

# Can We Control the Uncontrollable?

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- I have no actual or potential conflict of interest in relation to this program
- I have not used artificial intelligence in the development of this presentation

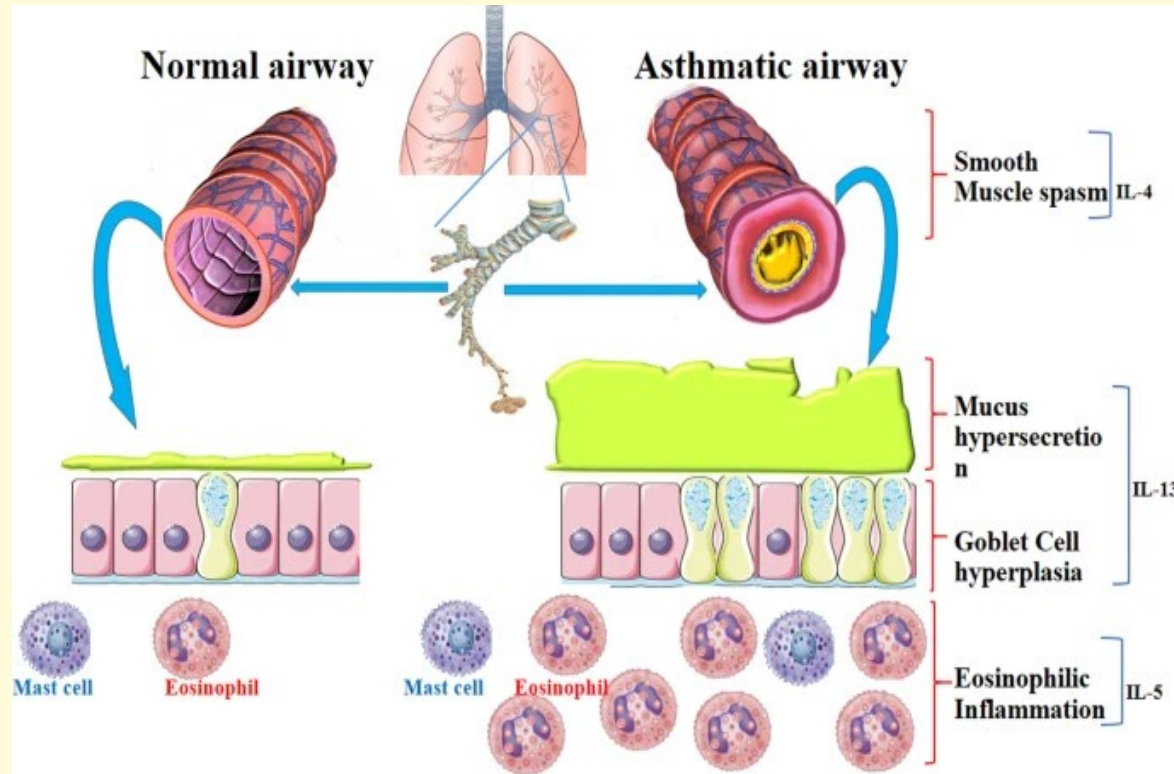
# Objectives

- Explain the treatment modality for a familiar and prevalent condition: Severe Asthma (SA)
- Identify when to consider alternate treatment options for asthma if uncontrolled
- Apply safe, innovative, and effective medical practice that will improve patient outcomes and their quality of life

