Asthma Guidelines: EPR-3 & 4, GINA and Yardsticks

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Disclosures

- Research: Clinical trials - GSK, Genentech, Astra Zeneca, SANOFI, TEVA
- Consultation/Advisory Board: – TEVA, GSK, AstraZeneca, SANOFI, Genentech, Novartis

Objectives

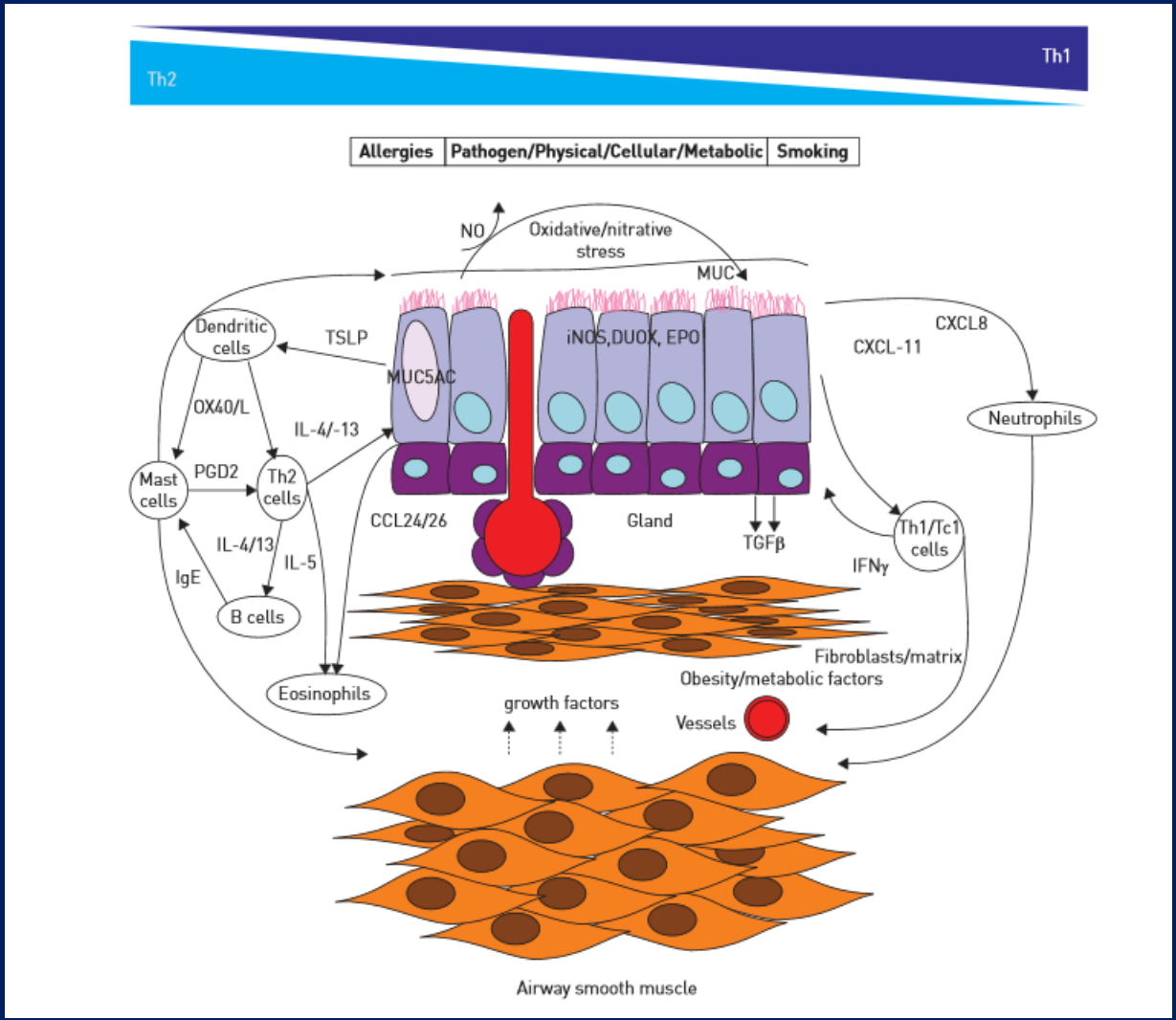
After this session participants will be able to:

- Have an increased understanding of asthma phenotypes
- Describe the asthma paradox and change in approaches to management of mild asthma
- Demonstrate understanding of GINA guidelines in 2019 and the use of asthma yardsticks
- Have an overview of the use of biologics in the treatment of severe asthma

What is Asthma?

- Asthma is a chronic disease characterized by recurrent episodes of:
  - wheezing
  - shortness of breath and
  - cough secondary to reversible airflow obstruction
- Bronchial hyperresponsiveness & airway Inflammation are hallmarks of asthma
- Asthma is a complex disorder that has many distinct pathophysiological mechanisms contributing to clinical signs and symptoms

Pathophysiology



ERJ 2014; 43:343-373

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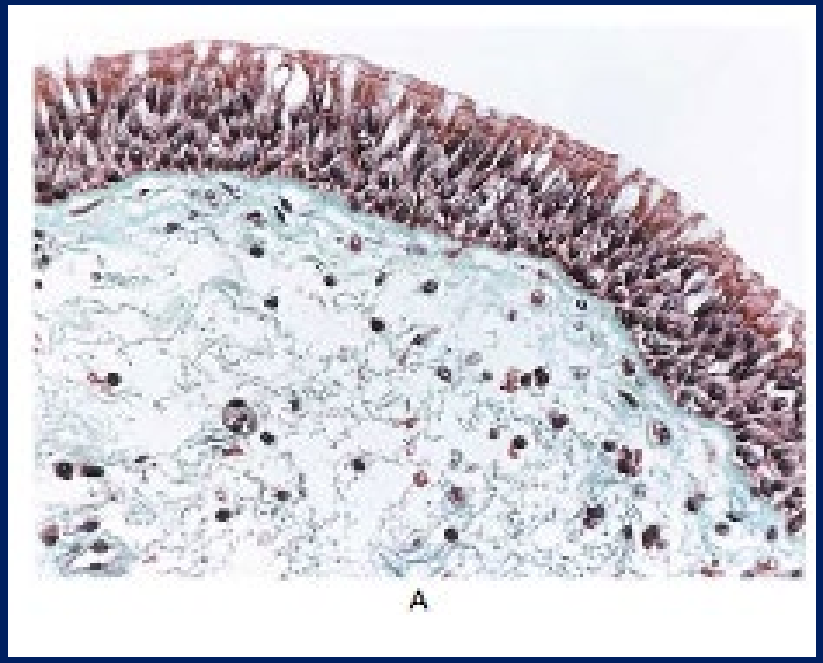
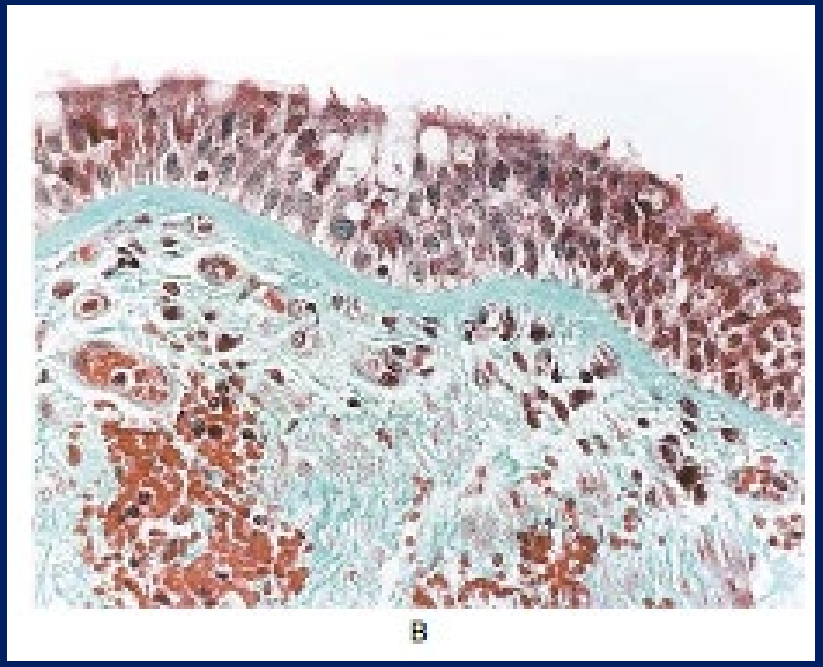
Pathology of Asthma



Normal Subject



Subject with mild asthma

The asthma subject has denuded epithelium, mucous gland hypertrophy, thickened reticular basement membrane and inflammatory cell infiltration in the mesenchyme.

Obtained from Busse et al. NEJM. 344;350-362.

What are asthma phenotypes and are they important?

Phenotype to Endotype

- Phenotype – the observable properties of an organism that are produced by the interaction of the genotype and the environment.

- Endotype - An "*endotype*" is proposed to be a subtype of a condition *defined* by a distinct pathophysiological mechanism. Criteria for *defining* asthma *endotypes* on the basis of their phenotypes and putative pathophysiology are suggested.

We have now moved to defining phenotypes of this heterogeneous disease

- Clinical:
- Fixed obstruction
- Obese
- Adult onset
- Exacerbation prone
- Treatment resistant

Pathologic:
Eosinophilic
Non-eosinophilic
Pauci-granulocytic

- Triggers
- Occupational
- Aspirin
- Exercise
- Menses

Phenotype suggests a clustering of characteristics, but may not describe underlying pathobiology that create these characteristics

Phenotypes to Endotypes

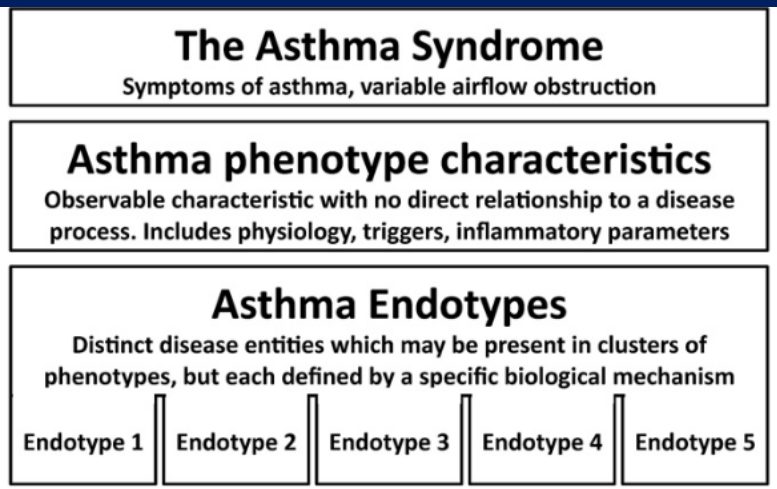
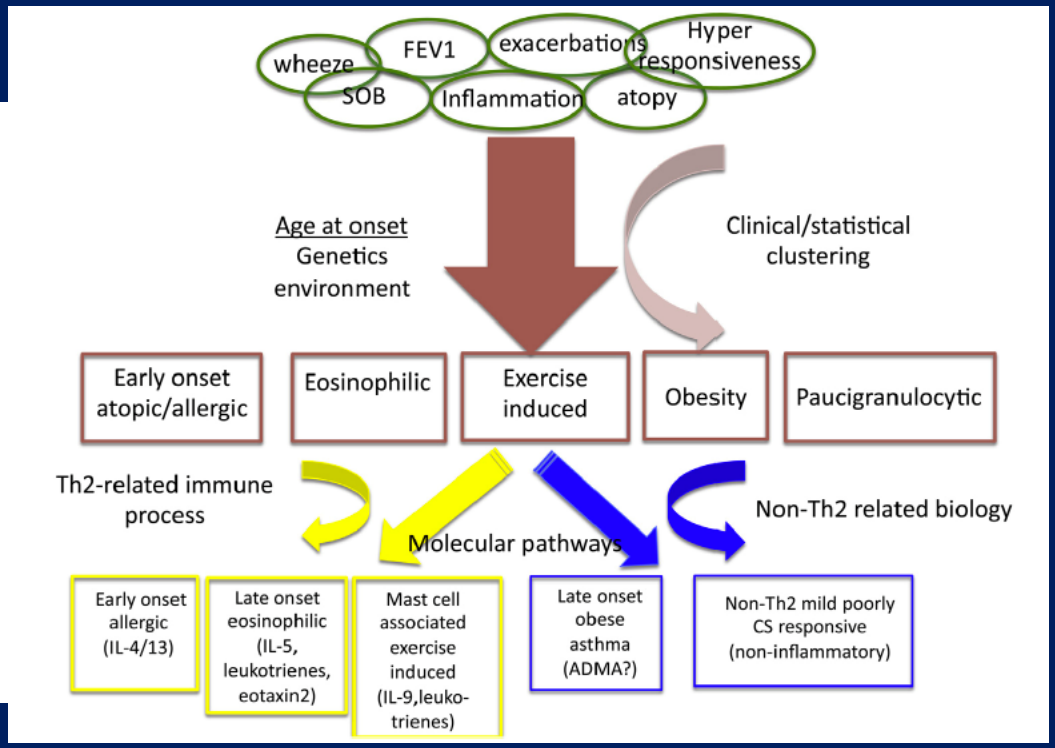


FIG 1. Asthma is made up of different endotypes, each characterized by its pathophysiology.



