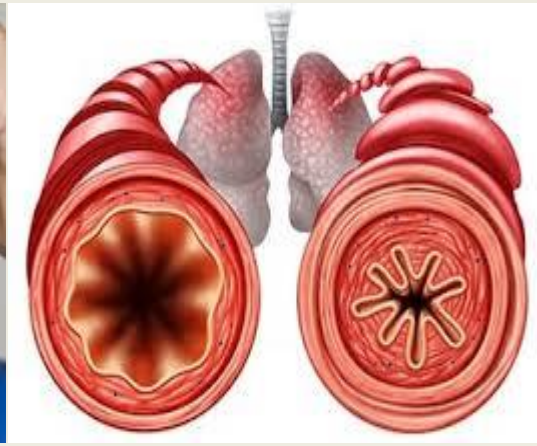
Asthma Management

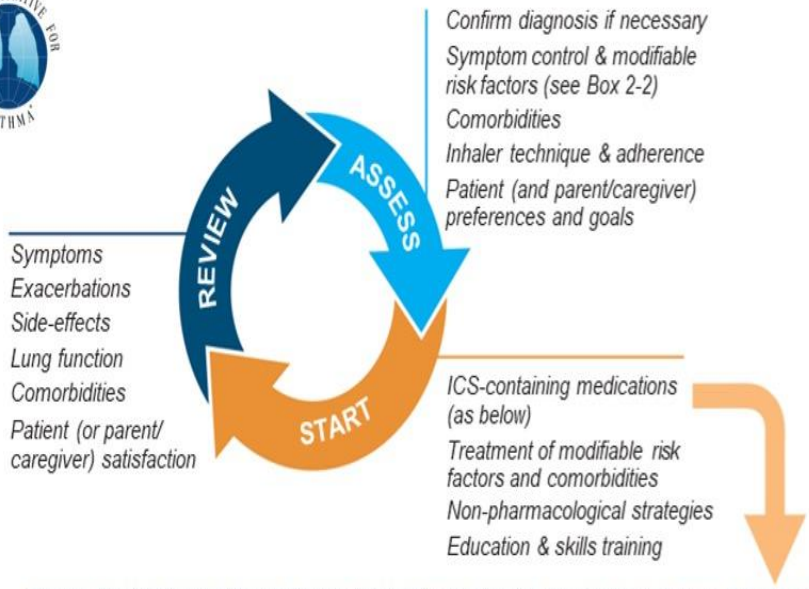



Dr. M. Hadi Alakkad

Stable Asthmatic Patient Approach

GINA 2024 – STARTING TREATMENT

in adults and adolescents 12+ years with a diagnosis of asthma



These recommendations are based on the (little) available evidence and consensus

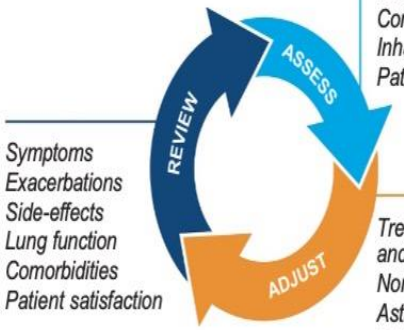
IF the patient has:	START WITH:	TRACK 1 (preferred)	OR	TRACK 2	
Daily symptoms, waking at night once a week or more and low lung function, or recent exacerbation	YES	Medium dose ICS-formoterol maintenance and reliever (MART)		Medium/high dose ICS-LABA + as-needed SABA (or ICS-SABA)	STEP 4
Symptoms most days, or waking at night once a week or more, or low lung function	YES	Low dose ICS-formoterol maintenance and reliever (MART)		Low dose ICS-LABA + as-needed SABA (or ICS-SABA)	STEP 3
Symptoms less than 3–5 days a week, with normal (or mildly reduced) lung function	YES	As-needed-only low dose ICS-formoterol		Low dose ICS + as-needed SABA (or ICS-SABA)	STEP 2
				Take low dose ICS whenever SABA is taken	STEP 1

Short course of OCS may also be needed for patients presenting during an exacerbation

In patients with symptoms 1–2 days a week or less, adherence with daily ICS would be very poor, so taking low-dose ICS whenever SABA is taken could reduce the risk of exacerbations

GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications including ICS (as below)
Education & skills training

TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed-only low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

TRACK 2: Alternative CONTROLLER and RELIEVER
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

