

SABA: drop it like it's hot?



TO RESCUE OR NOT TO RESCUE WITH
FORMOTEROL+BUDESONIDE

COLIN REEVE, BSP,CTE,CRE,CDE

Faculty/Presenter Disclosure

Faculty: Colin Reeve

Relationships with commercial interests:

- **Grants/Research Support: Not Applicable**
- **Speakers Bureau/Honoraria: Not Applicable**
- **Consulting Fees: Not Applicable**

Mitigating Potential Bias

Not Applicable

Learning Objectives

By the end of this presentation the participant should be able to:

- Describe the key therapeutic recommendation changes in the GINA 2019 Report
- Compare and contrast the recent evidence for budesonide-formoterol (BUD-FOR) prn therapy in the treatment of mild asthma

CTS evolution of Asthma Guidelines

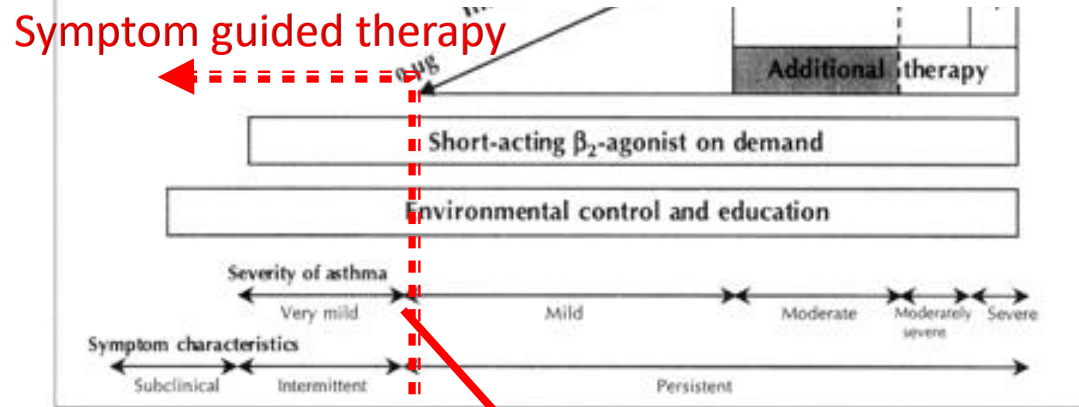
1999¹



2012²

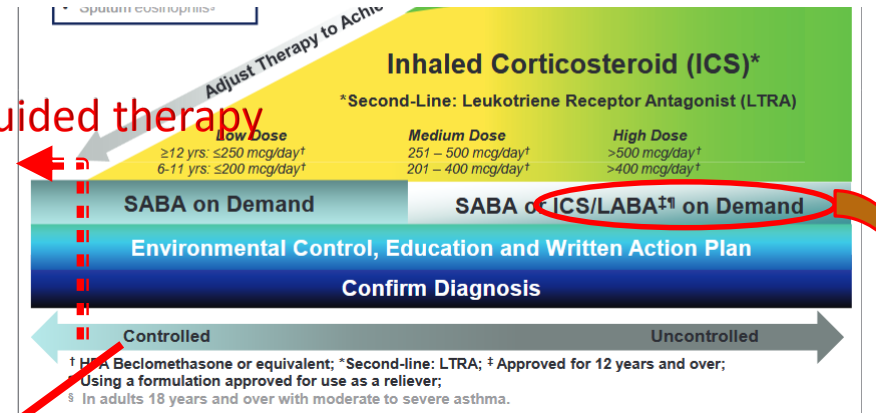
30% of adult asthma patients overuse SABA therapy³

50-75% of adult asthma patients have “mild asthma”⁴



What is mild vs very mild asthma? “Controlled” as a continuum?

