Severe asthma

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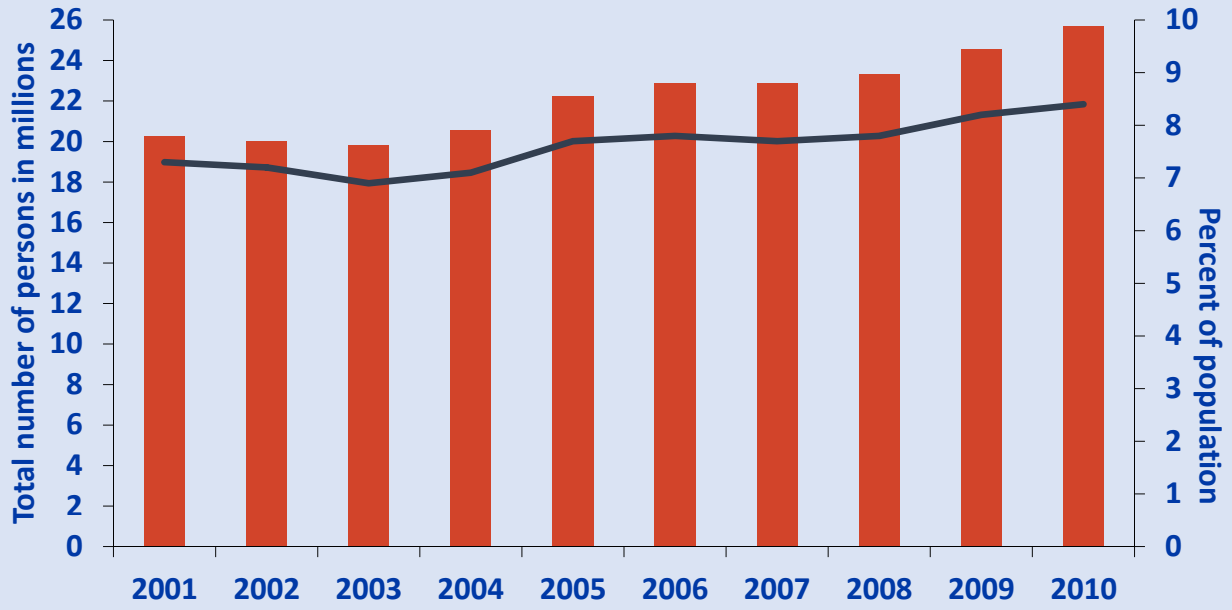
Asthma in the US

- Affects 26 million Americans, including >7 million children
- $56 billion in healthcare costs + lost productivity at work/school
- ***Prevalence continues to increase***



https://www.cdc.gov/asthma/most_recent_data.htm.
Larson K, et al. *Respir Res.* 2018;19(1):12. Kerkhof M, et al. *Thorax.* 2018;73(2):116-124.

Severe asthma

- 5-10% of the population of adults with asthma (0.5% of US population).
- Not a uniform disease, but a description of asthma patients with high medical needs caused by a variety of pathophysiologic mechanisms.
- Often poorly controlled by the current standard of care
- Health care is associated with more than 50% of the total US costs associated with asthma, $28 billion per year.
- Health care costs per patient are higher than those for DM, stroke or COPD.

Definition of Severe Asthma (2014 ATS/ERS Guidelines)

- Asthma which requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller and/or oral corticosteroids to prevent it from becoming uncontrolled or which remains uncontrolled despite treatment.

- Treatment with systemic CS for at least 50% of the previous year

When a diagnosis of asthma is confirmed and comorbidities have been addressed (misdiagnosis in 12-30%):

ERS/ATS Guidelines 2014

Advances over past 5 years

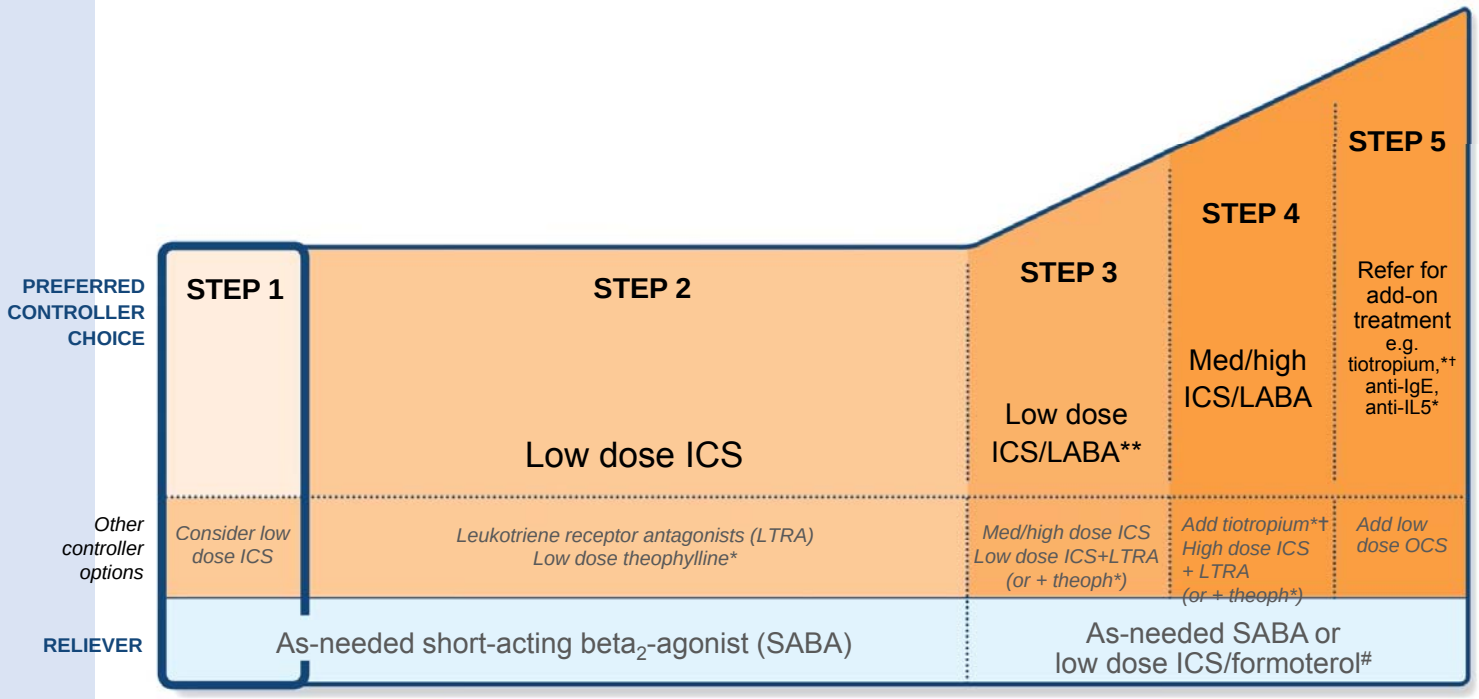
- Formulation of a standardized definition for severe asthma (ATS, ERS 2014)
- Evidence based treatment guidelines specifically for severe asthma
- Understanding of different phenotypic patterns and biomarkers
- Availability of novel targeted treatments.

Estimating Severity: 2007 NHLBI Guidelines

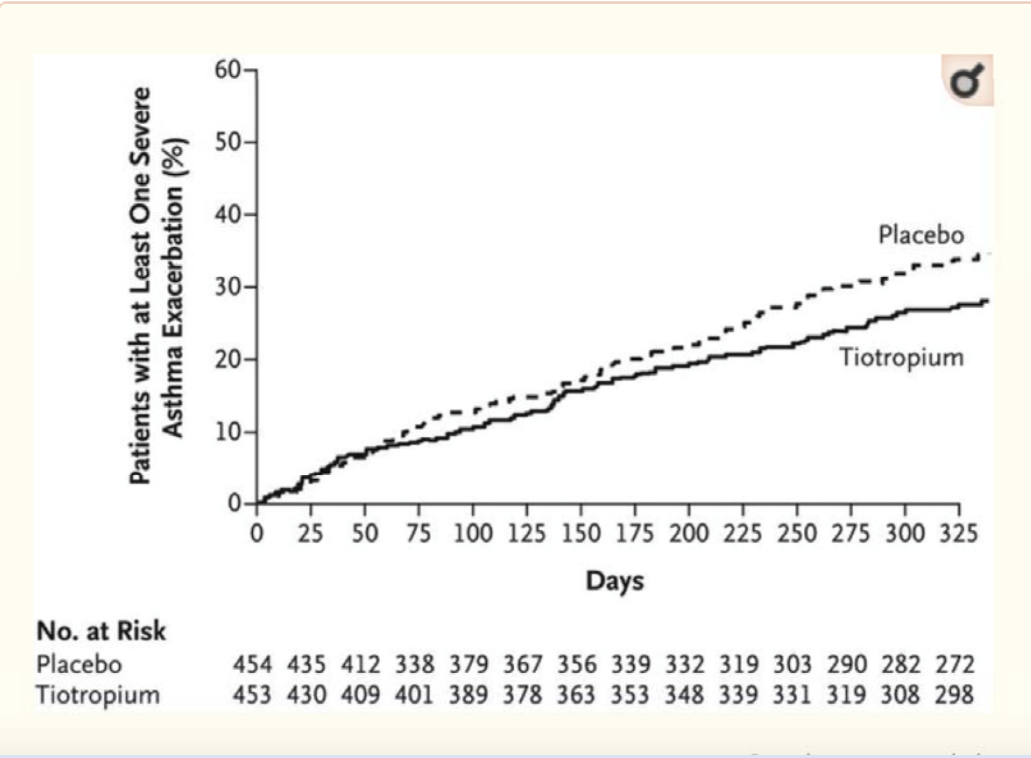
Severity assessment	Asthma severity			
	Intermittent	Persistent		
		Mild	Moderate	Severe
Symptoms	≤2d/wk	>2 d/wk but not daily	Daily	Throughout the day
Nighttime awakenings	≤2x/mo	3-4x/mo.	>1x/wk, but not nightly	Often 7x/wk
SABA use	≤2 d/wk	>2 d/wk, but not daily or >1x/d	Daily	Several times per day
Interference with ADL	None	Minor	Some	Extreme
Lung function	FEV_1 >80% predicted FEV_1/FVC normal	FEV_1 >80% predicted FEV_1/FVC normal	FEV_1 60-80% predicted FEV_1/FVC reduced 5%	FEV_1 <60% predicted FEV_1/FVC reduced >5%
Treatment step	Step 1	Step 2	Step 3	Step 4 or 5

National Asthma Education and Prevention Program, Third Expert Panel on the Diagnosis and Management of Asthma. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2007 Aug.