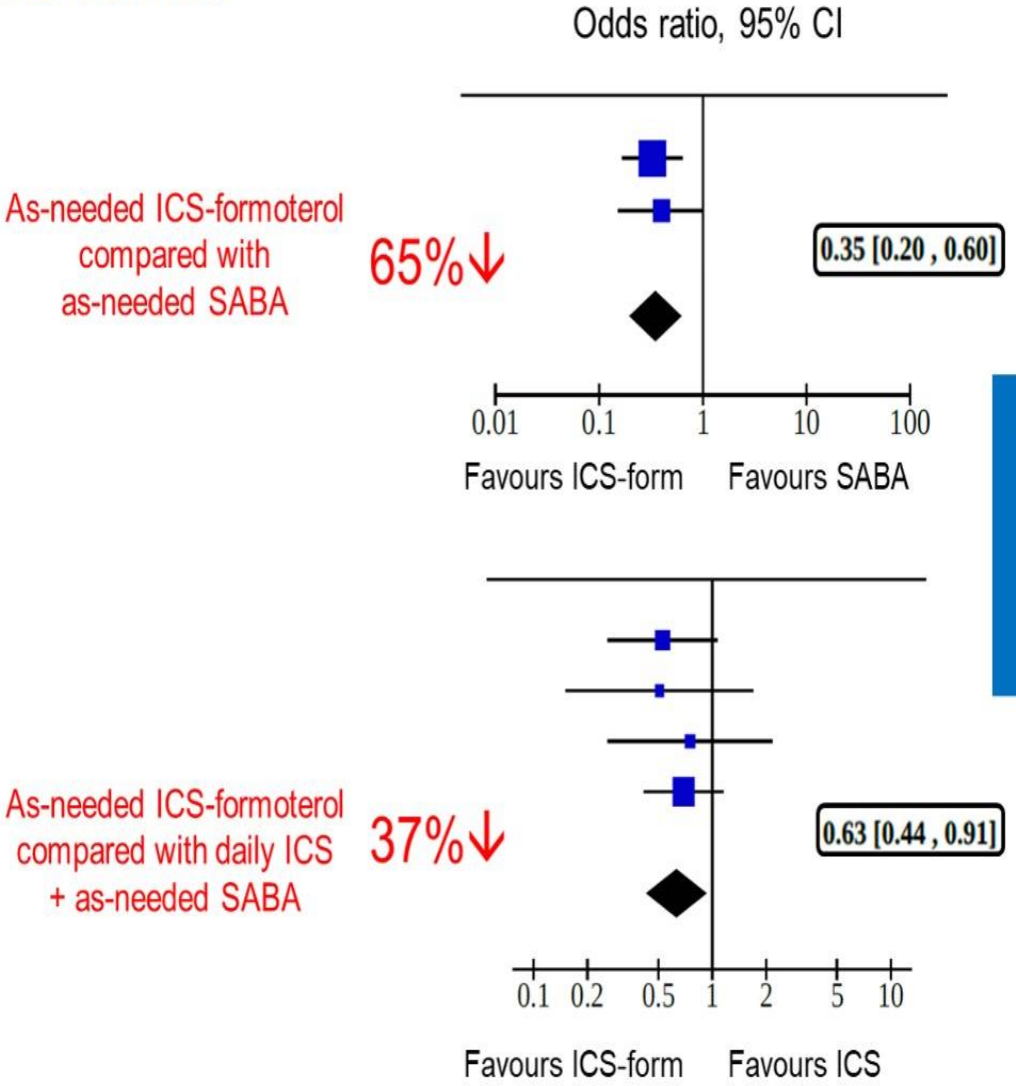
RELIEVER: As-needed ICS-SABA*, or as-needed SABA

See GINA severe asthma guide

Other controller options (limited indications, or less evidence for efficacy or safety – see text)				
Low dose ICS whenever SABA taken, or daily LTRA†, or add HDM SLIT*	*Medium dose ICS, or add LTRA†, or add HDM SLIT*	*Add LAMA or add LTRA† or add HDM SLIT, or switch to high dose ICS-only*	*Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects*	

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

As-needed-only ICS-formoterol reduces emergency visits and hospitalisations in patients with mild asthma



Approved by regulators in ~50 countries
Recommended in asthma guidelines of ~32 countries

From Crossingham et al, Cochrane Database Syst Rev 2021 (n=9565)

Assessment of asthma control

Ideally, patients should be seen **1-3 months** after starting treatment and every **3-12 months** thereafter

Asthma symptoms control tools for adults

Simple screening tools

A. Asthma symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice/week?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
• Any night waking due to asthma?	Yes☐ No☐			
• SABA reliever for symptoms more than twice/week?*	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

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Asthma symptoms control tools for adults

Asthma Control Test (ACT)

Asthma Control Test™

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
o	o	o	o	o
1	2	3	4	5

2. During the past 4 weeks, how often have you had shortness of breath?

More than Once a day	Once a day	3 to 6 times a week	Once or twice a week	Not at all
o	o	o	o	o
1	2	3	4	5

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a week	2 to 3 nights a week	Once a week	Once or twice	Not at all
o	o	o	o	o
1	2	3	4	5

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

3 or more times per day	1 or 2 times per day	2 or 3 times per week	Once a week or less	Not at all
o	o	o	o	o
1	2	3	4	5

5. How would you rate your asthma control during the past 4 weeks?

Not Controlled at All	Poorly Controlled	Somewhat Controlled	Well Controlled	Completely Controlled
o	o	o	o	o
1	2	3	4	5

Asthma symptoms control tools for adults

The asthma control test (ACT) is a validated, commonly used numeric tool to distinguish different levels of asthma symptom control. Possible scores range from **5 to 25**, with a higher score indicating better symptom control.

Asthma symptoms control tools for adults

ACT scores are classified as follows:

20-25, well-controlled asthma
16-19, not well-controlled
5-15, very poorly controlled

Role of lung function in assessing asthma control

Role of lung function in assessing asthma control

Lung function **does not correlate** strongly with asthma symptoms

Role of lung function in assessing asthma control

Lung function at individual visits is of **limited use for guiding treatment** because of its large (up to 20%) **visit-to-visit variation**

Role of lung function in assessing asthma control

Low FEV1 is **a strong independent** predictor of **risk of exacerbations** even after adjustment for symptom frequency

A low FEV_1 percent predicted:

- Identifies patients at risk of asthma exacerbations, independent of symptom levels, especially if FEV_1 is <60% predicted[96,105,162,163]
- Is a risk factor for lung function decline, independent of symptom levels[116]
- If symptoms are few, suggests limitation of lifestyle, or poor perception of airflow limitation,[164] which may be due to untreated airway inflammation.[152]

Normal FEV_1: A 'normal' or near-normal FEV_1 in a patient with frequent respiratory symptoms (especially when symptomatic) prompts consideration of alternative causes for the symptoms (e.g., cardiac disease, or cough due to post-nasal drip or gastroesophageal reflux disease;

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Persistent bronchodilator responsiveness: Finding significant bronchodilator responsiveness (increase in FEV_1 >12% and >200 mL from baseline)[35] in a patient taking ICS-containing treatment, or who has taken a SABA within 4 hours, or a LABA within 12 hours (or 24 hours for a once-daily LABA), suggests uncontrolled asthma, particularly poor adherence and/or incorrect technique.

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Role of lung function in assessing asthma control

Lung function should be assessed

- At **diagnosis or start of treatment**

- After 3-6 months of ICS- containing treatment to assess the patient's personal **best FEV1and**

Role of lung function in assessing asthma control

Lung function should be assessed

- Periodically thereafter (*e.g.* at least once **every 1–2 years**; **more often in at-risk patients** and those with **severe asthma**) to identify progressive **decline**.

