



The Summary and Context of Asthma Management in Thailand **What is new in GINA 2021**

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Virtual meeting 2021

The NEW GINA 2021

The Summary and Context of Asthma Management in Thailand

The Panel Discussion endorsed by Thai Asthma Council

11.40-11.45		<p>Opening and Welcome Orapan Poachanukoon MD, PhD. TU-CAAP, President of TAC</p>
11.45-12.00	Episode 1	<p>Guidance for managing COVID-19 and asthma</p> <ul style="list-style-type: none"> - Is COVID-19 increased in asthma patients? - Is asthma treatment (ICS, OCS, biologic) affecting COVID-19? - Dealing with asthma exacerbation coexisting with COVID-19 <p>Moderator: Orapan Poachanukoon MD, PhD. TU-CAAP, President of TAC Speaker: Nittha Oer-areemit MD Pulmonary and Critical Care Physician</p>
12.00-12.15	Episode 2	<p>What is new in GINA 2021?</p> <ul style="list-style-type: none"> - Does mild asthma matter and is intermittent asthma significant? - How to define severe asthma in 2021? - Is GINA 2021 new figure easy for clinical practice? <p>Moderator: Orapan Poachanukoon MD, PhD. TU-CAAP, President of TAC Speaker: Theerasuk Kawamatawong MD, FCCP Pulmonary and Critical Care Physician</p>
12.15-12.35	Episode 3	<p>Asthma guidelines: Adult vs. pediatric and local vs. global perspectives</p> <ul style="list-style-type: none"> - Asthma control and future risk assessment - Asthma management guidelines: Difference and similarity between adults and children - GINA and other guideline include TAC <p>Moderator & Speaker: Orapan Poachanukoon MD, PhD. TU-CAAP, President of TAC</p>
12.35-13.00	Episode 4	<p>Panel Discussion: Asthma management in Thailand for all age groups: Real life Practice</p> <p>Moderator: Orapan Poachanukoon MD, PhD. TU-CAAP, President of TAC Speaker 1: Watchara Boonsawat MD, PhD, President of EACC network Thailand Speaker 2: Nittha Oer-areemit MD Pulmonary and Critical Care Physician Speaker 3: Thitiwat Sriprasart MD Pulmonary and Critical Care Physician Speaker 4: Harutai Kamalaporn MD Pediatric Pulmonary Physician Speaker 5: Theerasuk Kawamatawong MD, FCCP Pulmonary and Critical Care Physician</p>
		<p>Closing remark Orapan Poachanukoon MD, PhD. TU-CAAP, President of TAC</p>



JOIN NOW!

Date: Tuesday 25th May 2021 / 11.40-13.00

SIGN 158

British guideline on the management of asthma

Quick reference guide
First published 2003
Revised edition published July 2019



Asthma: diagnosis, monitoring and chronic asthma management

NICE guideline
Published: 29 November 2017
www.nice.org.uk/guidance/ng80

2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group



July 2019

February 2020

December 2020

Global Initiative for Asthma (GINA)
What's new in GINA 2020?



GINA Global Strategy for Asthma Management and Prevention

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Global Initiative for Asthma (GINA)
What's new in GINA 2021?



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2020

April 2020



April 2021



2021

GINA

(Global Strategies for Asthma Management and Prevention)

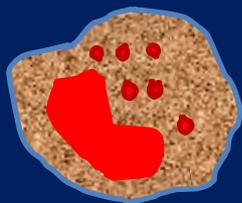
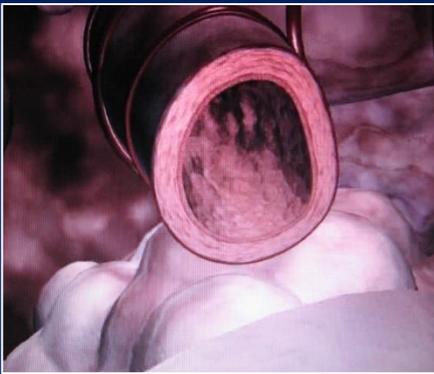


Asthma = Airway inflammation + Airway obstruction

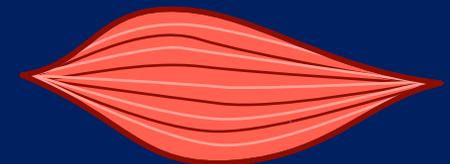
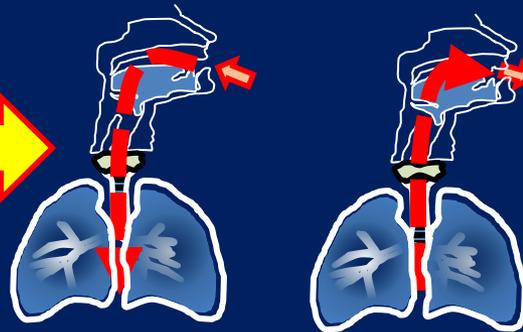
Normal airway