GINA guidelines



Addition of tiotropium to ICS/LABA in poorly controlled asthma reduces exacerbations by 21%



Kerstjens et al. N Engl J Med 2012

Uncontrolled Asthma

- Asthma symptoms that persist despite treatment
- May be indicated by:
  - High/daily use of rescue mediations (SABA)
  - Repeated need for oral corticosteroids
  - Frequent or severe exacerbations (ER/hospital visits for asthma)
  - Airflow limitation; FEV1 < 80% predicted

- May result from:
  - Resistance to therapies
  - Poor adherence
  - Inappropriate inhaler technique
  - Environmental factors
  - Comorbidities

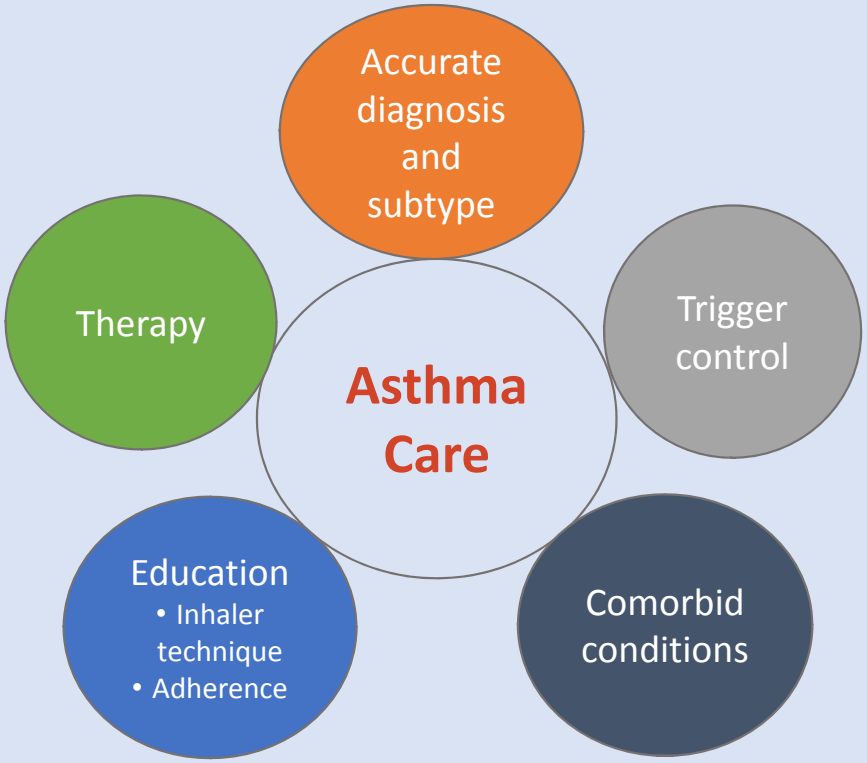
Uncontrolled Asthma

• GOAL Study (US)[1]	• Swedish database study[2]	• Italian registry study[3]

After treatment intensification:
• Total control achieved in only 19%-31% of patients
• Well controlled asthma achieved in 50%-63% of patients
	Poor asthma control in:
	• 28.2% of patients with mild-moderate asthma
	• 53.6% of patients with severe asthma
		Patients with severe, uncontrolled asthma:
		• 60.6% female, 83.1% had allergic asthma
		• ~30% with late onset of asthma
		• In the last 12 months:
		  • 55.7% had exacerbations
		  • 9.7% had ED visits
		  • 7.3% were hospitalized

1. Bateman ED, et al. *Am J Respir Crit Care Med.* 2004;170(8):836-844. 2. Larson K, et al. *Respir Res.* 2018;19(1):12.
3. Maio S, et al. *Allergy.* 2018;73(3):683-695.

Approach to Severe/Uncontrolled Asthma



Comorbidities in Asthma

➢*Comorbidities are common and can affect asthma control*

- Dutch survey of difficult-to-control asthma (N=914)[1]
  - *92% of patients had ≥1 comorbidity*
  - Comorbidities associated with older age, female gender, smoking history, and chronic prednisone use
- Analysis of the US National Health and Wellness Survey
  - Asthma patients with ≥1 allergic/asthma-related comorbidity (N = 1923)[2]
  - *54.4% had very poorly or not well-controlled asthma*
  - Patients with very poorly controlled asthma reported significantly greater decreases in quality of life, greater overall work impairment, and higher healthcare use (all $p < 0.05$)

1. Hekking PP, et al. *J Allergy Clin Immunol Pract.* 2018;6(1):108-113.
2. Lee LK, et al. *J Asthma.* 2018;55(2):208-219.

Nasal mometasone does not improve asthma controlled in poorly controlled asthma with symptoms of rhinitis/sinusitis

	N*	Change from randomization (SE)		Difference in change from randomization (95% CI)	P-value
		Mometasone	Placebo	Mometasone – Placebo	
cACT: Pediatric (ages 6-11) ↑					
Week 4	82	1.81 (0.58)	2.69 (0.54)	-0.88 (-2.47 ,0.71)	0.27
Week 12	75	3.40 (0.61)	3.05 (0.71)	0.34 (-1.52 ,2.21)	0.71
Week 24	71	4.15 (0.64)	4.53 (0.65)	-0.38 (-2.19 ,1.44)	0.68
ACT: Adolescent and adult (ages 12 and over) ↑					
Week 4	277	1.89 (0.26)	1.75 (0.31)	0.14 (-0.66 ,0.94)	0.72
Week 12	262	2.69 (0.30)	2.25 (0.32)	0.44 (-0.43 ,1.31)	0.32
Week 24	248	2.95 (0.31)	2.44 (0.38)	0.51 (-0.46 ,1.48)	0.30

Dixon A, JACI 2014

PPI use does not improve asthma outcomes in patients with asymptomatic GER

N	Treatment Group			P-value*	
	Placebo 193	Esomeprazole 200	IRR* (Eso:Plb) 95% CI	Eso vs Plb†	GER Interaction‡
Asthma episodes - type 1					
#Events	201	224			
Rate (events/person-year)	2.3	2.5	1.1 0.8, 1.5	0.66	0.93
Patients with ≥1 event, N(%)	42	42			
Exacerbation Components Peak flow, 30% drop					
#Events	141	180			
Rate (events/person-year)	1.7	2.1	1.2 0.8, 2.0	0.35	0.99
Patients with ≥1 event, N (%)	26	28			
Urgent Care					
#Events	53	51			

Mastronarde J NEJM 2010

Evaluation of Severe Asthma

- First step is to confirm the diagnosis (pre and post spirometry), check adherence to conventional therapies and optimize treatment of coexisting conditions (rhinitis, sinusitis, GER).
- Assess environmental factors, allergy referral for those with skin test or RAST positive.
- Implement an adequate trial of therapy with high dose ICS and LABA, consider adding LAMA as well.
- assess adherence and inhaler techniques since problems with these account for up to 50% of cases of uncontrolled asthma.

Phenotypes vs Endotypes

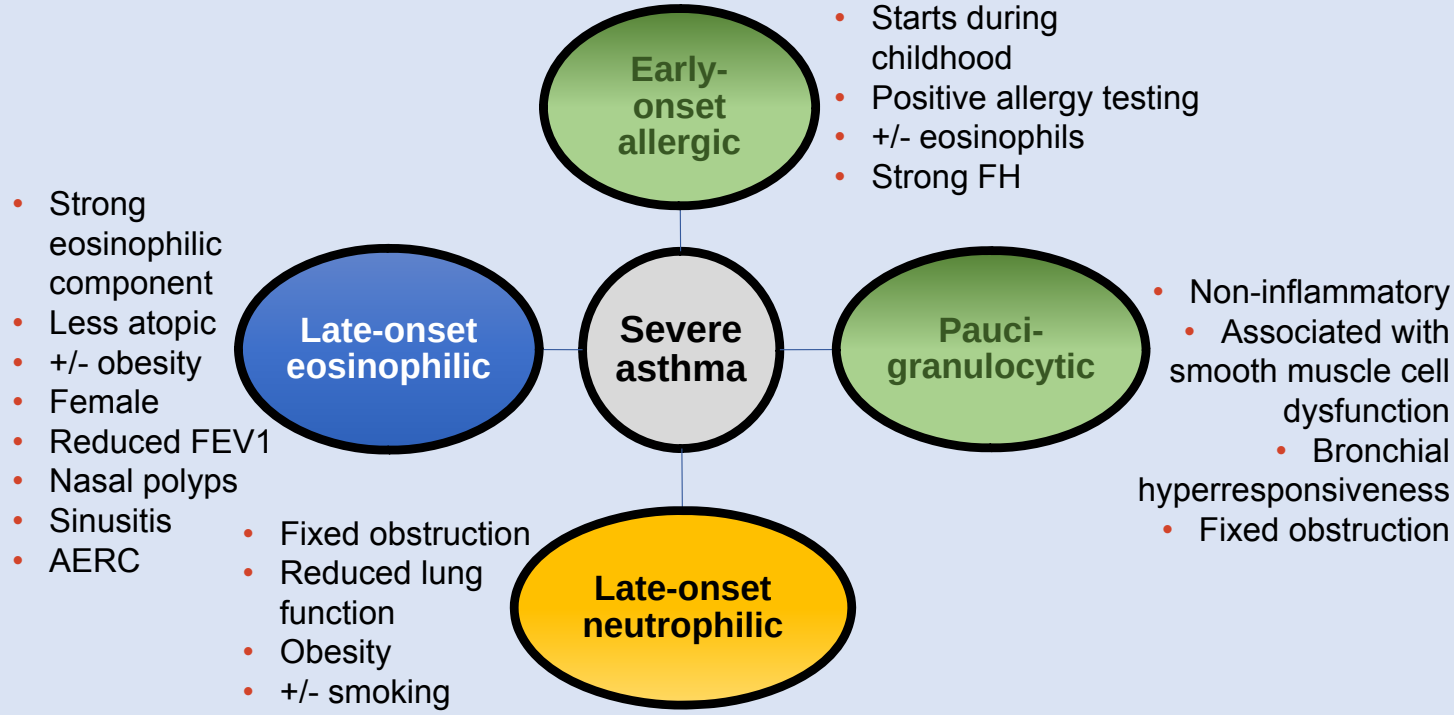
- Phenotypes:
  - Clinically observable characteristics of a disease
    - Examples: Allergic asthma, non-allergic asthma, obesity-related asthma, aspirin-sensitive asthma
- Endotypes:
  - Subtypes of a disease defined by intrinsic, distinct pathogenetic mechanisms
    - Examples: type 2 asthma, eosinophilic asthma, neutrophilic asthma
- Two specific endotypes (T2 high and low) important to distinguish when considering biologic therapy.

Agache I, et al. *Allergy.* 2012;67(7):835-846.