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# Background

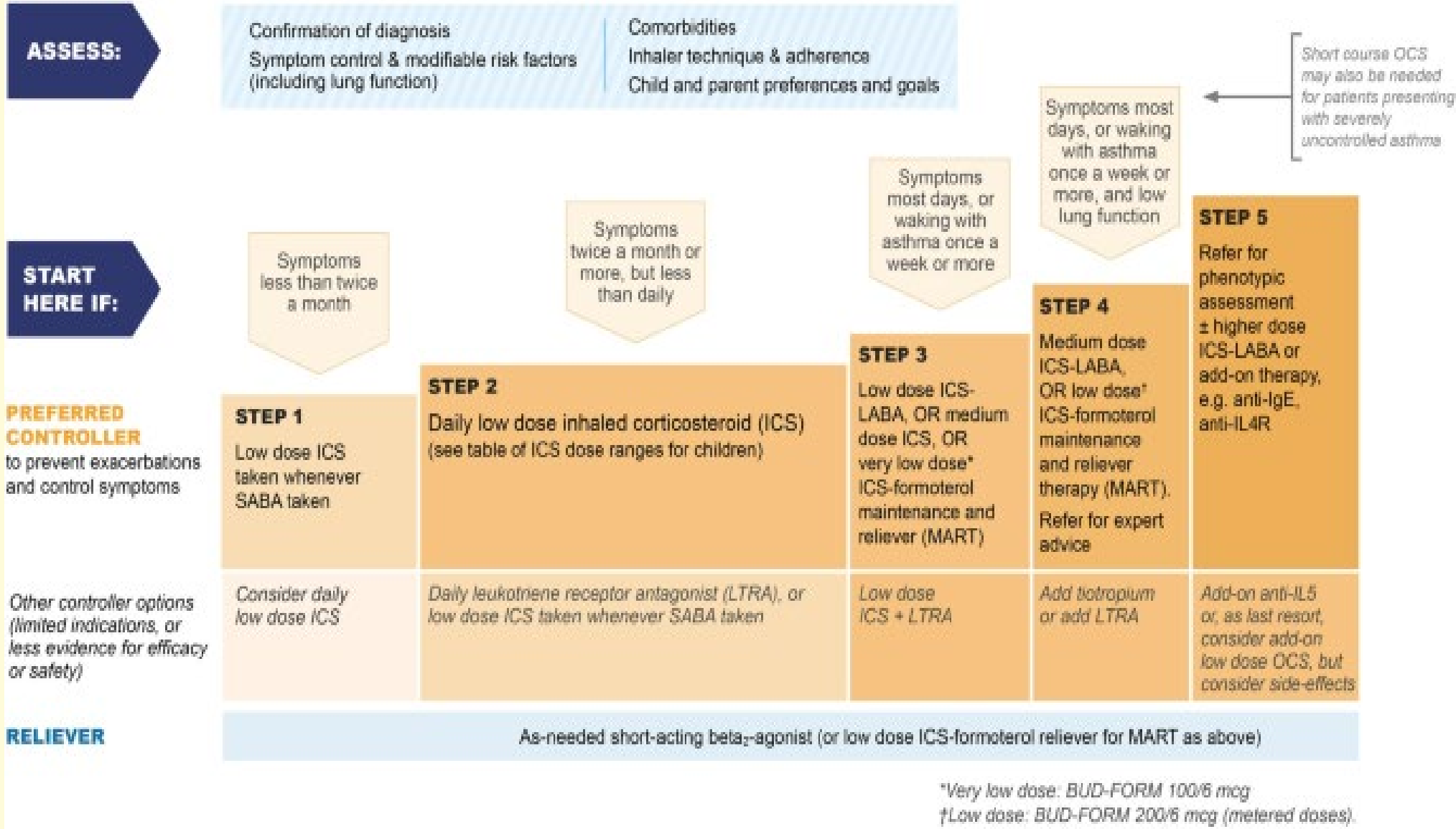


Athari, 2019  
Foster, 2017

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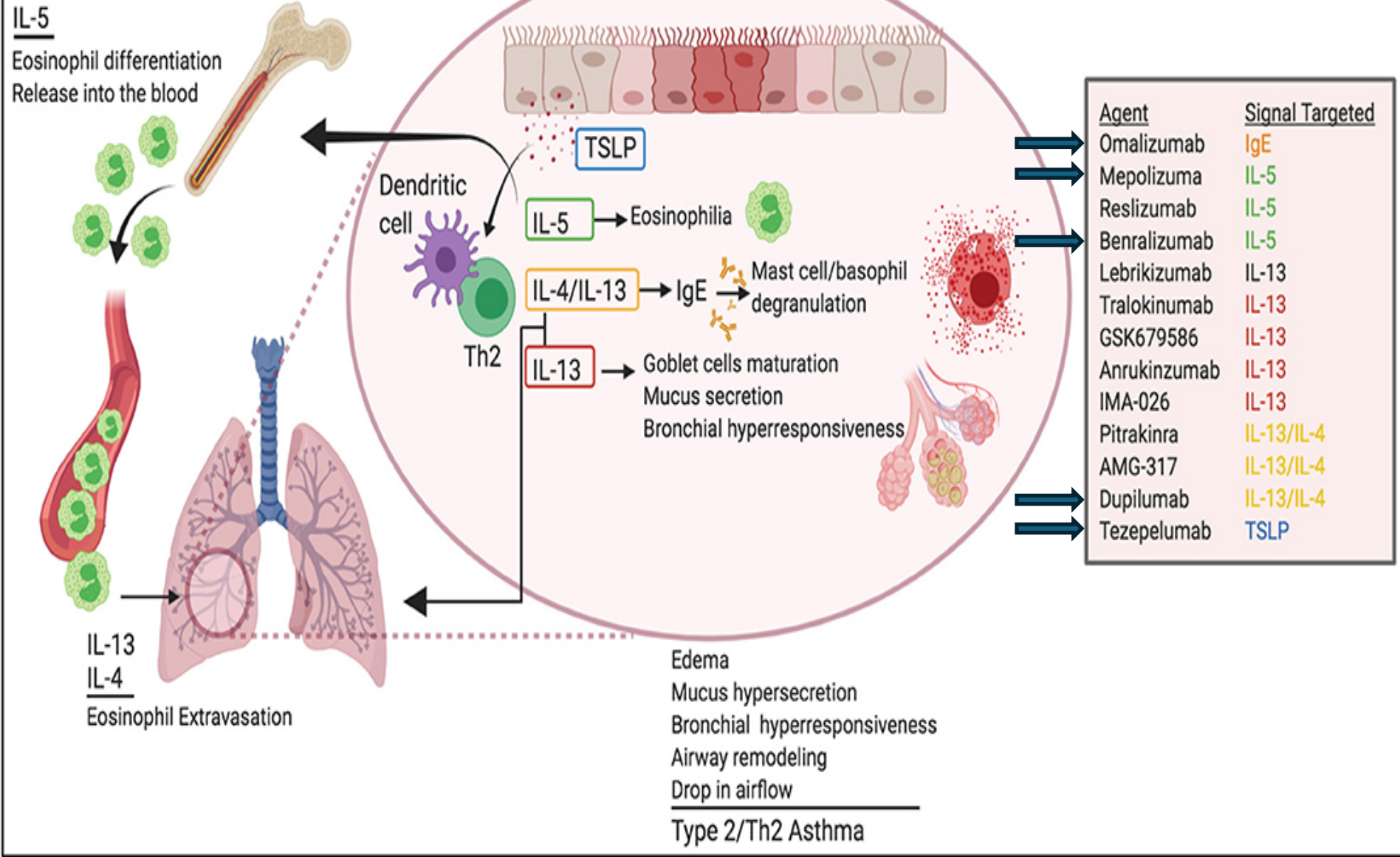






**IL-5**

Eosinophil differentiation  
Release into the blood



Agent	Signal Targeted
Omalizumab	IgE
Mepolizuma	IL-5
Reslizumab	IL-5
Benralizumab	IL-5
Lebrikizumab	IL-13
Tralokinumab	IL-13
GSK679586	IL-13
Anrakinzumab	IL-13
IMA-026	IL-13
Pitrakinra	IL-13/IL-4
AMG-317	IL-13/IL-4
Dupilumab	IL-13/IL-4
Tezepelumab	TSLP

IL-13  
IL-4  
Eosinophil Extravasation

Edema  
Mucus hypersecretion  
Bronchial hyperresponsiveness  
Airway remodeling  
Drop in airflow  
**Type 2/Th2 Asthma**