Endotype: underlying biologic or pathobiologic mechanism

Lotvall et al. JACI 2011;127:355-60

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Emphasis Shifting from Empiric to Targeted (Precision) Therapy

- Evidence-based
- One treatment for all

- Evidence-based
- Different treatments for groups of patients

- Evidence-based
- Individualized treatment for each patient

Willis JC, Lord GM. *Nat Rev Immunol*. 2015.

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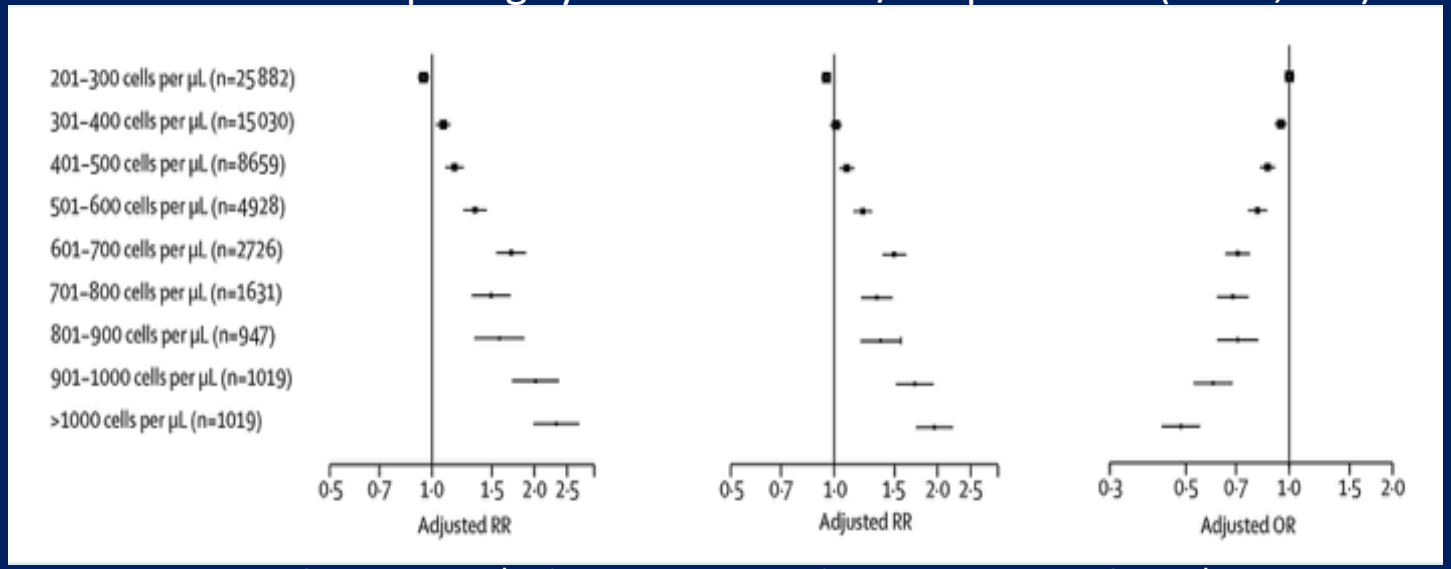
Relationship Between Blood Eosinophil Counts and Asthma Exacerbations

Claims database analysis examining eosinophil counts and exacerbations requiring systemic CS or ER/hospital care (N=61,841)



Severe Exacerbations | Acute Respiratory Events | Control

Price DB, et al. *Lancet Respir Med*. 2015

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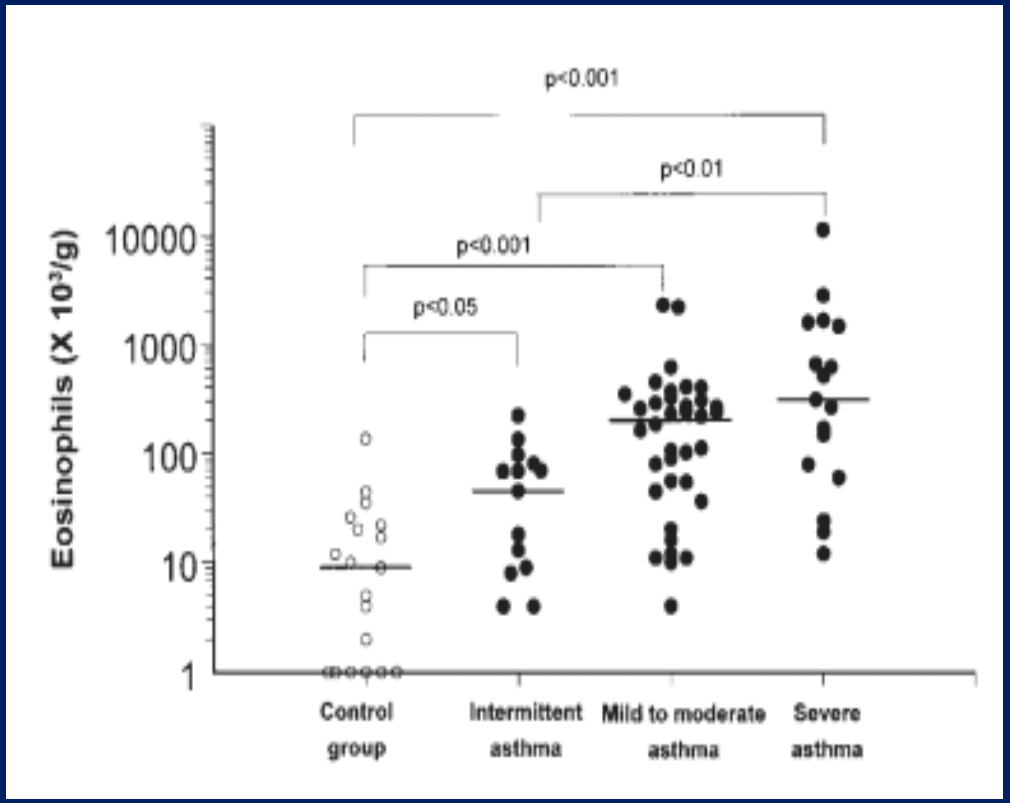
Sputum Eosinophils are Associated with Asthma Severity



Louis et al, *Am J Respir Crit Care Med*, 2000

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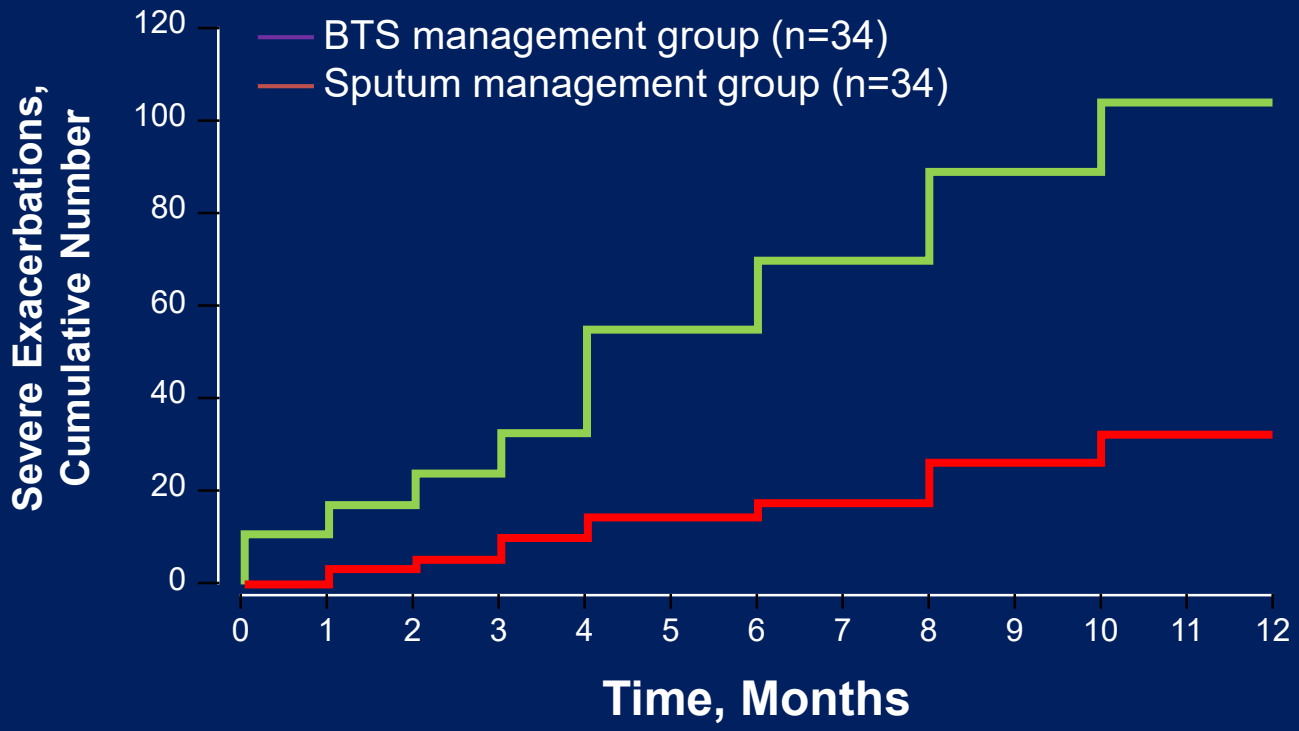
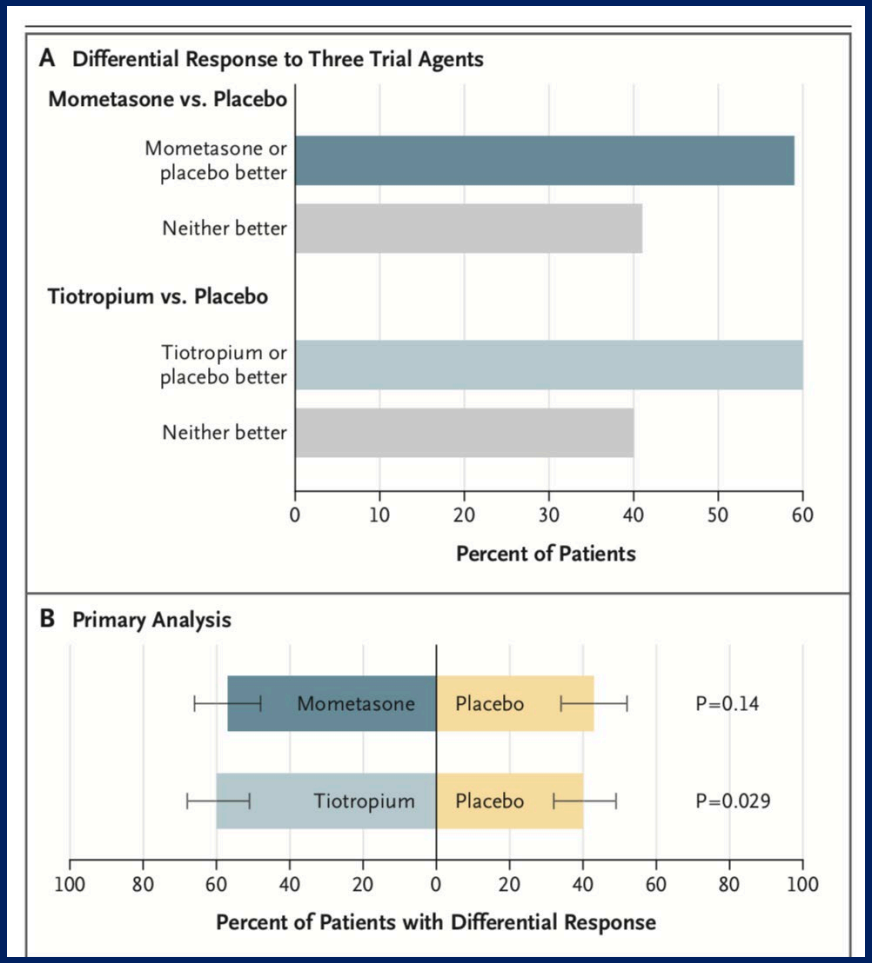