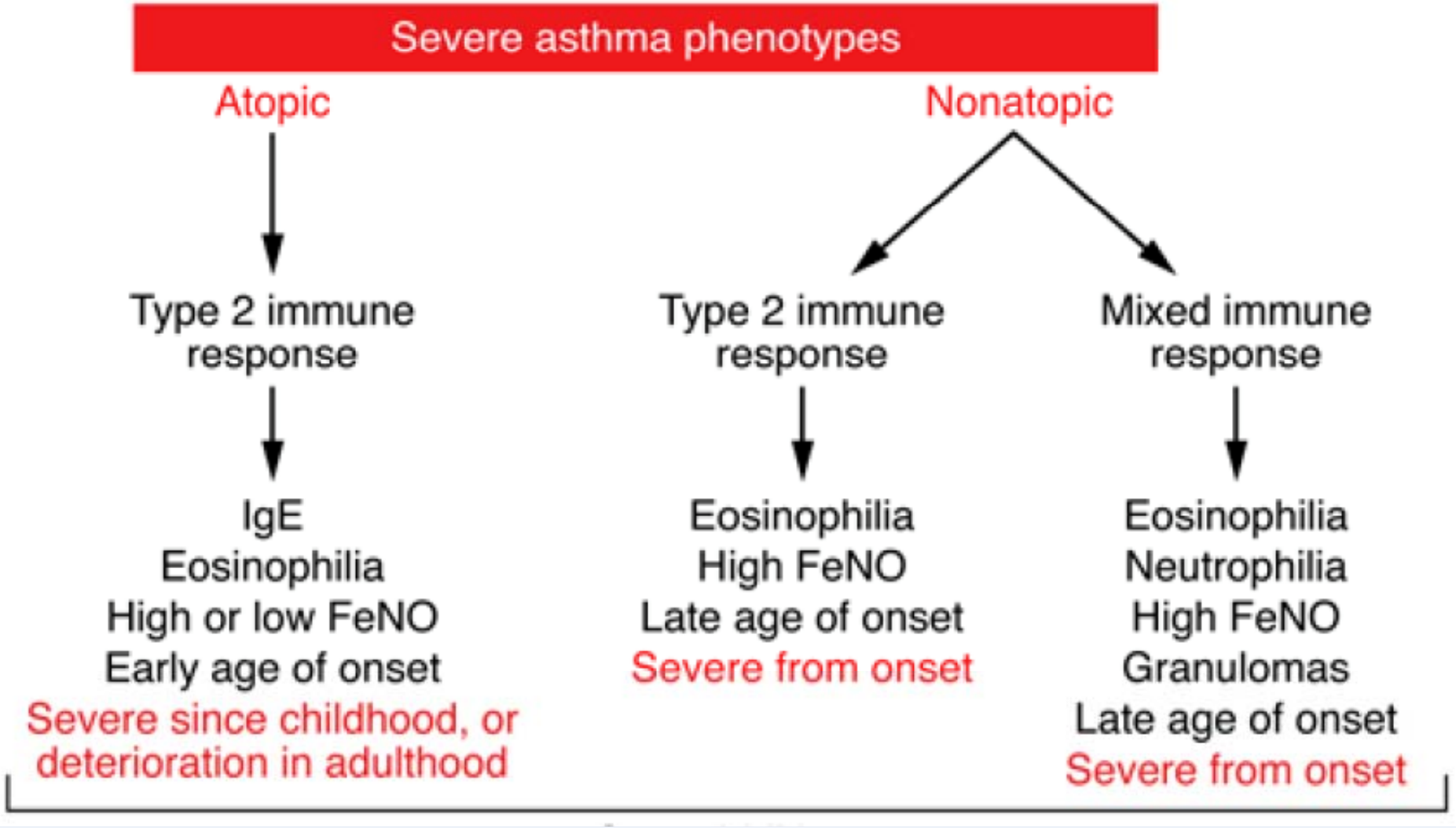
Asthma Phenotypes in Clinical Practice

- Treatment of asthma is moving toward a personalized treatment strategy based on patient specific characteristics and endotype rather than disease severity alone.
- Asthma phenotypes may help clinicians identify “treatable traits”
- Particularly relevant in severe disease
- Widely available tests that may guide selection of therapy:
  - Blood eosinophils
  - Serum IgE
  - Fractional exhaled nitric oxide (FENO)

Asthma Phenotypes



Opina MT, et al. *Curr Allergy Asthma Rep*. 2017;17(2):10.


Severe asthma phenotypes
Atopic
Nonatopic
Type 2 immune response
Type 2 immune response
Mixed immune response
IgE
Eosinophilia
High or low FeNO
Early age of onset
Severe since childhood, or deterioration in adulthood
Eosinophilia
High FeNO
Late age of onset
Severe from onset
Eosinophilia
Neutrophilia
High FeNO
Granulomas
Late age of onset
Severe from onset

Airway inflammation- Type 2

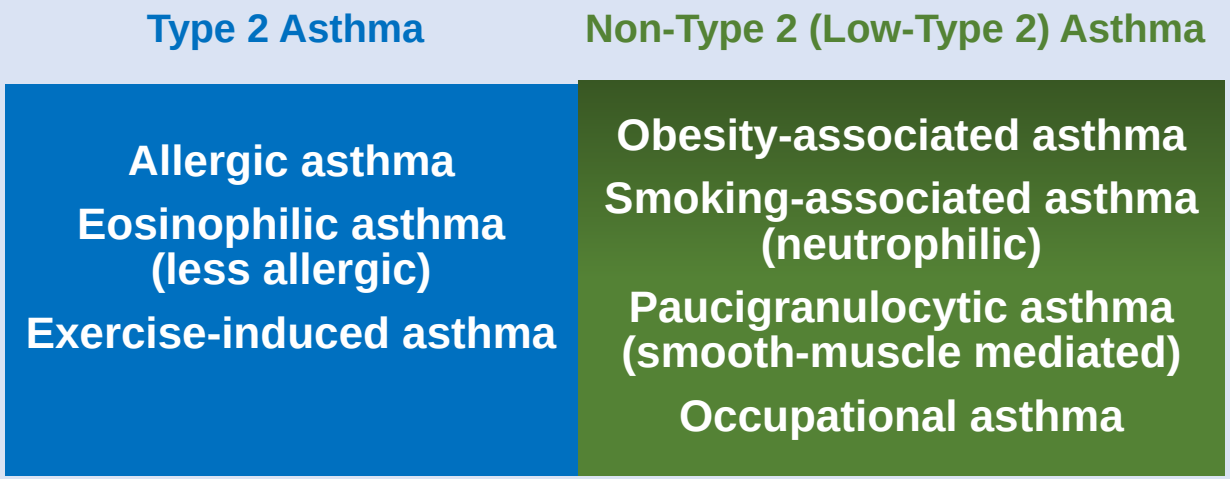
- Type 2 inflammation: IL-4, IL-5, IL-13 cytokines are produced by Th2 cells but also by innate lymphoid cells.
- About 50% of severe asthmatics exhibit Type 2 inflammation.
- characterized by eosinophils and may be accompanied by atopy (atopy more common in childhood onset).
- In mild to moderate asthma, type 2 inflammation is common and resolves after treatment with glucocorticoids.
- In severe asthma, active type 2 inflammation exists despite high dose therapy with inhaled or oral corticosteroids.
- Sputum eosinophilia (T2 inflammation) is seen in more than half of patients with severe asthma and has been labeled GC resistant asthma.

Which of the following is an example of an endotype in asthma?

A. Allergic asthma
B. Eosinophilic asthma
C. Obesity-related asthma
D. Aspirin-sensitive asthma

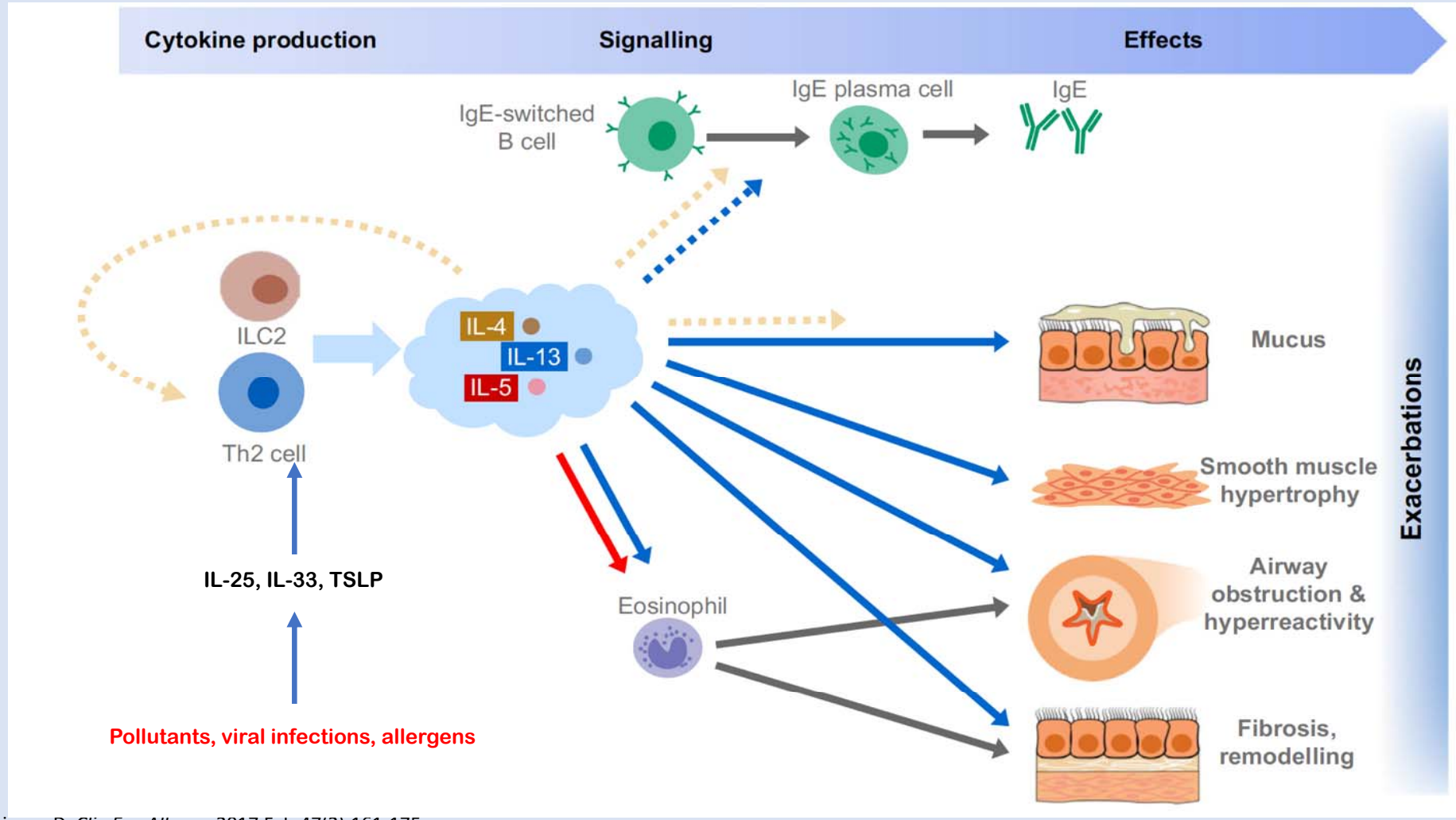
Type 2 Asthma

- Associated biomarkers include FENO, serum IgE, periostin, and blood and sputum eosinophil levels
  - FENO, IgE, eosinophil tests available for clinical use



Wenzel SE. *Nat Med*. 2012;18(5):716-725.

Effects of Type-2 Inflammation



Robinson D. *Clin Exp Allergy*. 2017 Feb;47(2):161-175.

Which of the following tests can be used to identify type 2 asthma?