Stepping up

Short- term step up (for 1-2 weeks)

A **short term increase** in maintenance ICS dose for **1-2 weeks** may be necessary (during viral infection or seasonal allergen).

This increase may be **initiated by the patient** according to their **written asthma action plan**

Sustained step up (for at least 2-3 months)

Some patients whose asthma is uncontrolled or partially controlled may benefit **from increasing the maintenance dose**.

Sustained step up (for at least 2-3 months)

A **step up** in treatment may be recommended after **confirming** that the symptoms are

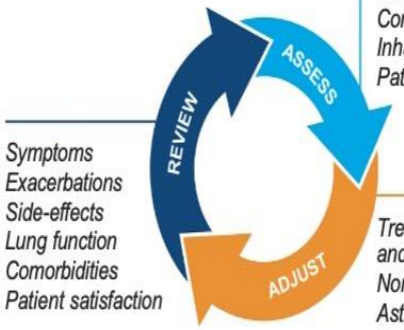
- **Due to asthma**,
- **Inhaler technique**
- **Adherence** are satisfactory
- **Modifiable risk factor** such as smoking have been addressed

Stepping Down

Once good **asthma control** has been achieved and maintained for **2-3 months** and lung function has reached a plateau, treatment can often be reduced, without loss of asthma control.

GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications including ICS (as below)
Education & skills training

TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed-only low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

TRACK 2: Alternative CONTROLLER and RELIEVER
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed ICS-SABA*, or as-needed SABA

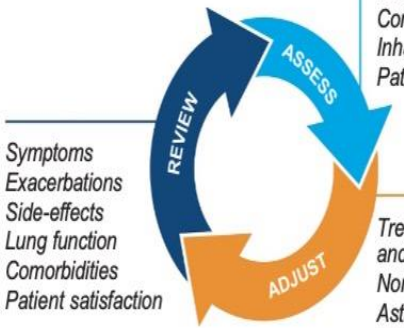
See GINA severe asthma guide

Other controller options (limited indications, or less evidence for efficacy or safety – see text)				
Low dose ICS whenever SABA taken, or daily LTRA†, or add HDM SLIT*	*Medium dose ICS, or add LTRA†, or add HDM SLIT*	*Add LAMA or add LTRA† or add HDM SLIT, or switch to high dose ICS-only*	*Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects*	

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications including ICS (as below)
Education & skills training

TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed-only low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

TRACK 2: Alternative CONTROLLER and RELIEVER
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed ICS-SABA*, or as-needed SABA

See GINA severe asthma guide

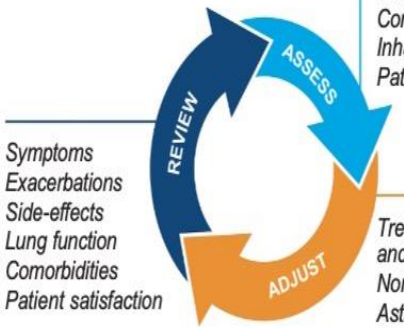
Other controller options (limited indications, or less evidence for efficacy or safety – see text)				
Low dose ICS whenever SABA taken, or daily LTRA†, or add HDM SLIT*	*Medium dose ICS, or add LTRA†, or add HDM SLIT*	*Add LAMA or add LTRA† or add HDM SLIT, or switch to high dose ICS-only*	*Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects*	

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

GINA 2024 Box 4-6

GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications including ICS (as below)
Education & skills training

TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed-only low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

TRACK 2: Alternative CONTROLLER and RELIEVER
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed ICS-SABA*, or as-needed SABA

See GINA severe asthma guide

Other controller options (limited indications, or less evidence for efficacy or safety – see text)				
Low dose ICS whenever SABA taken, or daily LTRA†, or add HDM SLIT*	*Medium dose ICS, or add LTRA†, or add HDM SLIT*	*Add LAMA or add LTRA† or add HDM SLIT, or switch to high dose ICS-only*	*Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects*	

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

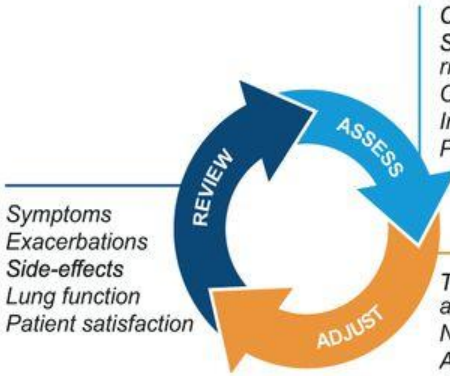
Assessing Asthma Severity

Assessing Asthma Severity

Sever Asthma is defined that remains **unconrolled** despite optimized treatment with **high dose ICS-LABA,** or that requires high dose ICS-LABA to **prevent it from becoming uncontrolled**

Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks)
Education & skills training

Sever Asthma Controlled or uncontrolled step 5

CONTROLLER and **PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-formoterol

RELIEVER: As-needed low-dose ICS-formoterol

CONTROLLER and **ALTERNATIVE RELIEVER**
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-LABA

RELIEVER: As-needed short-acting β2-agonist

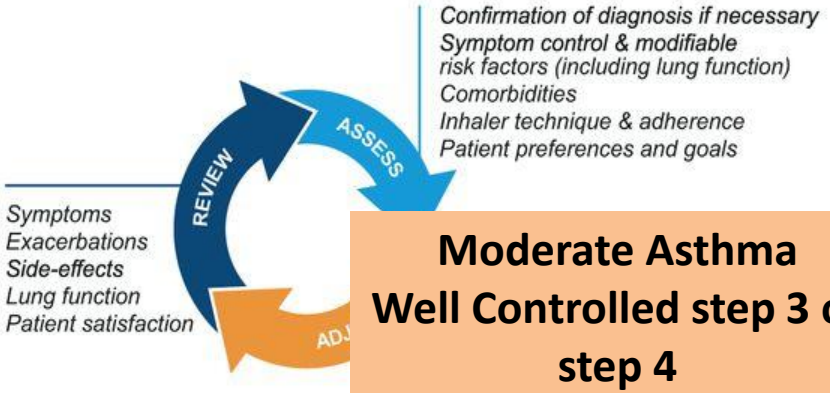
Other controller options for either track				
	Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects*