# So which biologic do we choose?

This -umab That -umab



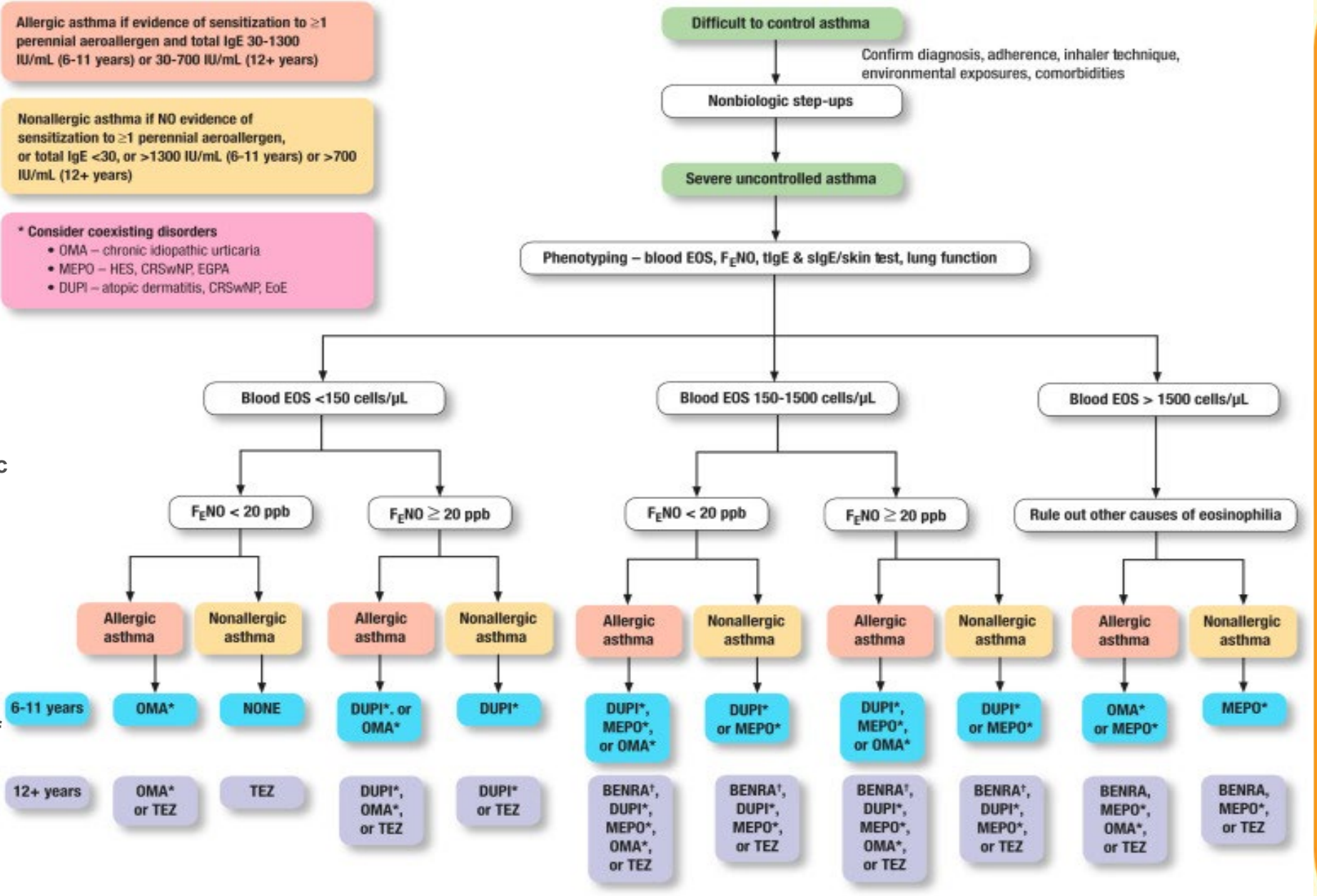


**BENRA:** Benralizumab  
**CRSwNP:** chronic rhinosinusitis with nasal polyposis  
**DUPI:** dupilumab  
**EGPA:** eosinophilic granulomatosis with polyangiitis  
**EoE:** eosinophilic esophagitis  
**EOS:** eosinophils  
**HES:** hypereosinophilic syndrome  
**MEPO:** mepolizumab  
**OMA:** omalizumab  
**TEZ:** tezepelumab  
 \*Consider coexisting atopic disorders  
 †BENRA: considered if EOS ≥ 300 cells/μL

Allergic asthma if evidence of sensitization to ≥1 perennial aeroallergen and total IgE 30-1300 IU/mL (6-11 years) or 30-700 IU/mL (12+ years)

Nonallergic asthma if NO evidence of sensitization to ≥1 perennial aeroallergen, or total IgE <30, or >1300 IU/mL (6-11 years) or >700 IU/mL (12+ years)

\* Consider coexisting disorders  
 • OMA – chronic idiopathic urticaria  
 • MEPO – HES, CRSwNP, EGPA  
 • DUPI – atopic dermatitis, CRSwNP, EoE