A. DLCO
B. Fractional excretion of nitric oxide
C. Sputum neutrophil count
D. Serum acute phase reactants

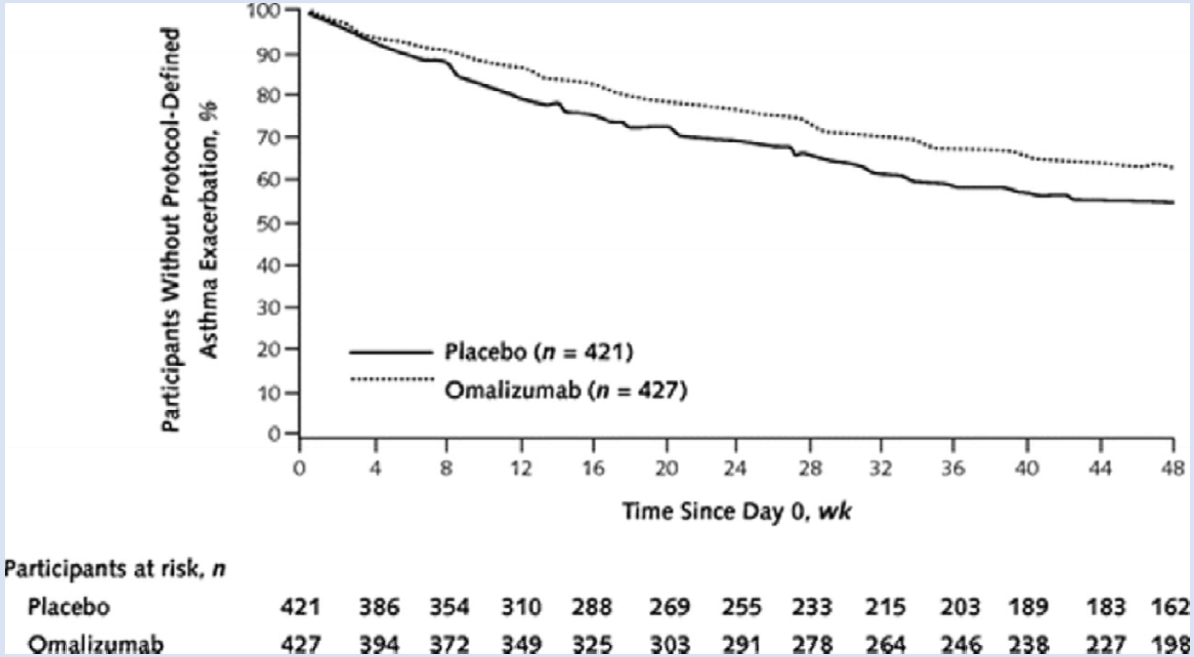
Phenotype targeted therapy – personalized medicine

- Biomarkers can help target therapies to the correct patients.
- Measurable type 2 biomarkers include FeNO, IgE and sputum/blood eosinophils.
- IgE and allergy skin or RAST testing are biomarkers for allergic asthma.
- mAb to IL-5 (mepolizumab, rezluzimab, benraluzimab) and IL-4/13 (dupilumab) were specifically developed for severe eosinophilic asthma (persistent blood eos despite treatment with ICS or oral steroids).
- Currently, no targeted treatments are available for non eosinophilic asthma.

Omalizumab

- Monoclonal Ab that binds to free IgE preventing binding of IgE to the high affinity receptor on mast cells and basophils. Approved for moderate to severe atopic asthma (2003)
- In adults, indicated for IgE $\geq$ 30 or <700 KU/L (>1,300 in children aged 6 to 11 years) and at least one positive skin test or RAST. **Elevated IgE not necessary.**
- In those on ICS/LABA, reduces exac by 25-35%. FeNO >20ppb associated with better response and 50% reduction in exacerbations.
- Trial of 3-6 months to assess for clinical response; continue indefinitely if favorable response.
- Risk of anaphylaxis 0.1%

Omalizumab in severe allergic asthma inadequately controlled with ICS/LABA



Participants at risk, *n*													
Placebo	421	386	354	310	288	269	255	233	215	203	189	183	162
Omalizumab	427	394	372	349	325	303	291	278	264	246	238	227	198

25% fewer exacerbations with omalizumab compared with placebo

Hanania, Annals Internal Mediine 2011

Omalizumab: Clinical Trials

Study	Patient population	Outcomes
Hanania et al. 2011[1]	Patients with severe asthma inadequately controlled on ICS/LABA (N=850)	• Reduced rate of exacerbations (0.66 vs 0.88 per patient; P=0.006)
Busse et al. 2011[2]	Inner-city children, adolescents and young adults with persistent asthma (N=419)	• 24.5% reduction in number of days with asthma symptoms (from 1.96 to 1.48 per 2 weeks; P<0.001) • Reduced proportion of subjects with ≥1 exacerbation from 48.8% to 30.3% (P<0.001)
Humbert et al. 2005[3]	Patients with inadequately controlled asthma on ICS/LABA with reduced lung function and recent history of exacerbations (N=419)	• Reduced adjusted clinically significant exacerbation rate by 26% (P=0.042) • Reduced severe asthma exacerbation rate (0.24 vs 0.48; P=0.002)

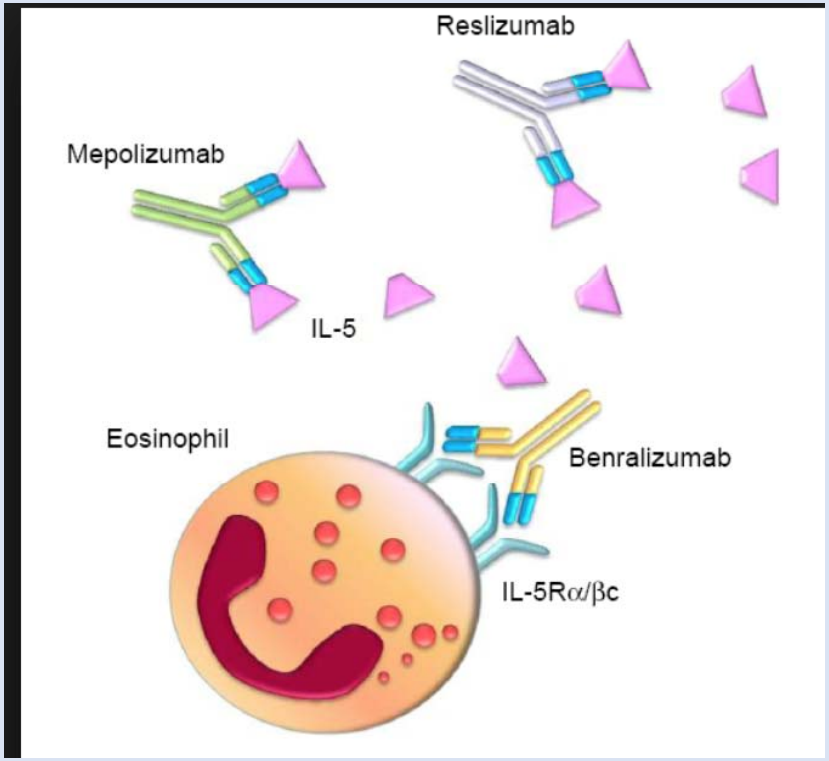
1. Hanania NA, et al. *Ann Intern Med.* 2011;154(9):573-582.
2. Busse WW, et al. *N Engl J Med.* 2011;364(11):1005-1015.
3. Humbert et al. *Allergy.* 2005;60(3):309-316.

Anti-IgE Therapy: Evidence Summary

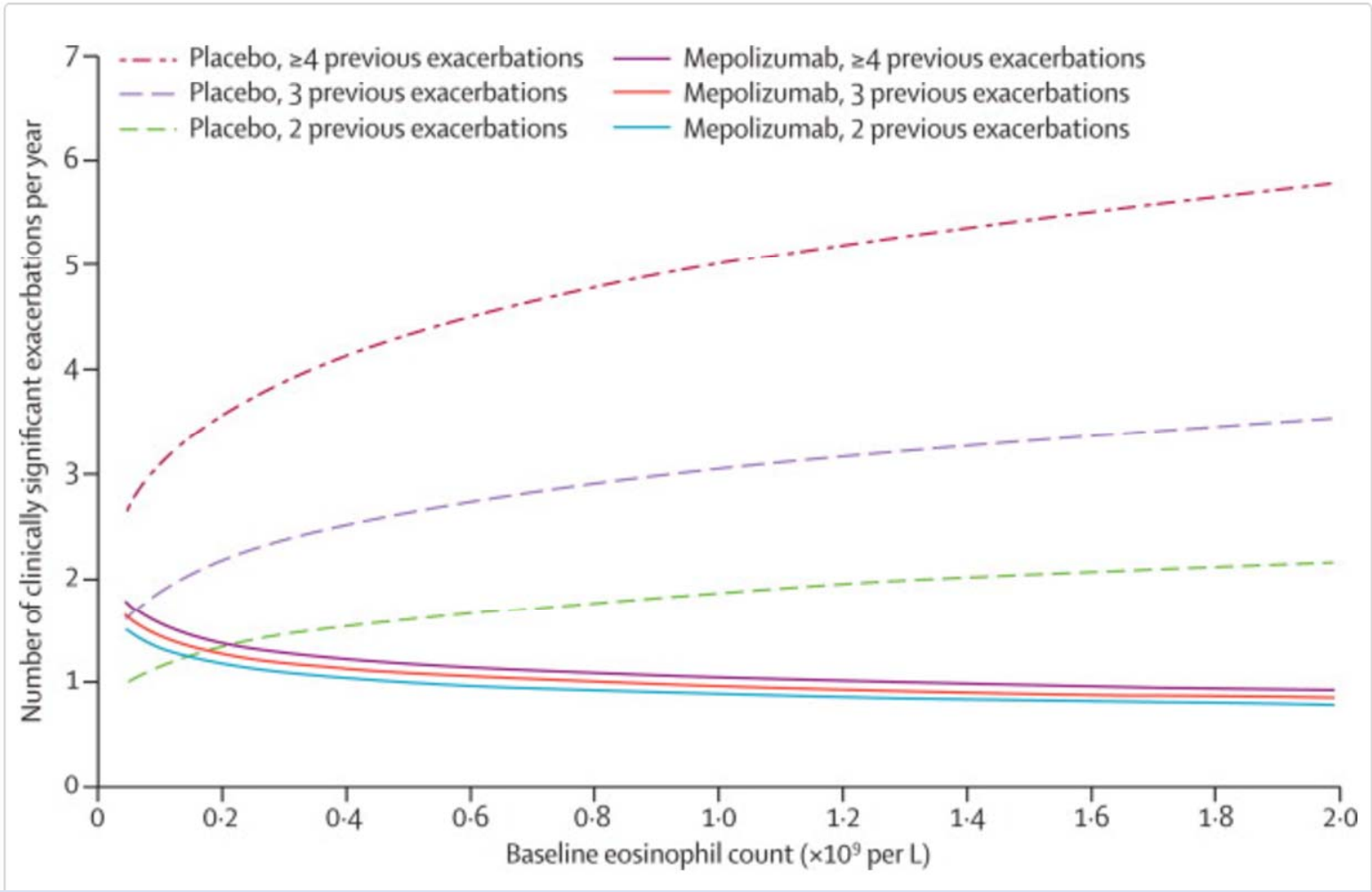
- Efficacy of anti-IgE therapy in multiple studies, compared to placebo:
  - *Improved* quality of life
  - *Reduced* exacerbations
  - *Reduced* emergency department visits
  - *Reduced* hospitalizations
  - *Reduced* corticosteroid requirements

Holgate S, et al. *J Allergy Clin Immunol.* 2005;115(3):459-465; Humbert M, et al. *Allergy.* 2005;60(3):309-16; Hanania NA, et al. Ann Intern Med. 2011;154(9):573-82; Busse WW, et al. *N Engl J Med.* 2011;364(11):1005-1015.