Green et al, *Lancet*, 2002

Sputum Eosinophils Impact Response to Inhaled Asthma Therapies



Lazarus S. NEJM 2019

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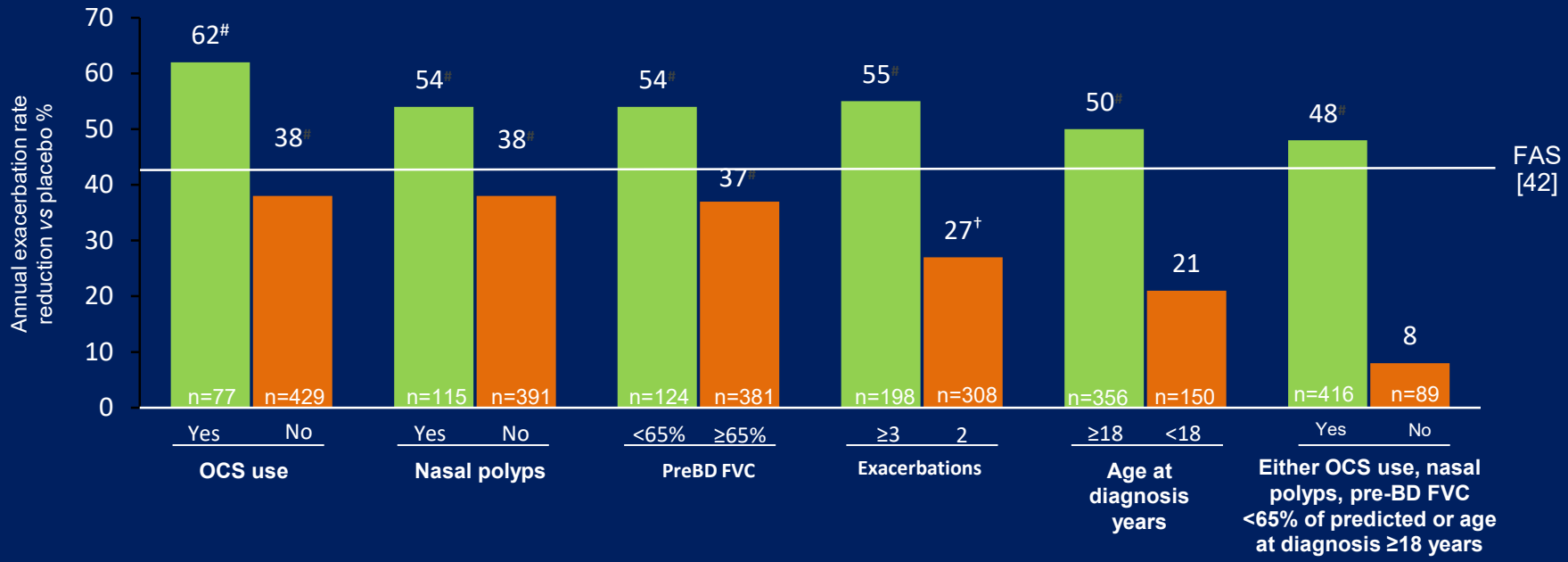
Baseline predictors of response to benralizumab treatment

Five clinical predictors of response with benralizumab were identified:
OCS use, nasal polyps, pre-BD FVC <65%, ≥3 exacerbations and ≥18 years of age at asthma diagnosis



#Nominal P-value <0.001; †Nominal P-value >0.01–≤0.05

Patients with eosinophil counts at baseline ≥300 cells/μL. Patient population had high-dosage ICS/LABA. All P-values were nominal

BD, bronchodilator; FAS, full analysis set; FVC, forced vital capacity; LABA, long-acting β_2-agonist; OCS, oral corticosteroid

Bleecker ER, et al. Eur Respir J 2018;52(4):pii:1800936

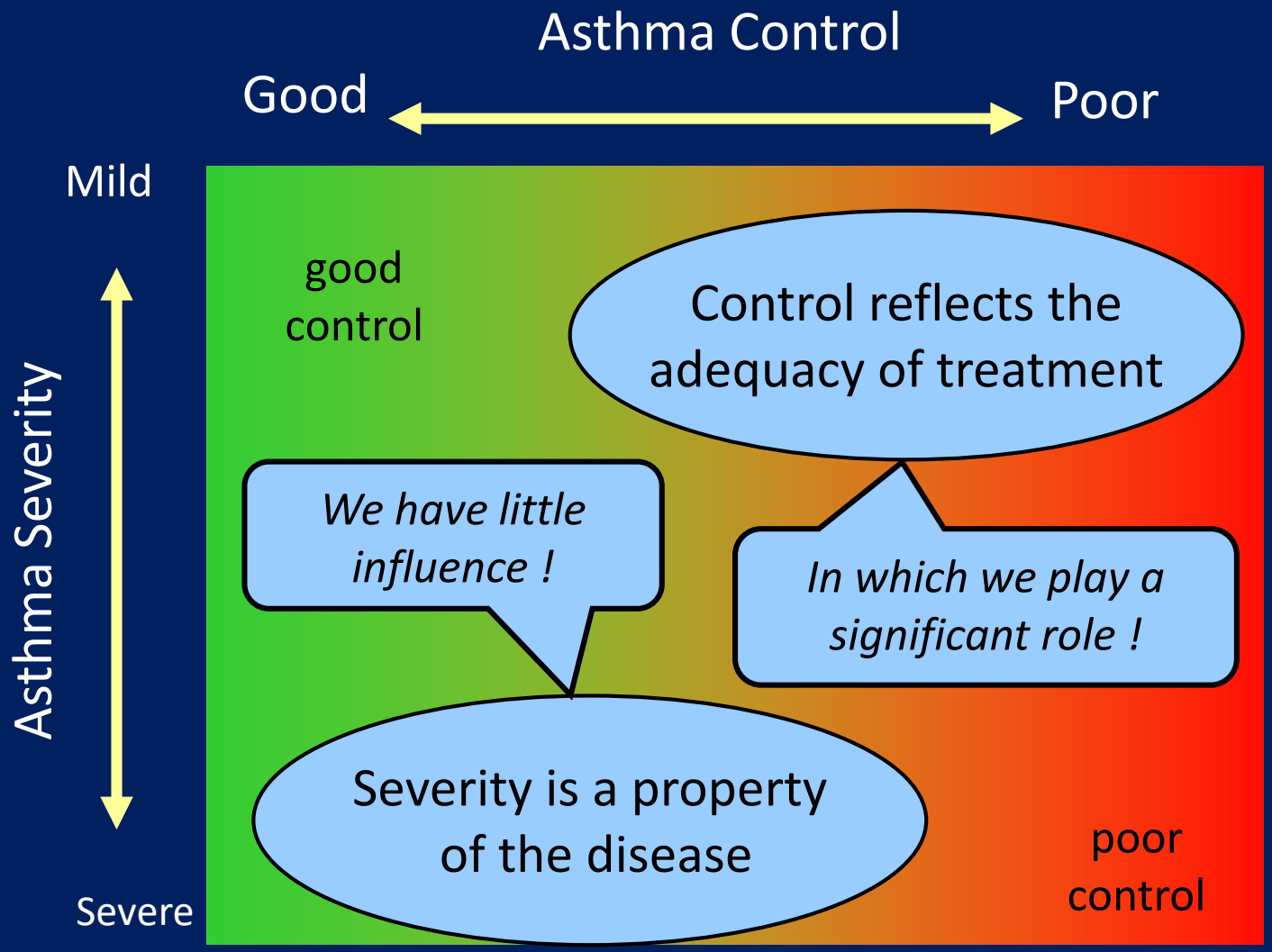
Review of Current NAEPP Guidelines and Ongoing Updates

Classifying Severity in Patients ≥12 Years Not Currently Taking Long-Term Controllers

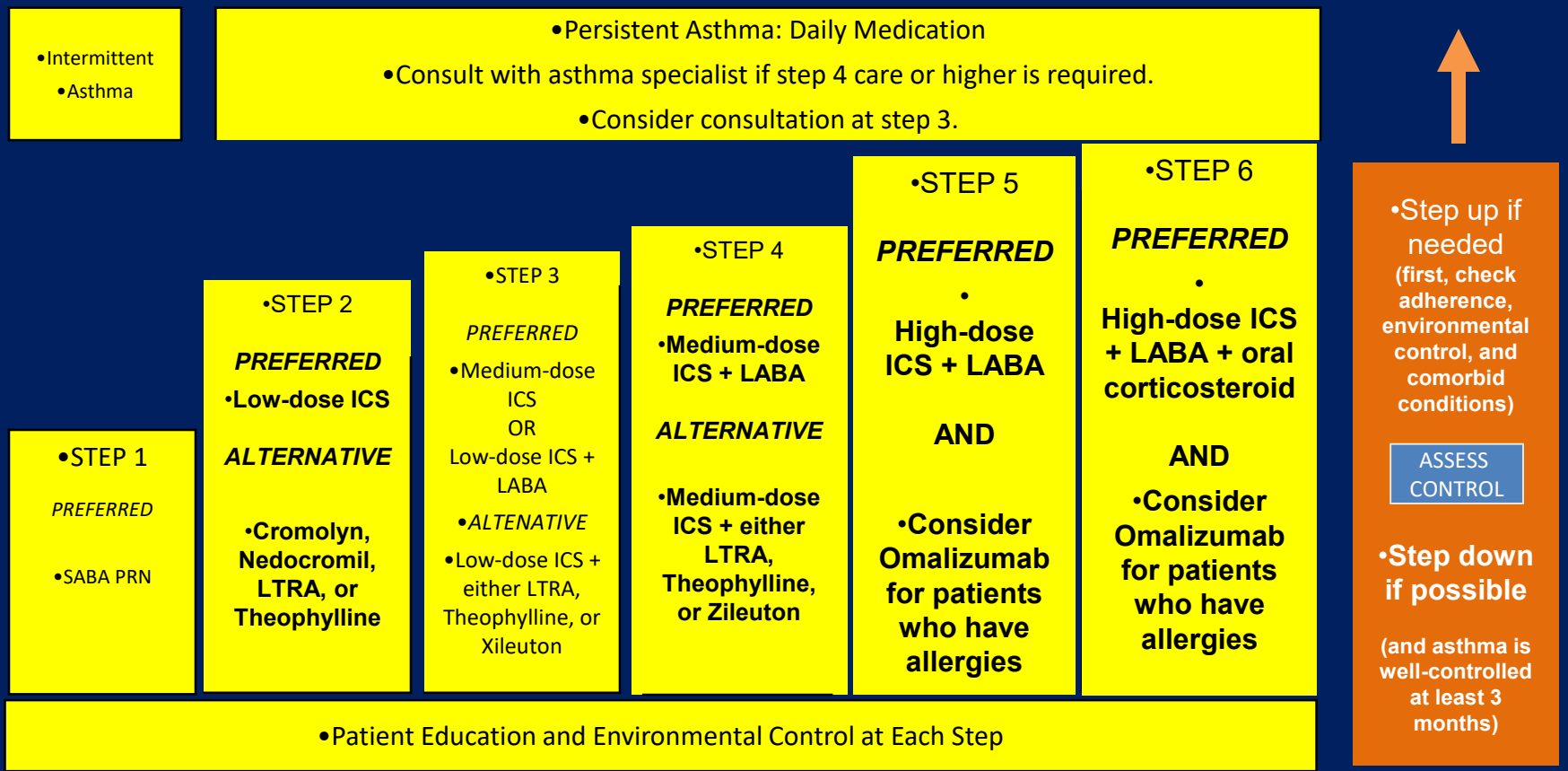
Components of Severity		Classification of Asthma Severity (Youths ≥12 of Age and adults)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8-19 yr 85% 20-39 yr 80% 40-59 yr 75% 60-80 yr 70%	**Symptoms**	**≤2 days/week**	**>2 days/week but not daily**	**Daily**	**Throughout the day**
	Nighttime awakenings	**<2x/month**	**3-4x/month**	**>1x/week but not nightly**	**Often 7x/week**
	Short-acting $beta_2$-agonist use for symptom control	**≤2 days/week**	**>2 days/week but not daily**	**Daily**	**Several times per day**
	Interference with normal activity	**None**	**Minor limitation**	**Some limitation**	**Extremely limited**
	Lung function	• **Normal FEV_1 between exacerbations** • **FEV_1 >80% predicted** • **FEV_1/FVC normal**	• **FEV_1 <80% predicted** • **FEV_1/FVC normal**	• **FEV_1 >60% but <80% predicted** • **FEV_1/FVC reduced 5%**	• **FEV_1 <60% predicted** • **FEV_1/FVC reduced >5%**
Risk	**Exacerbations (consider frequency and severity)**	**0-2/year** ←	**>2/year** **Frequency and severity may fluctuate over time →** **Relative annual risk of exacerbations may be related to FEV_1 →**		

NHLBI. National Asthma Education and Prevention Program. Full report of the Expert Panel: Guidelines for the diagnosis and management of asthma (EPR-3) DRAFT, page 115. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/epr3/index.htm. Accessed February 8, 2007.

Emphasizing Control Rather Than Severity



NAEPP Stepwise Approach for Managing Asthma in Patients ≥ 12 Years of Age



- Quick-Relief Medication for All Patients:
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of systemic oral corticosteroids may be needed.
- Caution: Increasing of beta-agonist or use >2x/week for symptom control indicates inadequate control and the need to step up treatment.