Early asthma attack

Severe asthma attack



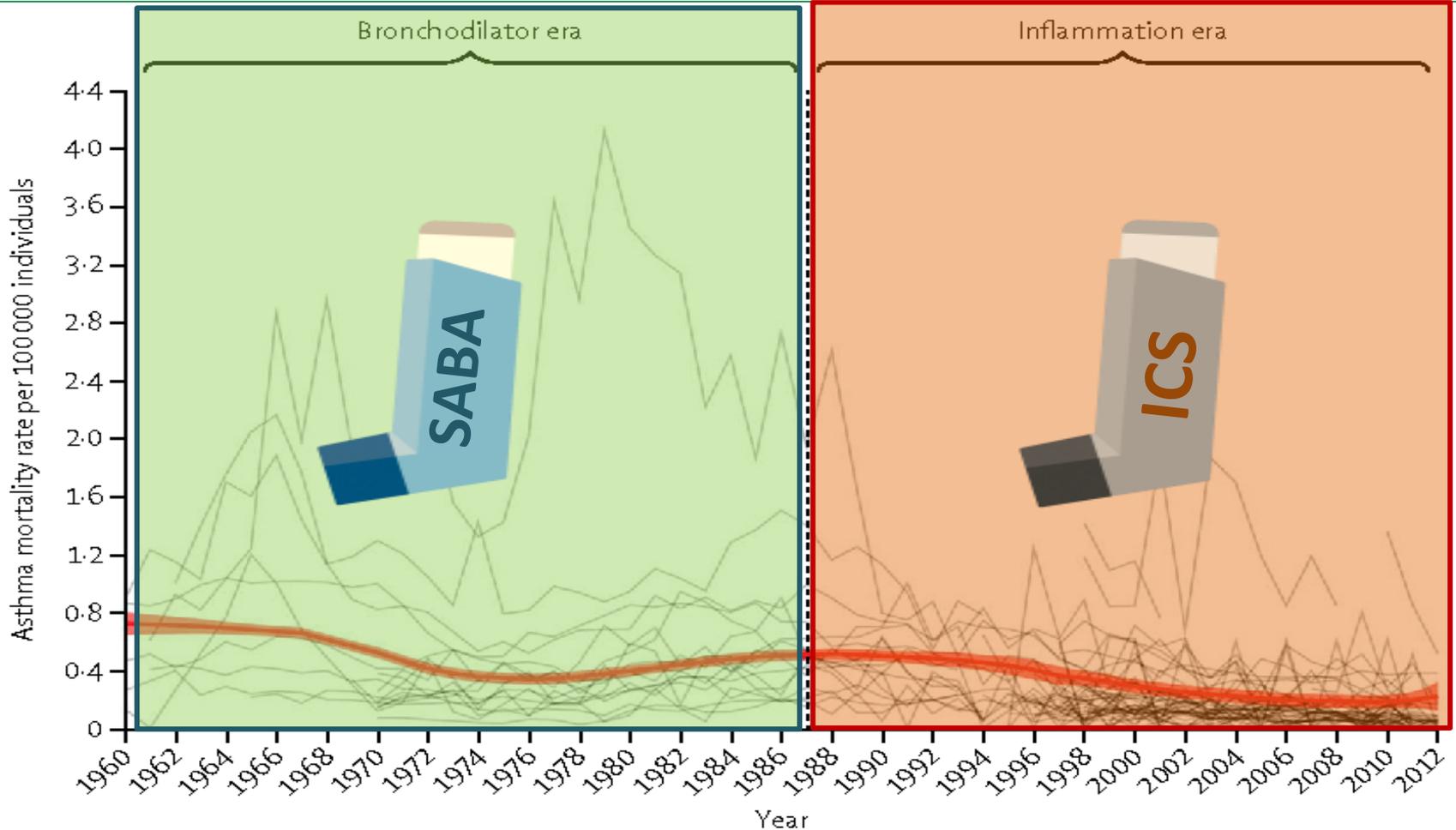
Eosinophil



Airway smooth muscle

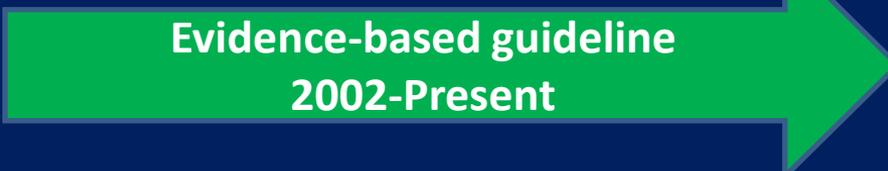
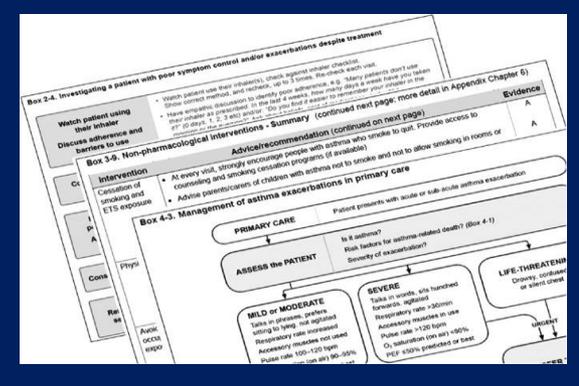
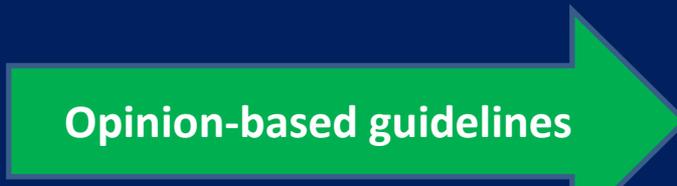
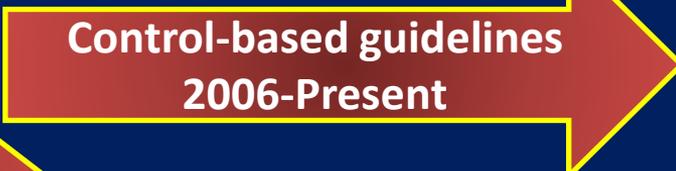
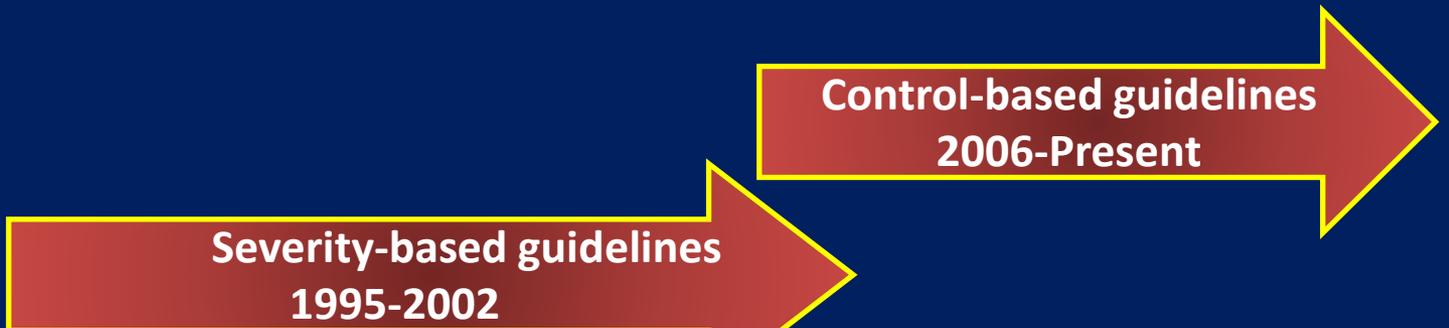
From Bronchodilator to Inflammation Era

Asthma mortality in patients 5–34 y in 46 countries (1960-2012)

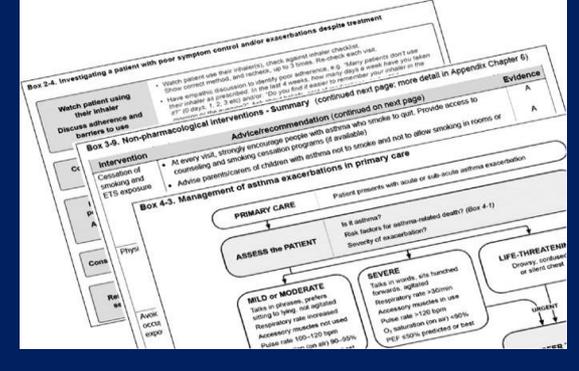


Evolution of GINA strategy

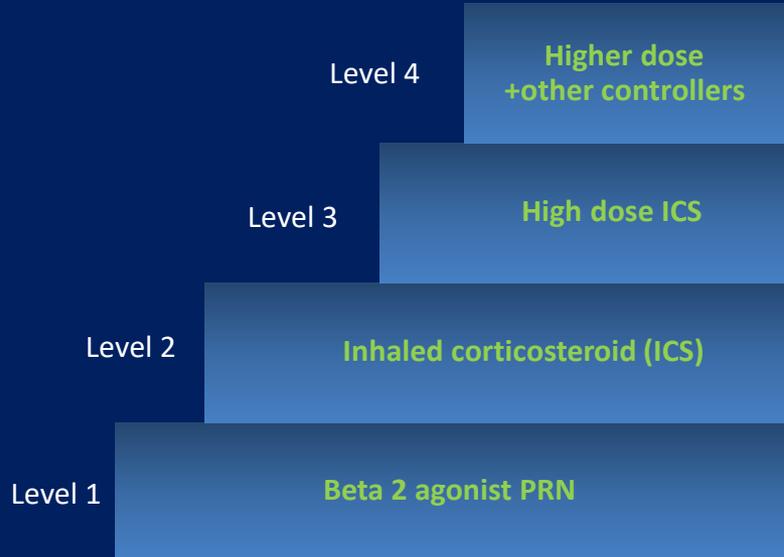
Paradigm change in the conception of guidelines for the management and treatment of asthma



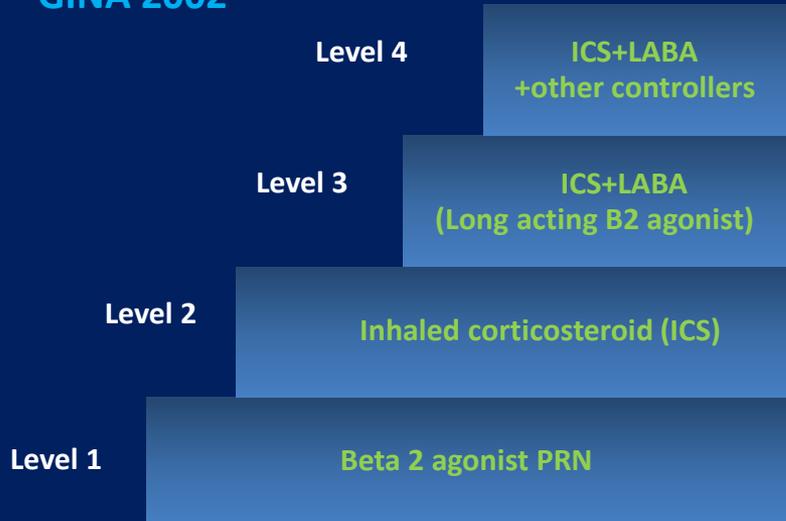
1980 1985 1990 1995 2000 2005 2010 2015.....2019



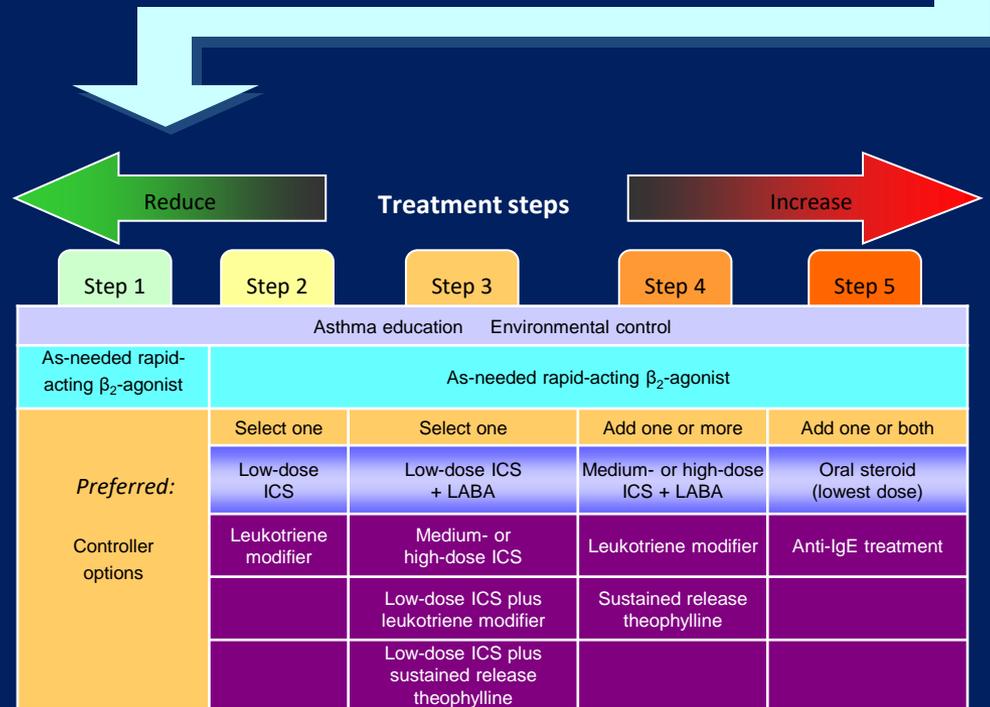
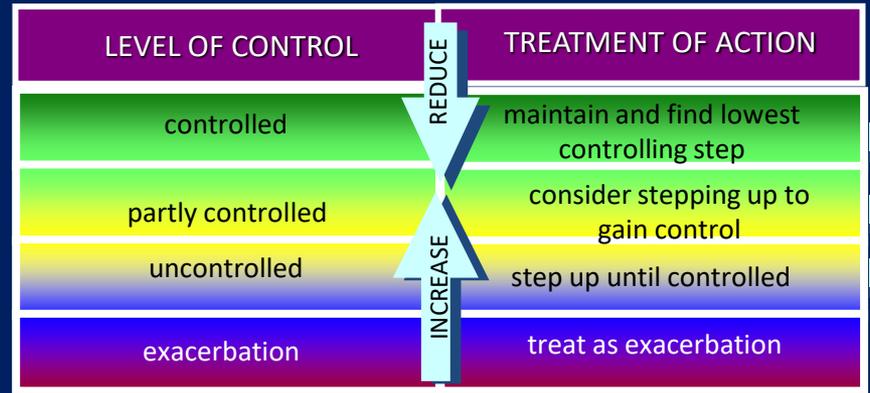
GINA 1995



GINA 2002



GINA 2006





Classification of Severity

CLASSIFY SEVERITY Clinical Features Before Treatment			
	Symptoms	Nocturnal Symptoms	FEV ₁ or PEF
STEP 4 Severe Persistent	Continuous Limited physical activity	Frequent	≤ 60% predicted Variability > 30%
STEP 3 Moderate Persistent	Daily Attacks affect activity	> 1 time week	60 - 80% predicted Variability > 30%
STEP 2 Mild Persistent	> 1 time a week but < 1 time a day	> 2 times a month	≥ 80% predicted Variability 20 - 30%
STEP 1 Intermittent	< 1 time a week Asymptomatic and normal PEF btw attacks	> 2 times a month	≥ 80% predicted Variability < 20%

The presence of one feature of severity is sufficient to place patient in that category.