IL-5 promotes eosinophil activation and survival



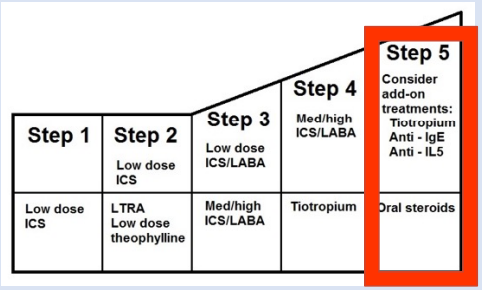
Blood eosinophil count correlates with increased exacerbations



Pavord, Lancet 2012

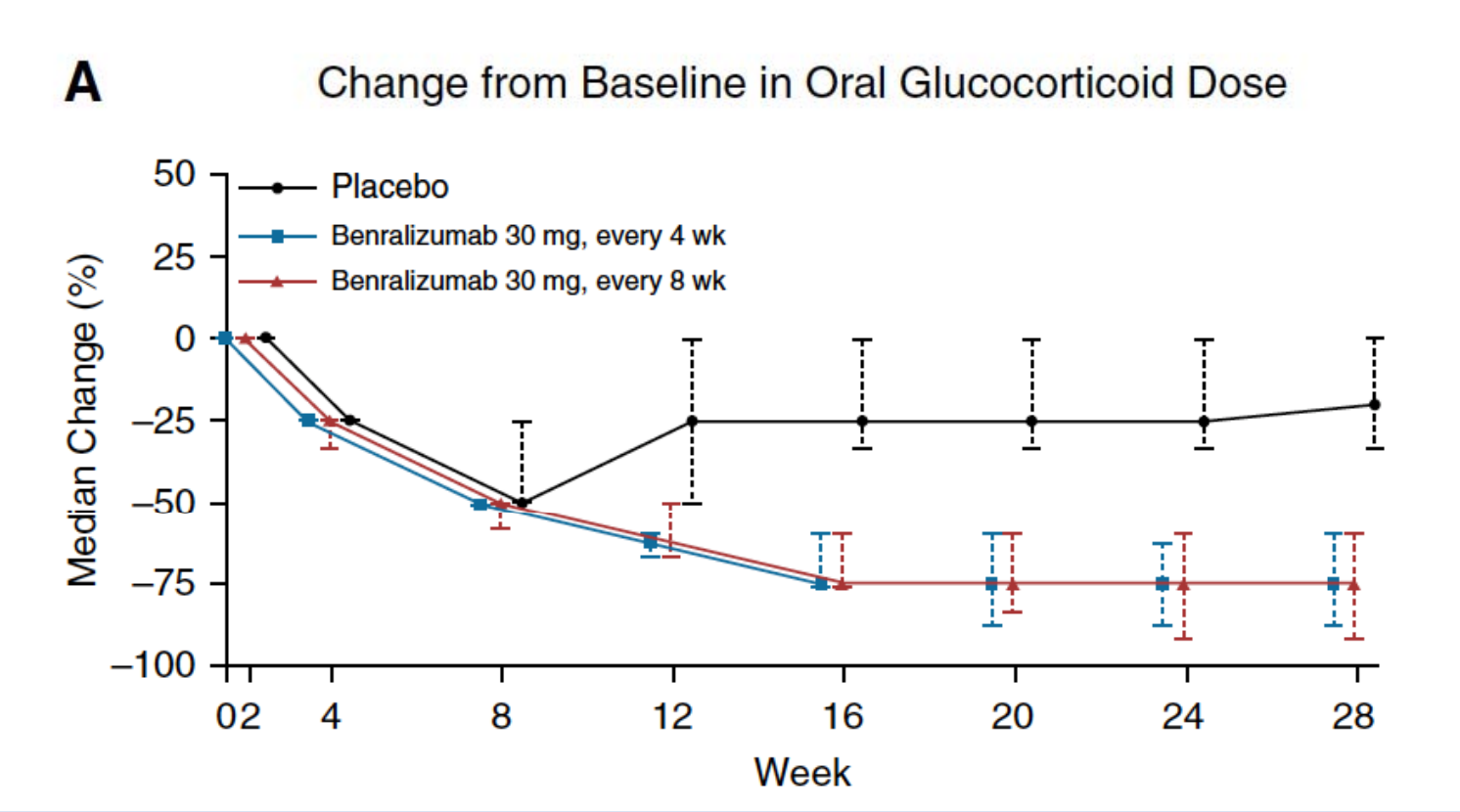
Anti-IL-5 Therapy

- Agents: IL-5 antibodies: mepolizumab, reslizumab,
- IL-5 receptor antibody: benralizumab
- Developed to treat eosinophilic asthma
- Efficacy in clinical trials:
  - In patients with blood eosinophils ≥150 (or ≥400) cells/mcL
    - Reduced exacerbations approx 50%
    - Reduced emergency department visits
    - Improved lung function
    - Reduced oral corticosteroid use (50%)



Bel EH, et al. *N Engl J Med.* 2014;371(13):1189-1197; Ortega HG, et al. *N Engl J Med*. 2014;371(13):1198-1207; Castro M, et al. *Lancet Respir Med.* 2015;3(5):355-366; Bjermer L, et al. *Chest.* 2016;150(4):789-798.

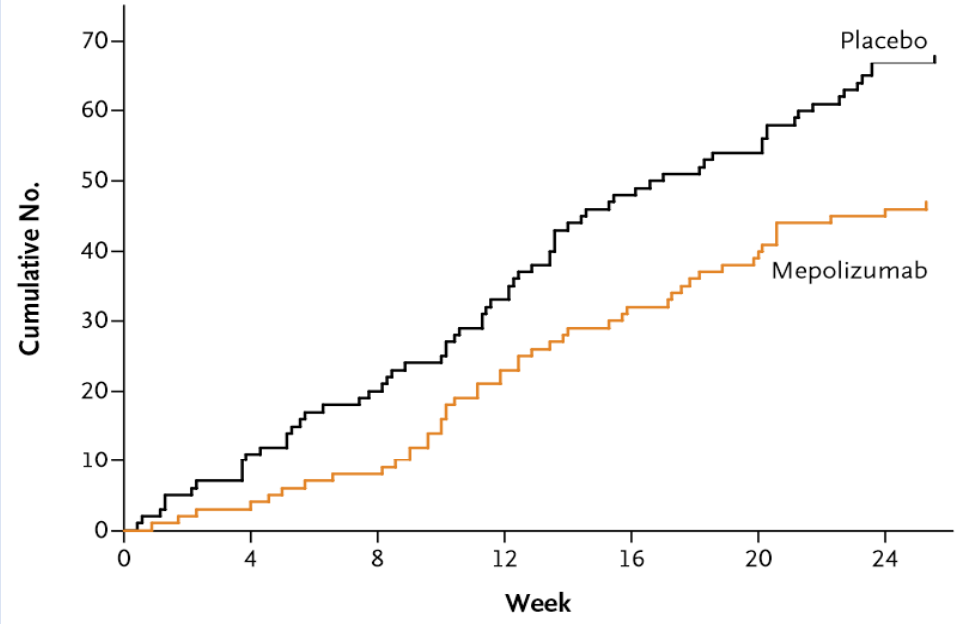
Benralizumab leads to reduction in oral steroid dose



Nair P NEJM 2017

Mepolizumab reduces exacerbations

Cumulative rate of clinically significant exacerbations

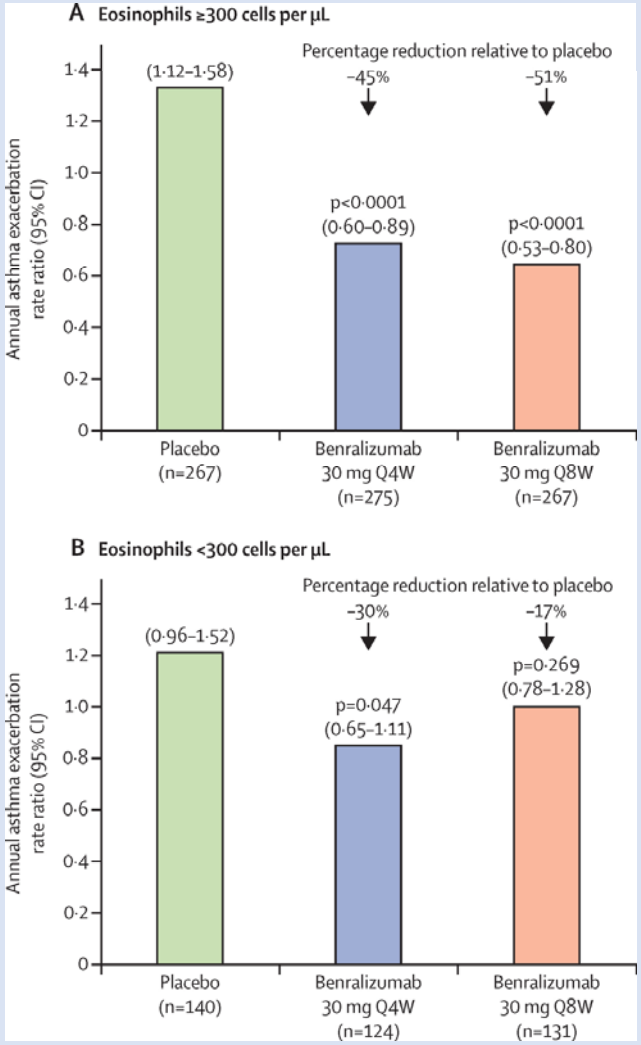


- Mepolizumab 100 mg q4weeks vs placebo
- Reduced annualized rate of exacerbations by 32% vs placebo at week 24 (P=0.04)

Bel EH, et al. *N Engl J Med*. 2014 25;371(13):1189-1197.

Benralizumab effectiveness based on blood eosinophil count

Direct, rapid and near
complete depletion of eosinophils



Fitzgerald; Lancet Resp Med 2018

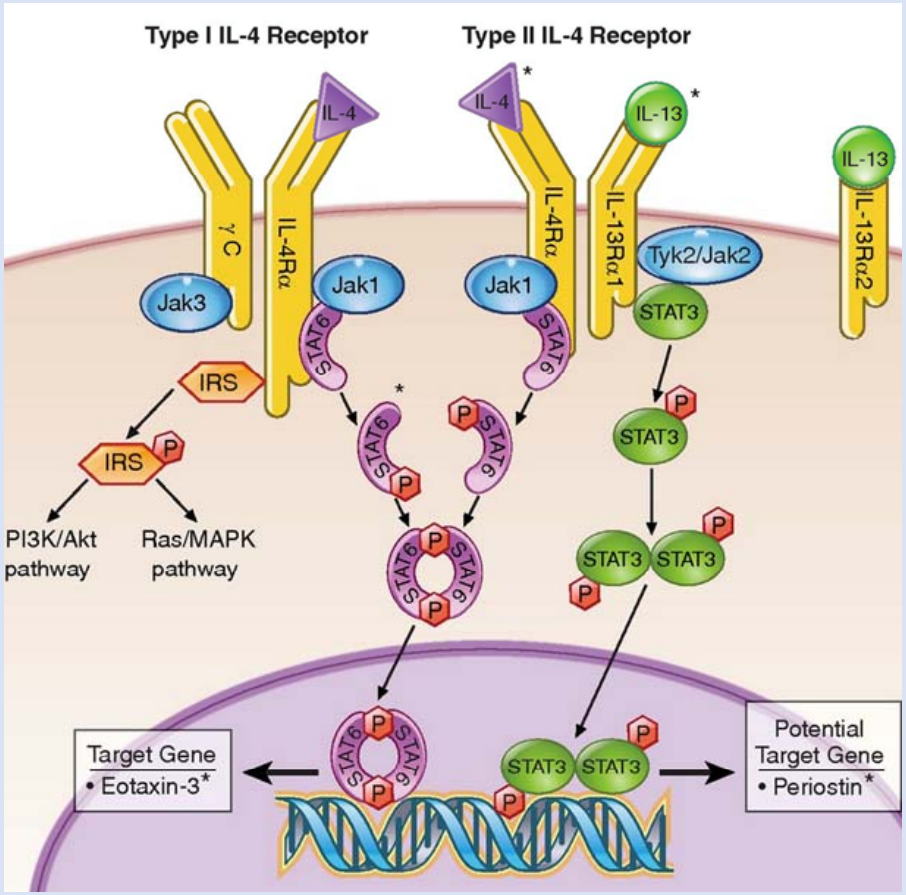
Anti-IL-5 Therapy: Clinical Trials

Agent	Study	Outcome
Mepolizumab Eo≥150	Ortega et al.[1] (N=576)	• 53% lower exacerbation rate vs placebo (P<0.001) • Zoster vaccine 4 weeks prior to initiation. • Reduction in glucocorticoid dose 2.39-times more likely vs placebo (P=0.008)
	Bel et al.[2] (N=135)	
Reslizumab Eo ≥ 400	Castro et al.[3] (N=953)	• Reduced exacerbation rate vs placebo (rate ratio 0.50 [study 1] and 0.41 [study 2]; both P<0.0001) • Significantly improved FEV_1 vs placebo (160 mL increase with 3.0 mg/kg dose; P=0.0018) • 3 cases of anaphylaxis, black box warning.
	Bjermer et al. [4] (N=315)	
Benralizumab Eo ≥ 150	Nair et al.[5] (N=220)	• 75% reduction in median final glucocorticoid dose vs 25% reduction with placebo (P<0.001)
	FitzGerald et al.[6] (N=1306)	• Lower annual exacerbation rate vs placebo • Rate 0.60 (q4weeks; P=0.0018), 0.66 (q8weeks; P=0.0188) vs. 0.93 (placebo):
	Ferguson et al.[7] (N=351)	• 80 mL greater improvement in FEV_1 vs placebo (P=0.04)