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Updates NAEPP Guidelines Ongoing

- Intermittent use of ICS and long acting muscarinic antagonists in asthma
  - Includes intermittent ICS dosing/ use of ICS/LABA as reliever therapy

- Effectiveness and safety of bronchial thermoplasty in asthma management

- Fraction of exhaled nitric oxide clinical utility in asthma management

Mensah et al. JACI 2018; 142:744-748

Updates NAEPP Guidelines Ongoing

- Effectiveness of indoor allergen reduction in asthma management

- The role of immunotherapy and asthma management
  - Covers both subcutaneous and sublingual immunotherapy

Mensah et al. JACI 2018; 142:744-748

GINA (Global Initiative for Asthma) Strategy 2019 Updates

Background to changes in 2019 - the risks of 'mild' asthma

- Patients with apparently mild asthma are at risk of serious adverse events
  - 30–37% of adults with acute asthma
  - 16% of patients with near-fatal asthma
  - 15–20% of adults dying of asthma

  } had symptoms less than weekly in previous 3 months *(Dusser, Allergy 2007)*
- Exacerbation triggers are variable (viruses, pollens, pollution, poor adherence)
- Inhaled SABA has been first-line treatment for asthma for 50 years
  - This dates from an era when asthma was thought to be a disease of bronchoconstriction
  - Patient satisfaction with, and reliance on, SABA treatment is reinforced by its rapid relief of symptoms, its prominence in ED and hospital management of exacerbations, and low cost
  - Patients commonly believe that *"My reliever gives me control over my asthma"*, so they often don't see the need for additional treatment

Background to changes in 2019 - the risks of SABA-only treatment

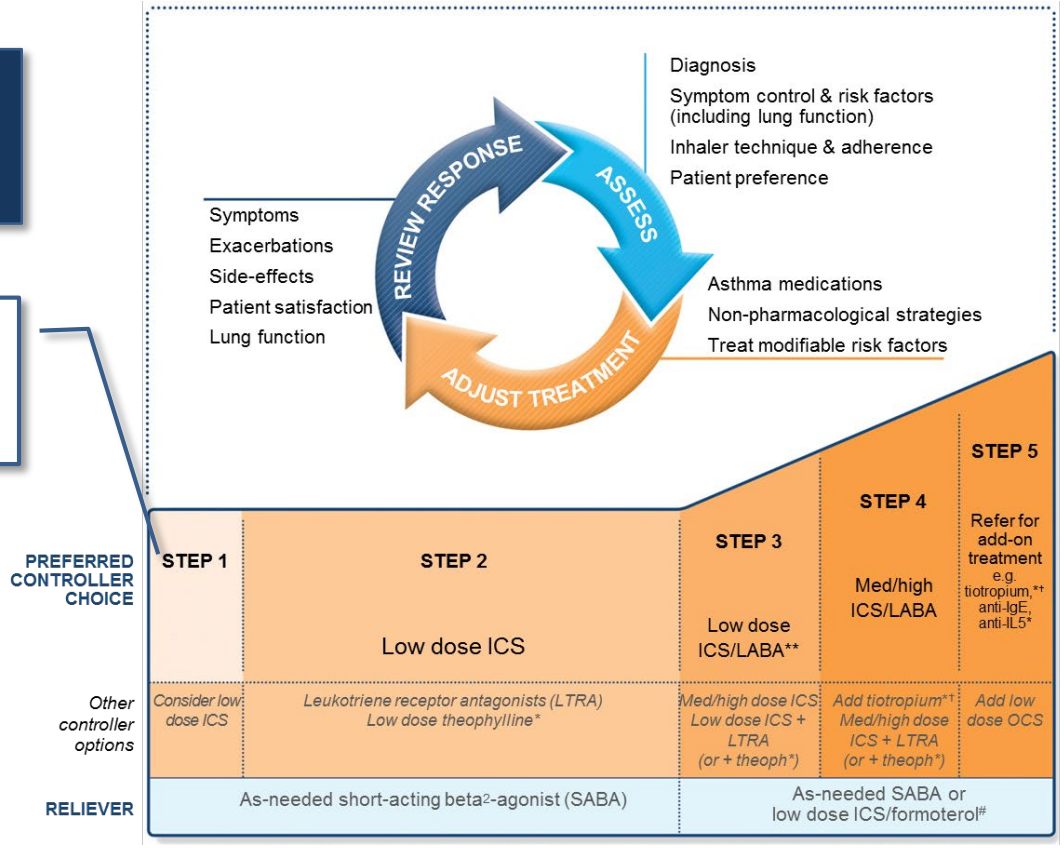
- Regular or frequent use of SABA is associated with adverse effects
  - β-receptor downregulation, decreased bronchoprotection, rebound hyperresponsiveness, decreased bronchodilator response *(Hancox, Respir Med 2000)*
  - Increased allergic response, and increased eosinophilic airway inflammation *(Aldridge, AJRCCM 2000)*

- Higher use of SABA is associated with adverse clinical outcomes
  - Dispensing of ≥3 canisters per year (average 1.7 puffs/day) is associated with higher risk of emergency department presentations *(Stanford, AAAI 2012)*
  - Dispensing of ≥12 canisters per year is associated with higher risk of death
    (Suissa, AJRCCM 1994)

GINA 2018 – main treatment figure

Step 1 treatment is for patients with symptoms <twice/month and no risk factors for exacerbations

Previously, no controller was recommended for Step 1, i.e. SABA-only treatment was 'preferred'



*Not for children <12 years

**For children 6-11 years, the preferred Step 3 treatment is medium dose ICS

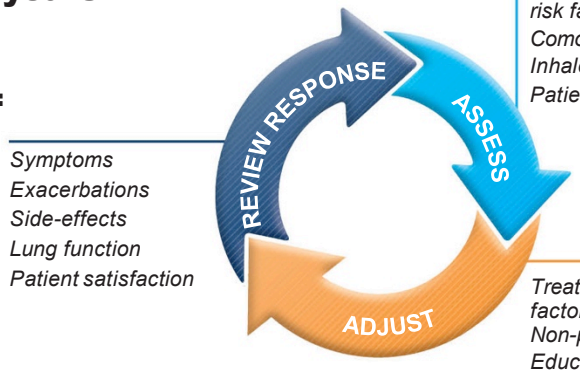
#For patients prescribed BDP/formoterol or BUD/formoterol maintenance and reliever therapy

† Tiotropium by mist inhaler is an add-on treatment for patients ≥12 years with a history of exacerbations

Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response



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

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

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

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	As-needed low dose ICS-formoterol *	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA Refer for phenotypic assessment ± add-on therapy, e.g.tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options	*Low dose ICS taken whenever SABA is taken †*	*Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †*	*Medium dose ICS, or low dose ICS+LTRA #*	*High dose ICS, add-on tiotropium, or add-on LTRA #*	*Add low dose OCS, but consider side-effects*
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* Off-label; data only with budesonide-formoterol (bud-form)
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‡ 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 FEV >70% predicted

Box 3-5A

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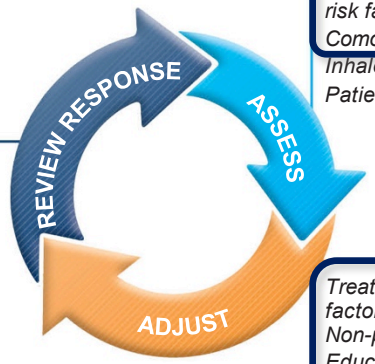

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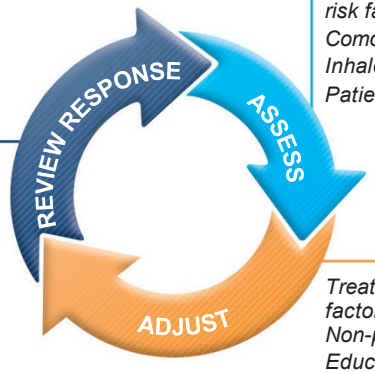
Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response

'Controller' treatment means the treatment taken to prevent exacerbations

Asthma medication options:
Adjust treatment up and down for individual patient needs



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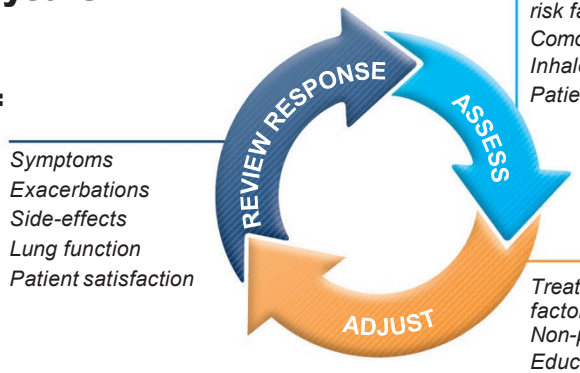

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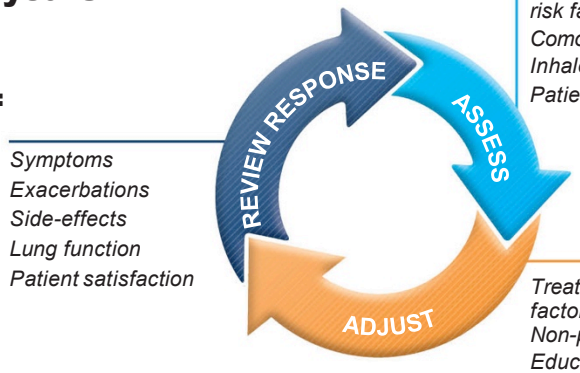

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Step 2 - other controller options

Low dose ICS taken whenever SABA taken (off-label, separate or combination inhalers)

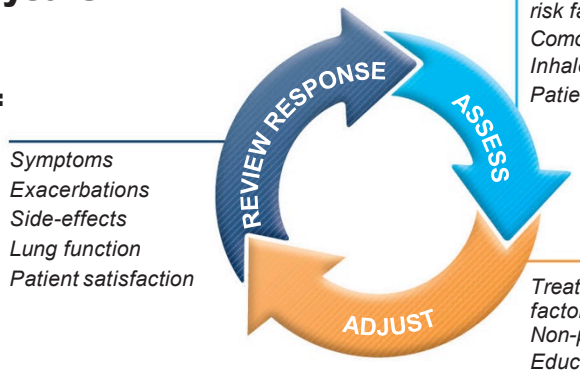
- Evidence
  - Two RCTs showed reduced exacerbations compared with SABA-only treatment
    - BEST, in adults, with combination ICS-SABA *(Papi, NEJMed 2007)*
    - TREXA, in children/adolescents, with separate inhalers *(Martinez, Lancet 2011)*
  - Three RCTs showed similar or fewer exacerbations compared with maintenance ICS
    - TREXA, BEST
    - BASALT in adults, separate inhalers, vs physician-adjusted treatment *(Calhoun, JAMA 2012)*

- Values and preferences
  - High importance given to preventing severe exacerbations
  - Lower importance given to small differences in symptom control and the inconvenience of needing to carry two inhalers
  - Combination ICS-SABA inhalers are available in some countries, but approved only for maintenance use
- Another option: leukotriene receptor antagonist (less effective for exacerbations)

Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response



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

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

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

Step 4 treatment is medium dose ICS-LABA; high dose now in Step 5

Asthma medication options:
Adjust treatment up and down for individual patient needs

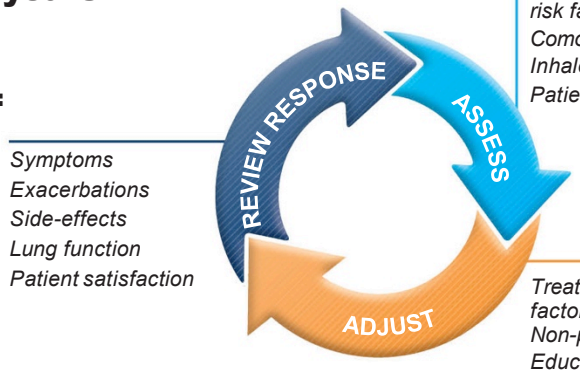
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	As-needed low dose ICS-formoterol *	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA Refer for phenotypic assessment ± add-on therapy, e.g.tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options	*Low dose ICS taken whenever SABA is taken †*	*Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †*	*Medium dose ICS, or low dose ICS+LTRA #*	*High dose ICS, add-on tiotropium, or add-on LTRA #*	*Add low dose OCS, but consider side-effects*
PREFERRED RELIEVER	As-needed low dose ICS-formoterol *		As-needed low dose ICS-formoterol ‡		
Other reliever option	*As-needed short-acting β_2 -agonist (SABA)*				

* 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 FEV >70% predicted

Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response



Confirmation of diagnosis if necessary
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Asthma medications