GINA asthma symptom control

(Exclude FEV₁ from control assessment)

Asthma symptoms control

WC

PC

UC

In the past 4 weeks, has the patient had :

- Daytime asthma symptoms (>2/wk) Yes No
- Any night awakening due to asthma Yes No
- **Reliever (SABA)** for symptoms (>2 /wk) Yes No
- Any activity limitation due to asthma Yes No

None 1-2 3-4
of these of these of these



* WC= well controlled, PC= Partly controlled and UC =Uncontrolled asthma

Future risk factor of poor outcome



Poor asthma outcome

Risk factors of exacerbation

- **Uncontrolled symptoms**
- **Inadequate ICS**
- **High SABA use (≥ 3 canisters/yr)**
- ≥ 1 exacerbation in last 12 mo
- Low FEV₁; high BD reversibility
- Incorrect inhaler technique and/or poor adherence
- Smoking
- Obesity, chronic rhinosinusitis, pregnancy
- Blood eosinophilia
- Elevated FeNO in adults with allergic asthma taking ICS
- Ever intubated for asthma

Risk factors for developing fixed AO

- No ICS treatment
- Smoking
- Occupational exposure
- Mucus hypersecretion
blood eosinophilia
- Pre-term birth, low BW

Risk factors of medication side effect

- Frequent oral steroids
- High dose/potent ICS
 - P450 inhibitors

GINA 2021

Selection of asthma treatment options



**Patient
priorities
and
preferences**

**Patient
behavior
(adherence)**

**Populations,
Health
systems and
medication
access**

**Underlying
disease
processes**

**Feasibility
in clinical
practice
for
implementation**

Asthma pharmacology

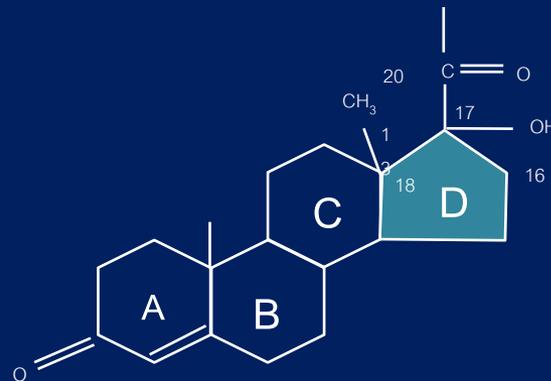
Treatment options in GINA 2021

Airflow obstruction



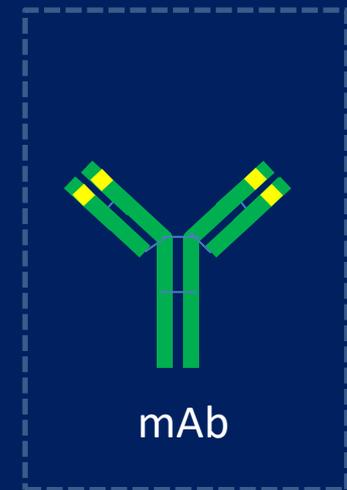
Bronchodilators

Airway inflammation



Anti-inflammatory

Targeted therapy



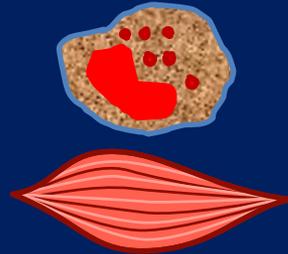
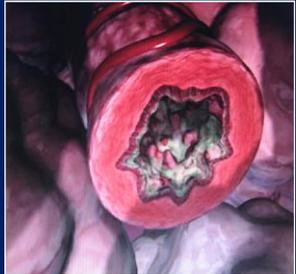
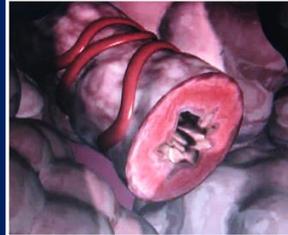
Monoclonal Ab

Persistent use of SABA in asthma

Real world situation

Education & information

- ✓ Asthma = disease of **bronchospasm**
- ✓ Asthma = disease of airway **inflammation**



Patient satisfaction on SABA & reliance

- ✓ **Rapid** symptoms relieve
- ✓ Prominence in ED-ICU care
- ✓ **Low cost**



Patient believe in SABA

- ✓ Asthma reliever provides asthma control
- ✓ Asthma controller takes time (**no benefit**)



Steroid phobia and ignorance & SABA addiction

Regular use of SABA vs. Higher use of SABA

Adverse effect on asthma

Decreased broncho-protection



- β -receptor downregulation
- Rebound AHR
- \downarrow bronchodilator response
- \uparrow allergic response
- \uparrow eosinophilic inflammation

Adverse clinical outcome



- Dispensing of ≥ 3 canisters per year (≈ 1.7 puffs/d) is associated with \uparrow of ER visits
- Dispensing of ≥ 12 canisters per year is associated with higher risk of death

Hancox. Respir Med. 2000 ;94(8):767-71.

Aldridge. Am J Respir Crit Care Med. 2000 ;161(5):1459-64.

Stanford, Ann Allergy Asthma Immunol. 2012;109(6):403-7

Suissa. Am J Respir Crit Care Med. 1994;149(3 Pt 1):604-10.

Benefits of ICS and non-formoterol LABA in asthma

**Airway
inflammation**

**Smooth muscle
dysfunction**

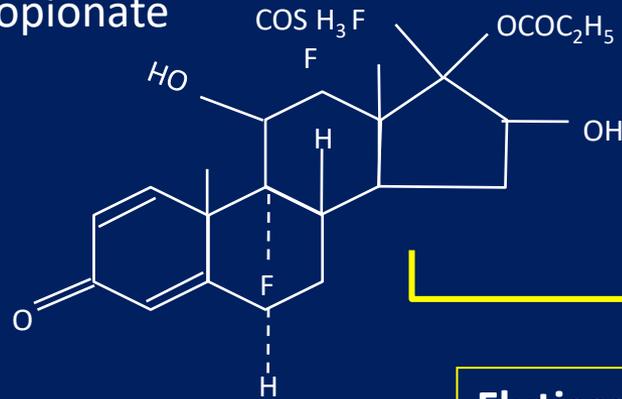
ICS



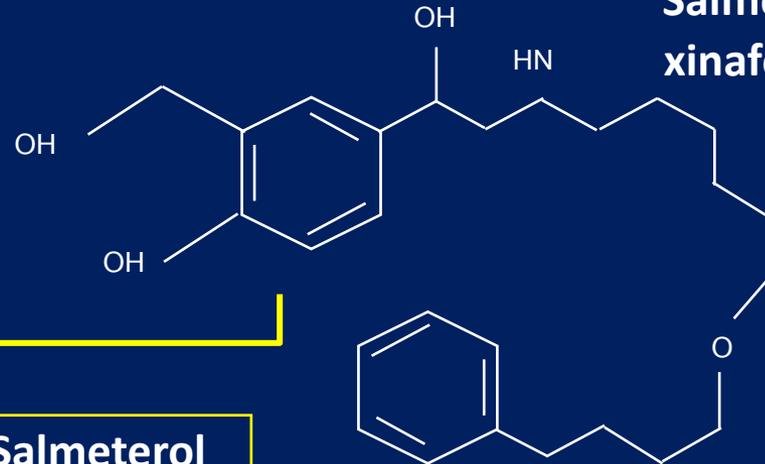
LABA



Fluticasone
propionate



Salmeterol
xinafoate



**Fluticasone
propionate**

**Salmeterol
xinafoate**

**Fluticasone
propionate**

**Vilanterol
trifenatate**

**Fluticasone
propionate**

**Formoterol
fumarate**

Benefits of ICS and formoterol LABA in asthma

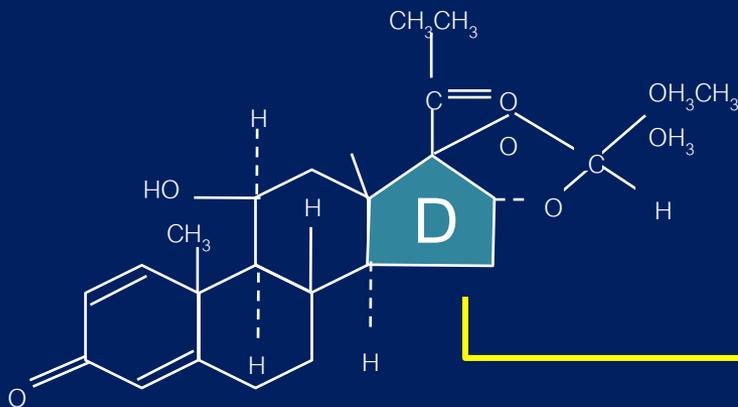
Airway
inflammation

Smooth muscle
dysfunction

ICS



Budesonide



LABA

Formoterol



Budesonide
(BUD)

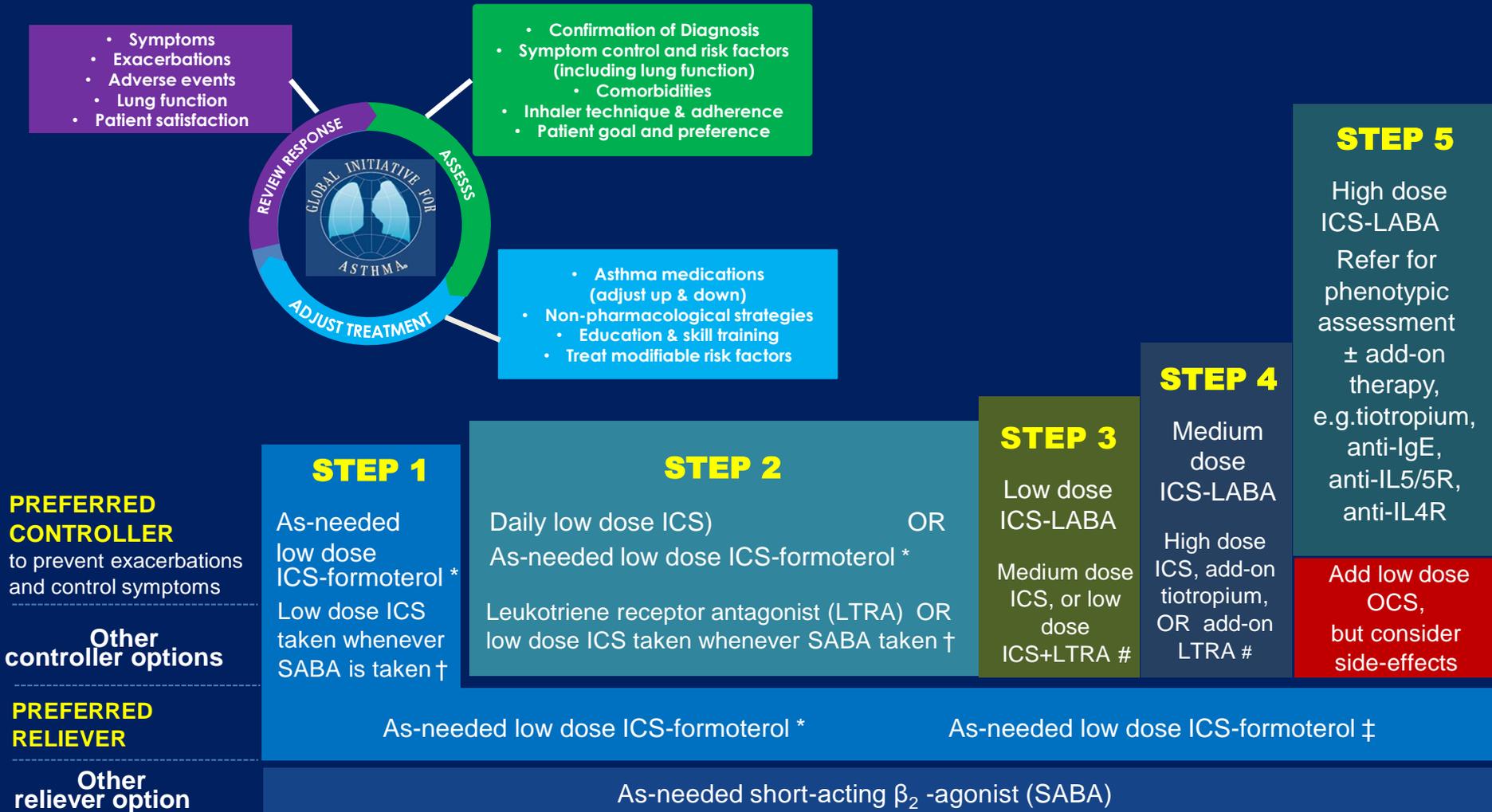
Formoterol
fumarate

Beclomethasone
dipropionate (BDP)