Assessing Asthma Severity

Moderate Asthma is curruntly defined as asthma that is **well controlled with step 3 or step 4 treatment**

Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Sever Asthma Controlled or uncontrolled step 5

Moderate Asthma Well Controlled step 3 or step 4

tracks)

CONTROLLER and **PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-formoterol

RELIEVER: As-needed low-dose ICS-formoterol

CONTROLLER and **ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-LABA

RELIEVER: As-needed short-acting β2-agonist

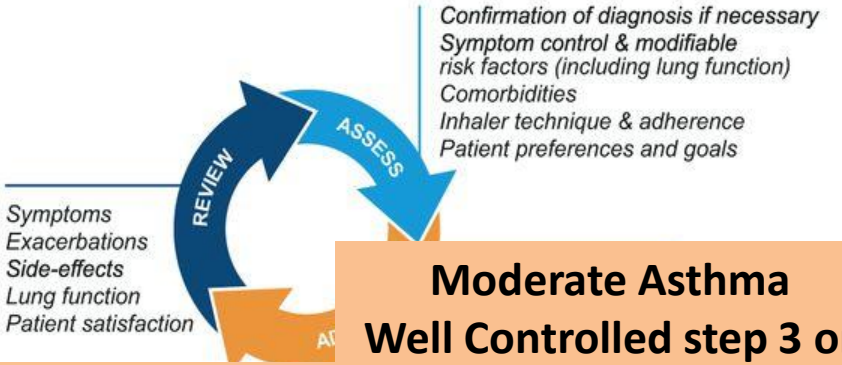
Other controller options for either track				
	Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects*

Assessing Asthma Severity

Mild Asthma is curruntly defined as asthma that is **well controlled with as needed ICS-Formoterol**, or with **low dose ICS plus as needed SABA**

Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Sever Asthma Controlled or uncontrolled step 5

Moderate Asthma Well Controlled step 3 or step 4

Mild Asthma well Controlled step 1 or step 2

tracks)

CONTROLLER and **PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-formoterol

RELIEVER: As-needed low-dose ICS-formoterol

CONTROLLER and **ALTERNATIVE RELIEVER**
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-LABA

RELIEVER: As-needed short-acting β2-agonist

Other controller options for either track				
	Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects*

Assessing Asthma Severity

By this retrospective definition, **asthma severity** can only be assessed **after good asthma control** has been achieved and treatment stepped down to find the patient's minimum effective dose, or if **asthma remains uncontrolled** despite at least several months of **optimized maximal therapy**

STEP 5

Add-on LAMA

Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

STEP 5

Add-on LAMA

Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects

SEVERE ASTHMA PHENOTYPES

Clinical Phenotypes

Well-established severe asthma **clinical phenotypes** are based on a combination of clinical characteristics that have been validated in clustering analyses of patients. These include

