Apogee
CLINICAL IMMERSION

Current Treatment of Asthma

Eileen Wang MD, MPH

National Jewish Health®
Breathing Science is Life.®

Objectives

- Goals of asthma management and treatment challenges
- Guideline-directed therapy (Global Initiative for Asthma or GINA)
- Treatment landscape
- Recent updates to recommendations
- Selecting a biologic and factors to consider

Evolution of Asthma Concepts

1960-1980s

- Bronchospasm
- Smooth Muscle Focus

1990-2000s

- Inflammation
- Asthma Control: Impairment and Risk

2010-current

- Precision Medicine
- Clinical Phenotypes
- Inflammatory Endotypes
- Airway Epithelium
- Barrier Dysfunction
- Airway Hyperresponsiveness
- Mucus Plugging
- Population Health and Health Inequities

Szefler S.J. *J Allergy Clin Immunol* 2018; 142:773-780.
Singh, S. et al. *Diagnostics* 2023; 13(4): 808.

GINA goal of asthma management

The goal is to achieve the **best possible long-term asthma outcomes** for each patient:

- Long-term symptom control, which may include:
  - Few/no asthma symptoms, quickly relieved
  - No sleep disturbance
  - Unimpaired physical activity
- Long-term asthma risk minimization, which may include:
  - No exacerbations
  - Improved or stable personal best lung function
  - No requirement for maintenance oral corticosteroids
  - No medication side-effects

When discussing best possible long-term outcomes with a patient, consider:

- Their asthma phenotype
- Clinical features
- Multimorbidity
- Risk factors (e.g. poor adherence, smoking, persistent airflow limitation)
- Availability, cost and adverse effects of medications
- The patient's goals (these may be different from medical goals)

- Assessing symptom control is not enough! Patients with few asthma symptoms can still have severe or fatal exacerbations related to individual risk factors or external triggers (viruses, allergen, pollution)
- Encourage referral for expert advice for patients with difficult-to-treat or severe asthma

Patient Questionnaires

1. In the past **4 weeks**, how much of the time did your **asthma** keep you from g

All of the time (1)	Most of the time (2)	Some of the time (3)

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

More than once a day (1)	Once a day (2)	3 to 6 times a week (3)

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

4 or more nights a week (1)	2 or 3 nights a week (2)	Once a week (3)

4. During the past **4 weeks**, how often have you used your rescue inhaler o

3 or more times per day (1)	1 or 2 times per day (2)	2 or 3 times per week (3)

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

Not controlled at all (1)	Poorly controlled (2)	Somewhat controlled (3)

AMERICAN LUNG ASSOCIATION.

The American Lung Association supports the Asthma Control Test and does not endorse products.

If your score is 19 or less, your asthma may
Talk to your doctor.

In the past 2 weeks, has coughing, wheezing, shortness of breath, or chest tightness:

1. Bothered you during the day on **more than 4 days**? Yes No
2. Woke you up from sleep **more than 1 time**? Yes No
3. Limited the activities you want to do **every day**? Yes No
4. Caused you to use your rescue inhaler or nebulizer **every day**? Yes No

Primatene® MIST (Amphastar Pharmaceuticals) or Epinephrine

ProAir RespiClick® (Teva Respiratory, LLC) or Albuterol sulfate

Proventil® HFA (Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.) or Albuterol sulfate

Ventolin® HFA (GlaxoSmithKline) or Albuterol sulfate

Xopenex HFA® (Sunovion Pharmaceuticals Inc.) or Levalbuterol tartrate

Albuterol sulfate or Xopenex® (Sunovion Pharmaceuticals Inc.) or Levalbuterol HCl

Please see all prescribing information for all products.

In the past 2 weeks:

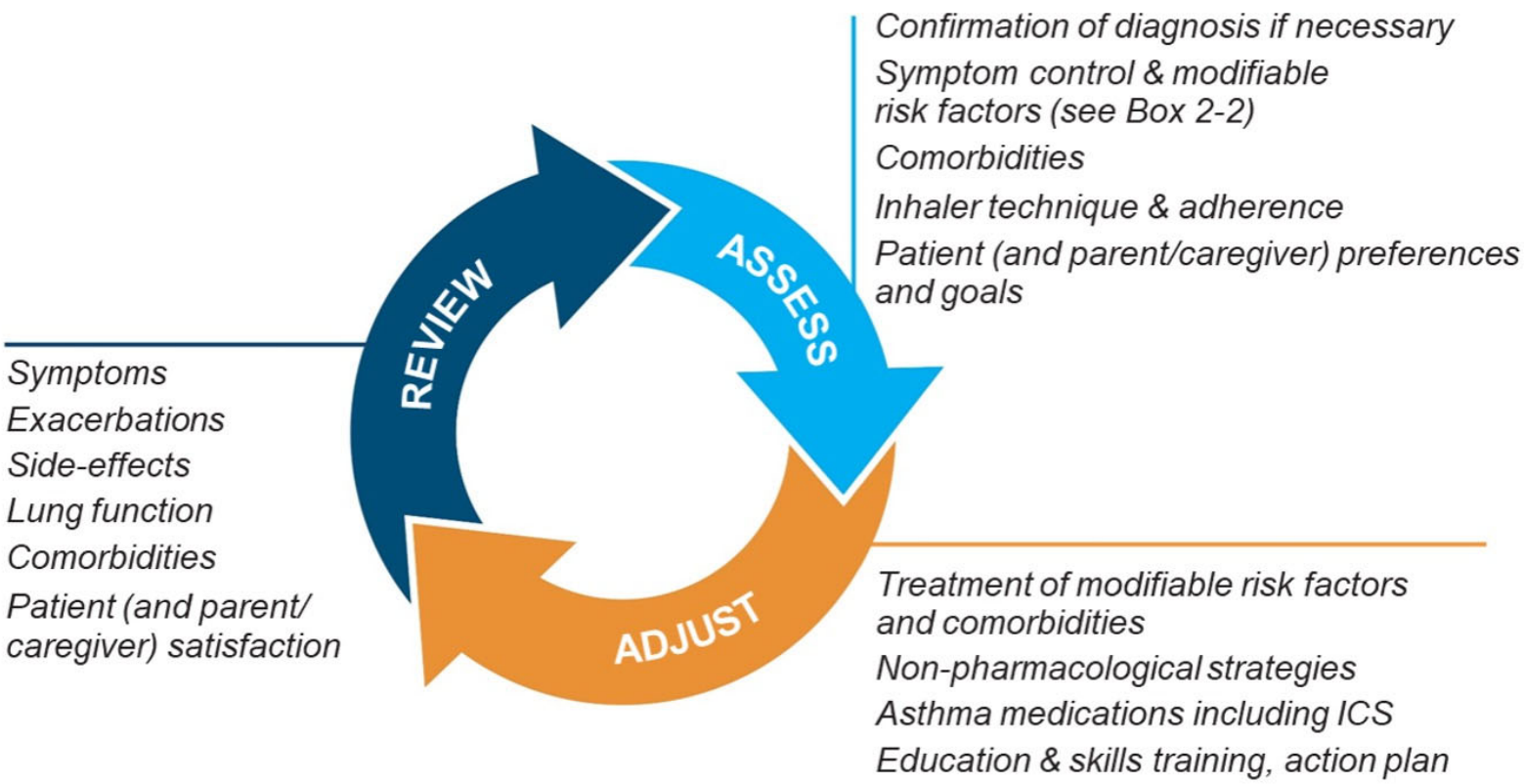
5. Did you have to limit your social activities (such as visiting with friends/relatives or playing with pets/children) because of your asthma? Yes No
6. Did coughing, wheezing, shortness of breath, or chest tightness limit your ability to exercise? Yes No
7. Did you feel that it was difficult to control your asthma? Yes No

In the past 12 months, has coughing, wheezing, shortness of breath, or chest tightness:

8. Caused you to take steroid pills or shots, such as prednisone or Medrol®*? Yes No
9. Caused you to go to the emergency room or have unplanned visits to a health care provider? Yes No
10. Caused you to stay in the hospital overnight? Yes No