Formoterol
fumarate

Adults & adolescents 12+ years

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* Off-label; data only with Budesonide-formoterol

† Off-label; separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever for patients prescribed BUD-form or BDP-form maintenance and reliever therapy

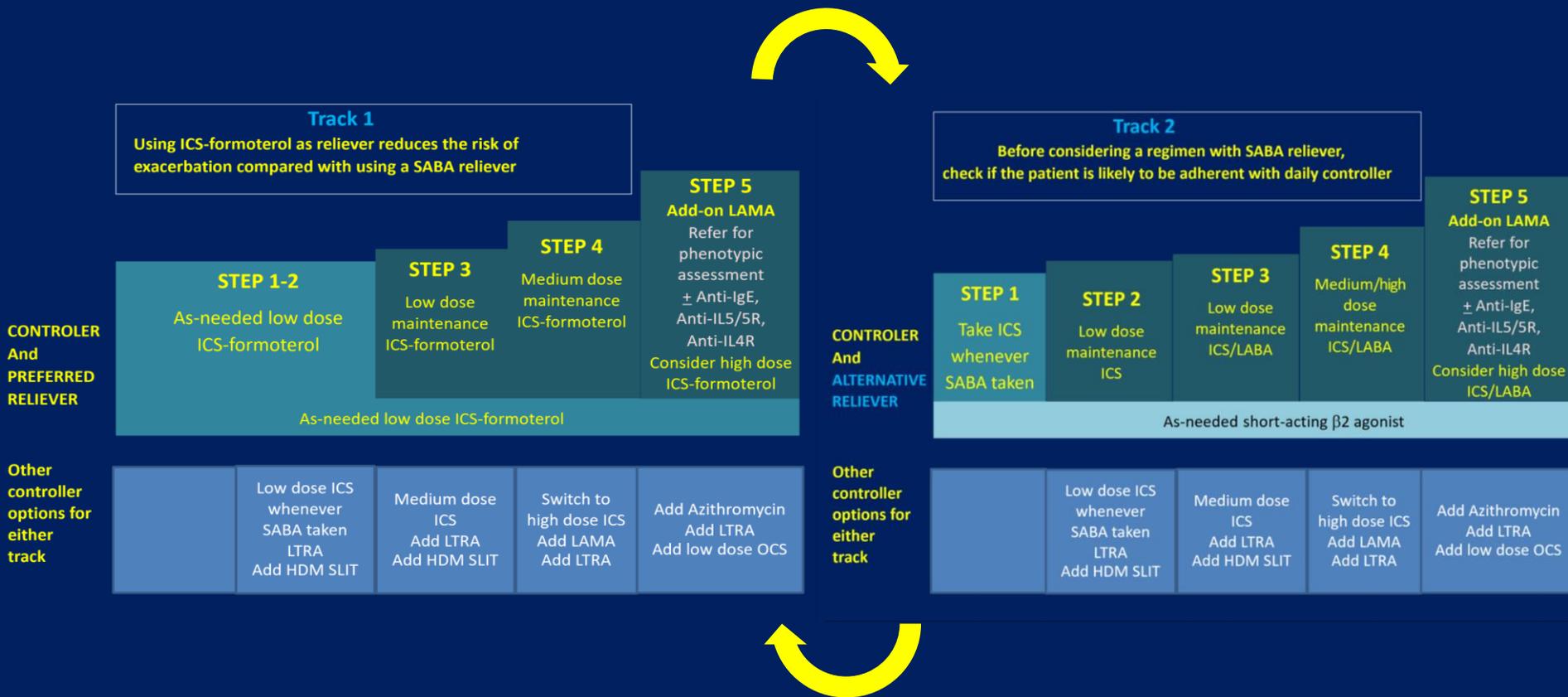
Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV₁ >70% predicted

Treatment may be

Stepped up/down within a track using the same reliever at each step OR

Switched between tracks

According to the patient's needs and preferences



Asthma controllers & relievers in adults & adolescents 12+ years

Track 1

Using ICS-formoterol as reliever reduces the risk of exacerbation compared with using a SABA reliever

**CONTROLLER
And
PREFERRED
RELIEVER**

STEP 1-2

As-needed low dose
ICS-formoterol

STEP 3

Low dose
maintenance
ICS-formoterol

STEP 4

Medium dose
maintenance
ICS-formoterol

STEP 5

Add-on LAMA

Refer for
phenotypic
assessment
± Anti-IgE,
Anti-IL5/5R,
Anti-IL4R
Consider high dose
ICS-formoterol

As-needed low dose ICS-formoterol

**Other
controller
options for
either
track**

Low dose ICS
whenever
SABA taken
LTRA
Add HDM SLIT

Medium dose
ICS
Add LTRA
Add HDM SLIT

Switch to
high dose ICS
Add LAMA
Add LTRA

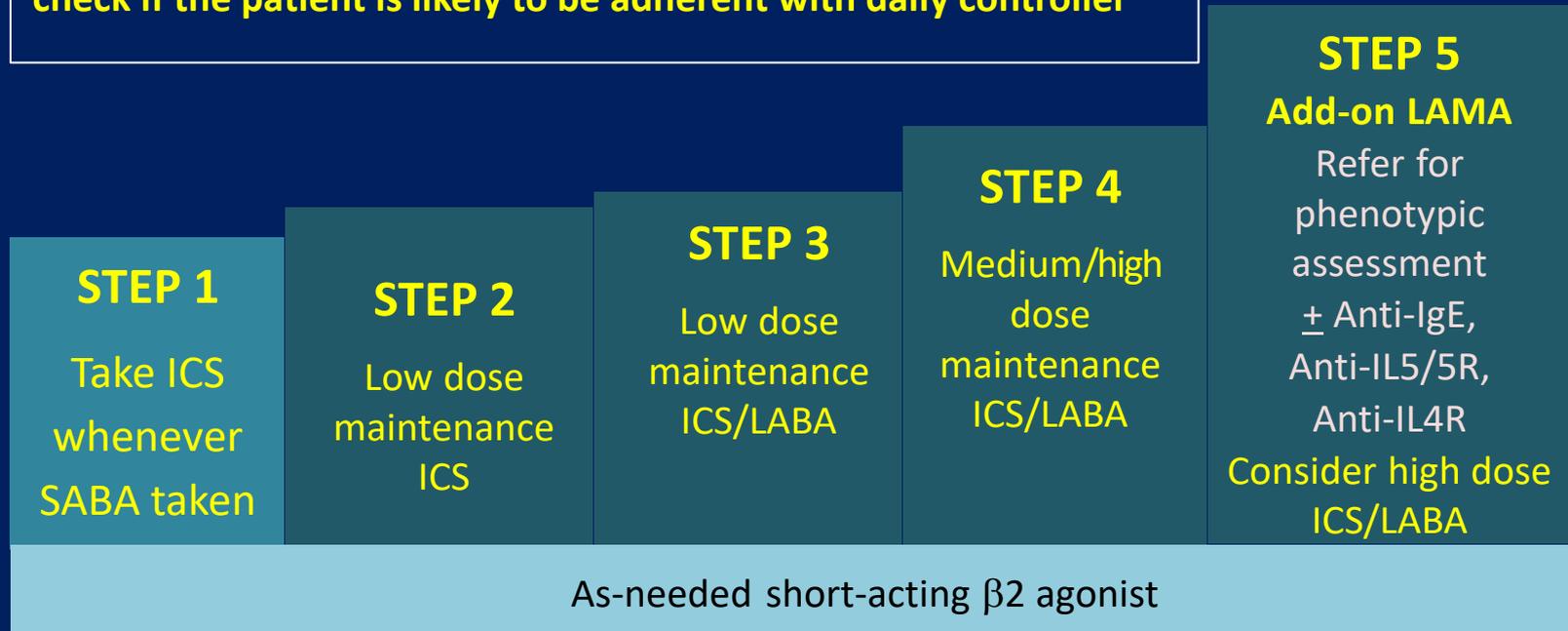
Add Azithromycin
Add LTRA
Add low dose OCS

Asthma controllers & relievers in adults & adolescents 12+ years

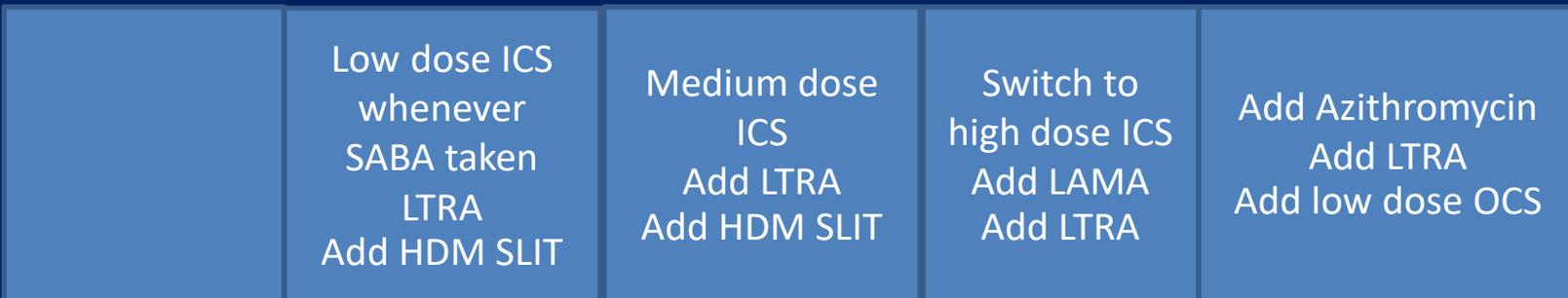
Track 2

Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

**CONTROLLER
And
ALTERNATIVE
RELIEVER**



Other controller options for either track



GINA treatment figure now shows two tracks

With the two reliever choices across asthma severity
Based on evidence about outcomes