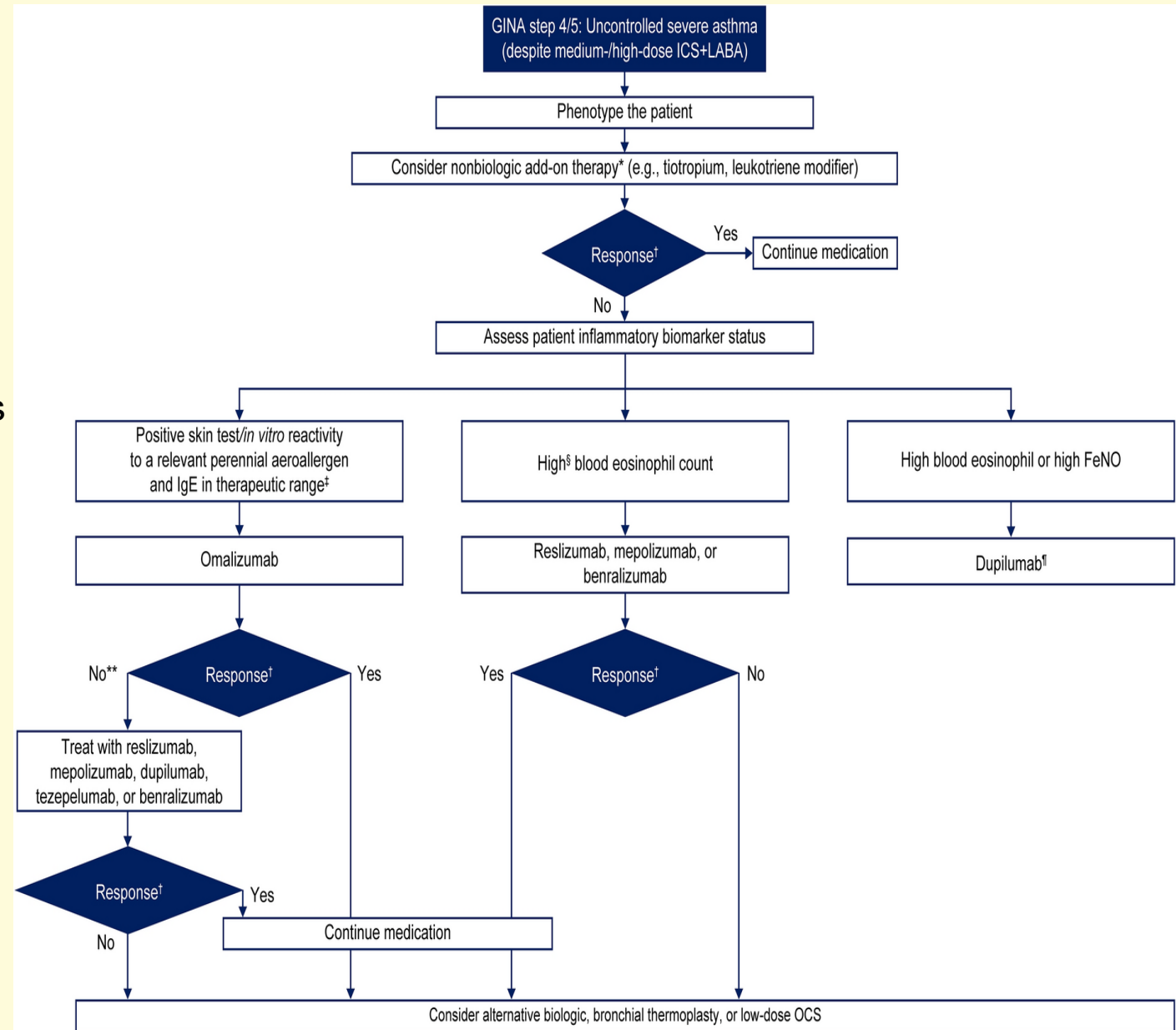
# Is the uncontrolled “controlled”?

## - Consider

- Asthma control
- Lung function
- Adverse events
- Use of systemic corticosteroids
- Pt satisfaction
- Biomarker trends

## - Evaluate response

- > Super responder
- > Partial responder
- > Non-responder
- > Inconclusive response



**Table II Adverse effect profiles of biologics for asthma**

<b>Biologic agent</b>	<b>Common adverse reactions</b>	<b>Agent-specific adverse reactions/safety concerns</b>	<b>Rare agent-specific adverse reactions/safety concerns</b>
Omalizumab	Injection-site reactions	Serum sickness, hypereosinophilic conditions (EGPA)	Anaphylaxis (black box warning)
Mepolizumab	Injection-site reactions	Helminthic infections, hypereosinophilic conditions (EGPA)	Hypersensitivity reactions, herpes zoster infection
Dupilumab	Injection-site reactions, URI/nasopharyngitis	Transient eosinophilia, helminthic infection, conjunctivitis (with atopic dermatitis)	Hypersensitivity reactions
Benralizumab	Injection-site reactions, nasopharyngitis	Helminthic infections,	Hypersensitivity reactions
Tezepelumab	Injection-site reactions, nasopharyngitis, URI, headache	Pharyngitis, arthralgia, back pain, hypersensitivity reactions	

These profiles are presented irrespective of patient age.