Total YES Answers ☐

Asthma treatment is not ‘set and forget’, and not just medications

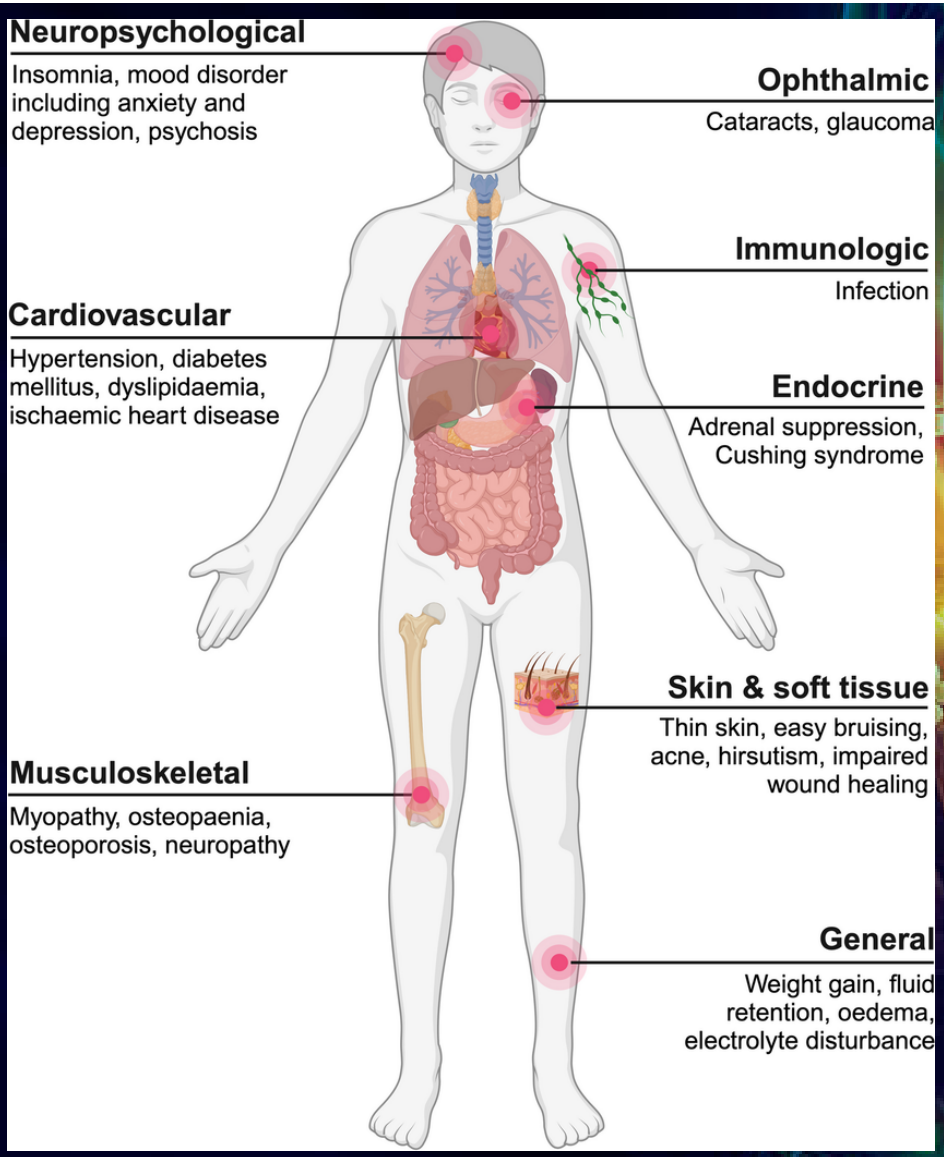


Treatment Complexity, Challenges, and Barriers

- Misdiagnosis
- Lack of recognition of uncontrolled or severe asthma
- Confounders and co-morbidities
- Medication access and cost
- Access to subspecialty care
- Medication administration complexity
- Biologic therapies
- Glucocorticoid resistance

Up to half of patients do not achieve well-controlled status with guideline-based treatment

Systemic Corticosteroids Potential Adverse Effects



Liu D., et al. (2024). Current Transplantation Reports. 11. 197-206. 10.1007/s40472-024-00441-9.

SHORT-ACTING BETA$_2$-AGONIST (SABA) BRONCHODILATORS
relax tight muscles in airways and offer quick relief of symptoms such as coughing, wheezing and shortness of breath for 3-6 hours

Albuterol Sulfate Inhalation Solution
0.63, 1.25 mg, 2.5mg; 3 mL
G N

ProAir RespiClick®
90 mcg
albuterol sulfate inhalation powder
1 2 3 A

Proventil® HFA
90 mcg
albuterol sulfate
1 2 3 A G

Ventolin® HFA
90 mcg
albuterol sulfate
1 2 3 A G

Xopenex®
0.31, 0.63, 1.25 mg; 3 mL
levalbuterol hydrochloride inhalation solution
A G N

Xopenex HFA®
45 mcg
levalbuterol tartrate
A G

SABA and ICS
contains SABA to relax airway muscles and offer quick relief of symptoms, and inhaled corticosteroid (ICS) to reduce inflamed airways

AIRSUPRA®
90/80 mcg
albuterol and budesonide
1 2 3 A

INHALED CORTICOSTEROIDS (ICS)
reduce and prevent swelling of airway tissue; they do not relieve sudden symptoms of coughing, wheezing or shortness of breath

Alvesco® HFA
80, 160 mcg
ciclesonide
1 2 3 A

Arnuity® Ellipta®
50, 100, 200 mcg
fluticasone furoate inhalation powder
1 2 3 A

Asmanex® HFA
50, 100, 200 mcg
mometasone furoate
1 2 3 A

Asmanex® Twisthaler®
110, 220 mcg
mometasone furoate inhalation powder
1 2 3 A

Fluticasone Propionate Diskus Inhalation Powder
50, 100, 250 mcg
authorized generic of Flovent Diskus
1 2 3 A

Fluticasone Propionate HFA
44, 110, 220 mcg
authorized generic of Flovent HFA
1 2 3 A

Pulmicort Flexhaler®
90, 180 mcg
budesonide inhalation powder
1 2 3 A

Pulmicort Respules®
0.25, 0.50, 1.0 mg; 2 mL
budesonide inhalation suspension
A G N

QVAR Redihaler®
40, 80 mcg
beclomethasone dipropionate
1 2 3 A

LONG-ACTING BETA$_2$-AGONIST (LABA) BRONCHODILATORS
relax tight muscles in airways and offer lasting relief of symptoms such as coughing, wheezing and shortness of breath for at least 12 hours

Brovana®
15 mcg; 2 mL
arformoterol tartrate inhalation solution
C N

Perforomist®
20 mcg; 2 mL
formoterol fumarate inhalation solution
C N

Serevent® Diskus®
50 mcg
salmeterol xinafoate inhalation powder
1 2 3 A C

Striverdi® Respimat®
2.5 mcg
olodaterol hydrochloride
1 2 3 C

MUSCARINIC ANTAGONISTS (ANTICHOLINERGICS)
relieve cough, sputum production, wheeze and chest tightness associated with chronic lung diseases

SHORT-ACTING

Atrovent® HFA
17 mcg
ipratropium bromide
1 2 3 C

LONG-ACTING

Incruse® Ellipta®
62.5 mcg
umeclidinium inhalation powder
1 2 3 C

Ipratropium Bromide Inhalation Solution
0.5/3 mg; 3 mL
C G N

Spiriva® HandiHaler®
18 mcg
tiotropium bromide inhalation powder
C

Spiriva® Respimat®
1.25, 2.5 mcg
tiotropium bromide
1 2 3 A C

Tudorza® Pressair®
400 mcg
aclidinium bromide inhalation powder
1 2 3 C

Yupelri®
175 mcg; 3 mL
revefenacin inhalation solution
C N

COMBINATION MEDICATIONS
contain ICS and LABA

Advair Diskus®
100/50, 250/50, 500/50 mcg
fluticasone propionate and salmeterol inhalation powder
1 2 3
A C G

Advair® HFA
45/21, 115/21, 230/21 mcg
fluticasone propionate and salmeterol xinafoate
1 2 3 A G

AirDuo® RespiClick®
55/14, 113/14, 232/14 mcg
fluticasone propionate and salmeterol inhalation powder
1 2 3 A G

Breo® Ellipta®
50/25, 100/25, 200/25 mcg
fluticasone furoate and vilanterol inhalation powder
1 2 3
A C G

Breyna®
80/4.5, 160/4.5 mcg
budesonide and formoterol fumarate dihydrate (approved generic of Symbicort)
1 2 3 A C

Dulera®
50/5, 100/5, 200/5 mcg
mometasone furoate and formoterol fumarate dihydrate
1 2 3 A

Symbicort®
80/4.5, 160/4.5 mcg
budesonide and formoterol fumarate dihydrate
1 2 3 A C G

Wixela Inhub®
100/50, 250/50, 500/50 mcg
fluticasone propionate and salmeterol xinafoate (approved generic of Advair Diskus)
1 2 3 A C

contain LABA and long-acting muscarinic antagonist (LAMA)

Anoro® Ellipta®
62.5/25 mcg
umeclidinium and vilanterol inhalation powder
1 2 3 C

Bevespi Aerosphere®
9/4.8 mcg
glycopyrrolate and formoterol fumarate
1 2 3 C

Duaklir® Pressair®
400/12 mcg
aclidinium bromide and formoterol fumarate
1 2 3 C

Stiolto® Respimat®
2.5/2.5 mcg
tiotropium bromide and olodaterol
1 2 3 C

contain ICS, LABA and LAMA

Trelegy® Ellipta®
200/62.5/25 mcg, 100/62.5/25 mcg
fluticasone furoate, umeclidinium and vilanterol inhalation powder
1 2 3 A C

