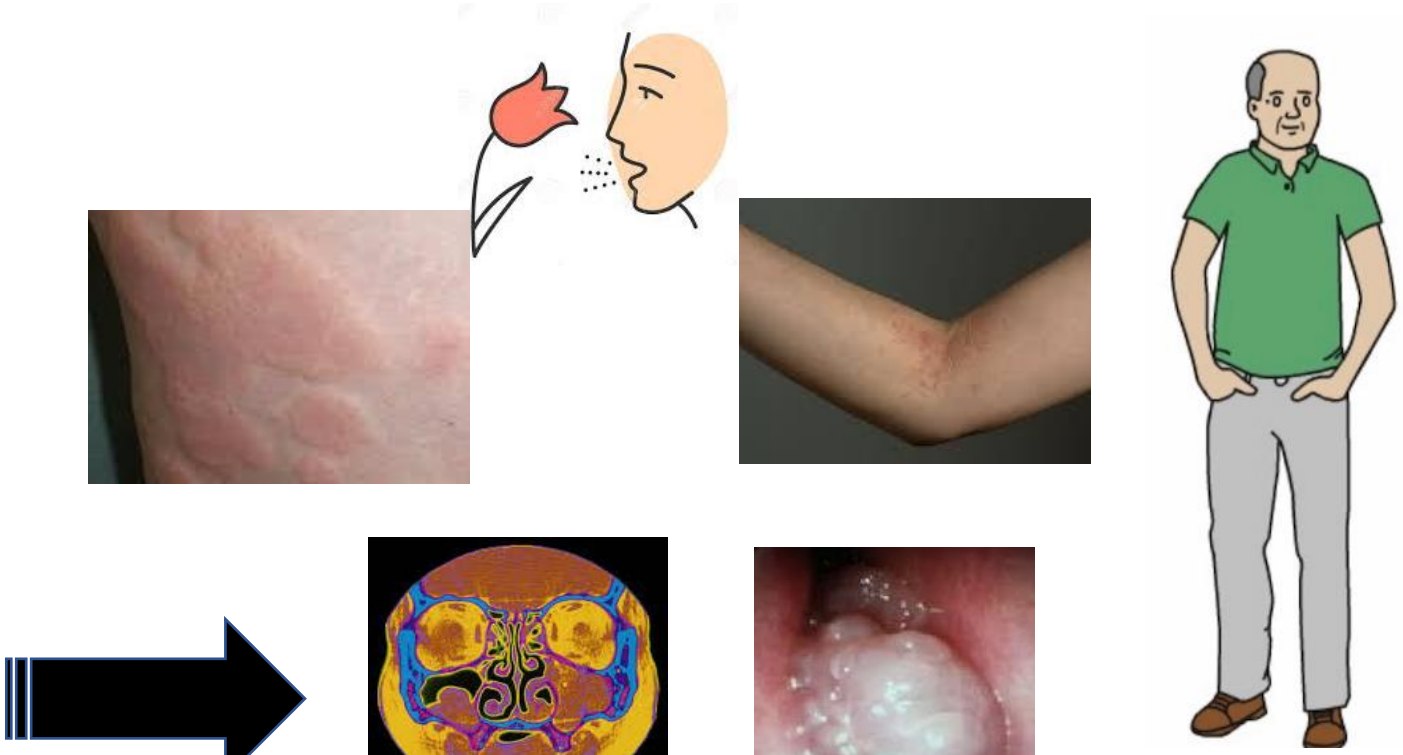
World Allergy Organization Journal 2013, 6(Suppl 1):P3

Which Patients with Severe Asthma ?