Track 1

(the preferred approach)
with low dose ICS-formoterol
as the reliever

Using **ICS-formoterol as reliever** reduces the risk of exacerbations compared with using a **SABA reliever**

Track 2

(an alternative approach)
with SABA
as the reliever

if Track 1 is not **possible**
or is **not preferred** by a patient
with **no exacerbations** on their
current controller therapy

Patient is likely to be **adherent**
with **daily controller**

ICS-formoterol as reliever VS. SABA reliever

- Similar symptom control
- Similar lung function

GINA treatment figure now shows two tracks

With the two reliever choices across asthma severity
Based on evidence about outcomes

Track 1

(the preferred approach)
with low dose **ICS-formoterol**
as the reliever

At any treatment step has
asthma symptoms, patients
use low dose **ICS-formoterol**
for symptom relief

In Steps 3–5, patients take
ICS-formoterol as **daily
controller treatment**
(maintenance and reliever
therapy-MART)

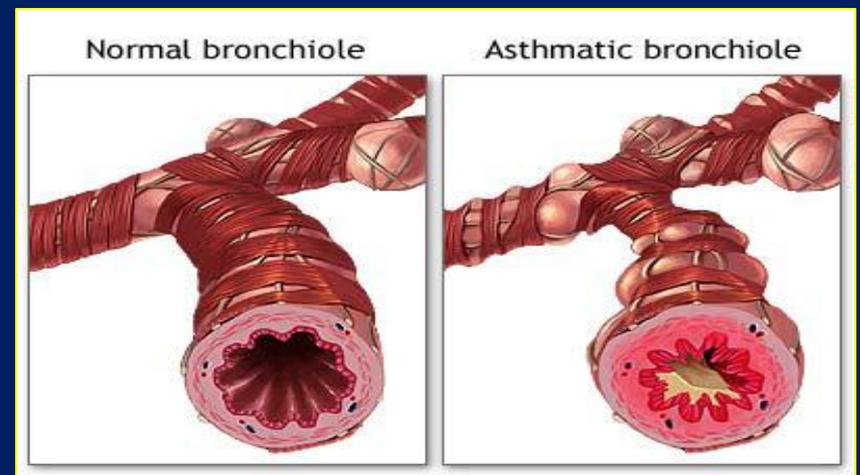
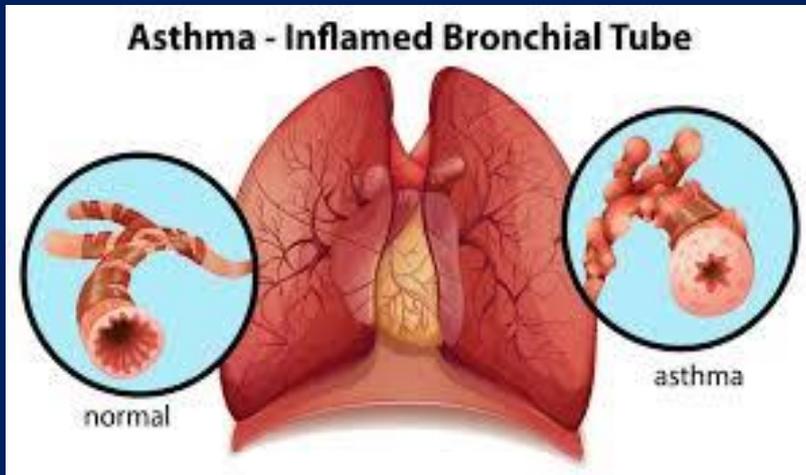
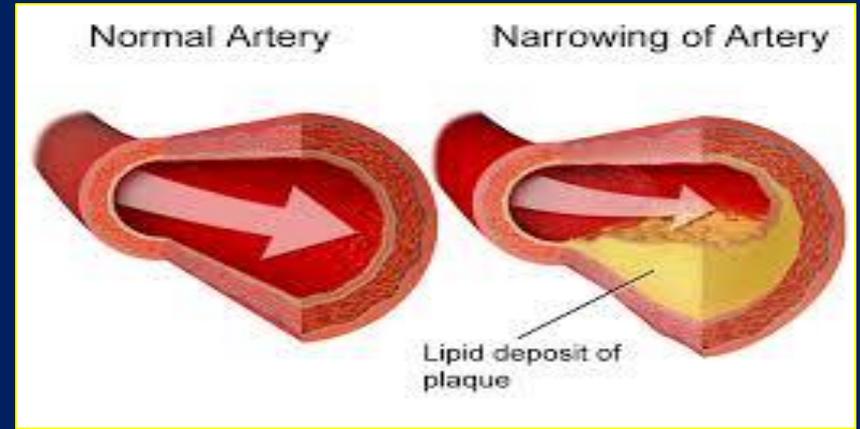
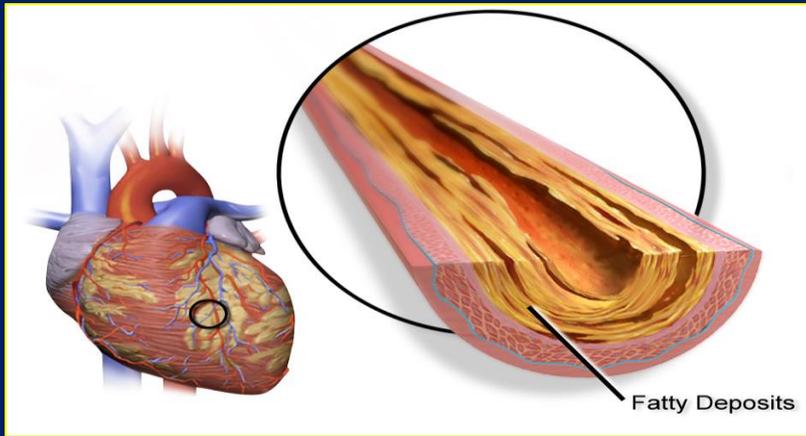
Track 2

(an alternative approach)
with **SABA**
as the reliever

Patient takes a **SABA and low
dose ICS together** for symptom
relief
ICS taken right after the SABA

In Steps 2–5, patient takes **ICS-
containing controller med**
regularly every day
Patients uses **SABA (alone)** for
symptom relief

Bronchospasm in asthma and coronary stenosis in ischemic heart disease
Bronchodilator SABA vs. Vasodilator-Nitrate
Anti platelet for plaque rupture vs. ICS for airway inflammation

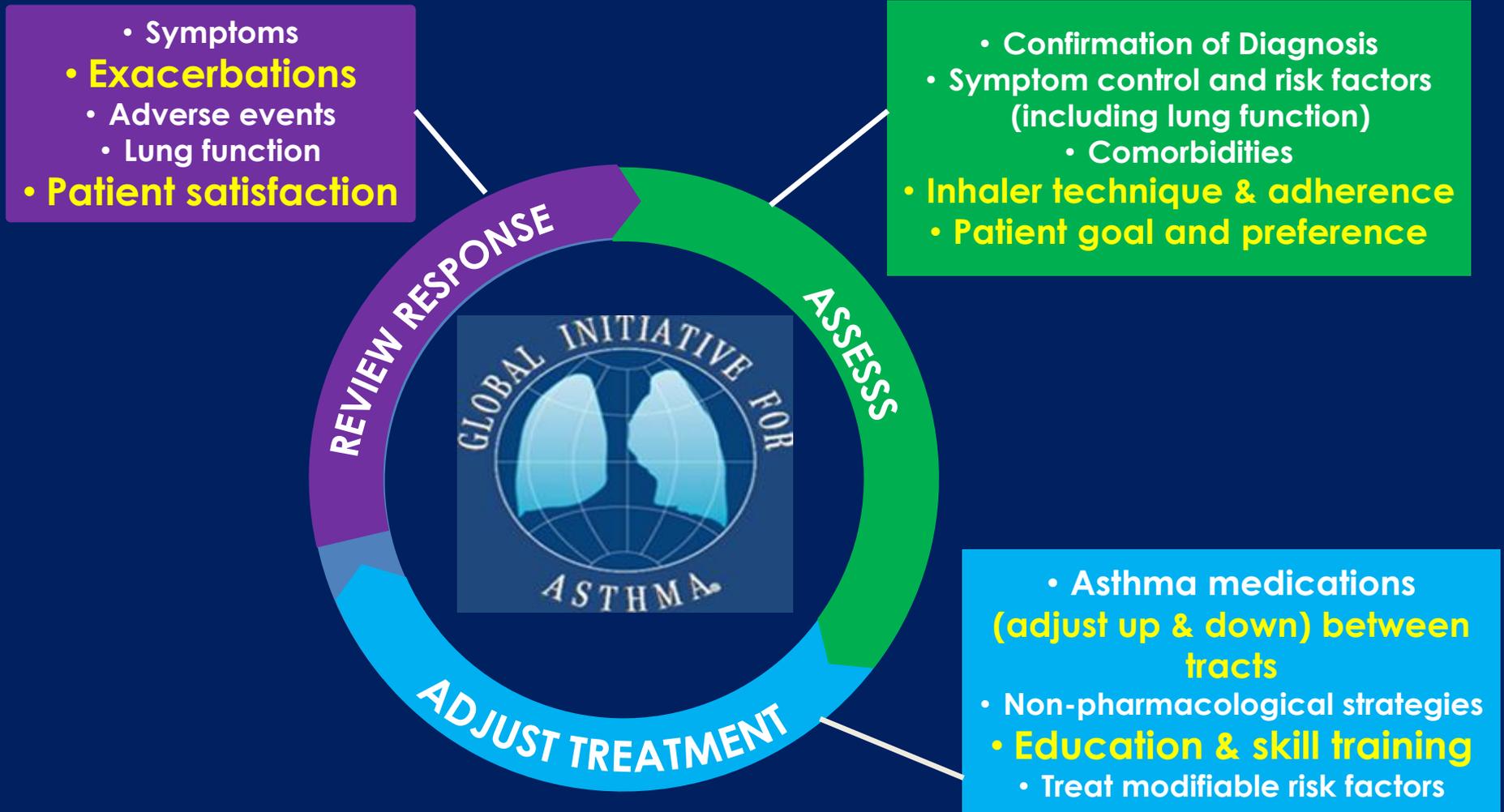


Asthma treatment track for adults and adolescents

Track 1 and Track 2

Features	GINA Track 1	GINA Track 2
Controller	Maintenance ICS/formoterol	ICS or ICS/LABA
Reliever for asthma symptoms at any step	 <p>As needed ICS/formoterol</p> <p>Single inhaler for symptoms</p>	 <p>SABA</p> <p>ICS taken right after SABA</p>
Patient profiles & Conditions for use	Patient is likely to be poorly adherent with daily ICS	<ul style="list-style-type: none"> - Patient is likely to adhere to daily ICS containing regimens & SABA - No exacerbation on current Rx - unavailable drug in track 1 - not preferred by patient
Benefits and drawbacks of track	<ul style="list-style-type: none"> -ICS/form better reduced risk of exacerbation than SABA reliever - Max as-needed ICS/formoterol dose $\leq 72 \mu\text{g}/\text{day}$ - Rinsing mouth after use - Pre-exercise - Beclomethasone/FORM???? 	Higher dose of ICS for step up Severe asthma (high dose ICS)