Breztri Aerosphere®
160/9/4.8 mcg
budesonide, glycopyrrolate and formoterol fumarate
1 2 3 C

contain SABA and short-acting muscarinic antagonist (SAMA)

Combivent® Respimat®
20/100 mcg
ipratropium bromide and albuterol
1 2 3 C

Ipratropium Bromide and Albuterol Sulfate Inhalation Solution
0.5mg/2.5mg; 3ml
C G

BIOLOGICS
target cells and pathways that cause airway inflammation; delivered by injection or IV

Cinqair®
62.5/25 ml
reslizumab
A

Dupixent®
100, 200, 300 mg
dupilumab
A

Fasenra®
30 mg
benralizumab
A

Nucala®
100 mg
mepolizumab
A

Tezspire®
210 mg
tezepelumab-ekko
A

Xolair®
75 to 375 mg
omalizumab
A

PDE4 INHIBITORS
target lung inflammation and reduce exacerbations

Daliresp®
250, 500 mcg
roflumilast
C

LEUKOTRIENE MODIFIERS
block chemicals called leukotrienes that cause airway inflammation; available as tablet or granules

Singulair®
4, 5, 10 mg
montelukast
A

Zafirlukast
10, 20 mg
A

Zileuton
600 mg
A

Allergy & Asthma NETWORK

EDITORIAL
GINA 2019

GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents

Helen K. Reddel [1], J. Mark FitzGerald [2], Eric D. Bateman [3], Leonard B. Bacharier [4], Allan Becker [5], Guy Brusselle [6], Roland Buhl [7], Alvaro A. Cruz [8], Louise Fleming [9], Hiromasa Inoue [10], Fanny Wai-san Ko [11], Jerry A. Krishnan [12], Mark L. Levy [13], Jiangtao Lin [14], Søren E. Pedersen [15], Aziz Sheikh [16], Arzu Yorgancioglu [17] and Louis-Philippe Boulet [18]

Audience Response

- Why is short acting beta agonist (SABA) therapy alone no longer recommended?

A. Regular use of SABA is associated with increased airway hyperresponsiveness

B. SABA treats inflammation but inadequately treats bronchoconstriction

C. Overuse of SABA is not associated with significant benefits or risks

Why Not SABA alone?

- Does not treat underlying inflammation
  - Treats symptoms but not disease
- Those with mild to moderate asthma have been shown to still be at risk of severe and fatal exacerbations
  - Can be unpredictable
  - Up to 27% of deaths due to asthma are in patients with occasional symptoms
- Data supporting risk in regular use or overuse of SABA
  - Increased airway hyperresponsiveness, exacerbation risk and mortality
- Starting with SABA alone trains patients early that it is their primary asthma medication
- **For children 6-11, adolescents, and adults, GINA does not recommend treatment of asthma with SABA alone.**

Nwaru BI, et al. Eru Respir J. 2020.
Bergström S, et al. Respir Med 2008.
Cole s, et al. BMJ Open 2013.
GINA 2024.

GINA 2024

Adults and Adolescents 12-17 years

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
As-needed-only low dose ICS-formoterol*

RELIEVER:

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
Take ICS whenever SABA taken*

Children 6-11 years

PREFERRED CONTROLLER
to prevent exacerbations and control symptoms

STEP 1
Low dose ICS taken whenever SABA taken*

GINA 2024 Box 4-6; slide 1/4

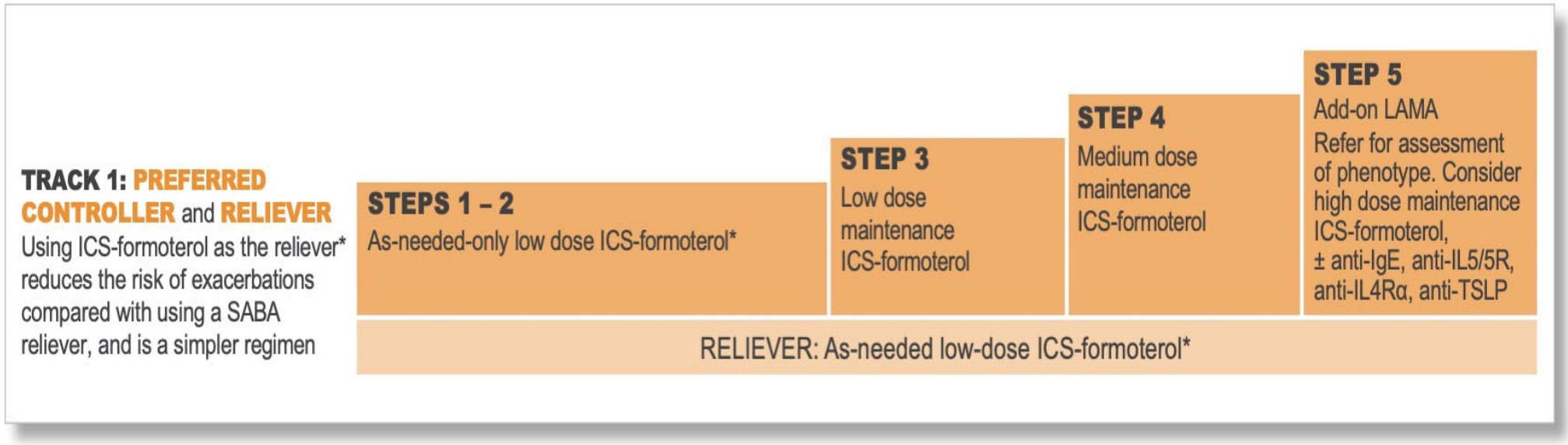
What is Anti-Inflammatory Reliever or Rescue (AIR)?

Definitions

- Anti-inflammatory reliever or rescue (AIR): pairing inhaled corticosteroid with bronchodilator for **reliever therapy**
  - Examples are ICS/formoterol (ICS/LABA) and ICS/albuterol (ICS/SABA)
- Maintenance and reliever therapy (MART)
- Single maintenance and reliever therapy (SMART)