*EGPA*, Eosinophilic granulomatosis with polyangiitis; *URI*, upper respiratory tract infection.

# Case Presentation

10-year-old male with past medical history of severe uncontrolled asthma, obesity, atopic dermatitis, and non-allergic rhinitis who presented with several severe asthma exacerbations requiring multiple hospitalizations, ICU admissions, intubations, AVCO2R and ECMO treatment. Initially, he was solely followed by Pediatric Pulmonology and his controller medications included conventional agents (Symbicort and Spiriva). Unfortunately, severe exacerbations were frequently recurrent and associated with frequent respiratory infections requiring hospitalizations. At that time, he had been admitted 18 times for asthma exacerbations, 16 of those were associated with infectious processes. He was then also referred to Allergy and Immunology (AI) for co-management of these issues.

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# Case Presentation

- Spirometry testing performed at his initial visit
  - (FEV1/FVC)= 64% (65.5/89.6)
  - FEF25-75= 24%
    - Consistent with lower airway disease + moderate obstruction
- Labs:
  - Eosinophilia (Eos:# 800 cells/uL, Eos%:13.7)
  - IgE 89 IU/mL
    - Consistent with patient's atopic history

# Case Presentation cont.

Given this case:

- SA, uncontrolled
- Poor lung function
- Age at the time
- Labs

What biologic would you start him on?

Biologics: Overview, Dosing, and Efficacy						
Biologics Comparison	Omalizumab (Xolair)	Mepolizumab (Nucala)	Benralizumab (Fasenra)	Reslizumab (Cinqair)	Dupilumab (Dupixent)	Tezepelumab (Tezspire)
Patient website	<a href="http://xolair.com">xolair.com</a>	<a href="http://nucala.com">nucala.com</a>	<a href="http://fasenra.com">fasenra.com</a>	<a href="http://cinqair.com">cinqair.com</a>	<a href="http://dupixent.com">dupixent.com</a>	<a href="http://tezspire.com">tezspire.com</a>
Approved age	≥ 6 years	≥ 6 years	≥ 12 years	≥ 18 years	>6 years	≥ 12 years
Available for home injection?	Yes	Yes	Yes	No	Yes	Yes
Dosing (SQ= subcutaneous, under the skin)	Based on total IgE and weight SQ every 2-4 weeks	≥12: 100 mg SQ every 4 weeks 6-11: 40 mg SQ every 4 weeks	30 mg SQ every 4 weeks x 3 doses, then 30 mg SQ every 8 weeks	3 mg/kg IV every 4 weeks	Dosing depends on age, weight, indication: every 2-4 weeks	210mg SQ every 4 weeks
Mechanism of Action	IgE antagonist	IL-5 antagonist	IL-5 antagonist	IL-5 antagonist	IL-4 and IL-13 dual inhibitor	Thymic stromal lymphopoietin (TSLP) inhibitor
Qualifying lab data	Total IgE ≥ 30 IU/mL	Eosinophils ≥ 150 cells/μL	Eosinophils ≥ 150 cells/μL	Eosinophils ≥ 400 cells/μL	None required but benefits seen with Eosinophils > 150- 300 cells/uL	None required

# Case Presentation cont.

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Hing, 2023

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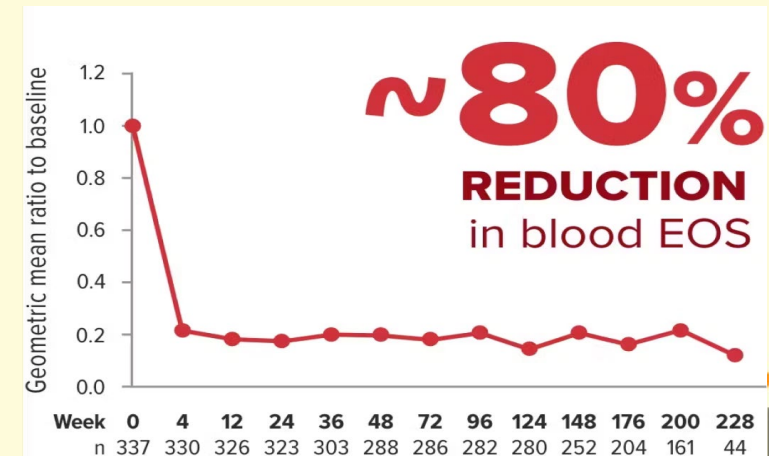
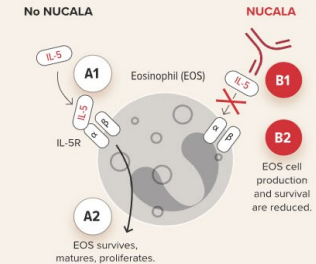