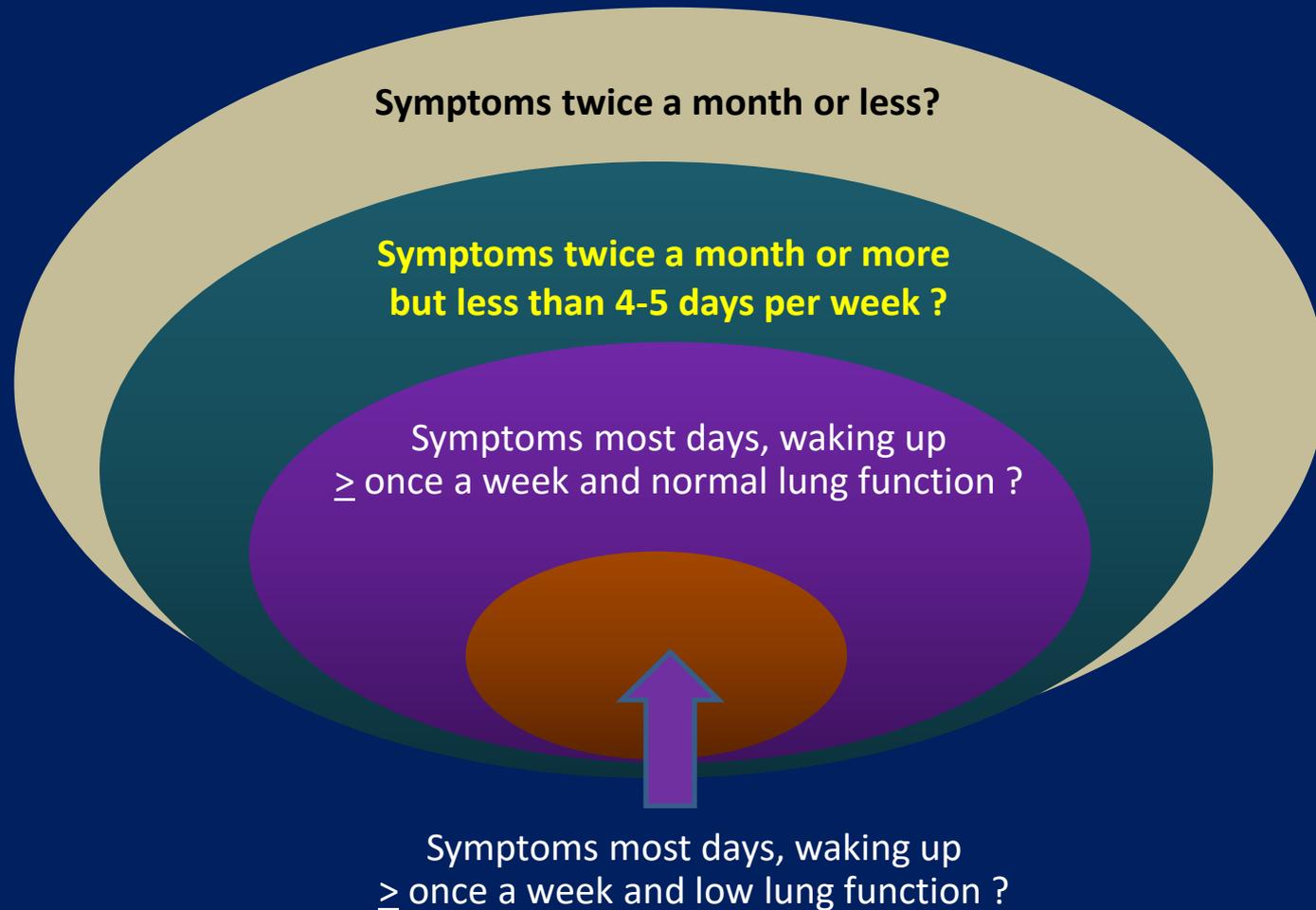
Personalized asthma management



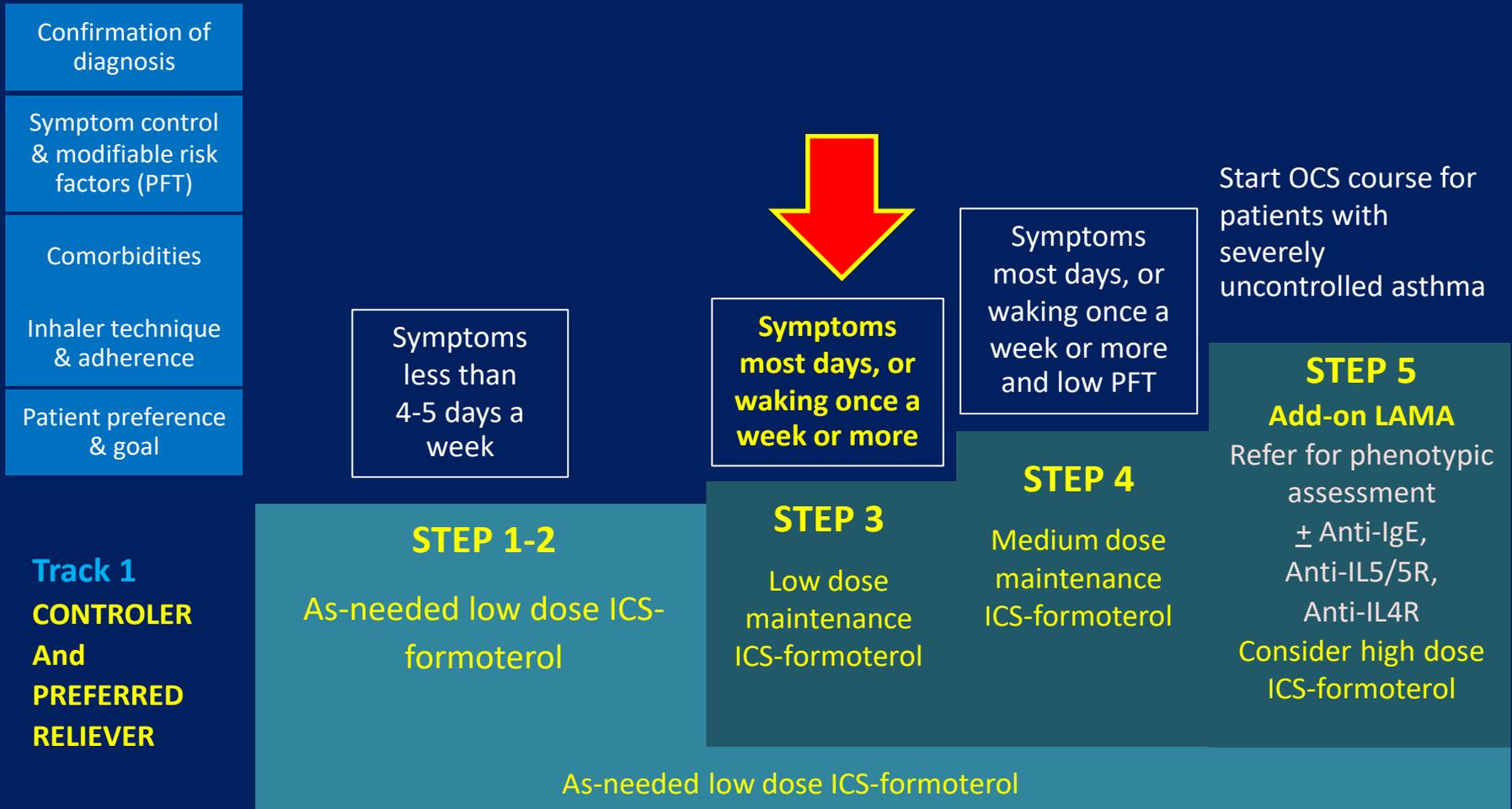
NOT just about medications, NOT one-size-fits-all