See severe asthma Pocket Guide for details about Step 5

Asthma medication options:
Adjust treatment up and down for individual patient needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
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Other controller options	*Low dose ICS taken whenever SABA is taken †*	*Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †*	*Medium dose ICS, or low dose ICS+LTRA #*	*High dose ICS, add-on tiotropium, or add-on LTRA #*	*Add low dose OCS, but consider side-effects*
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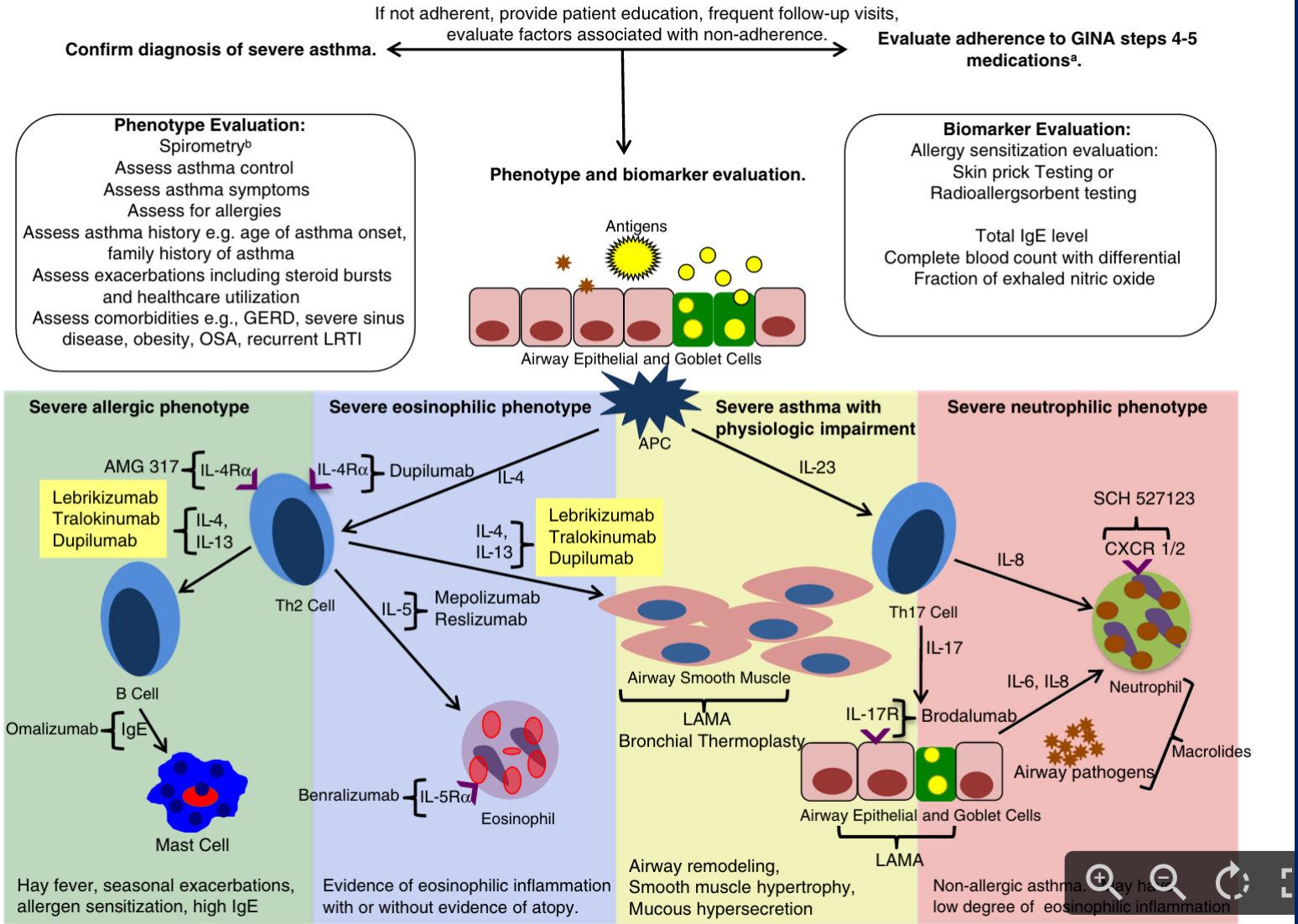
‡ Low-dose ICS-form is the reliever for patients prescribed bud-form or BDP-form maintenance and reliever therapy
# Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV >70% predicted

ATS/ERS Severe Asthma Definition

- Asthma that requires GINA steps 4-5 medications (high dose ICS and LABA and LTRA/theophylline for one year OR systemic CS ≥ 50% of the prior year to prevent loss of control.
- Uncontrolled asthma is defined as:
  - Poor symptom control, ACT <20, ACQ > 1.5
  - Frequent severe exacerbations ≥ 2 x/ year
  - At least one hospitalization, ICU stay of mechanical ventilation in past year
  - FEV1 < 80% with reduced FEV1/FVC

Chung et al. ERJ 2014; 43:343-373

Biologics for Severe Asthma Therapy



Opina et al. Curr Allergy Asthma Rep (2017) 17:10

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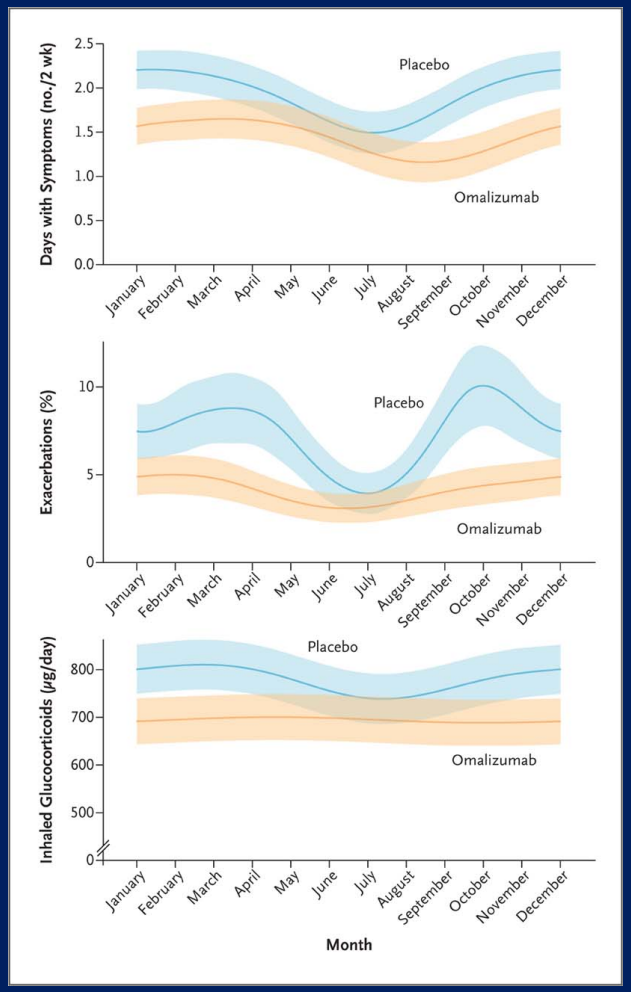
Omalizumab Decreases Seasonal Asthma Exacerbations



Busse WW et al. N Engl J Med 2011; 364:1005-1015

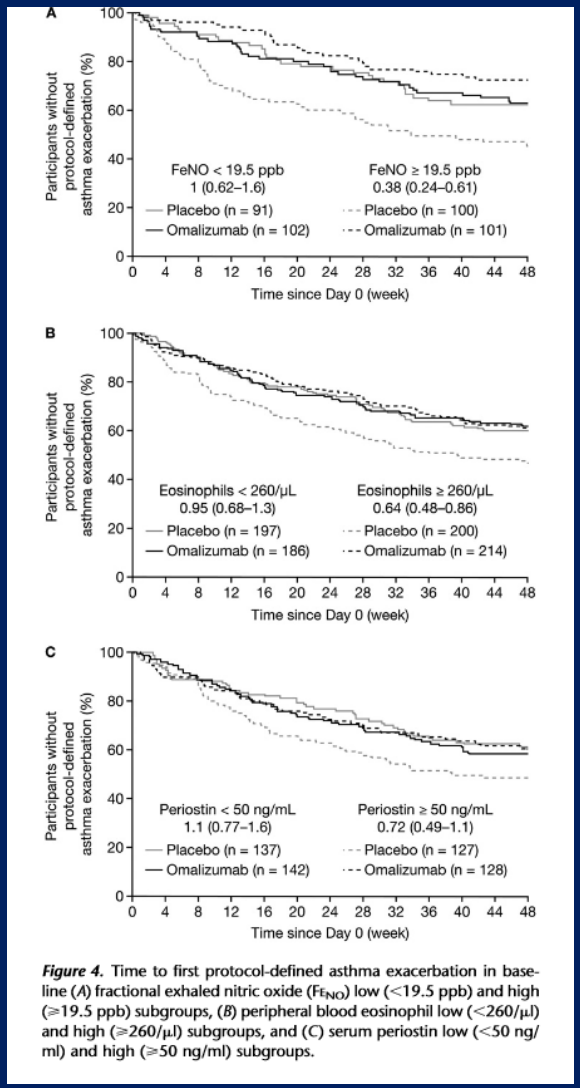


Figure 4. Time to first protocol-defined asthma exacerbation in baseline (*A*) fractional exhaled nitric oxide (Fe_{NO}) low (<19.5 ppb) and high (≥19.5 ppb) subgroups, (*B*) peripheral blood eosinophil low (<260/μl) and high (≥260/μl) subgroups, and (*C*) serum periostin low (<50 ng/ml) and high (≥50 ng/ml) subgroups.

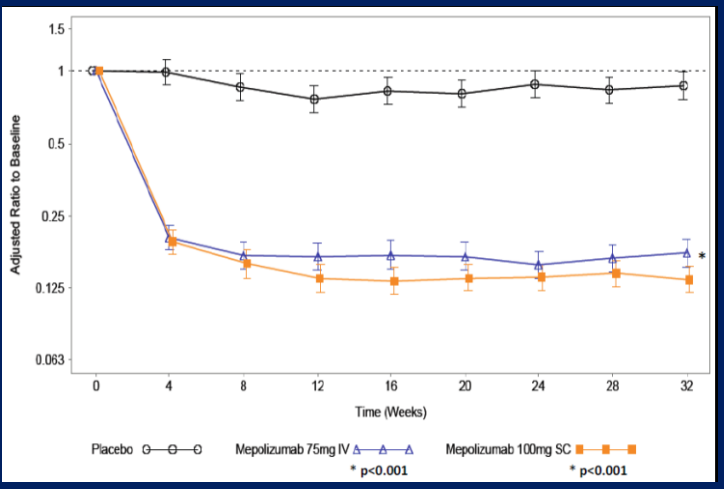
Hanania et al. AJRCCM. 2012;187:804-811

FeNO: 53% (95% [CI], 37–70; P=0.001) versus 16% (95% CI,32 to 46; P 0.45)

Eosinophils eosinophils,32% (95%CI,1148; 0.005)versus 9%(95%CI,24to 34;P 0.54)

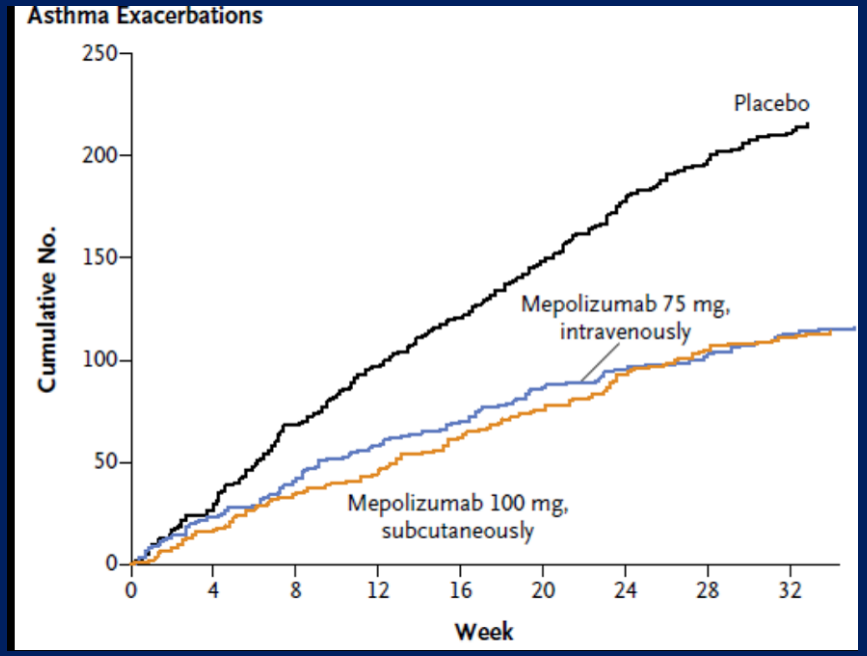
Periostin 30% (95% CI, 2 to 51; P=0.07)versus 3% (95% CI,43 to 32;P=0.94).

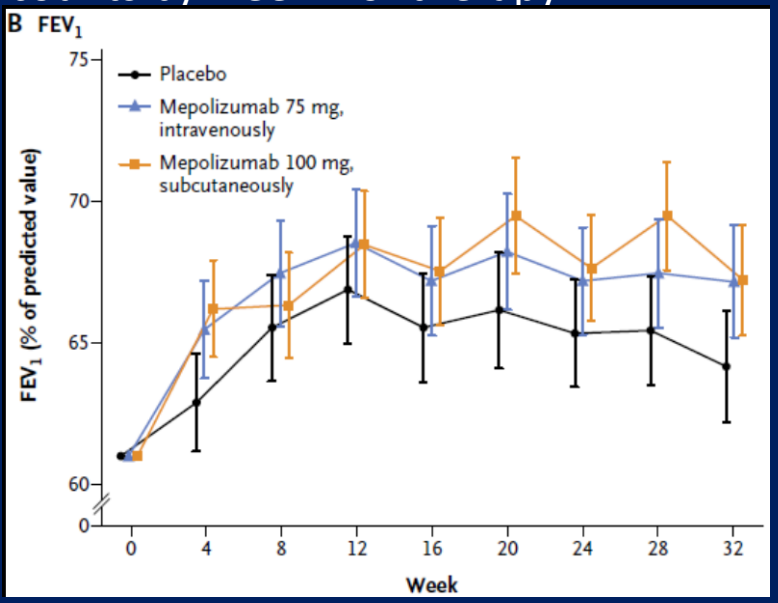
Mepolizumab Significantly Decreased Blood Eosinophils, Exacerbations and Improved Lung Function



Mepolizumab significantly reduces eosinophil counts by week 4 of therapy

Asthma Exacerbations were reduced by 47% with IV mepolizumab and 53% with SC mepolizumab





At week 32, the mean increase from baseline FEV1 was 100ml greater in the IV mepo grp (p=0.02) and 98ml greater in the SC group (p=0.03)

Ortega HG et al. NEJM 2014. 371:1198-1207

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Benralizumab in Severe Eosinophilic Asthma