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

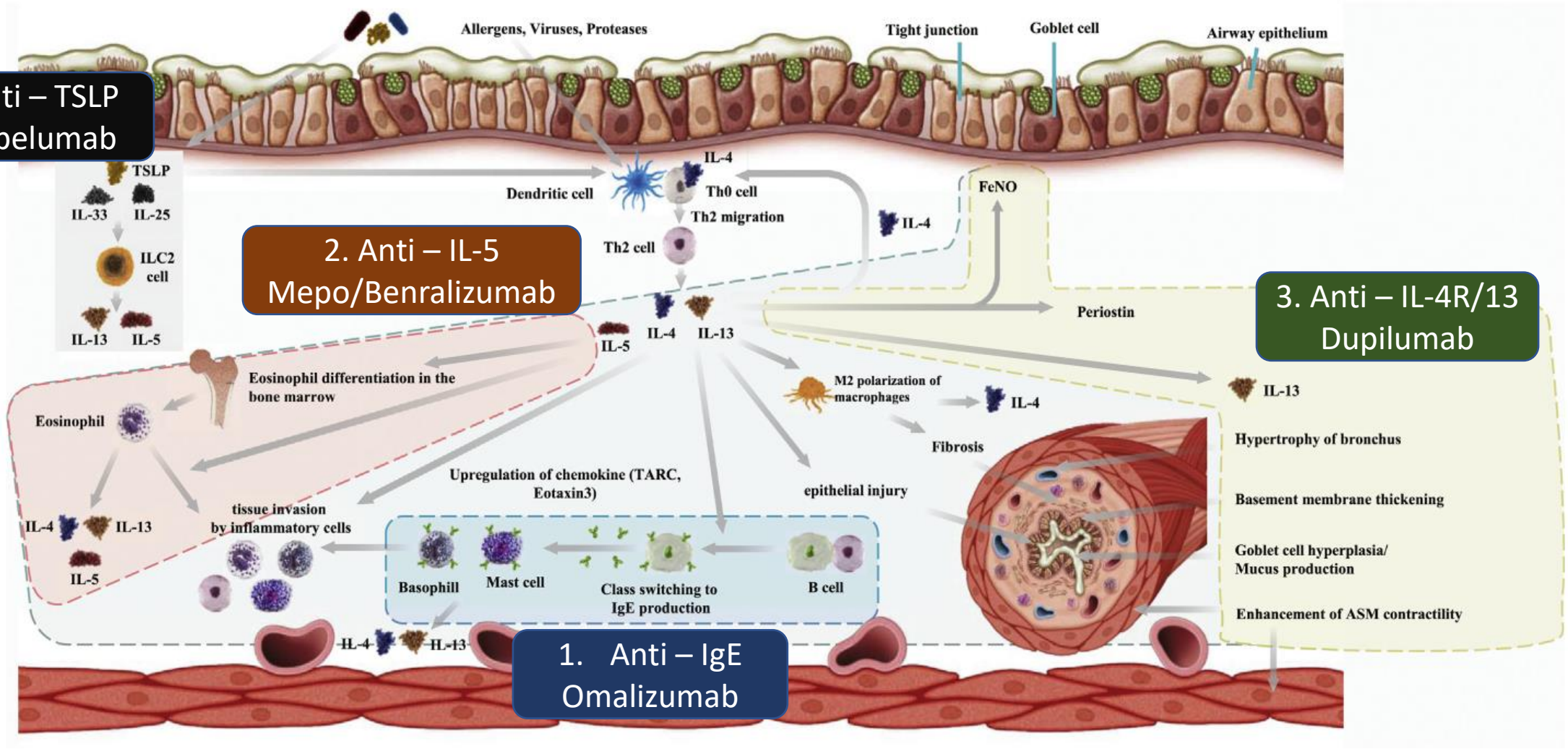
Choosing Appropriate Biologicals in Asthma- *Drivers*