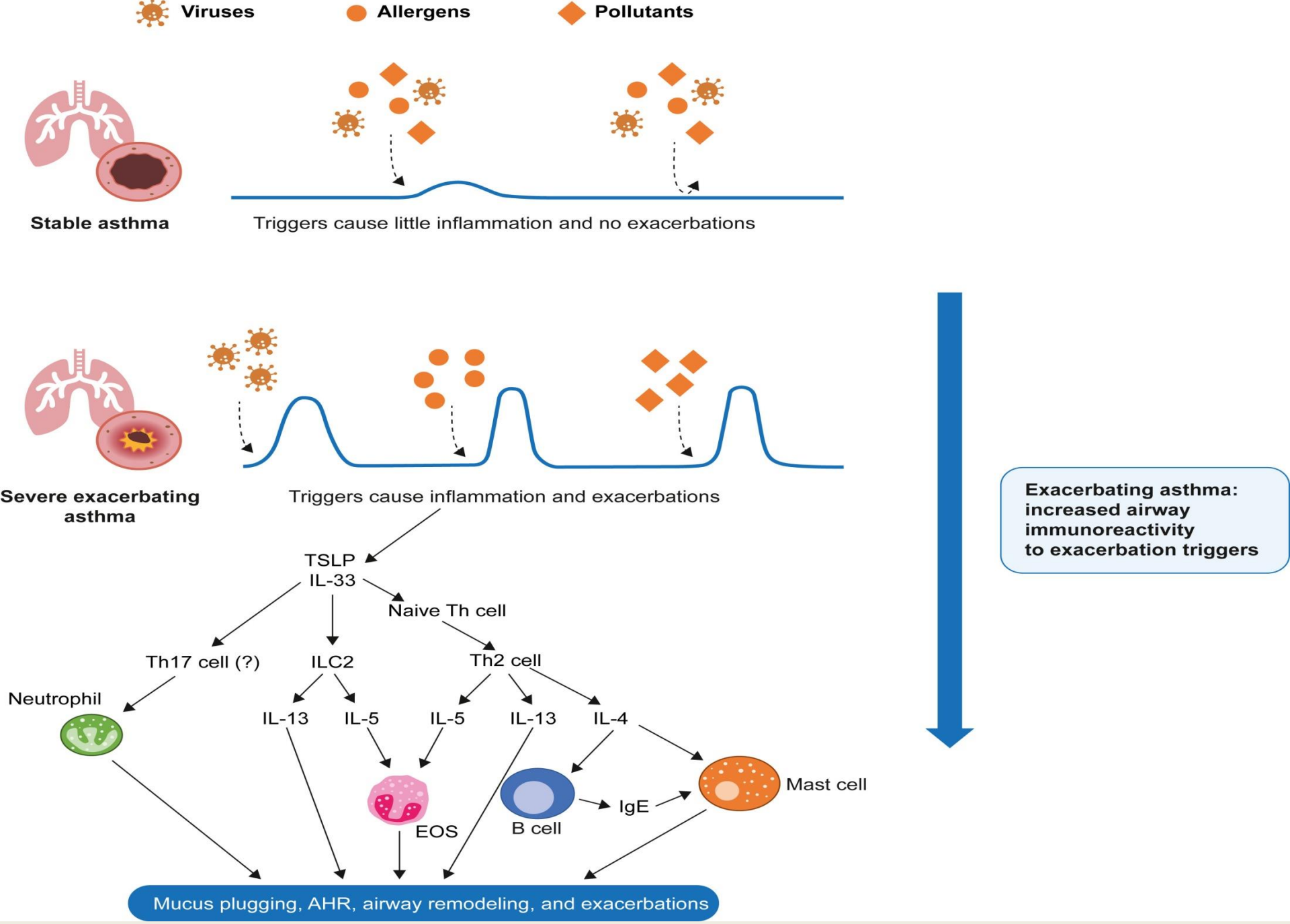
Clinical Phenotypes

- The **timing** of asthma **onset** (early vs late)
- **Atopy status** (allergic vs nonallergic),
- **Lung function** (persistence of airflow limitation),
- **Treatment response** (OCS resistance)

Clinical Phenotypes

- Other **comorbidities** (eg, **obesity**, chronic - **rhinosinusitis** with or without **nasal polyps**, gastroesophageal reflux disease, atopic dermatitis, urticaria, eosinophilic esophagitis, and **aspirin-exacerbated respiratory disease**).
- **Lung biopsy** Asthmatic granulomatosis

PHENOTYPING BASED ON BIOMARKERS OF INFLAMMATION



The Journal of Allergy and Clinical Immunology: In Practice Volume 12, Issue 4, April 2024, Pages 809-823

Asthma phenotypes are categorized into 2 main overarching inflammatory phenotypes defined by the predominant immunological pathways driving the disease pathology:

- **Eosinophilic (type 2 high asthma)**
- **Noneosinophilic (type 2 low asthma)**

Type 2/eosinophilic asthma

Approximately **70 percent of severe asthma** is associated with persistent elevation in markers of Type 2 inflammation (**blood eosinophils** and fraction of exhaled nitric oxide [FeNO])

Type 2/eosinophilic asthma

data from clinical trials suggest that blood levels of **eosinophils 150 /micro L** or **FeNO levels above 24 ppb** support an underlying active **Type 2 immune process**, which will respond to Type 2 specific therapy.

Neutrophilic asthma

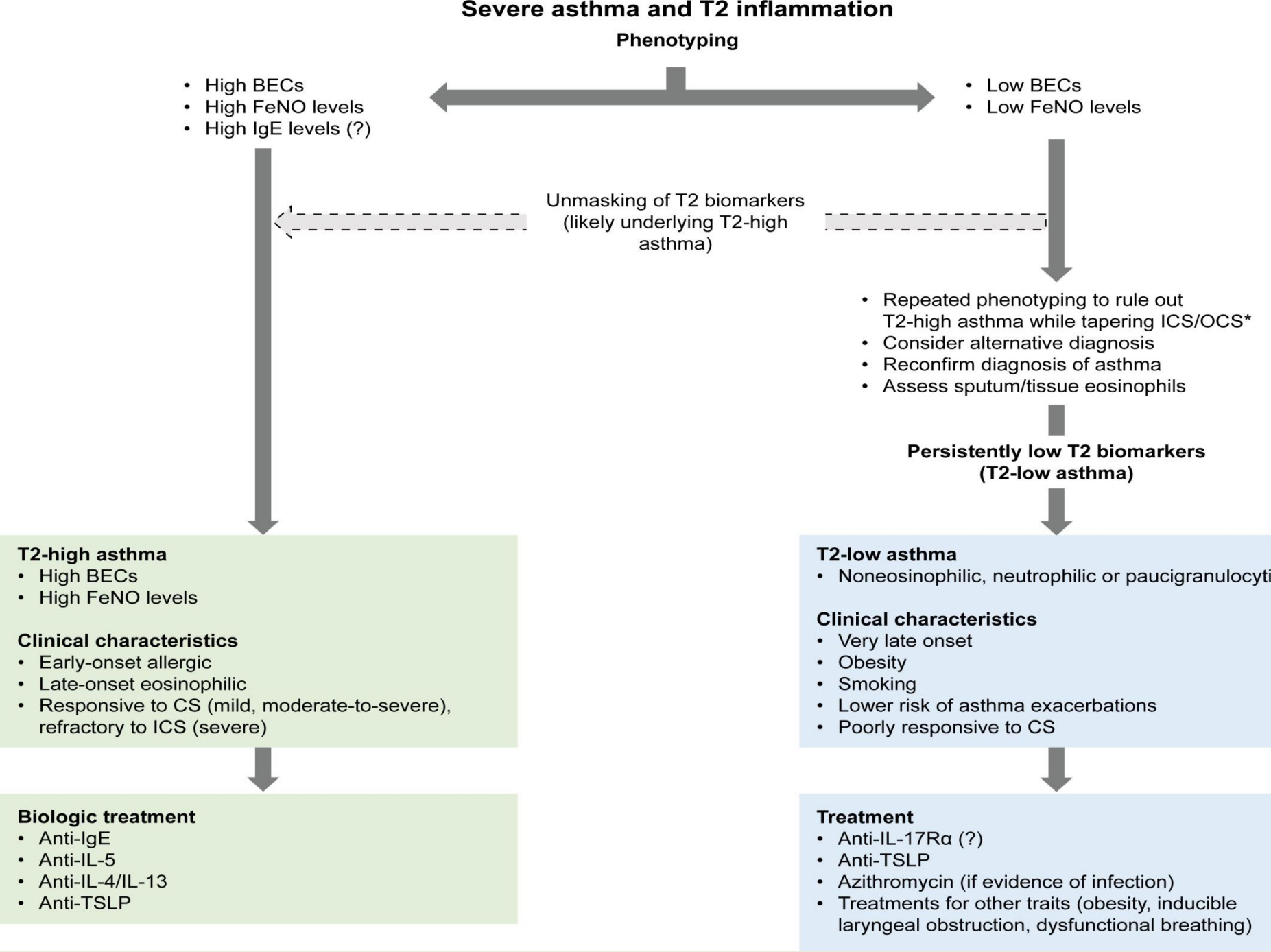
The existence of a neutrophilic asthma phenotype (eg, **40 to 60 percent neutrophils in induced sputum**) is **controversial**