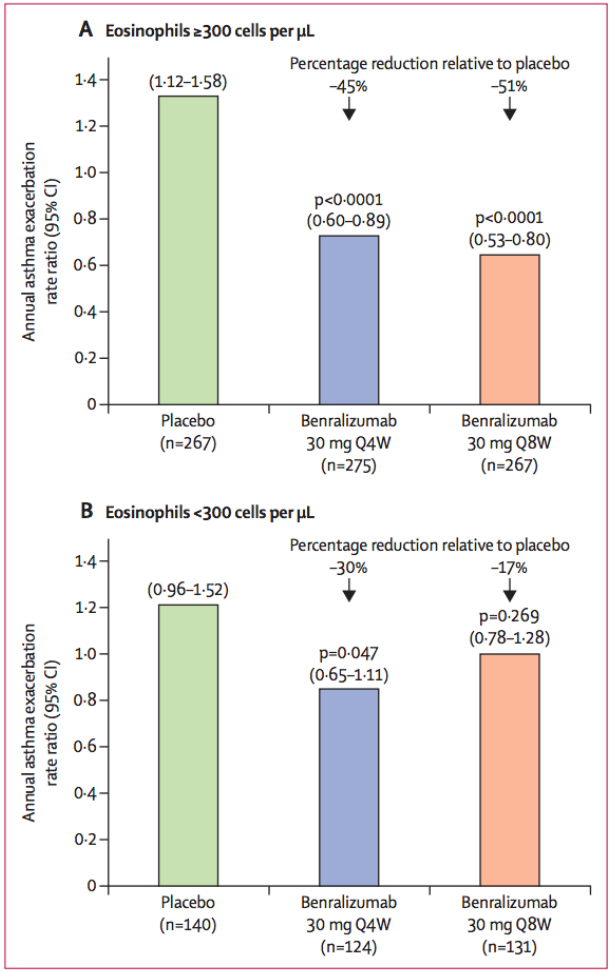

***Figure 2*: Annual asthma exacerbation rate estimates at 48 weeks according to baseline blood eosinophil concentrations**

Data for patients with baseline blood eosinophils (A) ≥300 cells per μL and (B) <300 cells per μL in the full analysis set are shown. Estimates were calculated using a negative binomial model, with adjustment for treatment, region, oral corticosteroid use at time of randomisation, and previous exacerbations. Q4W=every 4 weeks. Q8W=every 8 weeks (first three doses Q4W).

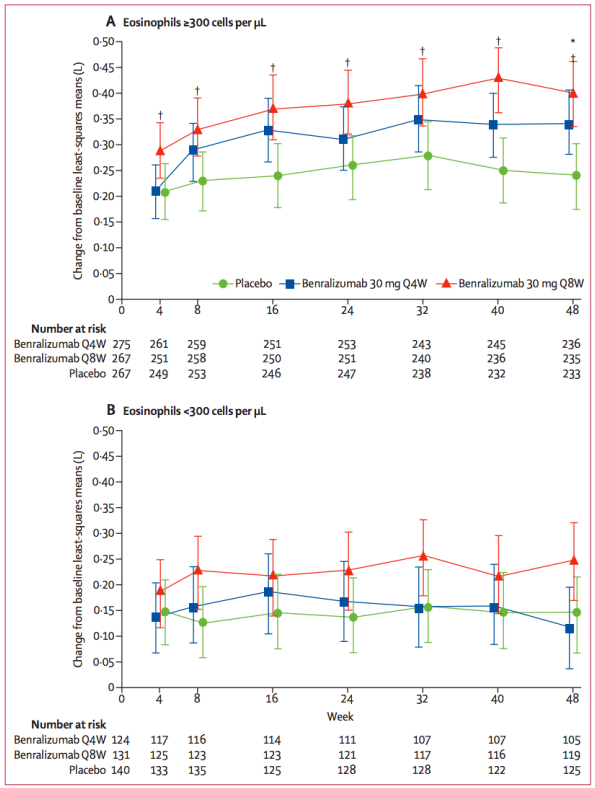

***Figure 3*: Change from baseline in prebronchodilator forced e blood eosinophil concentrations**

Bleecker et al. Lancet.2016: 2115-27

	SIROCCO		CALIMA[26]	
	Benralizumab Q4W	Benralizumab Q8W	Benralizumab Q4W	Benralizumab Q8W
Annual rate of exacerbations	↓ 45%	↓ 51%	↓ 36%	↓ 28%
Prebronchodilator FEV_1 (L)	↑ 0·106	↑ 0·159	↑ 0·125	↑ 0·116
Total asthma symptom score (score 0–6)*	↓ 0·08†	↓ 0·25	↓ 0·12†	↓ 0·23

All results are differences from placebo; week 48 results for SIROCCO and week 56 results for CALIMA. FEV_1=forced expiratory volume in 1 s. Q4W=every 4 weeks. Q8W=every 8 weeks (first three doses Q4W). *Reduced score suggests improvement. †Non-significant.

***Table 5*: Efficacy results for patients who received high-dosage inhaled corticosteroids plus long-acting β_2-agonists with baseline blood eosinophils at least 300 cells per μL in the CALIMA and SIROCCO studies**

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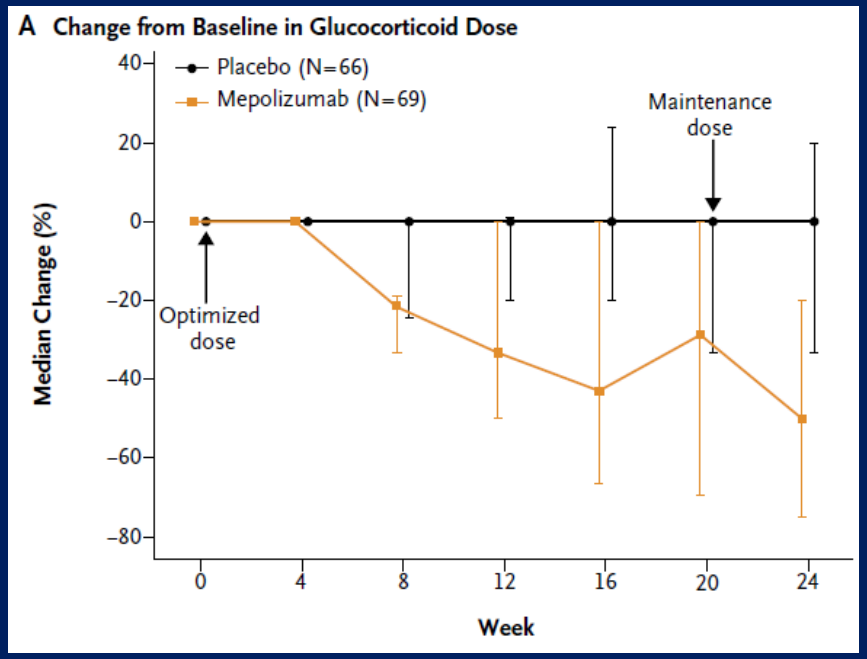
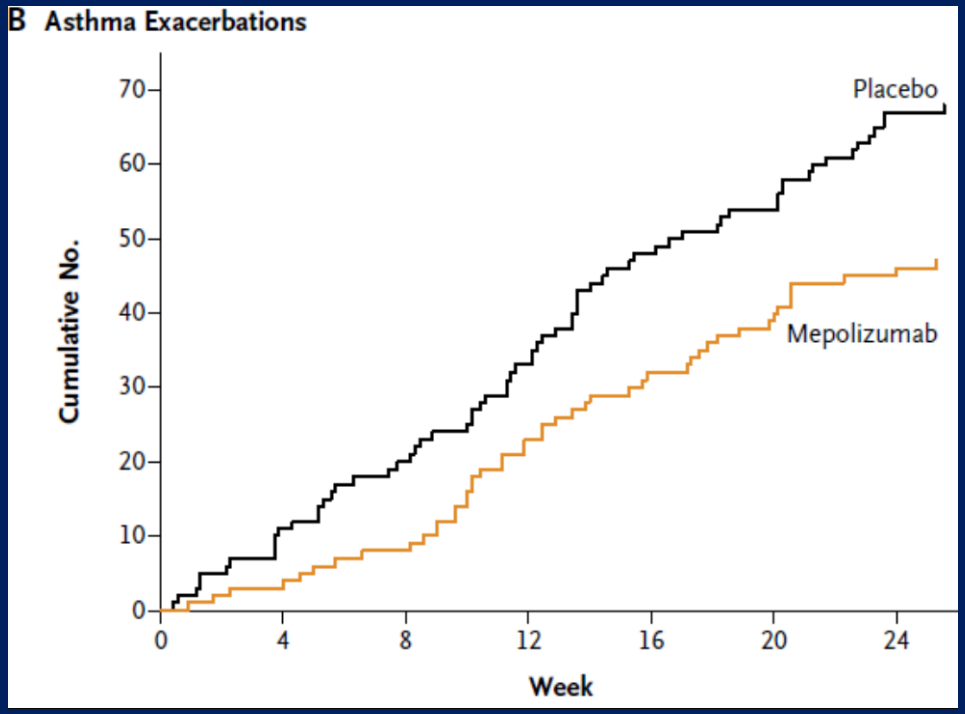
Mepolizumab Decreased OCS Dose and Reduced Exacerbations Despite Significant Reduction in OCS Use



At 24 weeks, mean % reduction from baseline OCS dose was 50% in mepo group and no reduction in the placebo group



Relative reduction of 32% in exacerbations Compared with placebo (p=0.04)

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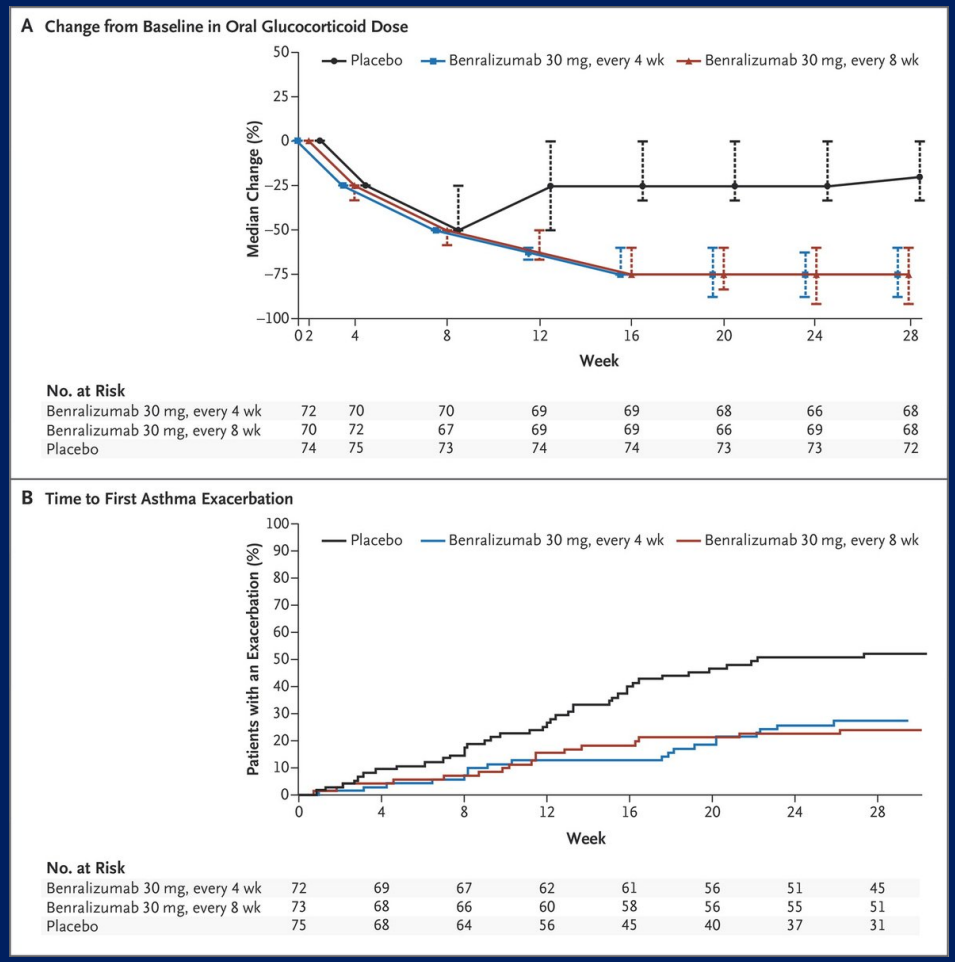
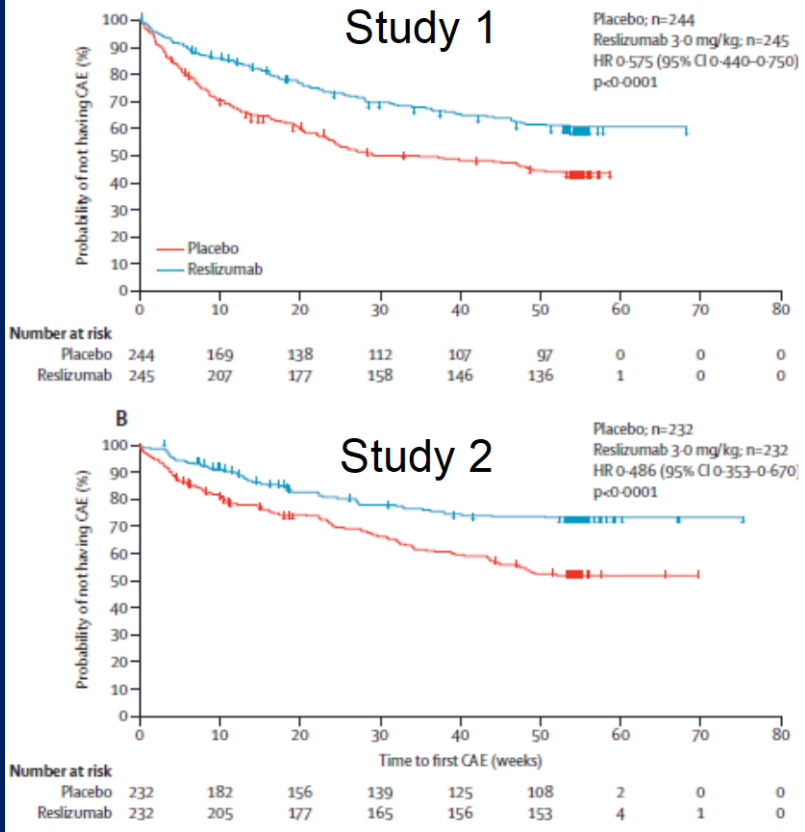
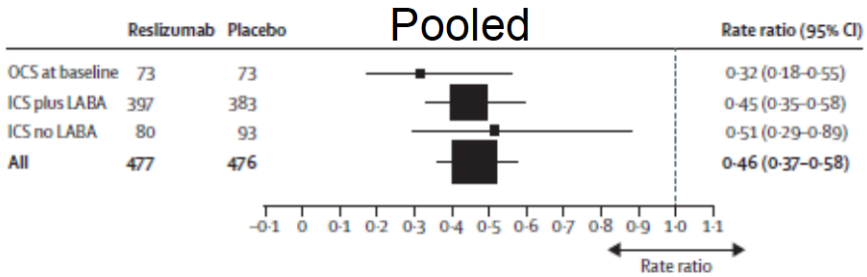
Steroid Sparing Effects of Benralizumab in Severe Eosinophilic Asthma