4. Anti – TSLP
Tezepelumab

2. Anti – IL-5
Mepo/Benralizumab

3. Anti – IL-4R/13
Dupilumab

1. Anti – IgE
Omalizumab



K. Matsunaga et al. / Allergology International 69 (2020) 187e196

Choosing Biologicals in SA : Match Expectations with Research

SA Outcomes	Omalizumab	Mepolizumab	Benralizumab
Reduction in Exacerbations	25% reduction	~ 50 %	40 -70 %
Reduction in maintenance dose of 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
Comorbidities	CRwNP Chronic Idiopathic Urticaria	EGPA (300 mg/ month) CRSwNP	WIP

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

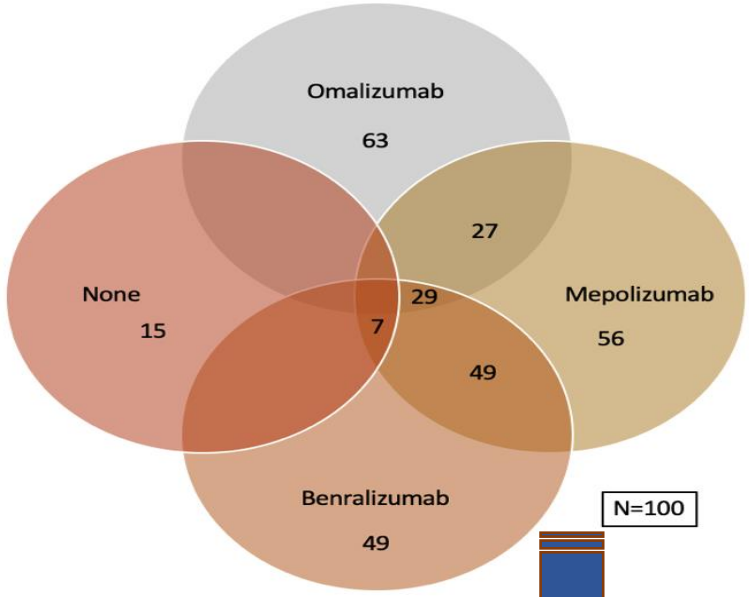
Deepak Talwar[1], Dhruv Talwar[2], Nitin Jain[3], Deepak Prajapat[4], Sourabh Pahuja[4]

[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

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

Lung India 2022;39:393-400.

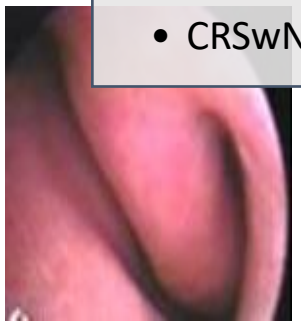
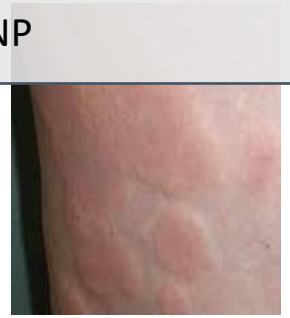
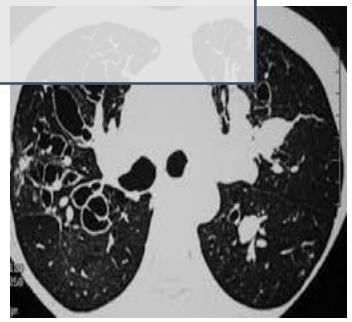
How to Choose Biologicals in Severe Asthma in India - 2024 !

Omalizumab

Childhood Onset asthma

Comorbidities :

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

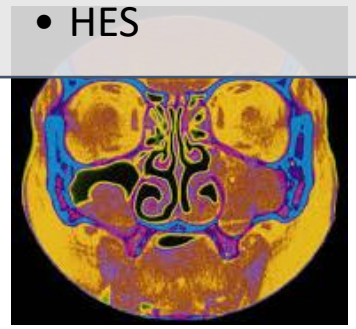
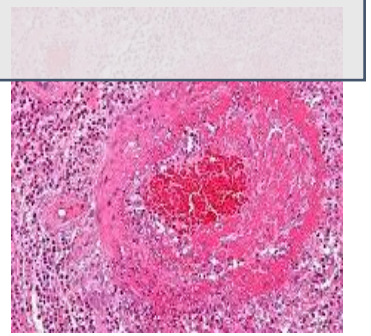