Symptom guided therapy



SMART Therapy:
BUD (Maintenance)
And **Reliever** (Therapy)



Asthma 2020

What we knew all along about asthma treatment (but refused to accept):

- Symptomatic reliever therapy is often overused often masking the underlying inflammatory disease processes of asthma³
- Airway inflammation>>>airway remodeling>>>fixed airway obstruction
- Under use of ICS therapy in asthma is associated with increased airway remodeling, ↑ exacerbation risk and ↑mortality⁵
- Even “mild” asthma is associated with increased risk of serious events ⁴

How do we fix this?



The NEW ENGLAND JOURNAL of MEDICINE

May 17, 2018

•Vol. 378 No. 20

ORIGINAL ARTICLES

Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma

P.M. O'Byrne and Others

SYGMA 1⁷

Symptom control

1865-1876 FREE

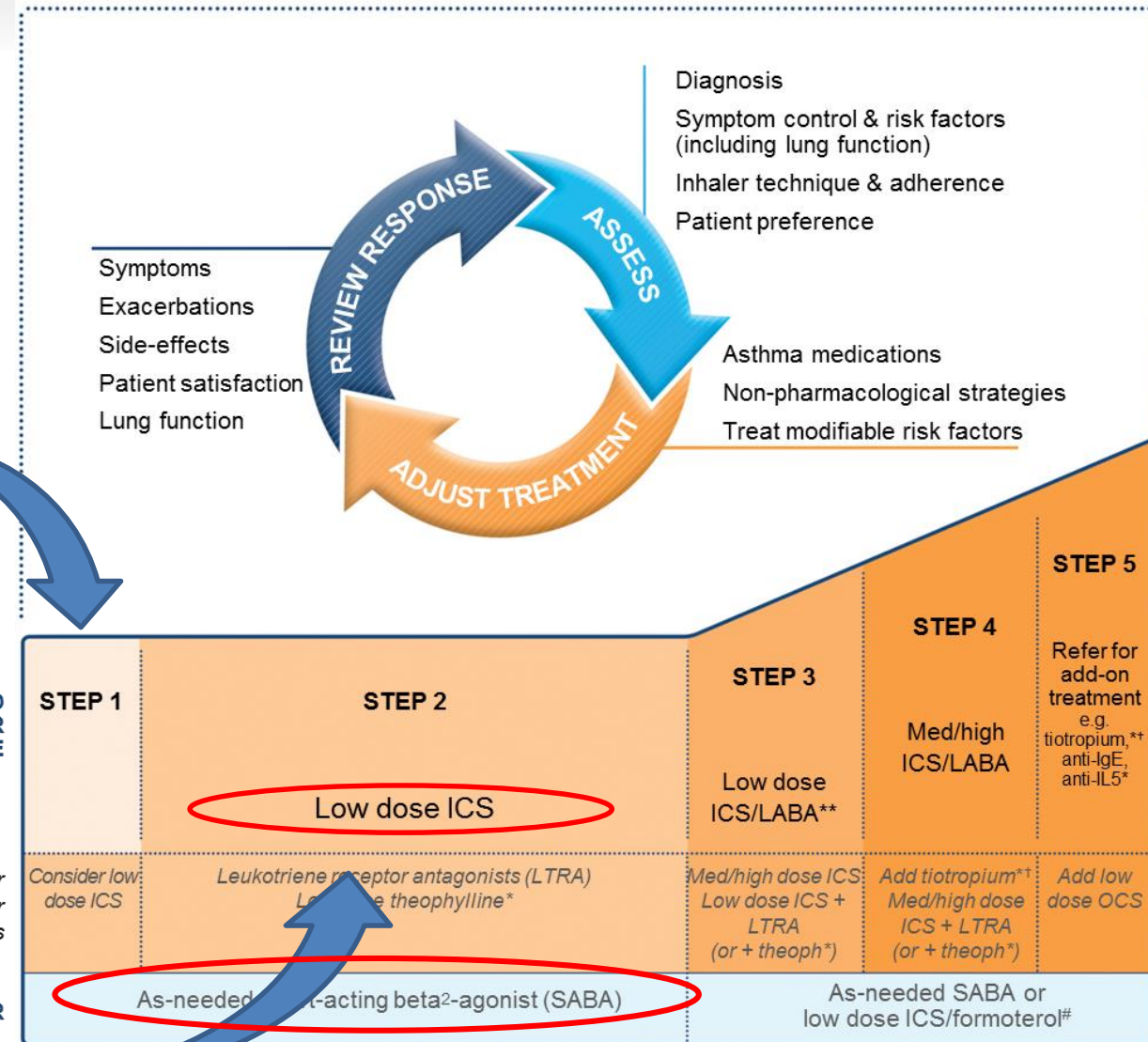
As-Needed Budesonide–Formoterol versus Maintenance Budesonide in Mild Asthma