Neutrophilic asthma

The specificity of neutrophilic inflammation for a particular subtype of asthma is **complicated** by the many confounding factors that can contribute to neutrophilia in sputum,

Neutrophilic asthma

- the use of inhaled glucocorticoids,
- air pollution,
- respiratory infection,
- sensitization to aspergillus,
- gastroesophageal disease



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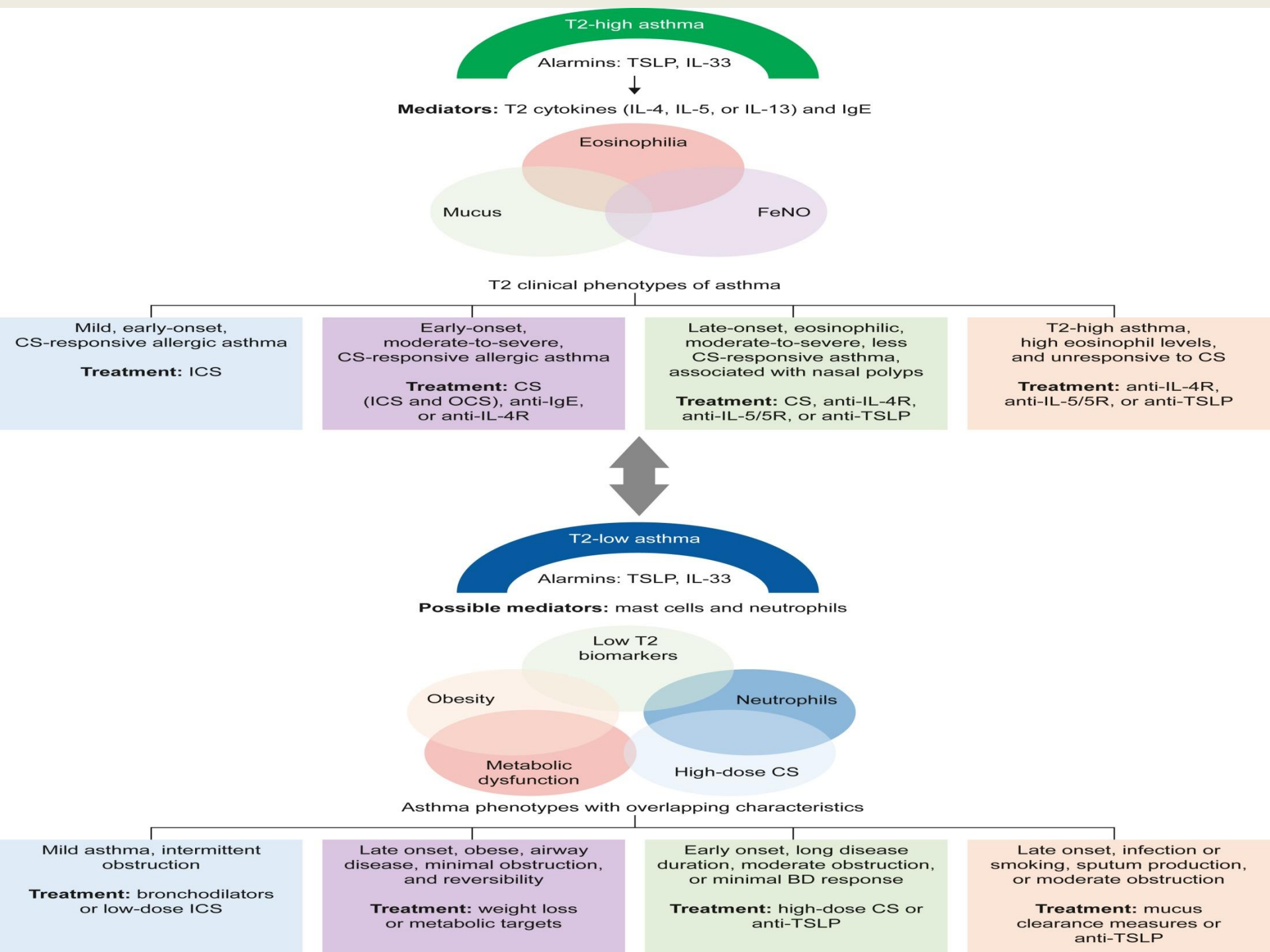
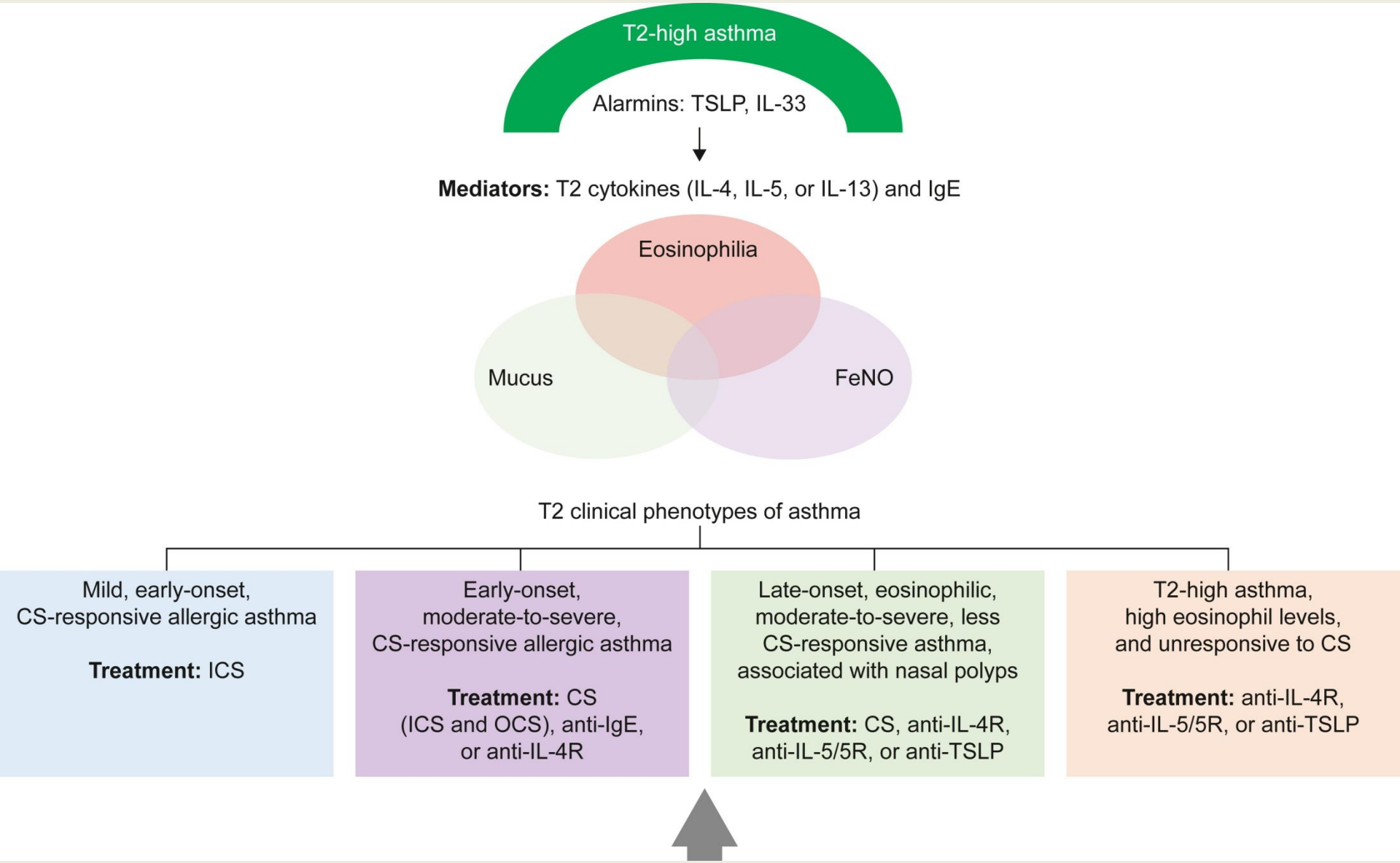