1. Bel EH, et al. *N Engl J Med*. 2014 25;371(13):1189-1197; 2. Ortega HG, et al. *N Engl J Med*. 2014;371(13):1198-1207; 3. Castro M, et al. *Lancet Respir Med* 2015;3: 355-366; 4. Bjermer L, et al. *Chest.* 2016;150(4):789-798; 5. Nair P, et al. *N Engl J Med.* 2017;376(25):2448-2458; 6. FitzGerald JM, et al. *Lancet.* Oct 29 2016;388(10056):2128-2141; 7. Ferguson GT, et al. *Lancet Respir Med.* Jul 2017;5(7):568-576.

Anti-IL-4/IL-13 Therapy

IL-4 and IL-13 signal through 2 overlapping receptors each containing a different subunit of the IL-4 alpha receptor. Promote production of IgE and recruitment of inflammatory cells, stiultes goblet cell hyperplasia, modulates airway hyperresponsiveness and airway remodeling



Cheng E, et al. *Am J Physiol Gastrointest Liver Physiol.* 2012;303(11):G1175-87.

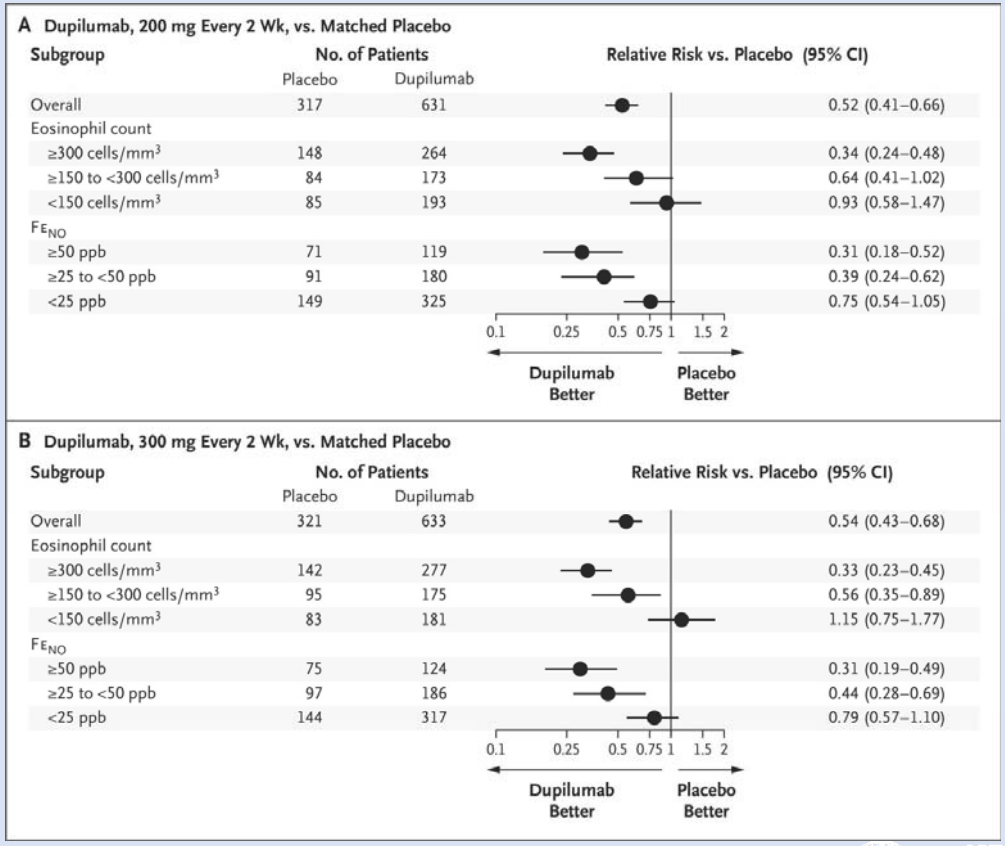
Dupilumab: Clinical Trials

Study	Patient population	Outcomes

Castro et al. 2018[1]	• Patients 12 years of age or older with uncontrolled asthma (N=1903)
	  • Add-on subcutaneous dupilumab at a dose of 200 or 300 mg every 2 weeks or matched-volume placebos for 52 weeks
		• Significantly lower rates of severe asthma exacerbation than those who received placebo
		  • 47.7% lower rate of severe asthma exacerbation among patients who received 200 mg dupilumab every 2 weeks than those who received placebo (P<0.001)
		• Better lung function and asthma control
		• Greater benefits were seen in patients with higher baseline levels of eosinophils

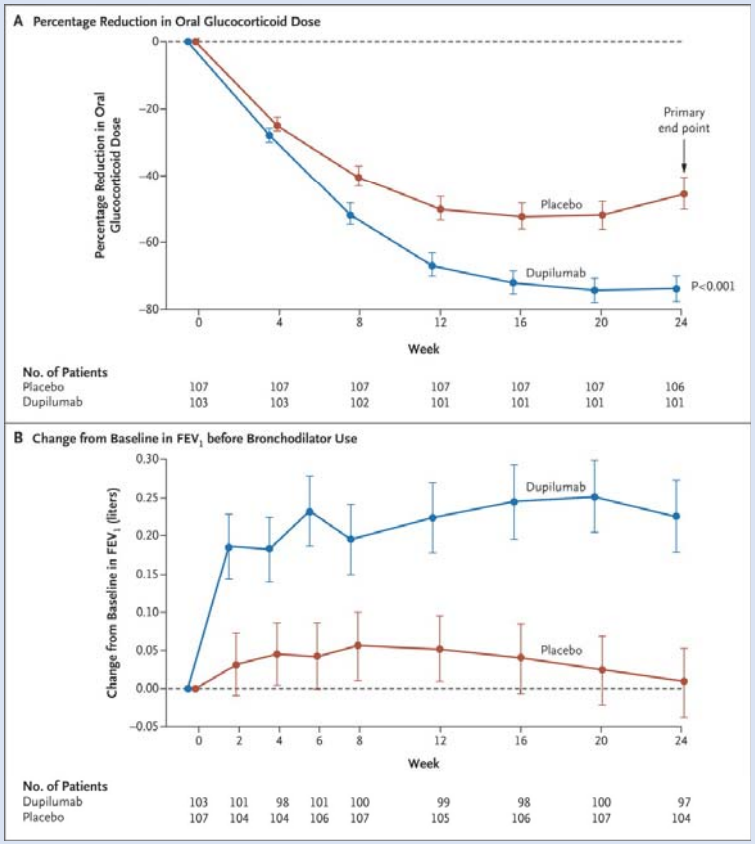
Castro M, et al. *N Engl J Med.* 2018;378(26):2486-2496.

Dupilumab reduces exacerbations in patients with eo count > 150



M Castro et al. N Engl J Med 2018;378:2486-2496.

Dupilumab reduces oral steroid dose and improves lung function in eosinophilic asthma



KF Rabe et al. N Engl J Med 2018;378:2475-2485.

Current FDA-approved Targeted Therapies

Monoclonal antibody	Target	Dosing	Dosing calculation	Treatable traits
Omalizumab	IgE	Subq q 2-4 weeks	IgE levels Weight	High IgE levels (30-700) + perennial allergens
Mepolizumab	IL-5	Subq q 4 weeks	100mg	Eosinophilic phenotype (> 150 cells/mcL)
Reslizumab	IL-5	IV q 4 weeks	Weight	Eosinophilic phenotype (> 400 cells/mcL)
Benralizumab	IL-5	Subq q 4 weeks x3, then q 8 weeks	30mg	Eosinophilic phenotype (> 150 cells/mcL)
Dupilumab	IL-4/ IL-13	Subq q 2 weeks	200mg or 300mg	Eosinophilic phenotype (>150 cells/mcL)

Bronchial thermoplasty

- Radiofrequency ablation of airway smooth muscle during three outpatient administered bronchoscopic sessions.

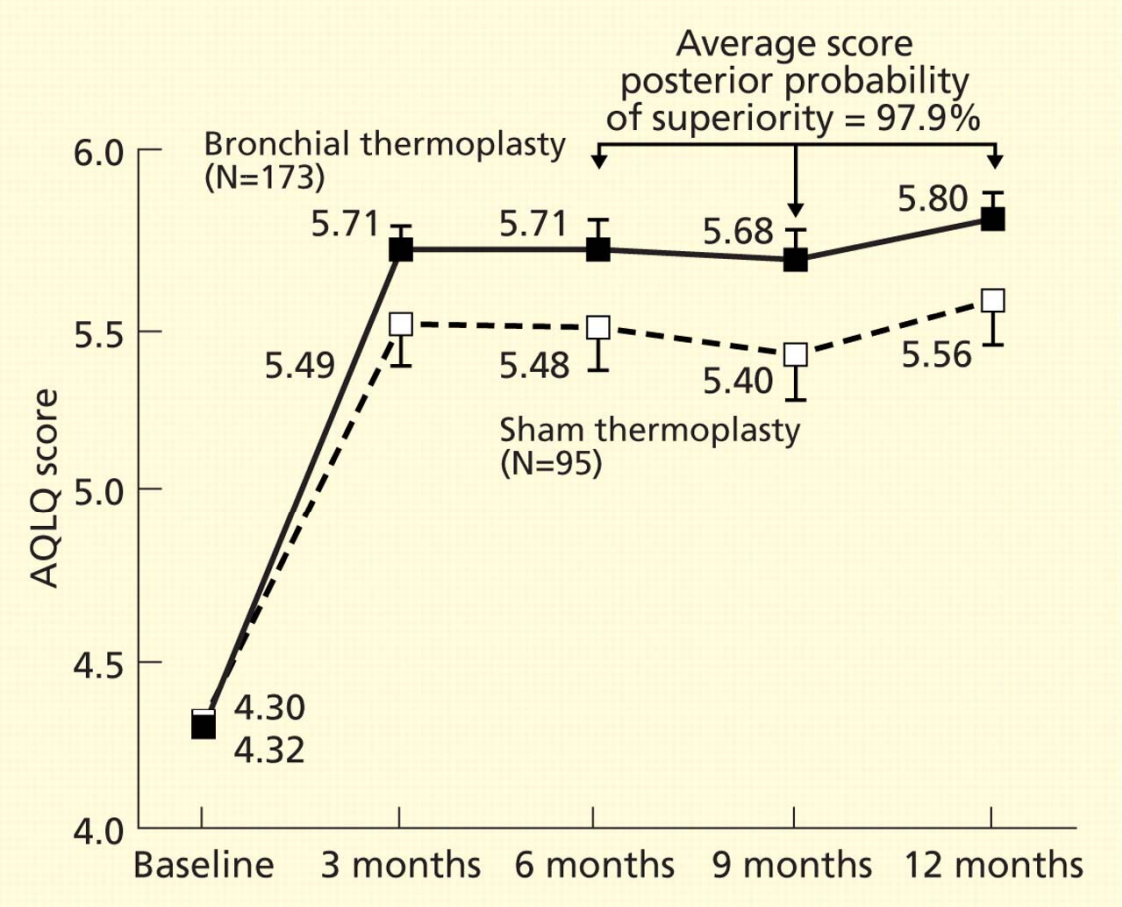
- Increase in exacerbations during the treatment periods and a large placebo effect, but reduced exacerbations and symptoms in the subsequent year. The trial excluded patients with three or more exacerbations per year, FEV1 < 60% or CRS.