Nair et al. NEJM 2017

Reslizumab in Severe Eosinophilic Asthma





- In two studies, the probability of not having an exacerbation by week 52 with placebo was 44% (95% CI 38–51) and 52% (95% CI 45–58), and with Reslizumab it was 61% (95% CI 55–67) and 73% (95% CI 67–79), respectively
- Reslizumab reduced the risk for asthma exacerbation compared with placebo in both studies ($P < 0.0001$)

Castro et al. Lancet Respir Med. 2015:3:355-66

Dupilumab Significantly Decreases OCS and Exacerbations in Moderate to Severe asthma

A Dupilumab, 200 mg Every 2 Wk, vs. Matched Placebo

Subgroup	No. of Patients		Relative Risk vs. Placebo (95% CI)
	Placebo	Dupilumab	
Overall	317	631	0.52 (0.41–0.66)
Eosinophil count			
≥300 cells/mm³	148	264	0.34 (0.24–0.48)
≥150 to <300 cells/mm³	84	173	0.64 (0.41–1.02)
<150 cells/mm³	85	193	0.93 (0.58–1.47)
Fe_{NO}			
≥50 ppb	71	119	0.31 (0.18–0.52)
≥25 to <50 ppb	91	180	0.39 (0.24–0.62)
<25 ppb	149	325	0.75 (0.54–1.05)

0.1 0.25 0.5 0.75 1 1.5 2

Dupilumab Better — Placebo Better

B Dupilumab, 300 mg Every 2 Wk, vs. Matched Placebo

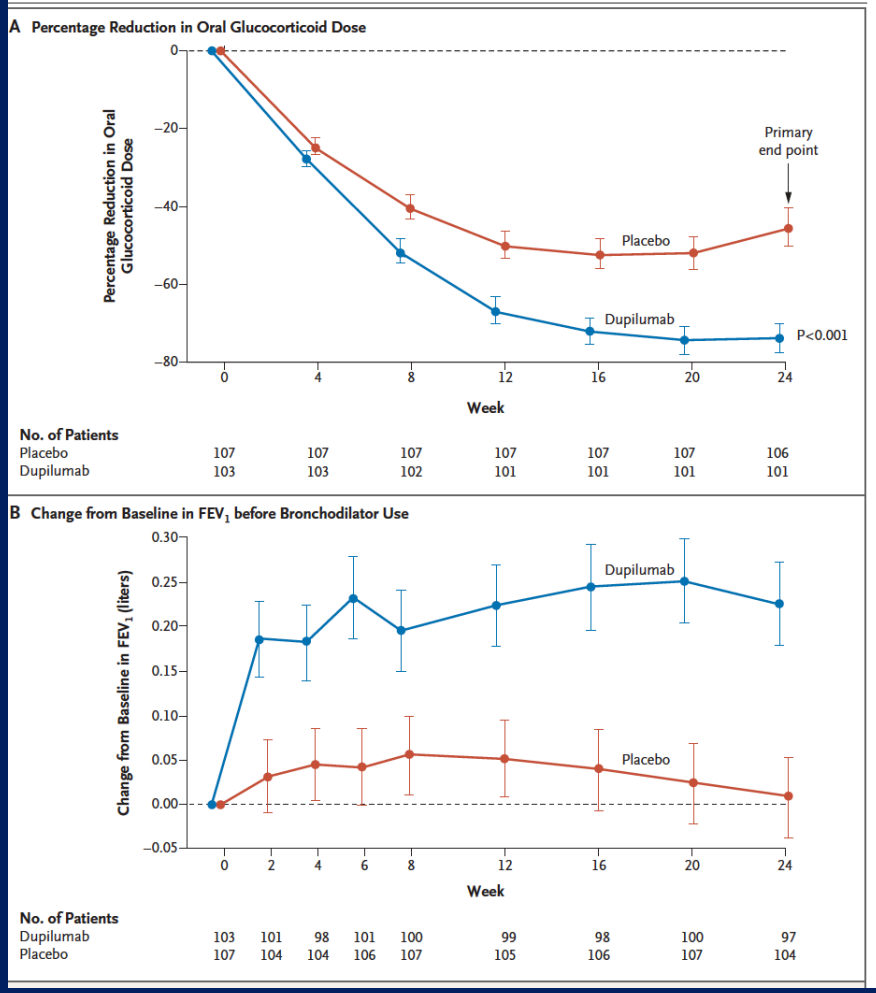
Subgroup	No. of Patients		Relative Risk vs. Placebo (95% CI)
	Placebo	Dupilumab	
Overall	321	633	0.54 (0.43–0.68)
Eosinophil count			
≥300 cells/mm³	142	277	0.33 (0.23–0.45)
≥150 to <300 cells/mm³	95	175	0.56 (0.35–0.89)
<150 cells/mm³	83	181	1.15 (0.75–1.77)
Fe_{NO}			
≥50 ppb	75	124	0.31 (0.19–0.49)
≥25 to <50 ppb	97	186	0.44 (0.28–0.69)
<25 ppb	144	317	0.79 (0.57–1.10)

0.1 0.25 0.5 0.75 1 1.5 2

Dupilumab Better — Placebo Better

Figure 1. Forest Plots of the Risk of Severe Asthma Exacerbations in the Intention-to-Treat Population and in Subgroups Defined According to Baseline Blood Eosinophil Count and Baseline Fe_{NO}.

Fe_{NO} denotes fraction of exhaled nitric oxide, and ppb parts per billion.



Rabe, C et al. N Engl J Med 2018;378:2475 and Castro et al. NEJM 378;26:2486

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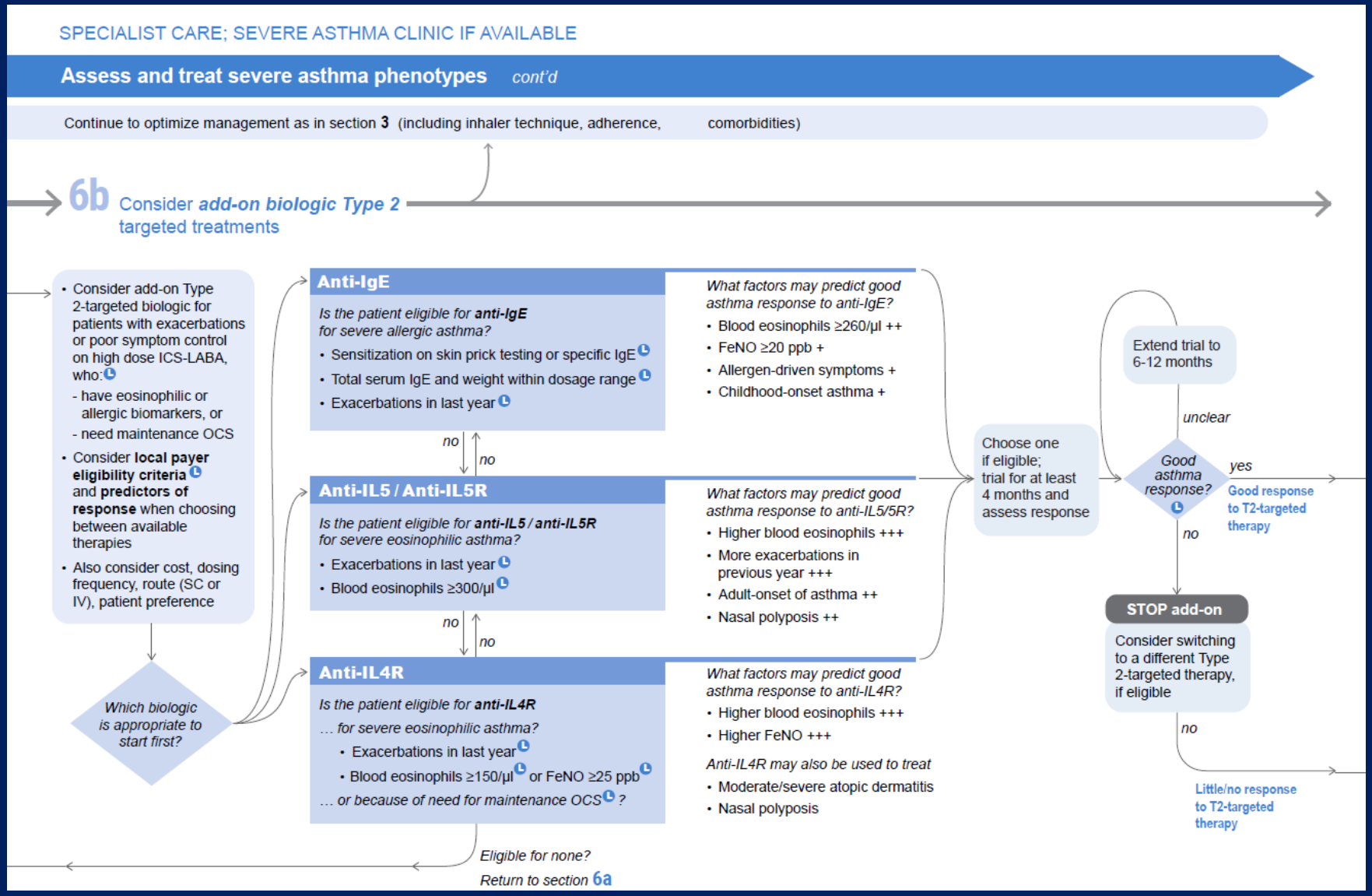
GINA Severe Asthma Algorithm



ATS/ERS Updated Guidelines 2019

- Blood eosinophil cut off of ≥150/ul can be used to guide anti IL5 therapy

- Eosinophil count of ≥260/ul or a FeNO >19.5ppb can be used to guide use of anti IgE therapy. Patients with both biomarkers have the best response

- Consider a trial of chronic macrolide therapy to decrease exacerbations in adults with persistently symptomatic or uncontrolled asthma on step 5 therapy

Holguin et al. ERJ 2019; In press

ATS/ERS Updated Guidelines 2019

- Suggest the use of anti IL5 and IL5r antibodies for the treatment of severe eosinophilic asthma (SEA)

- Suggest tiotropium for adults and adolescents >18 years of age with uncontrolled asthma on GINA step 4 or 5 therapy, irrespective of phenotype

- Suggest antiIL4/13 therapy in adults with SEA and OCS dependent asthma regardless of eosinophil count