Asthma severity

Driven by symptoms and lung function

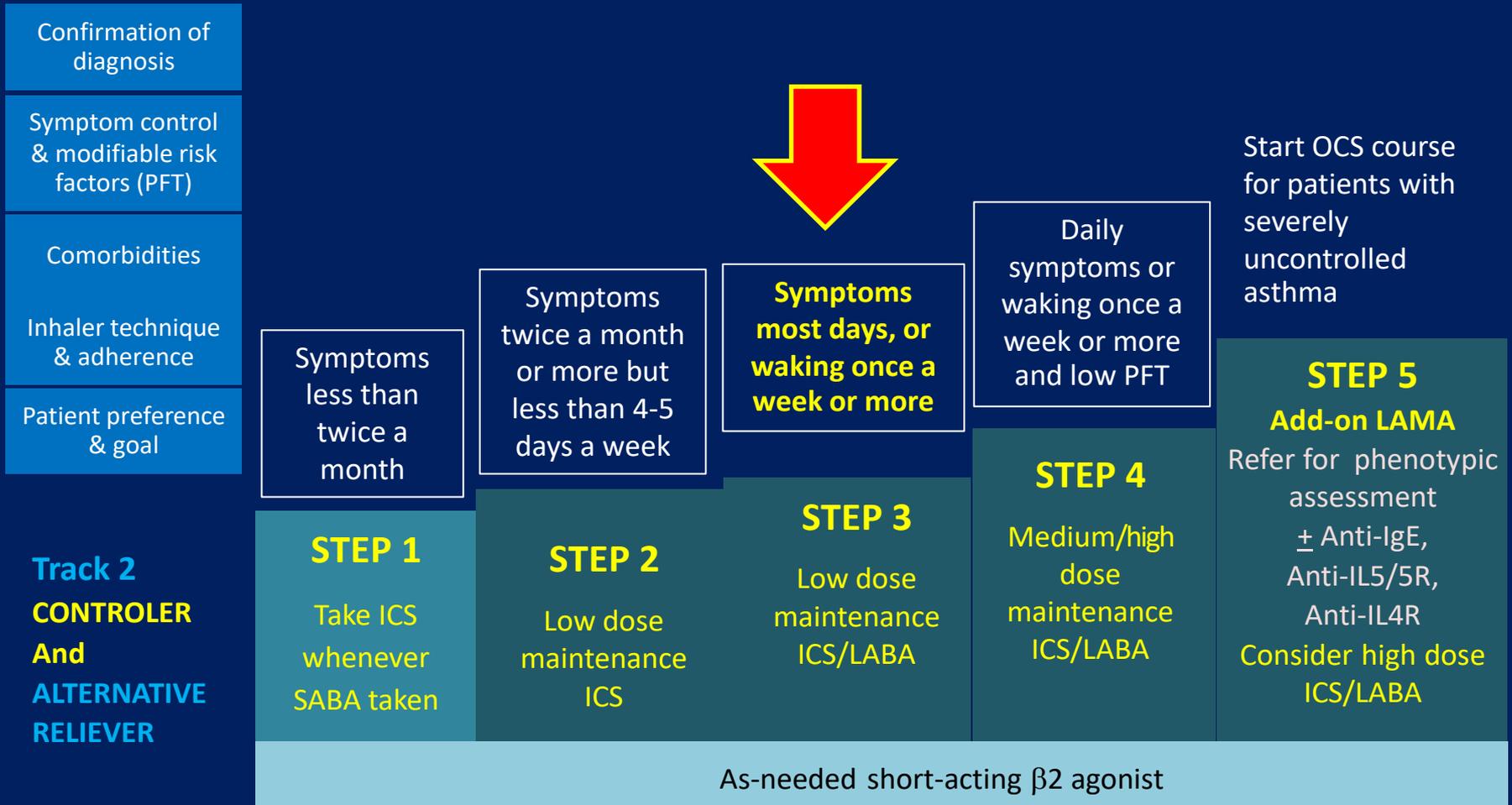


Starting treatment in adults & adolescents with diagnosis of asthma



- Track 1 is preferred if the patient is likely to be poorly adherent with daily controller
- ICS containing therapy is recommend even if symptoms are infrequent (it reduces risk of severe exacerbation and need for OCS)

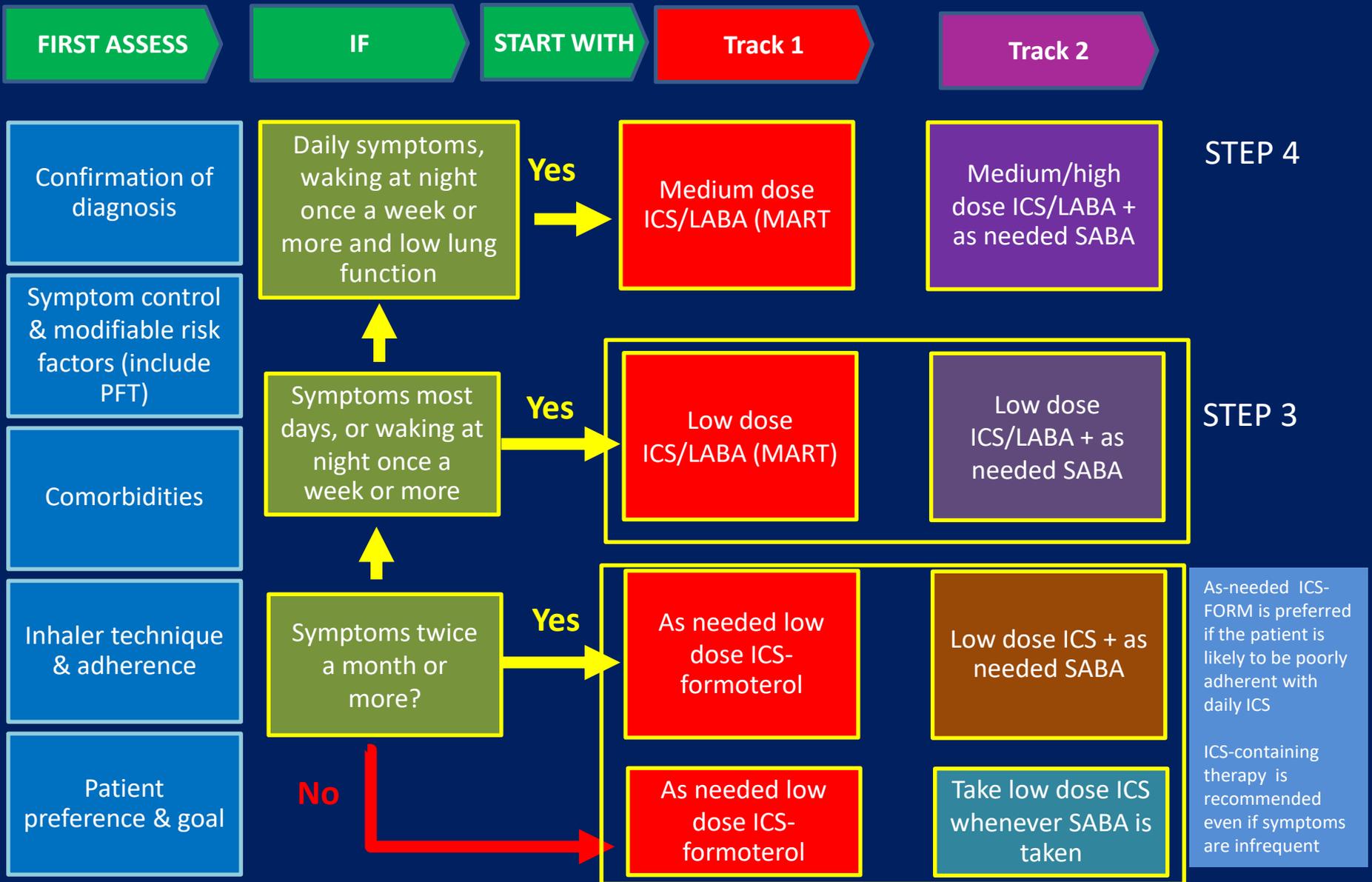
Asthma controllers & relievers in adults & adolescents 12+ years



- Track 2 before considering a regimen with SABA reliever check if the patient is likely to be adherent with daily controller
- ICS containing therapy is recommend even if symptoms are infrequent (it reduces risk of severe exacerbation and need for OCS)

Features for selection initial treatment Frequency of symptoms	Track 1 (Drug available and patient preference)	Track 2 (Likely adherence to daily treatment)
Symptoms less than twice a month AND no risk or exacerbation	As needed low dose ICS/formoterol (Evidence B)	Low dose ICS taken whenever SABA taken (Separate/same device) (Evidence B)
Symptoms or need of reliever twice a month or more	As needed low dose ICS/formoterol (Evidence A)	Low dose ICS with as-needed SABA (Evidence A)
Symptoms most day OR waking once a week OR risk factor exist	Low dose ICS/formoterol MART (Evidence A)	Regular Low dose ICS/LABA with as-needed SABA (Evidence A) OR Medium dose ICS (Evidence A)
Initial with severe uncontrolled asthma OR exacerbation	Medium dose ICS/formoterol MART (Evidence D) \pm OCS	Medium dose ICS/LABA with as-needed SABA (Evidence D) OR High dose ICS (Evidence A) \pm OCS

Suggested controller treatment for adults and adolescents with diagnosed asthma



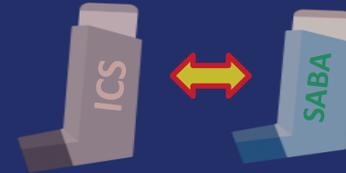
Track 1
CONTROLLER
And
PREFERRED
RELIEVER

Anti-Inflammatory Reliever Therapy (AIRT)



Maintenance and Reliever Therapy (MART)

Mild asthma (symptoms $< 2/m$ without risk factors)



Track 2
CONTROLLER
And
ALTERNATIVE
RELIEVER

Persistent asthma (symptoms $\geq 2/month$)



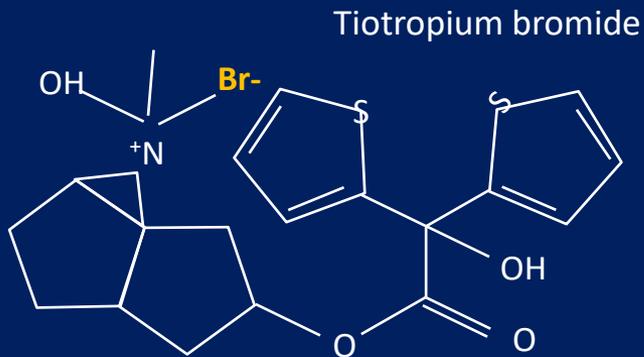
ICS/FORM vs. salbutamol as reliever (for infrequent symptoms)