Mepolizumab

Late Onset asthma

Comorbidities :

- Chronic Sinusitis with NP
- EGPA
- HES

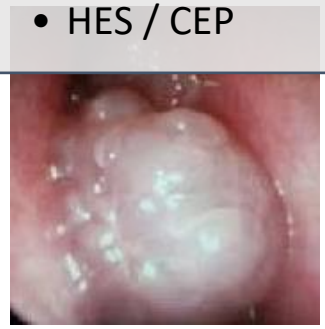
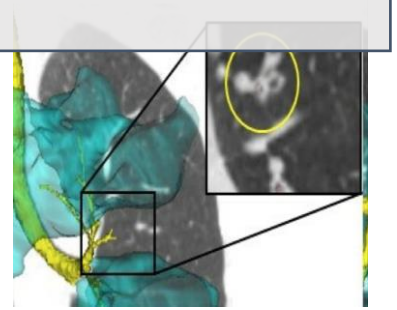



Benralizumab

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 2023***

Algorithm for Using Biologicals in Allergy's

Patient selection

- Allergic Disease : BA / CRS/Urticaria / Atopic Dermatitis/ Food Allergy
- Type 2 Inflammation: IgE / Eosinophil / Both
- On optimized. baseline therapy of underlying condition
- Poor control of disease
- Any OCS use

Choice of Biological

- Biological approved indication
- Local availability
- Experience
- Best fit choice if eligible more > 1 biological Approvals from
- Patients' preference
- Cost vs reimbursement

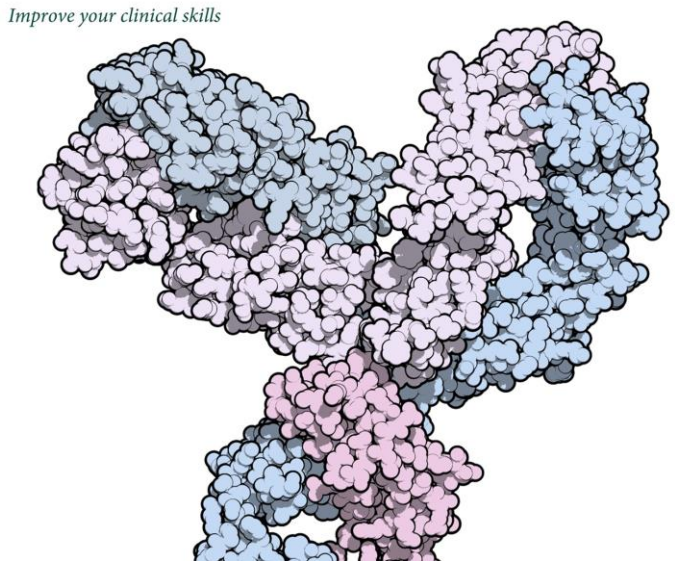
Treatment Response

- @ 16 weeks evaluate :
- QoL
- Disease control
- Exacerbations
- Hospitalizations
- ER visits
- Symptom burden reduction
- Decrease in treatment intensity
- OCS use

Biologicals In Allergies : Conclusions

Allergic Rhinitis	Omalizumab
CRSwNP	Dupulimab / Benralizumab / Mepolizumab
Chronic Idiopathic Urticaria	Omalizumab
Atopic Dermatitis	Dupulimab
Multifood Allergy	Omalizumab
Severe T_2 High Asthma	Omalizumab / Mepolizumab or Benralizumab

Thank You



Deepak Talwar

Director & Chair, Metro Centre for Respiratory Diseases

INDIA

METRO CENTRE FOR
Respiratory
Diseases