GINA 2024

Adults and Adolescents 12-17 years

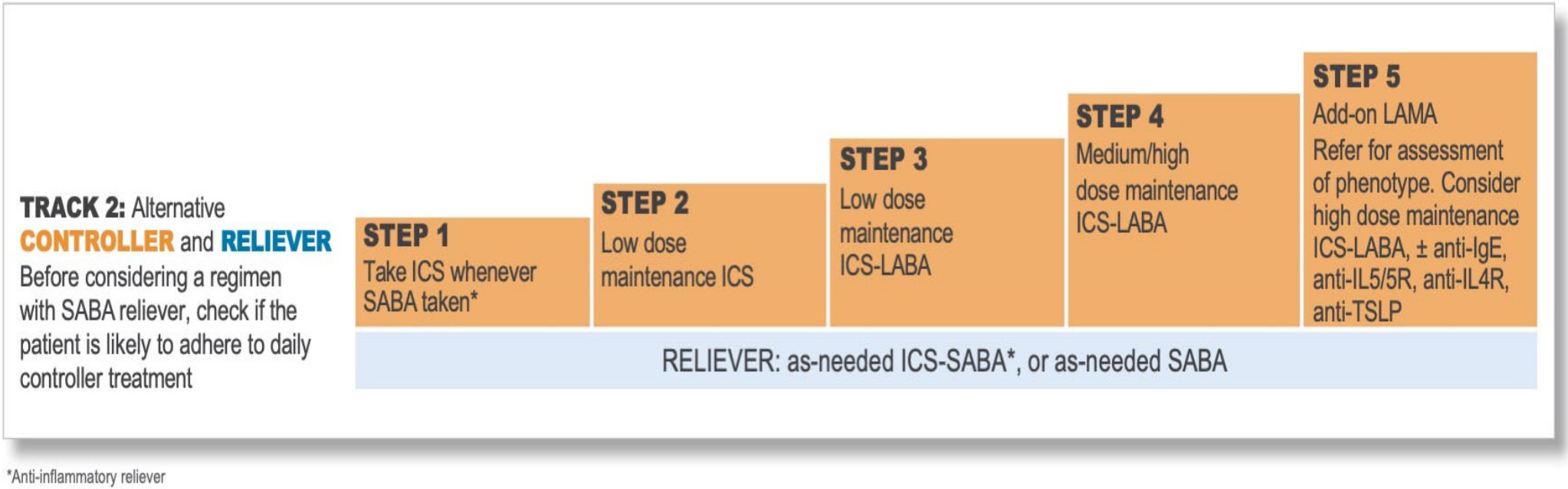


*Anti-inflammatory reliever

GINA 2024 Box 4-6; slide 1/4

GINA 2024

Adults and Adolescents 12-17 years

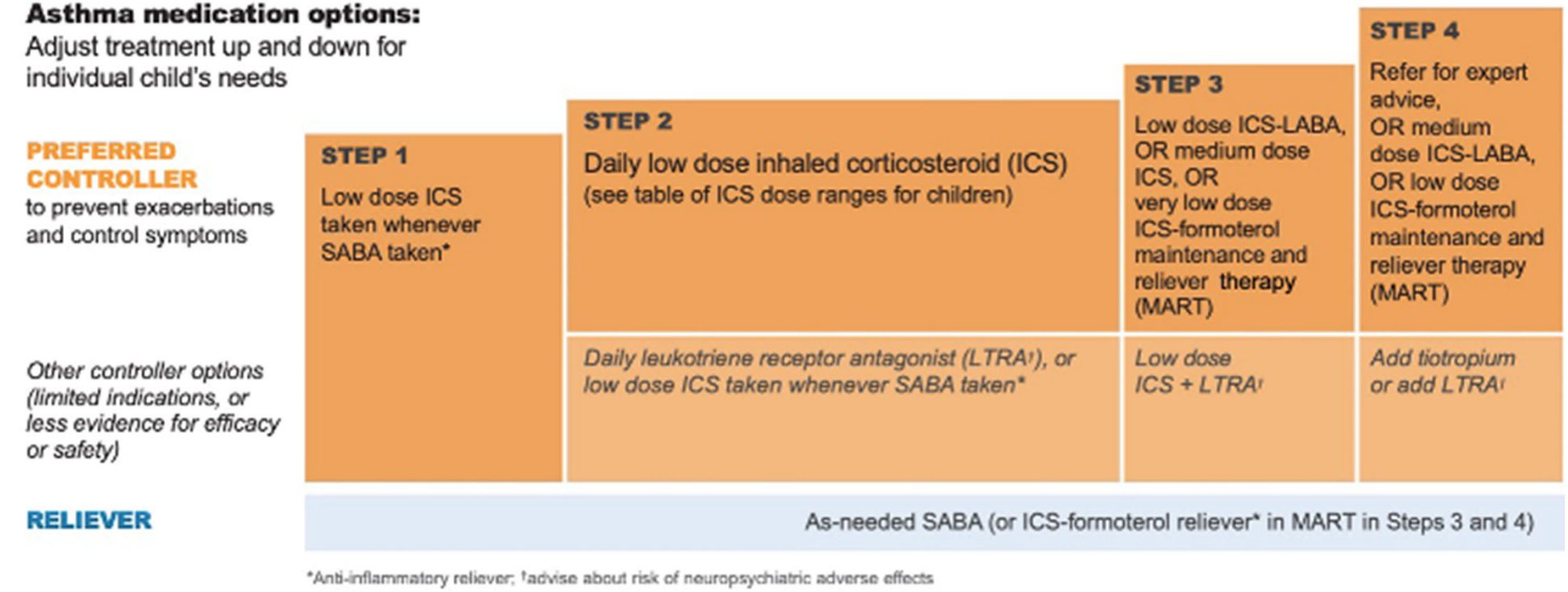


*Anti-inflammatory reliever

GINA 2024 Box 4-6; slide 1/4

GINA 2024

Children 6-11 years



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

GINA 2024 Box 4-12

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma

Authors: Paul M. O'Byrne, M.B., J. Mark FitzGerald, M.D., Eric D. Bateman, M.D., Peter J. Barnes, M.D., Nanshan Zhon Ph.D., Christina Keen, M.D., Carin Jorup, M.D., Rosa Lamarca, Ph.D., Stefan Ivanov, M.D., Ph.D., and Helen K. Reddel, M.B., B.S., Ph.D. Author Info & Affiliations

Published May 16, 2018 | N Engl J Med 2018;378:1865-1876 | DOI: 10.1056/NEJMoa1715274 | VOL. 378 NO. 20

SYGMA 1 Trial

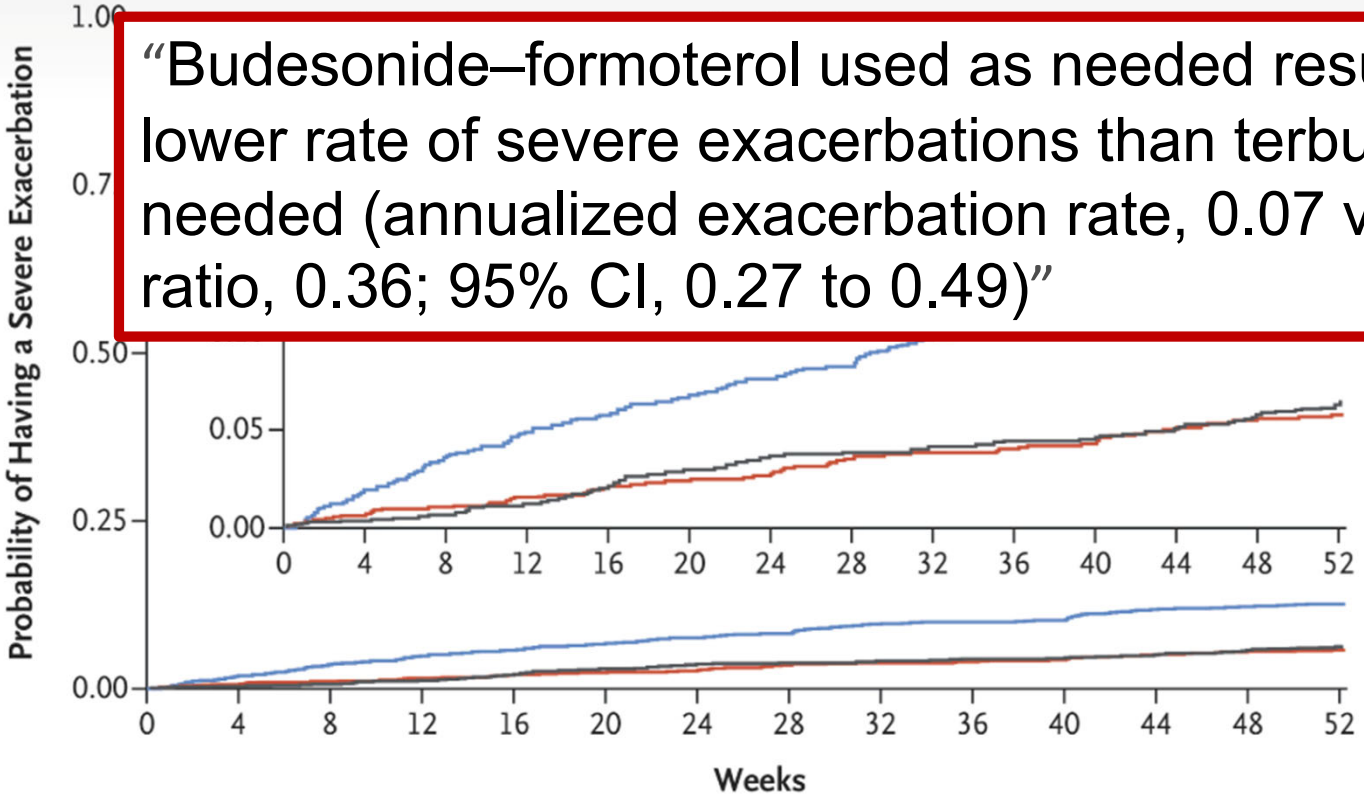
52-week study

12 years of age and older with mild asthma (appropriate for GINA step 2)

N=3836

Severe Exacerbation Risk Reduction with ICS-Formoterol

"Budesonide–formoterol used as needed resulted in a 64% lower rate of severe exacerbations than terbutaline used as needed (annualized exacerbation rate, 0.07 vs. 0.20; rate ratio, 0.36; 95% CI, 0.27 to 0.49)"



ded

SABA as needed

(N = 1282)

O'Byrne et al, NEJM 2018

Cochrane Library

Cochrane Database of Systematic Reviews

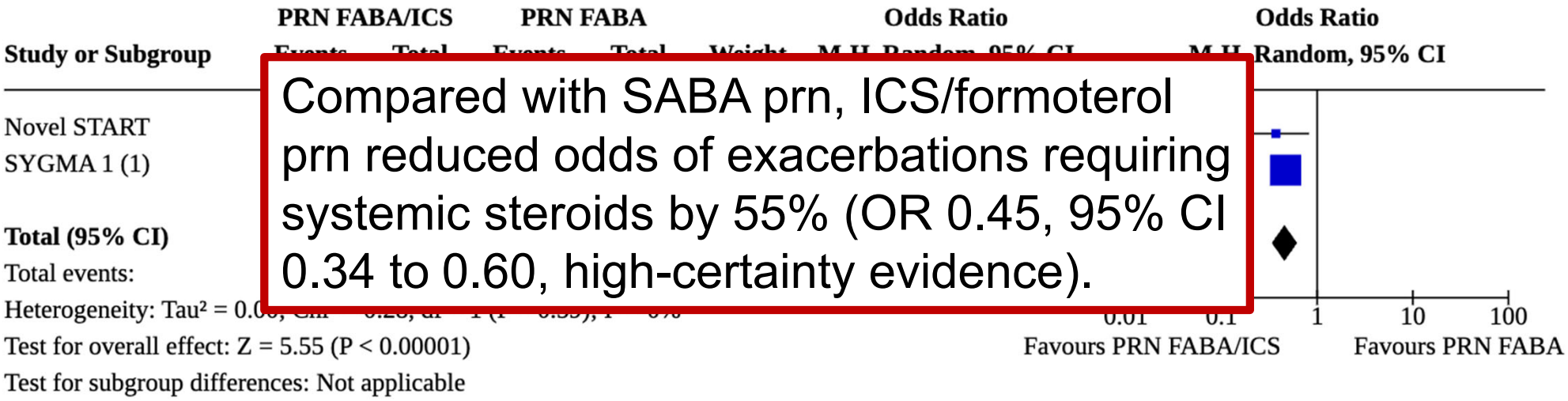
Combination fixed-dose beta agonist and steroid inhaler as required for adults or children with mild asthma (Review)

Crossingham I, Turner S, Ramakrishnan S, Fries A, Gowell M, Yasmin F, Richardson R, Webb P, O'Boyle E, Hinks TSC

Cochrane Database of Systematic Reviews 2021, Issue 5. Art. No.: CD013518.
DOI: 10.1002/14651858.CD013518.pub2.