Added-on therapy in GINA 2021 step 4-5

Bronchodilator vs. Anti-inflammatory drugs

Long-acting antimuscarinic (LAMA) beyond TIO



Tiotropium bromide
Umeclidinium bromide
Glycopyrronium bromide

Macrolides



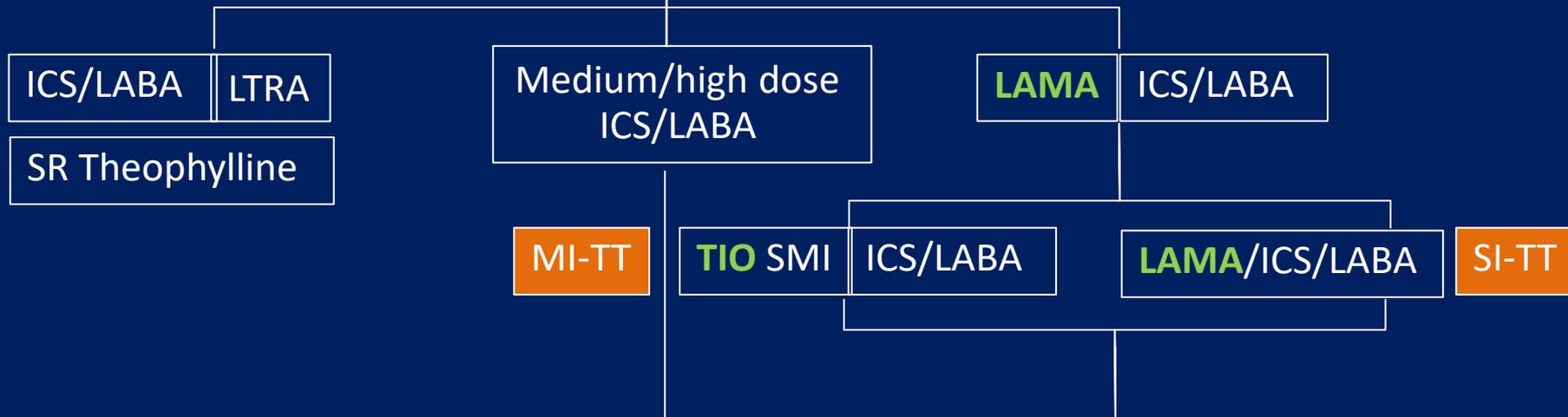
Clarithromycin
Azithromycin

LAMA beyond tiotropium in asthma

GINA step 4-5

Persistently uncontrolled despite low dose ICS-LABA step 3

- Check adherence
- Check device technique
- Check comorbid
- Check exposure



Step 5 recommendations; add-on LAMA include combination ICS-LABA-LAMA, if asthma is persistently uncontrolled despite ICS-LABA

LAMA for add-on ICS/LABA in asthma

Key concept from GINA 2021

MI-TT

TIO SMI ICS/LABA

Add-on tiotropium in separate inhaler (ages ≥ 6 y)

SI-TT

LAMA/ICS/LABA

Triple combinations (ages ≥ 18 y)

Adding LAMA to medium or high dose ICS-LABA modestly improves lung function (Evidence A) but not symptoms

Add-on LAMA modestly increased the time to severe exacerbation requiring OCS (Evidence B)

Ensure that patient receives sufficient ICS (> medium dose ICS/LABA, before considering adding a LAMA) for exacerbation

Single inhaler triple therapy (SI-TT) in asthma

ICS/LABA/LAMA

Generic name	Dose (FDC)	Manufacturer	Device
Beclomethasone dipropionate	100/6/12.5 µg BD	Chiesi (CHF 5993)	pMDI extrafine
Formoterol fumaratae	87/5/9 µg BD	TRIMBOW®	
Glycopyrronium bromide			
Fluticasone furoate	100/25/62.5 µg OD	GSK TRELEGY®	
Vilanterol trifenate			
Umeclidinium bromide			
Mometasone furoate	160/150/50 µg OD	Novartis (QVM149)	Breezhaler DPI
Indacaterol maleate			
Glycopyrronium bromide			

Long term azithromycin reduces asthma exacerbation

AZIZAST

AMAZES

AZMATICS

AZIZAST (24-week).
GG Brussel
Thorax. 2013;68(4):322-9.

AMAZES (48-week)
PG Gibson
Lancet. 2017.12;390:659-668

AZMATICS (12-week)
Hahn DL. J Am Board Fam
Med.2012;25 (4):442-459.

65% non-EOS (n=70)

Suggesting to try macrolide (before biologics) even in eosinophilic asthma for reducing exacerbation in at-risk patients

Eosinophilic asthmatics (sputum Eo \geq 3% **OR** blood Eo \geq 300/ μ L)

Fewer OCS course for exacerbation

Non-eosinophilic asthmatic (sputum Eo < 3% **OR** blood Eo < 300/ μ L)

Fewer ATBs for exacerbation

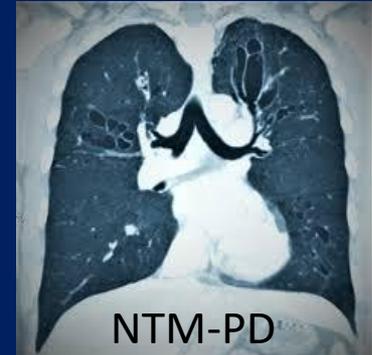
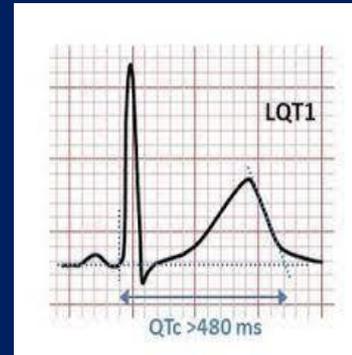
Severe asthmatics: fewer ATBs

Azithromycin for add-on ICS/LABA in asthma

Key concept from GINA 2021

250-500 mg a day 3 times a weekly

Before considering add-on azithromycin



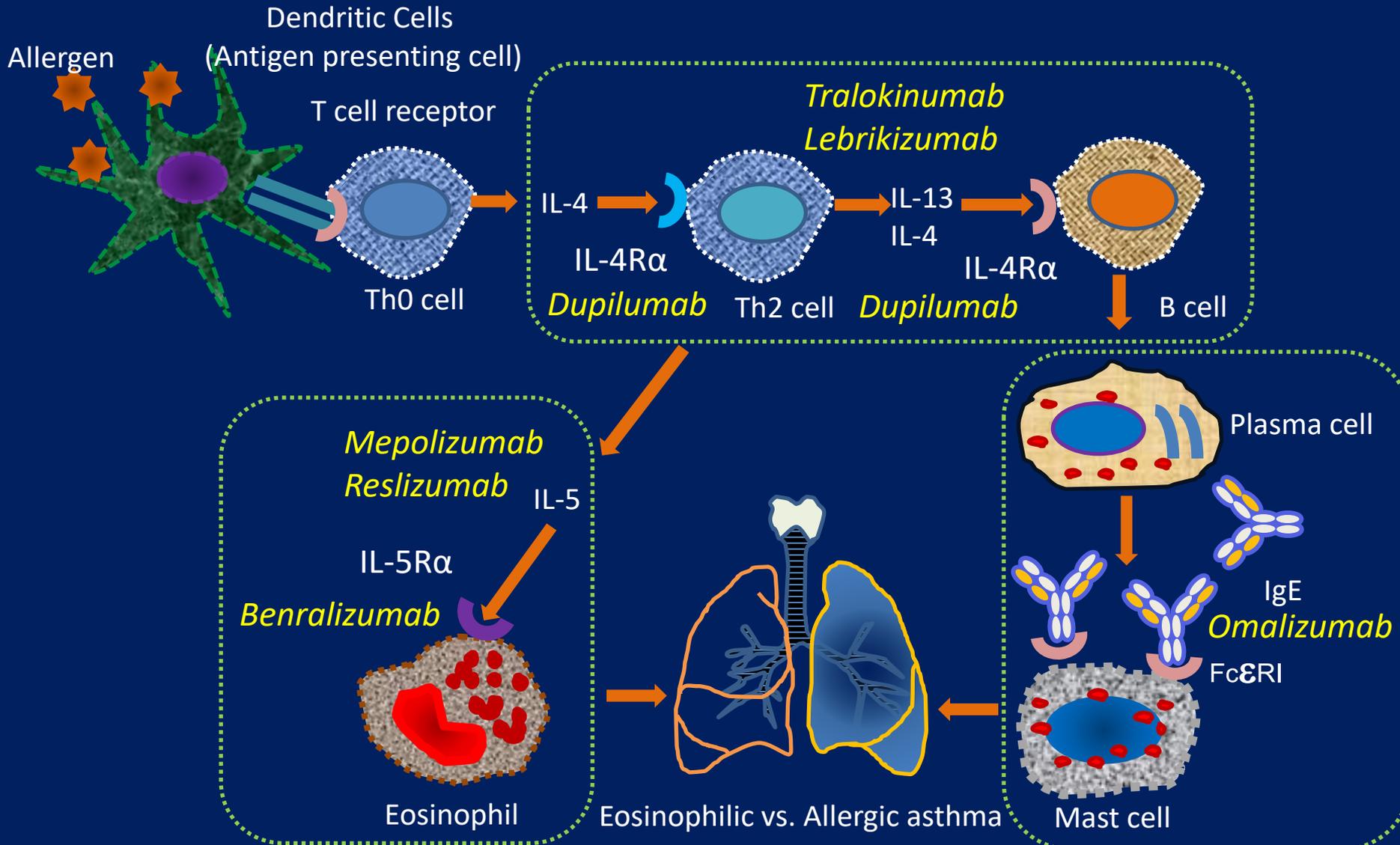
Significantly reduces exacerbations in patients taking **high dose ICS-LABA**

Significantly reduces exacerbations in patients with **eosinophilic or non-eosinophilic asthma**

No evidence published for azithromycin in asthma taking medium dose ICS-LABA

Targets for biologics

(Current and pipeline treatments for T2 predominant asthma)

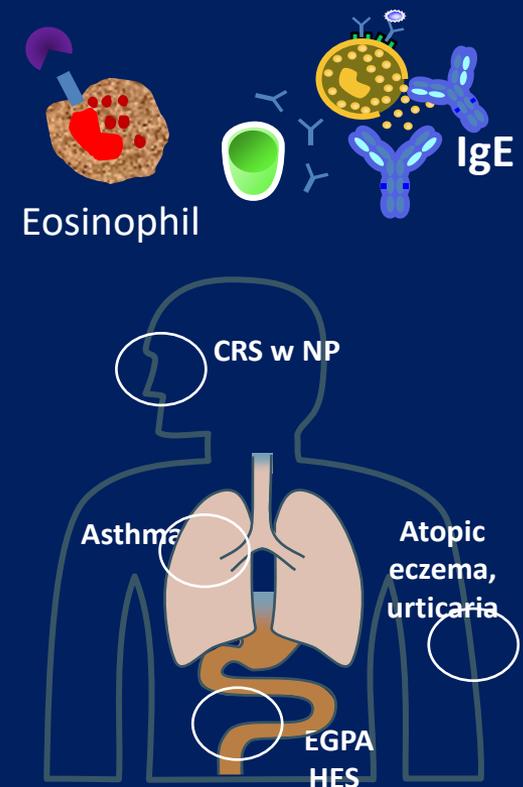


Additional indications for these therapies in Europe and/or USA

Type-2 biologics for non-asthmatic indications

- **Omalizumab**: chronic idiopathic urticaria, nasal polyposis
- **Mepolizumab**: hyper-eosinophilic syndrome (HES), eosinophilic granulomatosis with polyangiitis (EGPA)
- **Benralizumab**: no additional indications at present
- **Dupilumab**: chronic rhinosinusitis with nasal polyposis (CRSwNP), atopic dermatitis

Check local regulatory approvals and eligibility criteria





Thank you for your attention