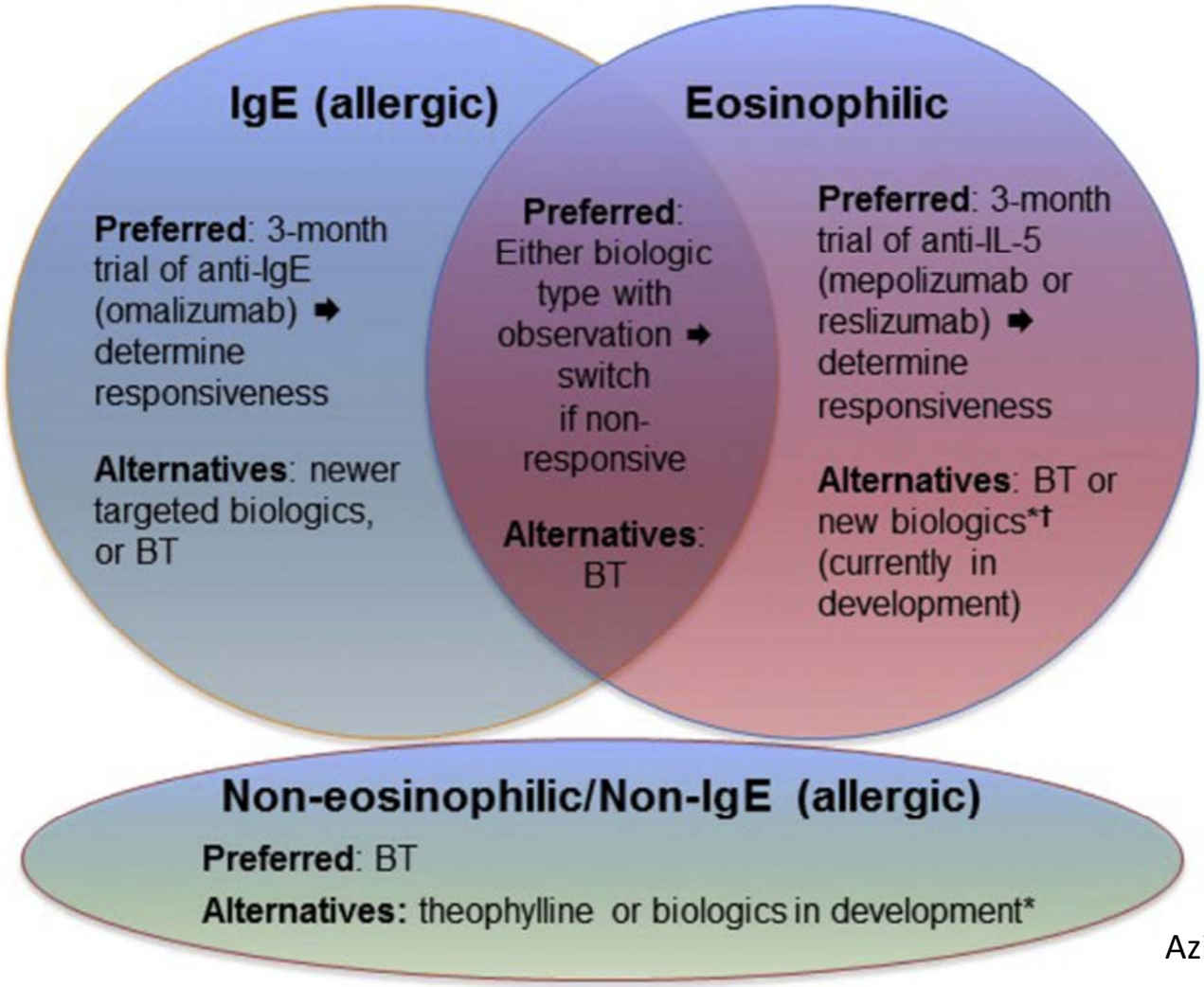
- Restrict to trials or registries.

Bronchial thermoplasty

-performed in bronchoscopy suite
-thermal energy to destroy bronchial smooth muscle cells in airways
-improves asthma quality of life, reduces exacerbations.

Thermoplasty improves asthma related quality of life

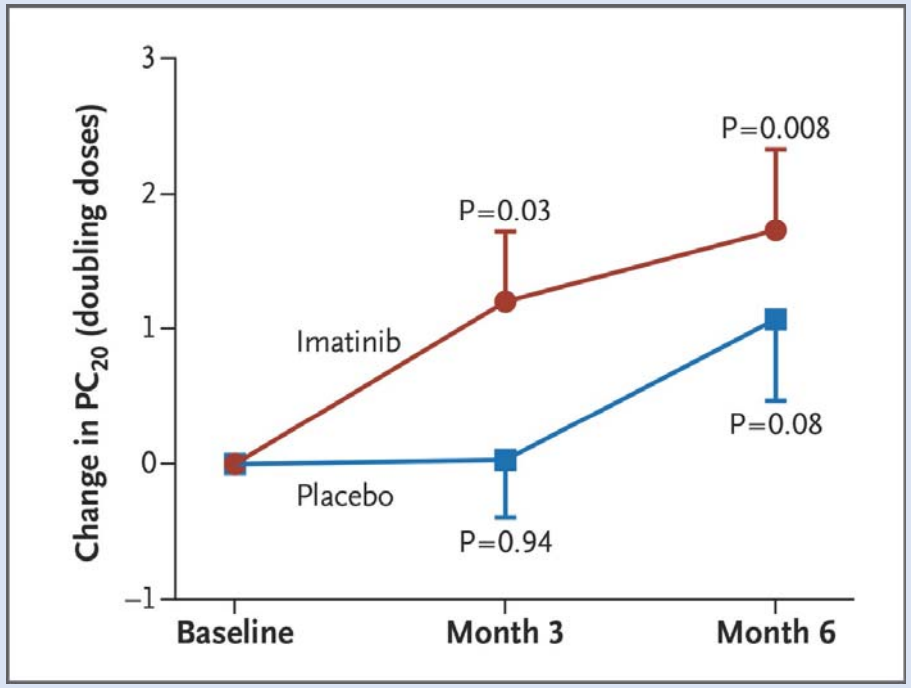


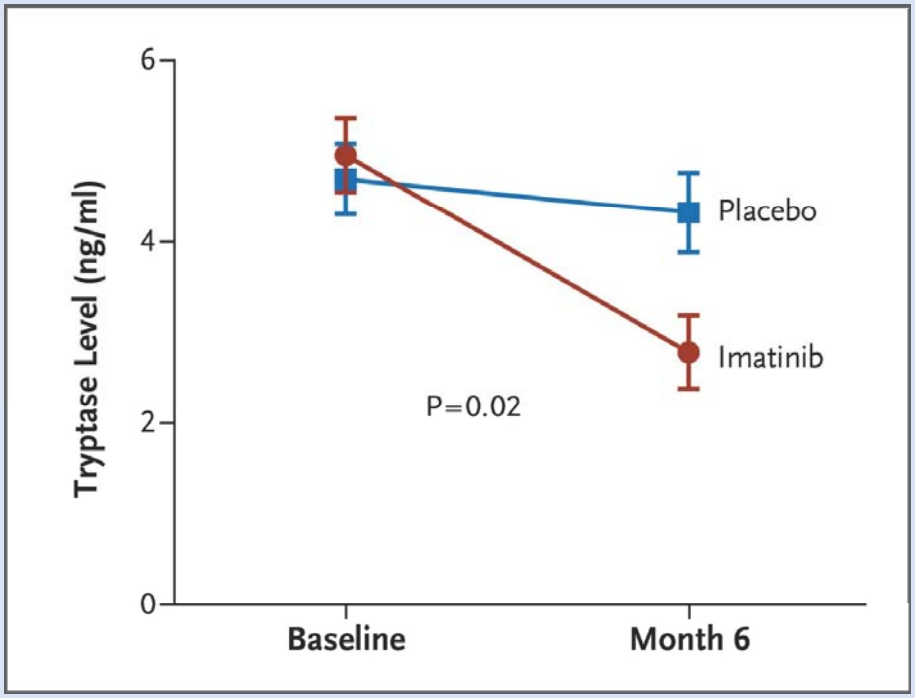


Azithromycin

Imatinib (KIT inhibitor) reduces airway hyper-responsiveness in severe asthma

KIT is a receptor for stem cell factor. Stem cell factor is increased in the serum of patients with asthma and correlates
With asthma severity. Imatinib reduces mast cell number and serum tryptase level in CML.

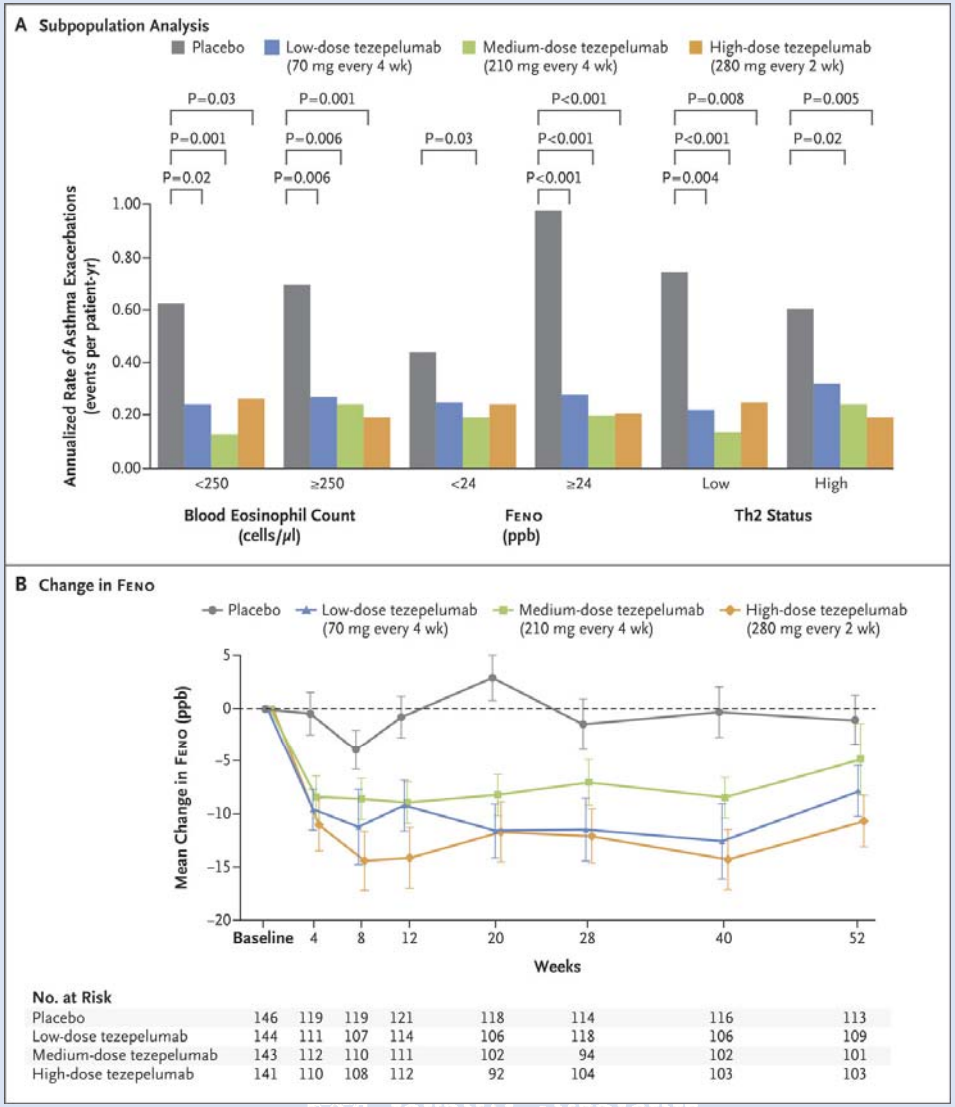




Cahill KN et al. N Engl J Med 2017;376:1911-1920.