ICS/Formoterol PRN and Reduction in Exacerbations Requiring Systemic Corticosteroid

Analysis 1.1. Comparison 1: As required fixed dose combination inhaler versus as required short acting beta agonist, Outcome 1: Asthma exacerbations requiring systemic steroid



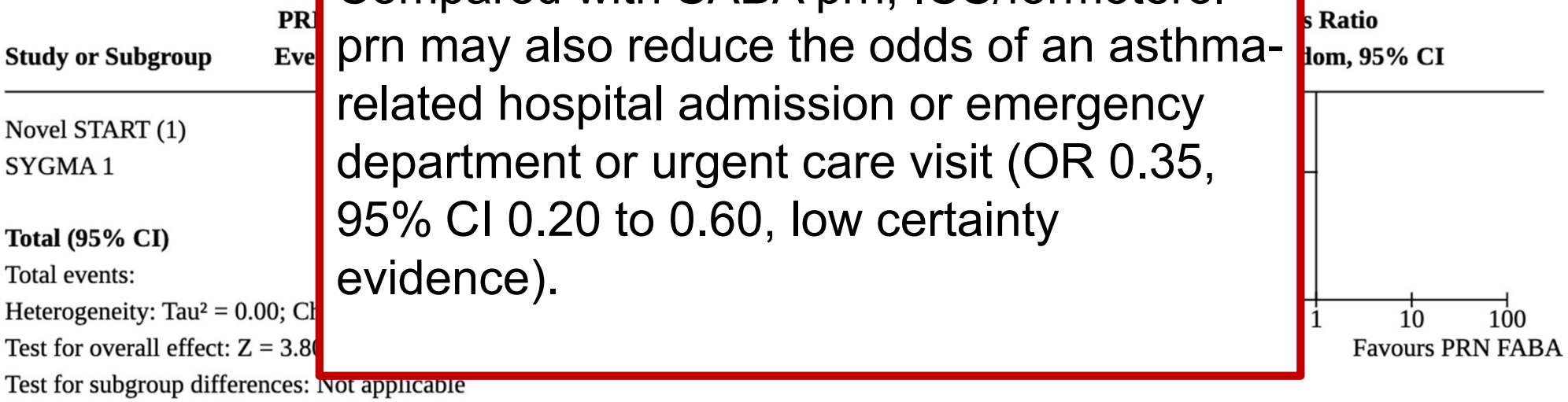
Compared with SABA prn, ICS/formoterol prn reduced odds of exacerbations requiring systemic steroids by 55% (OR 0.45, 95% CI 0.34 to 0.60, high-certainty evidence).

Crossingham I, Turner S, Ramakrishnan S, Fries A, Gowell M, Yasmin F, Richardson R, Webb P, O'Boyle E, Hinks TSC. Combination fixed-dose beta agonist and steroid inhaler as required for adults or children with mild asthma. *Cochrane Database of Systematic Reviews* 2021, Issue 5. Art. No.: CD013518.

ICS/Formoterol PRN and Reduction in Exacerbations Requiring Hospitalization, ED or UC Visit

Analysis 1.3. Comparison 1: As required fixed dose combination inhaler versus as required short acting beta agonist, Outcome 3: Exacerbations requiring hospital admission or emergency department / urgent care visit

Compared with SABA prn, ICS/formoterol prn may also reduce the odds of an asthma-related hospital admission or emergency department or urgent care visit (OR 0.35, 95% CI 0.20 to 0.60, low certainty evidence).



Crossingham I, Turner S, Ramakrishnan S, Fries A, Gowell M, Yasmin F, Richardson R, Webb P, O'Boyle E, Hinks TSC. Combination fixed-dose beta agonist and steroid inhaler as required for adults or children with mild asthma. *Cochrane Database of Systematic Reviews* 2021, Issue 5. Art. No.: CD013518.

Other Outcomes

- Compared with SABA alone, changes in asthma control or spirometry favored ICS/formoterol but were small and not clinically significant (less than the minimal clinically-important differences).

- No significant differences in asthma-associated quality of life or mortality.

- May reduce total systemic corticosteroid dose (mean difference -9.90 mg of cumulative dose of prednisolone over 52 weeks, 95% CI -19.38 to -0.42, 1 RCT, 443 participants, low-certainty evidence)

Audience Response

- For those with mild asthma, as needed ICS/formoterol, compared to as needed SABA, has been shown to:

A. Meaningfully improve asthma control
B. Reduce asthma-related mortality
C. Increase total systemic corticosteroid dose
D. Reduce risk of exacerbations requiring systemic corticosteroids

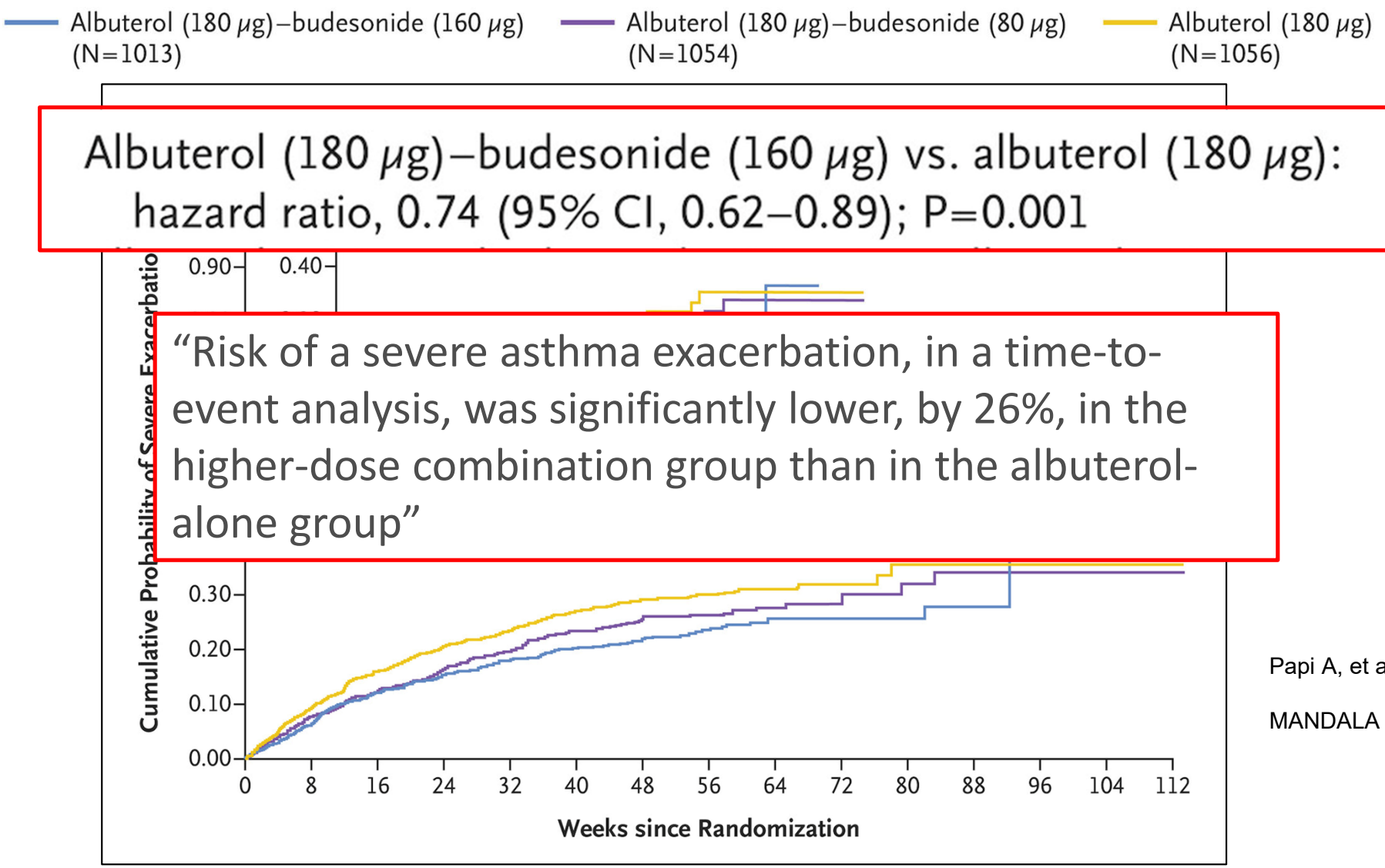
What about GINA Track 2 ICS/SABA?