Holguin et al. ERJ 2019; In press

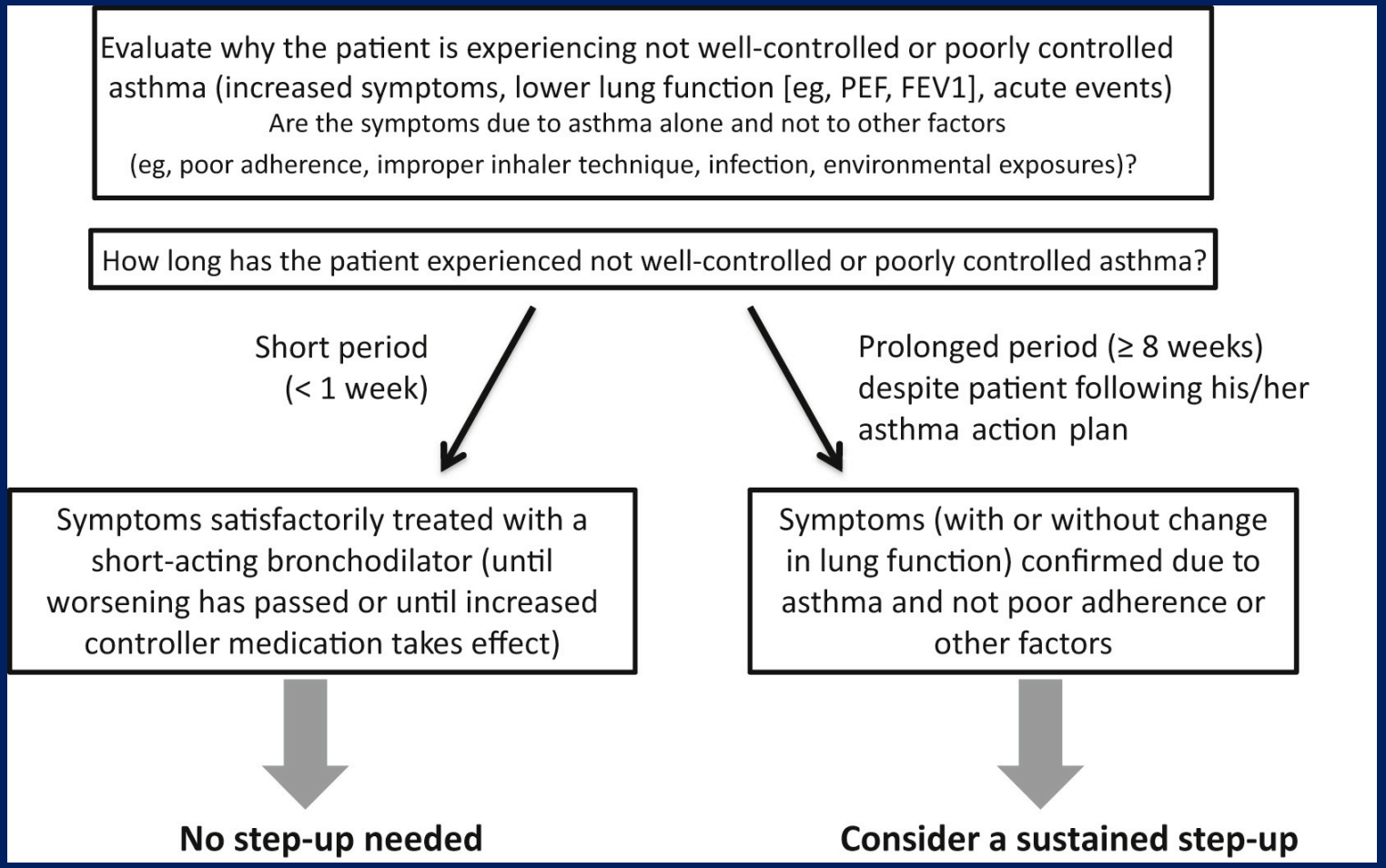
Asthma Yardstick

Asthma Yardstick

	Classification of asthma control		
Control component	**Well controlled**	**Not well controlled**	**Very poorly controlled**
Impairment			
Symptoms	≤2 days per week	>2 days per week	Throughout the day
Nighttime awakenings	≤2 times per month	1–3 times per week	≥4 times per week
Interference with normal activities	None	Some limitation	Extremely limited
Using SABA for symptoms (not prevention of EIB)	≤2 days per week	>2 days per week	Several times per day
FEV_1 or PEF	>80% predicted/personal best	60%–80% predicted/personal best	<60% predicted/personal best
Validated questionnaires			
ACT	≥20	16–19	≤15
ACQ	≤0.75	≥1.5	NA
ATAQ	0	1–2	3–4
Risk			
Exacerbations requiring OCS	≤1 per year	≥2 per year	
Progressive loss of lung function	Long-term follow-up required	Long-term follow-up required	Long-term follow-up required
Treatment-related adverse effects	May vary from none to troublesome/or worrisome. Intensity does not correlate with level of control but should be considered in overall assessment of risk.		

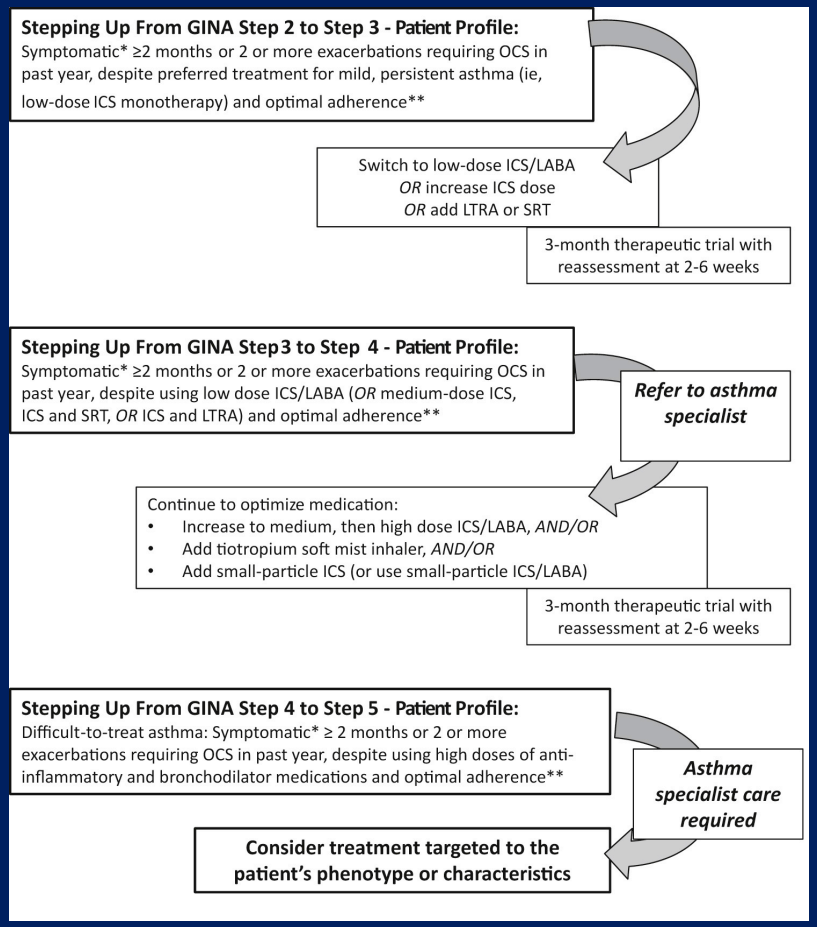
Chipps B et al. AAAI 2017; 118:133-142

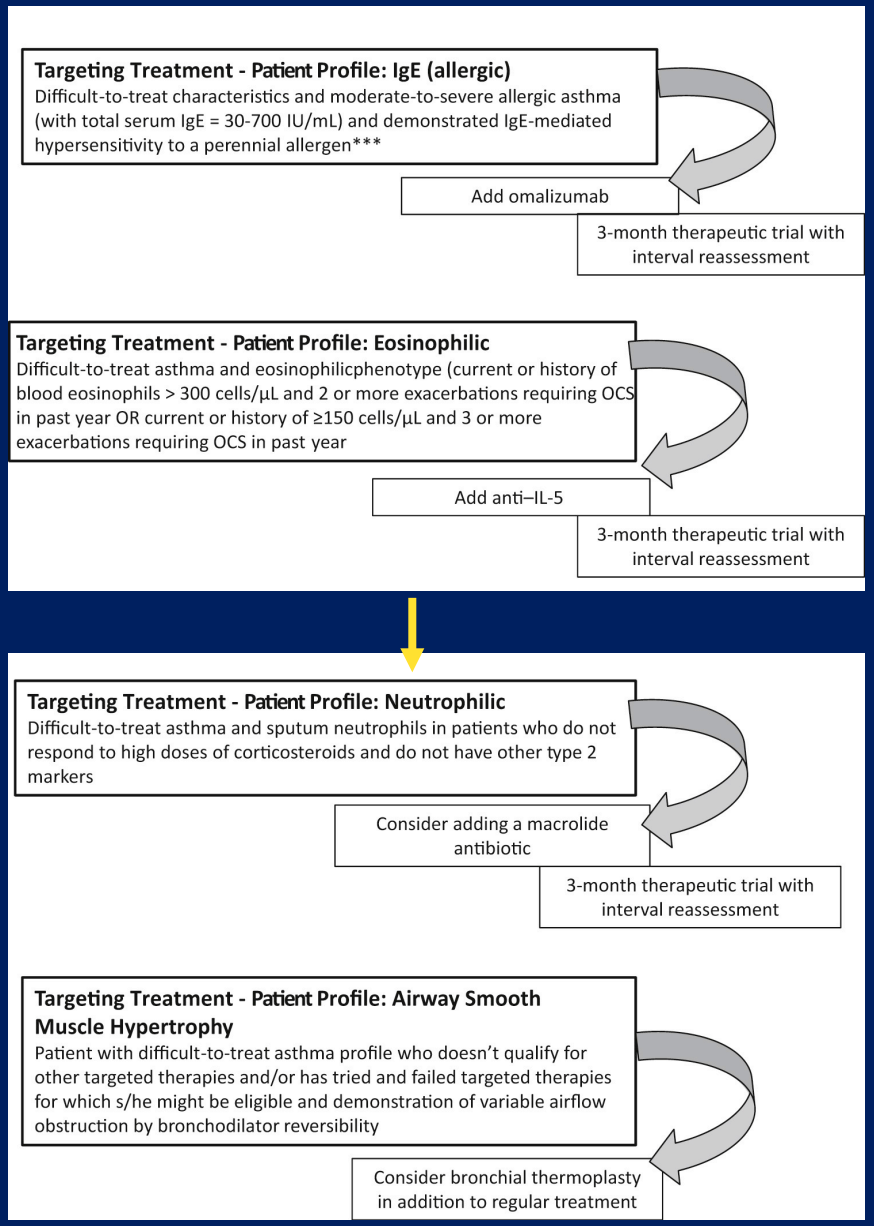
Asthma Yardstick



Annals of Allergy, Asthma & Immunology 2017 118, 133-142.e3DOI: (10.1016/j.anai.2016.12.010)

Asthma Yardstick





Annals of Allergy, Asthma & Immunology 2017 118, 133-142.e3DOI: (10.1016/j.anai.2016.12.010)

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Asthma Yardstick

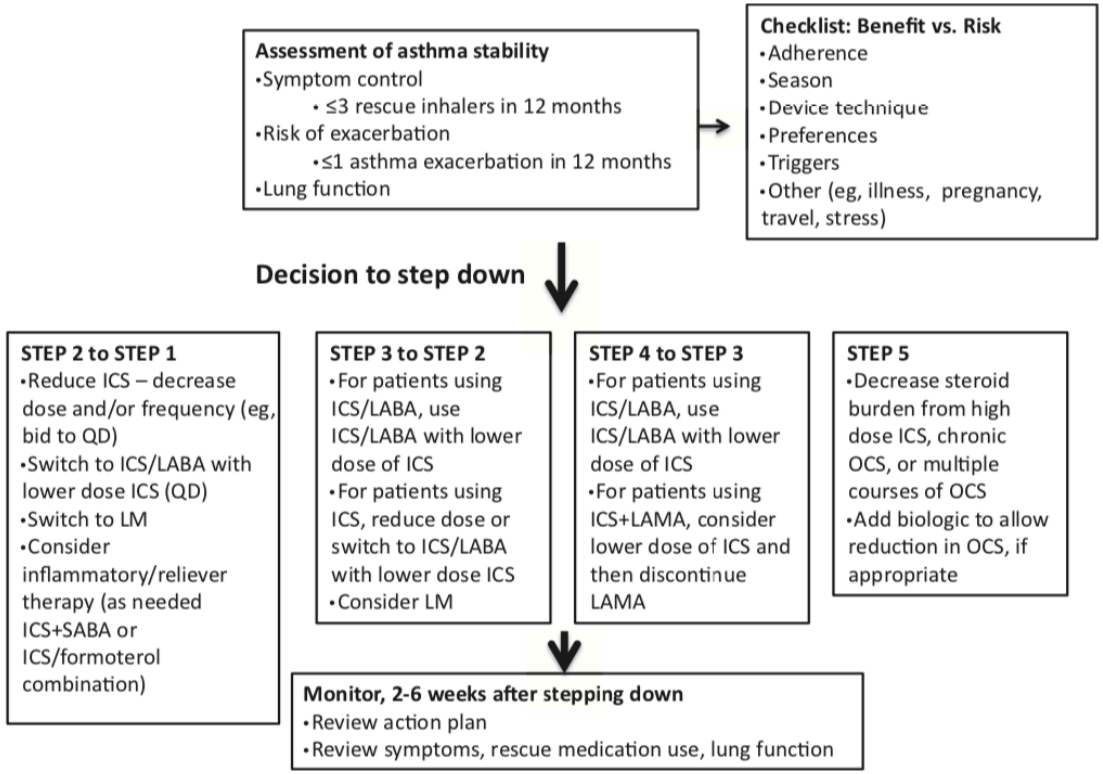

Figure 2. Recommendations for stepping down asthma therapy.[6] Abbreviations: FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroids; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic agent; LM, leukotriene modifier; OCS, oral corticosteroid; QD, once-a-day; SABA, short-acting $beta_2$-agonist.

Chipps B et al. AAAI 2017; 118:133-142

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Questions?