T2-high asthma
Alarmins: TSLP, IL-33
Mediators: T2 cytokines (IL-4, IL-5, or IL-13) and IgE
Eosinophilia
Mucus
FeNO
T2 clinical phenotypes of asthma
Mild, early-onset, CS-responsive allergic asthma
Treatment: ICS
Early-onset, moderate-to-severe, CS-responsive allergic asthma
Treatment: CS (ICS and OCS), anti-IgE, or anti-IL-4R
Late-onset, eosinophilic, moderate-to-severe, less CS-responsive asthma, associated with nasal polyps
Treatment: CS, anti-IL-4R, anti-IL-5/5R, or anti-TSLP
T2-high asthma, high eosinophil levels, and unresponsive to CS
Treatment: anti-IL-4R, anti-IL-5/5R, or anti-TSLP
T2-low asthma
Alarmins: TSLP, IL-33
Possible mediators: mast cells and neutrophils
Low T2 biomarkers
Obesity
Neutrophils
Metabolic dysfunction
High-dose CS
Asthma phenotypes with overlapping characteristics
Mild asthma, intermittent obstruction
Treatment: bronchodilators or low-dose ICS
Late onset, obese, airway disease, minimal obstruction, and reversibility
Treatment: weight loss or metabolic targets
Early onset, long disease duration, moderate obstruction, or minimal BD response
Treatment: high-dose CS or anti-TSLP
Late onset, infection or smoking, sputum production, or moderate obstruction
Treatment: mucus clearance measures or anti-TSLP