- Albuterol/budesonide FDA approved 2023 for adults

- For as-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations

- Phase 3 RCT: 3132 patients from North America, South America, Europe, South Africa
- Minimum duration 24 weeks
- Ages 4 and older with at least 1 severe exacerbation in last 12 months, FEV1 reversibility ≥ 12%, ACQ-5 ≥ 1.5, on medium to high-dose ICS (or low to high dose ICS/LABA)
- Maintenance therapy remained same
- Compared albuterol PRN to 2 doses of albuterol/budesonide in 1:1:1 ratio

Papi A, et al. NEJM 2022



Papi A, et al. NEJM 2022

MANDALA Trial

SHORT-ACTING BETA$_2$-AGONIST (SABA) BRONCHODILATORS
relax tight muscles in airways and offer quick relief of symptoms such as coughing, wheezing and shortness of breath for 3-6 hours

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Ventolin® HFA
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Xopenex®
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A G N

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A G

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40, 80 mcg
beclomethasone dipropionate
1 2 3 A

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C N

Perforomist®
20 mcg; 2 mL
formoterol fumarate inhalation solution
C N

Serevent® Diskus®
50 mcg
salmeterol xinafoate inhalation powder
1 2 3 A C

Striverdi® Respimat®
2.5 mcg
olodaterol hydrochloride
1 2 3 C

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1 2 3 C

LONG-ACTING

Incruse® Ellipta®
62.5 mcg
umeclidinium inhalation powder
1 2 3 C

Ipratropium Bromide Inhalation Solution
0.5/3 mg; 3 mL
C G N

Spiriva® HandiHaler®
18 mcg
tiotropium bromide inhalation powder
C

Spiriva® Respimat®
1.25, 2.5 mcg
tiotropium bromide
1 2 3 A C

Tudorza® Pressair®
400 mcg
aclidinium bromide inhalation powder
1 2 3 C

Yupelri®
175 mcg; 3 mL
revefenacin inhalation solution
C N

COMBINATION MEDICATIONS
contain ICS and LABA

Advair Diskus®
100/50, 250/50, 500/50 mcg
fluticasone propionate and salmeterol inhalation powder
1 2 3
A C G

Advair® HFA
45/21, 115/21, 230/21 mcg
fluticasone propionate and salmeterol xinafoate
1 2 3 A G

AirDuo® RespiClick®
55/14, 113/14, 232/14 mcg
fluticasone propionate and salmeterol inhalation powder
1 2 3 A G

Breo® Ellipta®
50/25, 100/25, 200/25 mcg
fluticasone furoate and vilanterol inhalation powder
1 2 3
A C G

Breyna®
80/4.5, 160/4.5 mcg
budesonide and formoterol fumarate dihydrate (approved generic of Symbicort)
1 2 3 A C

Dulera®
50/5, 100/5, 200/5 mcg
mometasone furoate and formoterol fumarate dihydrate
1 2 3 A

Symbicort®
80/4.5, 160/4.5 mcg
budesonide and formoterol fumarate dihydrate
1 2 3 A C G

Wixela Inhub®
100/50, 250/50, 500/50 mcg
fluticasone propionate and salmeterol xinafoate (approved generic of Advair Diskus)
1 2 3 A C

Allergy & Asthma NETWORK

Current Biologics

BIOLOGICS target cells and pathways that cause airway inflammation; delivered by injection or IV

Cinqair®
62.5/25 ml
reslizumab
A

Dupixent®
100, 200, 300 mg
dupilumab
A

Fasenra®
30 mg
benralizumab
A

Nucala®
100 mg
mepolizumab
A

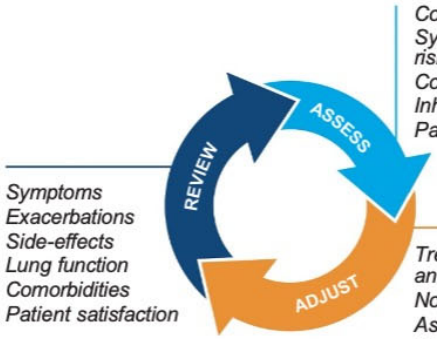
Tezspire®
210 mg
tezepelumab-ekko
A

Xolair®
75 to 375 mg
omalizumab
A

Allergy & Asthma NETWORK

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*			

See GINA severe asthma guide

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				

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*

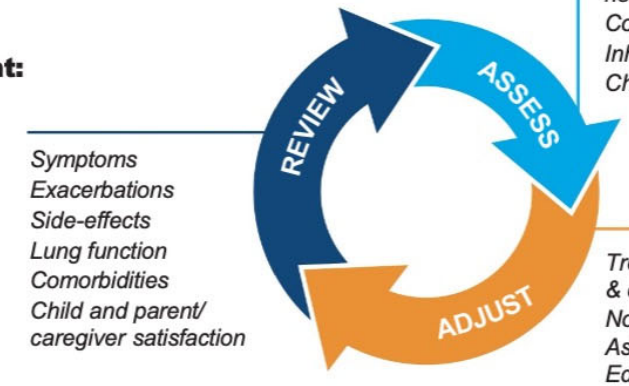
Other controller options (limited indications, or less evidence for efficacy or safety – see text)

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

GINA 2024 Box 4-6

GINA 2024 – Children 6–11 years

Personalized asthma management:
Assess, Adjust, Review



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

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Child and parent/ caregiver satisfaction

Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
Asthma medications including ICS
Education & skills training

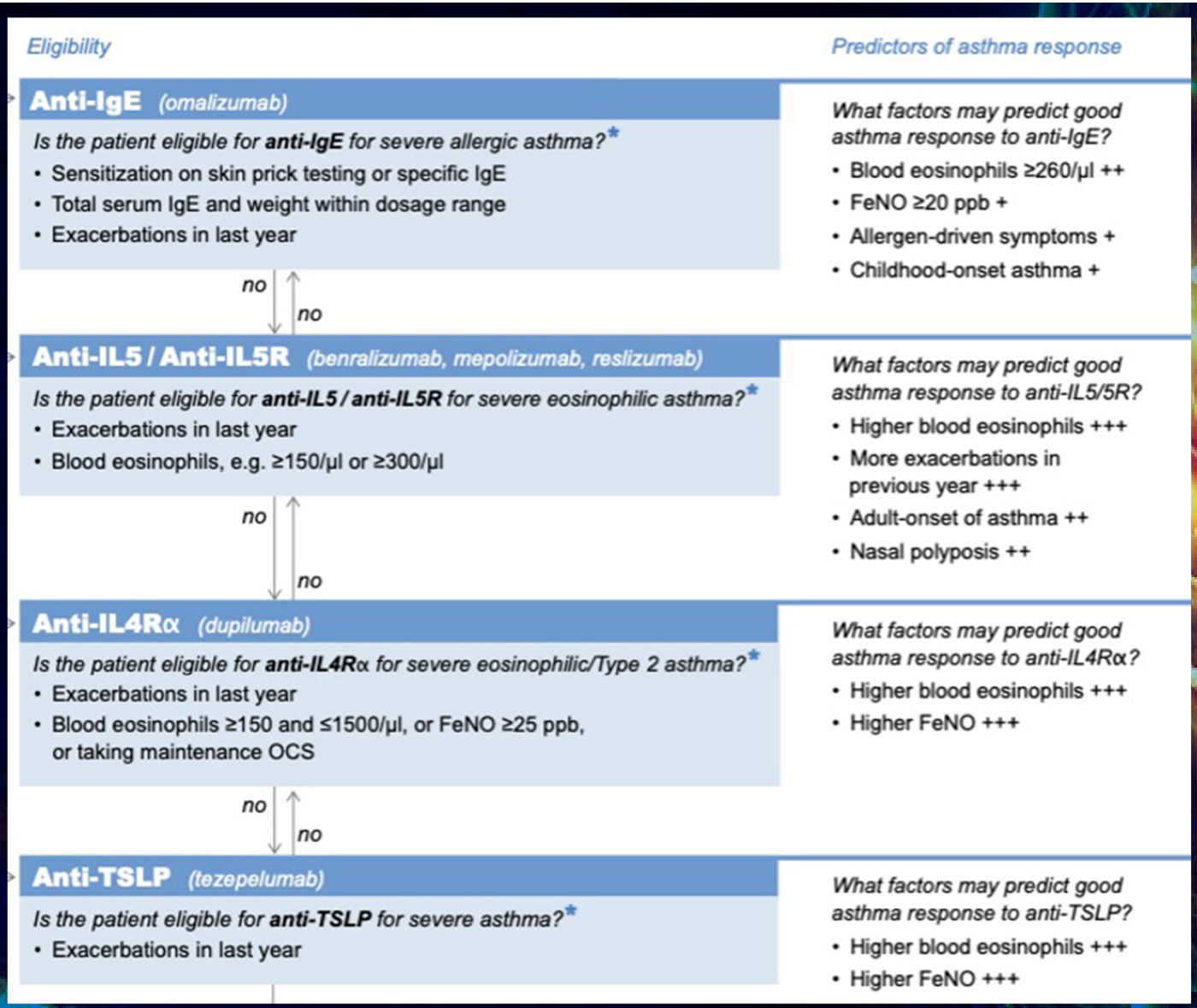
Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken*	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA, OR medium dose ICS, OR very low dose ICS-formoterol maintenance and reliever therapy (MART)	Refer for expert advice, OR medium dose ICS-LABA, OR low dose ICS-formoterol maintenance and reliever therapy (MART)	Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4Rα, anti-IL5
Other controller options (limited indications, or less evidence for efficacy or safety)		*Daily leukotriene receptor antagonist (LTRA†), or low dose ICS taken whenever SABA taken**	*Low dose ICS + LTRA†*	*Add tiotropium or add LTRA†*	*As last resort, consider add-on low dose OCS, but consider side-effects*
RELIEVER	As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)				