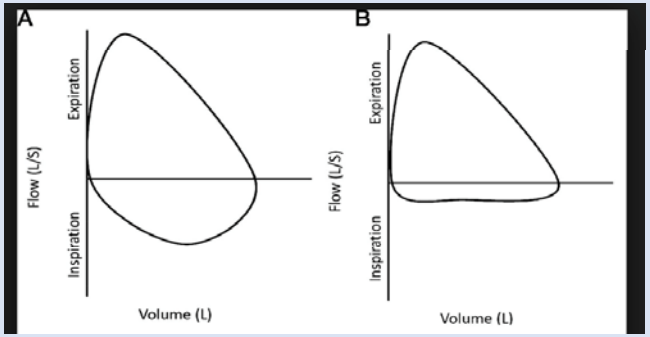
TEZEPELUMAB (TSLP INHIBITOR) EFFECT ON ASTHMA

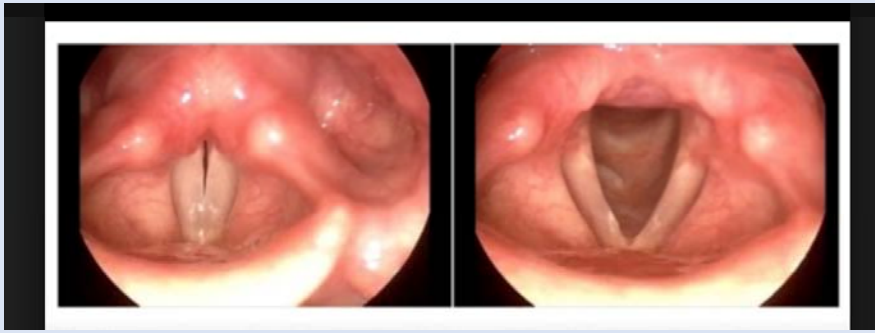
TSLP is central to regulation of T2 immunity, but many cell types relevant to asthma are activated By TSLP (mast cells, basophils, neutrophils)



Corren J et al. N Engl J Med 2017;377:936-946.

VOCAL CORD DYSFUNCTION





Suspect VCD:

- Exercise induced dyspnea, recurrent episodes of shortness of breath
- Frequent ED visits
- No response to asthma treatment
- Psychiatric comorbidities
- Respiratory distress without desaturation
- Inspiratory stridor
- Frequent intubations
- Rapid onset/rapid recovery
- Voice changes
- FEF/FIF50 > 1

Evaluation for Vocal cord dysfunction

- Difficult to diagnose if tested during asymptomatic period
- Often coexists with asthma but often misdiagnosed as asthma
- If normal spirometry, can perform methacholine to r/o asthma (ATS guidelines recommend doing I/E loops as the methacholine may promote VCD).
- Visualization of VC through laryngoscopy is recommended, but diagnostic only in about 50% of patients not actively having symptoms. Can perform during exercise
- Treatment: laryngeal control treatment, very effective; breathing techniques to control VC, anti-anxiety; botulinum toxin injection to laryngeal muscle in refractory cases.

Case

- 65 year old woman, asthma onset age 55 years; much worse beginning three years ago.
- Multiple steroid tapers despite high dose ICS/LABA, montelukast; taking 7.5mg prednisone daily at time of initial visit unable to wean.
- Daily symptoms, trouble exercising, trouble sleeping due to cough, wheeze, SOB.
- IgE 768, Blood eosinophil count 552
- Exacerbations often begin with sneezing
- RAST with allergy to cat dander and cockroach
- No obvious triggers in her home or work
- FEV1 56% predicted
- Chest CT LLL atelectasis, scattered bronchiolitis
- Two episodes short lived rash, never biopsied
- Sinus CT shows moderate disease

All of the following are appropriate interventions EXCEPT?

A. Initiate omalizumab

B. Initiate anti-IL5 antibody

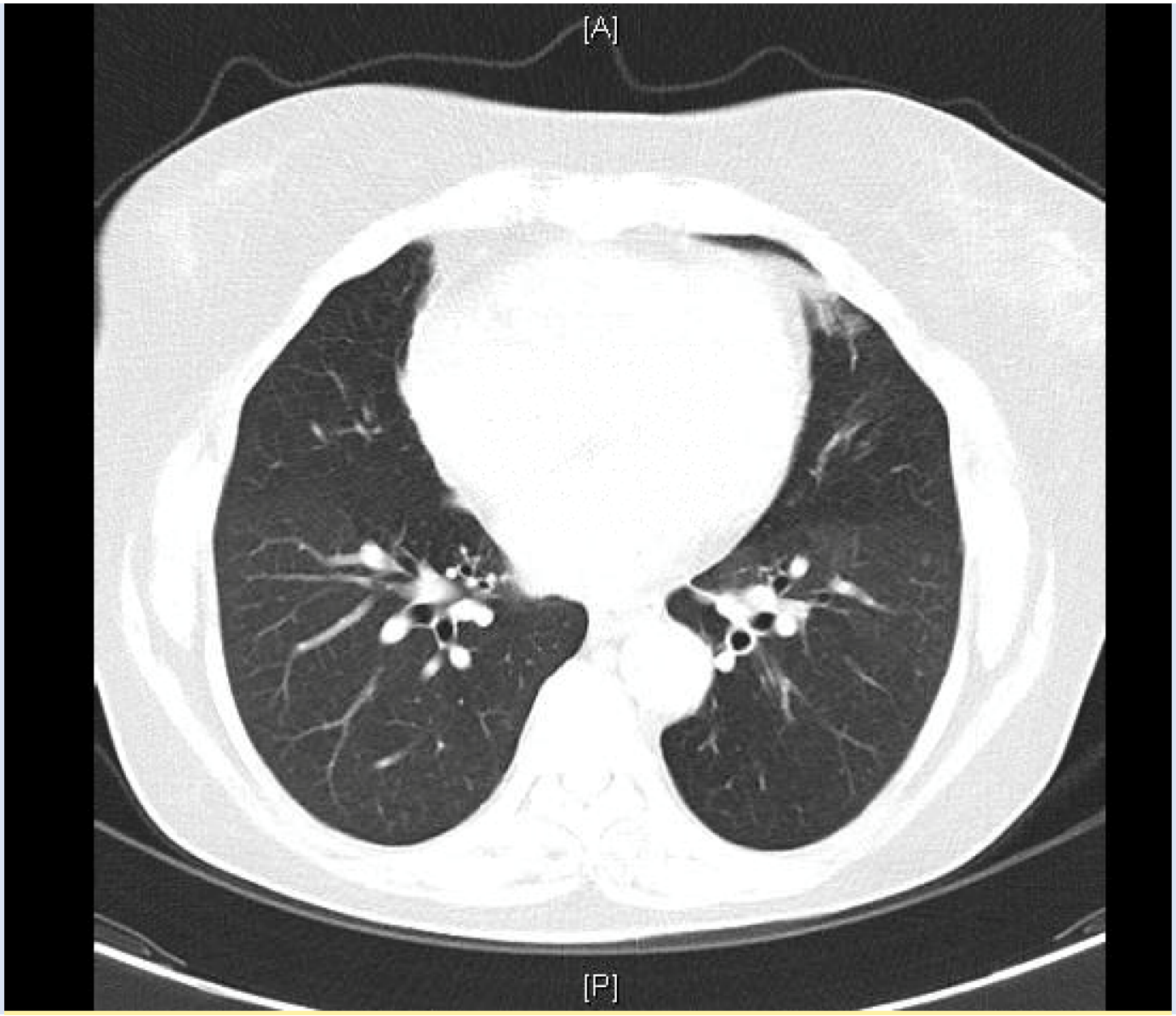
C. Allergen desensitization to cat and cockroach

D. Assess adherence

E. Review inhaler technique

Treatment

- Start omalizumab 375mg q2 weeks.
- After 6 months, able to wean off of prednisone.
- OK for 3 weeks, then recurrent wheeze and SOB, daily need for albuterol 2-3 times per day, wheeze on exam
- Eo count up from 552 to 1572.
- P-ANCA negative, ?Churg-Strauss without vasculitis
- Resume SLOW prednisone taper then maintain at 2.5mg daily
- Chest CT cylindrical LLL bronchiectasis, left lingular and RML atelectasis, b/l mild “tree in bud”
- Start mepolizumab 100mg daily (Shingrix vaccine). Doing well, pred stable at 2mg daily. Completely asymptomatic.


[A]
[P]

Another case

- 67 year old woman
- Lifelong asthma, very severe past 3 years, prednisone 10mg daily and still with symptoms.
- No allergy symptoms, RAST completely negative
- Continuous prednisone, unable to wean below 10mg daily prednisone, still with daily symptoms, interrupted sleep
- Multiple hospitalizations
- Moderate OVD on PFT
- Eo count ranges 110-440
- Start mepolizumab, no effect. Patient increasingly depressed.
- Empirically switch to reslizumab with marked improvement. Off prednisone for past 9 months.

Using Targeted Therapies in Practice

- Most patients with type 2 asthma can achieve good control with ICS/LABA
- About 5%-10% require additional treatment – targeted therapies
- Current biologics address type 2 inflammation only
- Before initiating targeted agents:
  - Identify asthma phenotype (if possible), eg, allergic asthma
  - Order appropriate testing, eg, serum IgE, eosinophils, FENO
- Choice of targeted agent based on features of asthma presentation and test results
  - Allergic asthma, anti-IgE or anti-IL5 or IL4/IL13
  - Eosinophilic asthma: anti-IL-5 or IL4/IL13

Summary

- Severe/uncontrolled asthma is difficult to treat
- Assess:
  - Adherence
  - Inhaler technique
  - Comorbidities
  - Environmental factors
- Asthma phenotypes/endotypes may inform treatment choices
- In appropriate patients, targeted therapies can reduce corticosteroid use, exacerbation rate, asthma symptoms and improve lung function and quality of life
- Use appropriate testing before selecting targeted therapy