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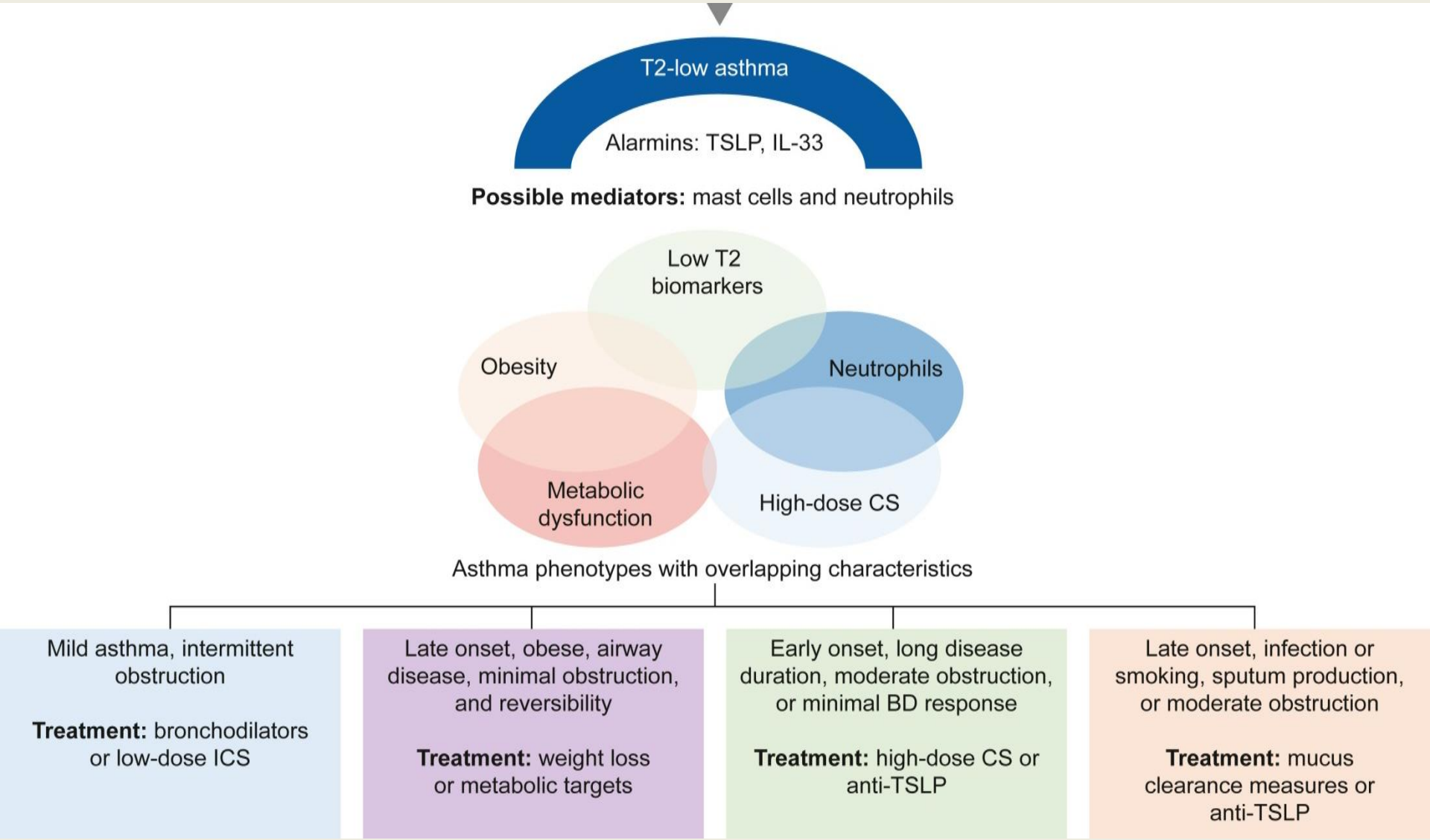

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NEW APPROACHES TO PHENOTYPING FOR THE DIAGNOSIS OF SEVERE ASTHMA AND THE MANAGEMENT OF

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Phenotyping early

Patients who are **not responding** well to **low-dose ICS and a long-acting b2-agonist** should be **phenotyped early** based on **BECs, FeNO levels, and lung function** to assess treatment adherence and to support appropriate treatment decisions.

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Phenotyping early

Elevated T2 biomarker levels have been associated with a **decline in lung function**, both in **healthy** individuals and in patients with **asthma.**

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such, **early phenotyping** using easily **accessible biomarkers** (blood eosinophils and FeNO) allows the **early initiation** of appropriate **targeted treatment** for patients with T2-high asthma, who typically have more severe asthma than those with T2-low asthma.

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Early treatment can

- prevent airway remodeling by **reducing inflammation and exacerbations**

- preventing lung function decline.

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Anti-IgE therapy (omalizumab)

The anti-IgE agent omalizumab is approved for use in patients age **six years and above** with

- With **moderate to severe persistent asthma eosinophilic phenotype** with **incomplete symptom control** with **inhaled glucocorticoid** treatment
- an **IgE level of 30 to 700** international units/mL,
- **positive allergen-skin** or **allergen-specific IgE** tests to a perennial allergen, and

Anti-IL-5 therapy

Interleukin (IL)-5 is **a pro-eosinophilic cytokine** that is a potent mediator of eosinophil hematopoiesis and contributes to eosinophilic inflammation in the airways. **Mepolizumab and reslizumab** are anti-IL-5 monoclonal antibodies [83];
benralizumab is an **anti-IL-5 receptor alpha** antibody

Anti-IL-5 therapy

is used for **add-on**, maintenance treatment of **uncontroled severe asthma** in patients who have an **eosinophilic phenotype**

Anti-IL-5 therapy

Clinical trial data suggest that efficacy requires an absolute blood **eosinophil count ≥150 micro/L** ,but this threshold is **less clear** in patients on daily **systemic glucocorticoids**.

Mepolizumab

is used for **add-on**, maintenance treatment of severe asthma in patients who are age **six years or older**

Mepolizumab

Mepolizumab is also approved for treatment of **chronic rhinosinusitis** and **nasal polyposis**

Reslizumab

add-on, maintenance therapy of severe asthma in patients who are **age 18 years or older**

Benralizumab

Benralizumab is a **monoclonal antibody directed against IL-5 receptor alpha** that is approved by the FDA as **add-on** therapy in patients **(≥12 years)**

It appears to be **more effective than anti-IL-5 antibodies** in **reducing eosinophil numbers**.

Anti-lL-4 receptor alpha subunit antibody (dupilumab)

Dupilumab is a fully **human monoclonal** antibody that binds to the alpha subunit of the IL-4 receptor. Through blockade of this receptor, dupilumab **inhibits** the activity of both **IL-4 and IL-13**, Type 2 cytokines that play akey role in allergy and asthma.

Anti-lL-4 receptor alpha subunit antibody (dupilumab)

Dupilumab is approved by the FDA for the treatment of **moderate-to-severe, eosinophilic** asthma in patients **age six years and older**

Anti-thymic stromal lymphopoietin (tezepelumab)

Thymic stromal lymphopoietin (TSLP) is an **epithelial cell-derived cytokine** that participates in **asthma inflammation.**

Tezepelumab is approved by the FDA **for add-on** maintenance therapy in patients with **severe asthma (both phenotypes)** who are **≥12 years of age**


Thank You