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

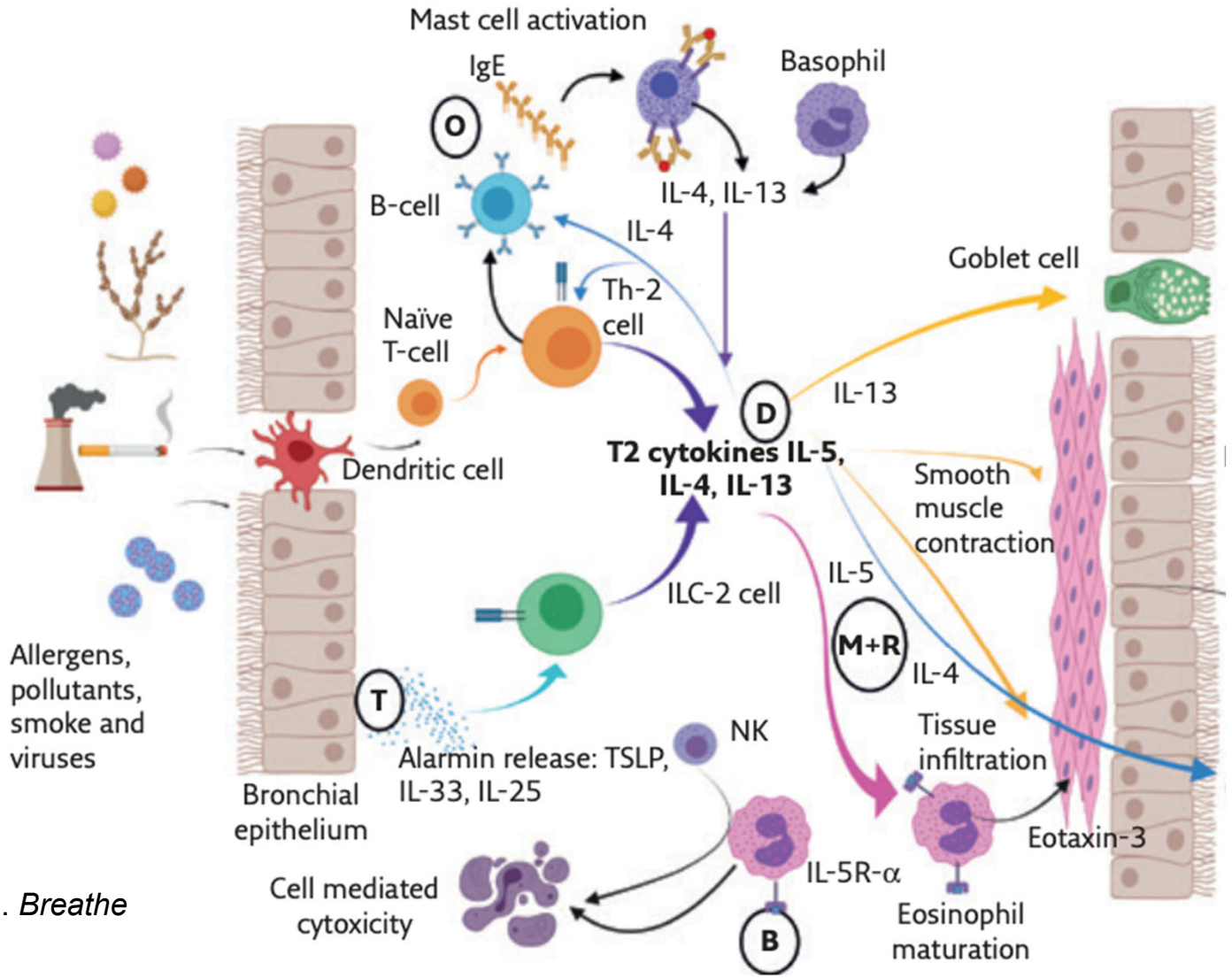
GINA 2024 Box 4-12

GINA



Biologic Targets

Key:
B: benralizumab;
D: dupilumab;
M+R: mepolizumab and reslizumab;
O: omalizumab;
T: tezepelumab

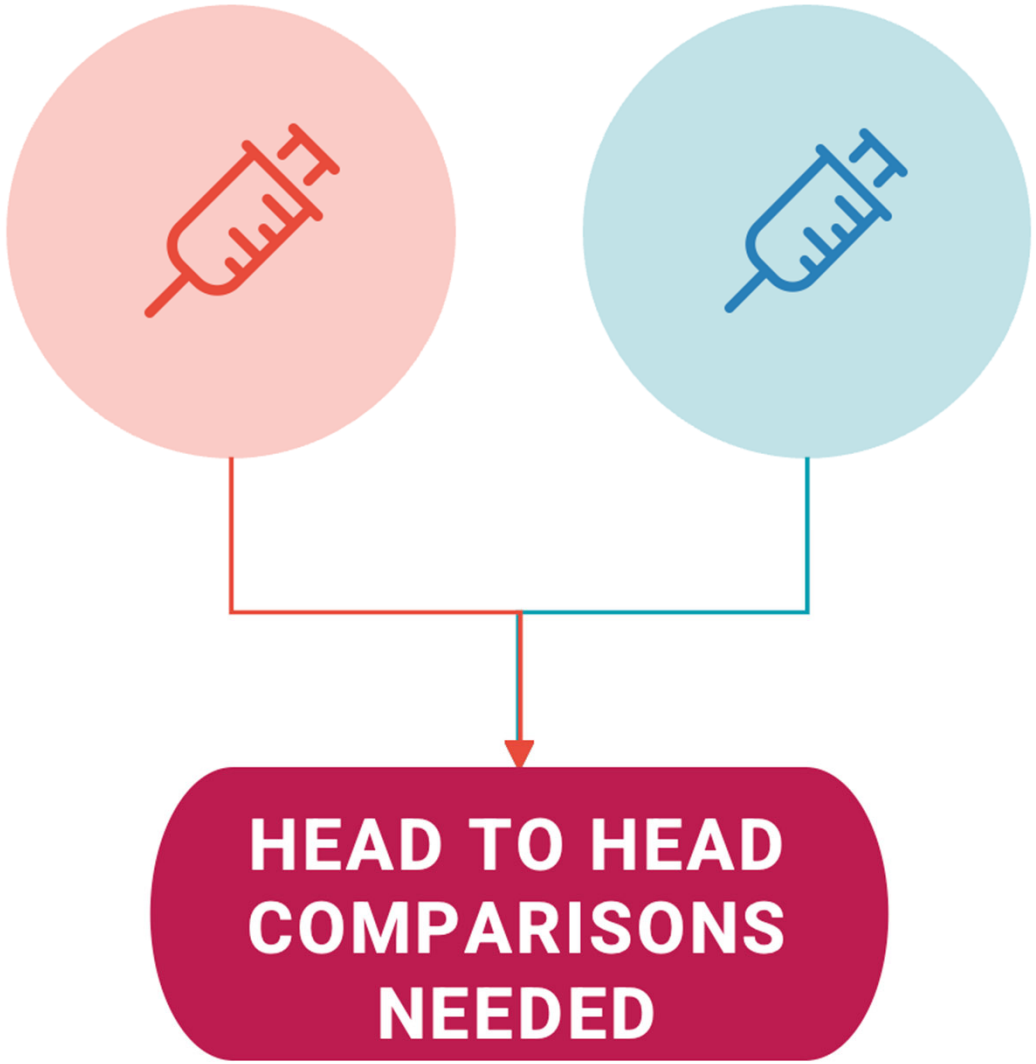


Kavanagh JE, Hearn AP, Jackson DJ. *Breathe* 2021; 17: 210144.