E.D. Bateman and Others

SYGMA 2⁸



Exacerbation reduction

1877-1887 FREE CME



Wait...ICS+Formoterol prn only?

- But...ICS needs to be taken regularly to reduce inflammation
- If patients overuse SABA therapy due to symptom guided treatment then...
 - Won't this just result in overuse of ICS and increase incidence of corticosteroid side effects?

	Intervention/Comparator	Population	Outcome	Results
SYGMA 1 <ul style="list-style-type: none"> • RCT • 52 Week • Phase III • 1:1:1 randomized 	 <p>I: Budesonide 200 µg-formoterol 6 µg prn + bid placebo</p> <p>Primary</p> <p>C(S): Terbutaline 0.5 mg prn + bid placebo</p> <p>Secondary</p> <p>C(NI): Budesonide 200 µg bid + terbutaline prn</p>	<ul style="list-style-type: none"> • 3849 patients randomized; 3836 analyzed • Age ≥12 years • Clinical Asthma dx • Mild Asthma (Step 2 GINA therapy required as per investigator) 	<p>Variable: <u># of weeks with well-controlled asthma</u></p>	<p>1) Primary (<u>Superiority Met</u>): 34.4% vs. 31.1% of weeks; odds ratio, 1.14; (95% CI, 1.00-1.30) P=0.046</p> <p>2) Secondary (<u>Non-inferiority not met</u>): 34.4% vs. 44.4%; odds ratio, 0.64; 95% CI, 0.57 to 0.73)</p>
SYGMA 2 <ul style="list-style-type: none"> • RCT • 52 Week • Phase III • 1:1 randomized 	 <p>I: Budesonide 200 µg-formoterol 6 µg prn + bid placebo</p> <p>C(NI): Budesonide 200 µg bid + terbutaline prn</p>	<p>4215 patients randomized; 4176 analyzed</p> <ul style="list-style-type: none"> • Age ≥12 years • Clinical Asthma dx • Mild Asthma (Step 2 GINA therapy required as per investigator) 	<p>Primary: Between group differences in <u>annualized rate of severe exacerbations</u>.</p> <p>Secondary:</p> <ul style="list-style-type: none"> • Time to 1st severe exacerbation • % of reliever-free days • ACQ-5 & AQLQ scores 	<p>1) Primary (<u>non-inferiority met</u>):</p> <ul style="list-style-type: none"> • 0.11 (95% CI, 0.10 to 0.13) in the BUD-FOR group <p>Vs.</p> <ul style="list-style-type: none"> • 0.12 (95% CI, 0.10 to 0.14) in the BUD maintenance group

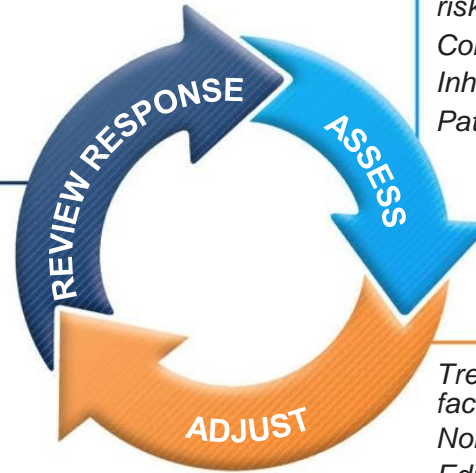
Adults & adolescents 12+ years



Personalized asthma management:

Assess, Adjust, Review response

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction



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

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

Asthma medication options:

Adjust treatment up and down for individual patient needs



PREFERRED CONTROLLER

to prevent exacerbations and control symptoms

Other controller options

PREFERRED RELIEVER

Other reliever option

STEP 1

As-needed low dose ICS-formoterol *
Low dose ICS taken whenever SABA is taken †

STEP 2

Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *
Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †



STEP 3

Low dose ICS-LABA

Medium dose ICS, or low dose ICS+LTRA #

STEP 4

Medium dose ICS-LABA

High dose ICS, add-on tiotropium, or add-on LTRA #

STEP 5

High dose ICS-LABA

Refer for phenotypic assessment ± add-on therapy, e.g. tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R

Add low dose OCS, but consider side-effects

As-needed low dose ICS-formoterol *

As-needed short-acting β_2 -agonist (SABA)

As-needed low dose ICS-formoterol for patients prescribed maintenance and reliever therapy ‡

* Off-label; data only with budesonide-formoterol (bud-form)

† 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

Still some unanswered questions...

Can other ICS-formoterol combinations be used as a prn reliever?

What about GINA 2012 “Step-1” patients? (Controlled asthma with $2 \leq$ reliever doses per week/no nocturnal sx)

- No symptom prompted therapy=further disease progression?

Budnesonide-formoterol prn vs. ICS maintenance + SABA:

- Is less ICS dose a good thing (less SE's/lower cost) or a bad thing? (more sx/progression of disease process)

GINA 2019 recommends as-needed low dose ICS-formoterol as a preferred reliever for Step 1 & 2 patients; what do I do with my patients already maintained on ICS +SABA therapy?

Cost?

Thank You!

References

1. Becker A. Canadian Asthma Consensus Report, 1999. Vol. 5, Canadian Journal of Allergy and Clinical Immunology. 2000. p. 44.
2. Loughheed MD, Lemiere C, Ducharme FM, Liciskai C, Dell SD, Rowe BH, et al. Canadian Thoracic Society 2012 guideline update : Diagnosis and management of asthma in preschoolers , children and adults. Loughheed, M. D., Lemiere, C., Ducharme, F. M., Liciskai, C., Dell, S. D., Rowe, B. H., ... Watson, W. (2012). Canadian Thoracic Society 201. Can Respir J. 2012;19(2):127–64.
3. Nwaru BI, Ekström M, Hasvold P, Wiklund F, Telg G, Janson C. Overuse of short-acting β 2 -agonists in asthma is associated with increased risk of exacerbation and mortality: A nationwide cohort study of the global SABINA programme. Eur Respir J [Internet]. 2020 Jan 16;1901872. Available from: <http://erj.ersjournals.com/lookup/doi/10.1183/13993003.01872-2019>
4. Dusser D, Montani D, Chanez P, De Blic J, Delacourt C, Deschildre A, et al. Mild asthma: An expert review on epidemiology, clinical characteristics and treatment recommendations. Vol. 62, Allergy: European Journal of Allergy and Clinical Immunology. 2007. p. 591–604.
5. Suissa S, Ernst P, Benayoun S, Baltzan M, Cai B. Low-dose inhaled corticosteroids and the prevention of death from asthma. N Engl J Med [Internet]. 2000 Aug 3;343(5):332–6. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/10922423>
6. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention [Internet]. Global Strategy for Asthma Management and Prevention. 2018. Available from: https://ginasthma.org/wp-content/uploads/2018/04/wms-GINA-2018-report-tracked_v1.3.pdf
7. O’Byrne PM, FitzGerald JM, Bateman ED, Barnes PJ, Zhong N, Keen C, et al. Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma. N Engl J Med. 2018 May 17;378(20):1865–76.
8. Bateman ED, Reddel HK, O’Byrne PM, Barnes PJ, Zhong N, Keen C, et al. As-Needed Budesonide–Formoterol versus Maintenance Budesonide in Mild Asthma. N Engl J Med. 2018 May 17;378(20):1877–87.