# Analysis and application

- **3 months following Nucala tx initiation**
  - **(FEV1/FVC)= 88.1%** vs prior: 64%
  - **FEF25-75= 96.5%** vs prior: 24%
  - **Eosinophilia resolution**  
Eos:# 0.0, Eos%:0  
vs prior: Eos:# 0.8, Eos%:13.7
- Admitted 3 x since Nucala vs. prior:18
  - 1. Uncomplicated asthma exacerbation 07/2021 (1 mo. after starting Nucala)
  - 2,3. Asthma exacerbations 2/2 viral infections (Rhinovirus 09/2021, COVID-19 01/2022)
  - 0 admissions for SA exacerbation since 01/2022

## TARGET EOSINOPHILS IN SEVERE ASTHMA WITH ANTI-IL-5 THERAPY

How NUCALA targets eosinophils



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# MOC Questions (Slido)







# MOC Questions (Slido)



# Review of Content

For those (> 6 yoa) with SA who have not responded to traditional tx:

- Get a detailed PE and history and counsel on trigger avoidance
- Investigate further
  - What are the triggers?
  - Comorbidities?
  - Compliance?
  - Control?
  - Lung function?
  - Biomarkers?
- Consult Peds Pulm and AI teams

Lizzo, 2024

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# Review of Content

- Consider adding biologic therapy when conventional options for SA are exhausted
- Evaluate which biologic would be best fit for uncontrolled SA candidates (i.e. according to age, triggers, biomarkers, etc.)
- After initiating biologic tx, is the uncontrolled ...“controlled?”
- When to “step down” after “stepping up”
- Re-evaluate: is the uncontrolled still... “controlled?”
- RCT’s published reveal evidence of biologics as efficacious tx for SA
  - reductions in annual rate of SA exacerbations by 40-50%

# Action Items

- Revolutionary developments in medicine are happening - keep thinking forward
- Prevention AND Treatment are goal
- Funding
- More research for biologics in pediatrics is necessary
  - Efficacy & Safety
  - Comparative studies measuring efficacy between biologics
  - Asthma endotypes and phenotypes classification to aid therapy and response
  - Biologic tx early on - can it change the course of SA in the long run?
  - Ensure diversity amongst research trials

Bacharier, 2023

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# References and additional reading

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# Resources

For patients and providers


- **Podcast:**
  - [About the Show — The Itch Podcast](#)  
([The Itch: Allergies, Asthma, Eczema & Immunology: #56 - Biologic Therapies for Asthma on Apple Podcasts](#))

- **Reading:**
  - [Biologics for the Management of Severe Asthma](#)  
( [www.aaai.org](#) > [Tools for the Public](#) > [Conditions Library](#) > [Library Articles: Asthma](#) > [Biologics for the Management of Severe Asthma](#) )

For providers

- **Reading:**
  - *“Biologics in the treatment of asthma in children and adolescents”*- Bacherier, Jackson 2023
- **Audio/Visual:**
  - Peer View Live (recorded) symposium session on *Selecting Targeted Treatment for Pediatric and Adult Patients with Uncontrolled, Moderate to Severe Asthma*- Bacherier, Kraft 2023

Apple Podcasts Preview



**#56 - Biologic Therapies for Asthma**  
The Itch: Allergies, Asthma, Eczema & Immunology  
Medicine

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In this episode, we explore a new form of asthma treatment, Biologics. These innovative treatments offer targeted relief by addressing the underlying causes of asthma, leading to improved symptom control and a better quality of life. Dr. G and Kortney discuss the current biologics for asthma treatment.

[Episode Website](#)

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38 min PLAY

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*Review articles*

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**Biologics in the treatment of asthma in children and adolescents** [Check for updates](#)

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