FDA-Approved Biologic Therapeutics for Asthma

Mechanism of Action	Drug	Approved Indications in US	Age (yrs)	Dosing and Frequency		Route/ Location
Anti-IgE	Omalizumab	2003 Asthma 2016 CSU 2020 CRSwNP 2024 Food Allergy	≥6	75-375 mg (based on weight, IgE level, age)	Q2W Q4W	SC: Clinic/Home
Anti-IL-5	Mepolizumab	2015 Asthma 2019 EGPA 2020 HES 2021 CRSwNP	≥ 6	40 mg (ages 6-11 years) 100 mg (ages ≥ 12 years) 300 mg (EGPA and HES)	Q4W	SC: Clinic/Home
	Reslizumab	2016 Asthma	≥ 18	3.0 mg/kg	Q4W	IV: Clinic/Home/ Infusion Center
Anti-IL-5Rα	Benralizumab	2018 Asthma 2024 EGPA	≥ 12	30mg	Q4W → Q8W	SC: Clinic/Home
Anti-IL-4Rα	Dupilumab	2017 A.D. 2018 Asthma 2019 CRSwNP 2022: EoE, Prurigo Nodularis	≥ 6	100, 200, or 300mg (based on age, weight for pediatric, eosinophilic vs OCS-dependent asthma)	Q2W	SC: Home
Anti-TSLP	Tezepelumab	2021 Asthma	≥ 12	210 mg	Q4W	SC: Clinic/Home

FDA-Approved Bio		Study Results	
Mechanism of Action	**Drug**	**Increased FEV1**	**mOCS Reduction**
Anti-IgE	Omalizur	✓	✓
Anti-IL-5	Mepolizu	✓	✓
	Reslizum	✓	✓
Anti-IL-5Rα	Benralizu	✓	✓
Anti-IL-4Rα	Dupiluma	✓	✓
Anti TSLP	Tezepelu	✓	✓



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2020;16:49; Lugogo N, et al. *Clin Ther.* 201
Nopsopon T, et al. *J Allergy and Clin Immu*

10(2):422-432; Castro M, et al. *Lancet*
et al. *All Asthma Clin Immunol*.
Crit Care Med. 2021;203:A1197;

UMJSTY^UJ FSI UWJINHYTWX TK WJXUTSXJ

HTR TWGNINYNUX

TWFQ HTWYNHTXYJWTNI ZXJ

XMFWJI IJHNXNTS R FPNSL

UWFHYNHFQ HTSXNIJWFYNTSX

How to Choose?

Stan: 27-year-old Man

Asthma history:
- Early mild childhood symptoms, worsened 2 years ago
- Last 12 months: OCS bursts x 5, ED visits x 4, hospital admission x 1, no intubation/mechanical ventilation
- Triggers: URIs, ragweed season, wildfire smoke

Past Medical History:
- Allergic rhinitis
- Anxiety

Past Social and Environmental History:
- Non-smoker
- No pets, evaporative cooler, mold/water damage

Current medication:
- High dose ICS/LABA twice daily
- LAMA daily
- Albuterol/budesonide prn
- Intranasal corticosteroids twice daily
- OCS bursts 4Xs last year

Current medications:
- High dose ICS/LABA twice daily
- LAMA daily
- Albuterol/budesonide prn
- Intranasal corticosteroids twice daily

Additional Information:
- Good inhaler technique, taking as prescribed

Pertinent findings on exam:
- Expiratory wheezing at bilateral bases

Pre-bronchodilator FEV_1: 70% predicted
Bronchodilator reversibility: 14%
ACT score: 14

Biomarkers of Type 2 Inflammation:
- Total serum IgE (IU/mL): 225
- Blood EOS (cells/µL): 350
- FeNO (ppb): 55
- Aeroallergen skin prick testing: + trees, grasses, weeds

Audience Response Question

After addressing his inhaler technique, through shared decision making, Stan opts to start on a biologic. Which of these would be a correct statement for this case?

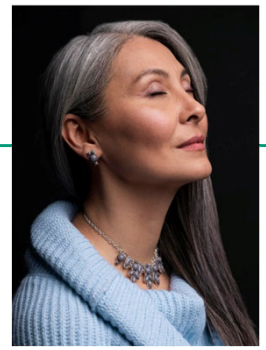
A. Anti-IL-5/5R would target Th1 inflammation
B. Anti-IgE would target his allergy-driven inflammation
C. Anti-IL-4Rα would target epithelial alarmins
D. Anti-TSLP would address his poorly controlled atopic dermatitis

Audience Response Question

Which therapy would you choose for Stan?

A. Anti-IgE (omalizumab)
B. Anti-IL-5/5R (mepolizumab, reslizumab, benralizumab)
C. Anti-IL-4Rα (dupilumab)
D. Anti-TSLP (tezepelumab)

Case 2: Susan, 57-year-old female patient



Asthma history:
- Early mild childhood symptoms, worsened 3 years ago
- Last 12 months: OCS bursts x 5, ED visits x 4, hospital admission x 1, no intubation/mechanical ventilation
- Triggers: URIs, wildfire smoke
- Lack of sense of smell and decreased taste

Past Medical History
- Recurrent sinusitis
- Chronic nonallergic rhinitis

Past Social and Environmental History:
- Non-smoker
- No pets, evaporative cooler, mold/water damage

Current medication:
- High dose ICS/LABA twice daily
- LAMA daily
- Albuterol/budesonide prn
- Intranasal corticosteroids twice daily
- OCS bursts 4Xs last year

Additional Information:
- Good inhaler technique, taking as prescribed

Pertinent findings on exam:
- Expiratory wheezing at bilateral bases
- Anterior rhinoscopy reveals polyps bilaterally

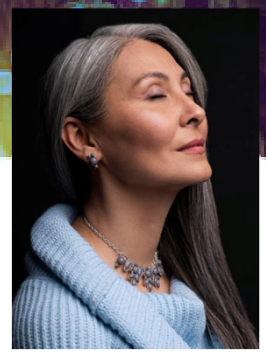
Pre-bronchodilator FEV_1: 70% predicted

Bronchodilator reversibility: 14%

ACT score: 14

Biomarkers of Type 2 Inflammation:
- Total serum IgE (IU/mL): 35
- Blood EOS (cells/µL): 800
- FeNO (ppb): 55
- Aeroallergen skin prick testing: negative

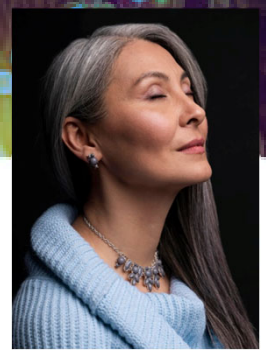
Audience Response Question



Which biologics have FDA-approved indications for both asthma and nasal polyps?

A. Omalizumab, tezepelumab, reslizumab
B. Mepolizumab, reslizumab, benralizumab
C. Omalizumab, dupilumab, benralizumab
D. Omalizumab, dupilumab, mepolizumab

Audience Response Question



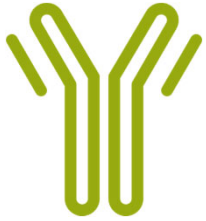
Which therapy would you choose for Susan?

A. Anti-IgE (omalizumab)
B. Anti-IL-5 (mepolizumab)
C. Anti-IL-4Rα (dupilumab)

Monitoring Response Considerations

EXACERBATING OR MIMICKING COMORBIDITIES

ADVERSE EFFECTS



NEUTRALIZING ANTIBODIES

NOT TAKING AS PRESCRIBED

WRONG TARGET/PATHWAY

Multidisciplinary Management

Nurse

- Comorbidity education
- Medication technique
- Peak flow teaching
- Smoking cessation
- Self-management

Physical Therapist

- Breath retraining
- Exercise capacity
- Physical activity
- Resistance training

Speech/language pathologist

- Breath retraining
- Vocal cord dysfunction exercises

Dietician

- Underweight
- Obesity
- Nutritional impact on asthma

Pharmacist

- Home med reviews
- Drug interactions
- Biologic teaching

Respiratory therapist

- Lung function

Social worker

- Social determinants of health
- Food insecurity
- Transportation, access issues

Key Points

- Goals of management include reduction of impairment and risk, reducing need for systemic corticosteroids
- GINA no longer recommends SABA alone therapy due to increased morbidity and mortality associated with regular use/overuse and strong data underlying ICS/formoterol or ICS/albuterol therapy
- GINA recommends anti-inflammatory reliever therapy. There is strong data that anti-inflammatory reliever as compared to SABA reliever reduces exacerbation risk across all severities of asthma.
- Reviewed growing treatment landscape.
- Discussed key factors to consider when selecting biologic to include shared decision-making.

Questions?