Immunotherapy/Biologics and Asthma

ATS Fellows Track Symposium 2020

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Introduction/Objectives

cs: severe asthma

elines thus far

Biologics selection and assessment

rse effects

ching biologics

r indications

t's now and what's next?

Asthma:
Inflammatory Changes
in Airway Wall

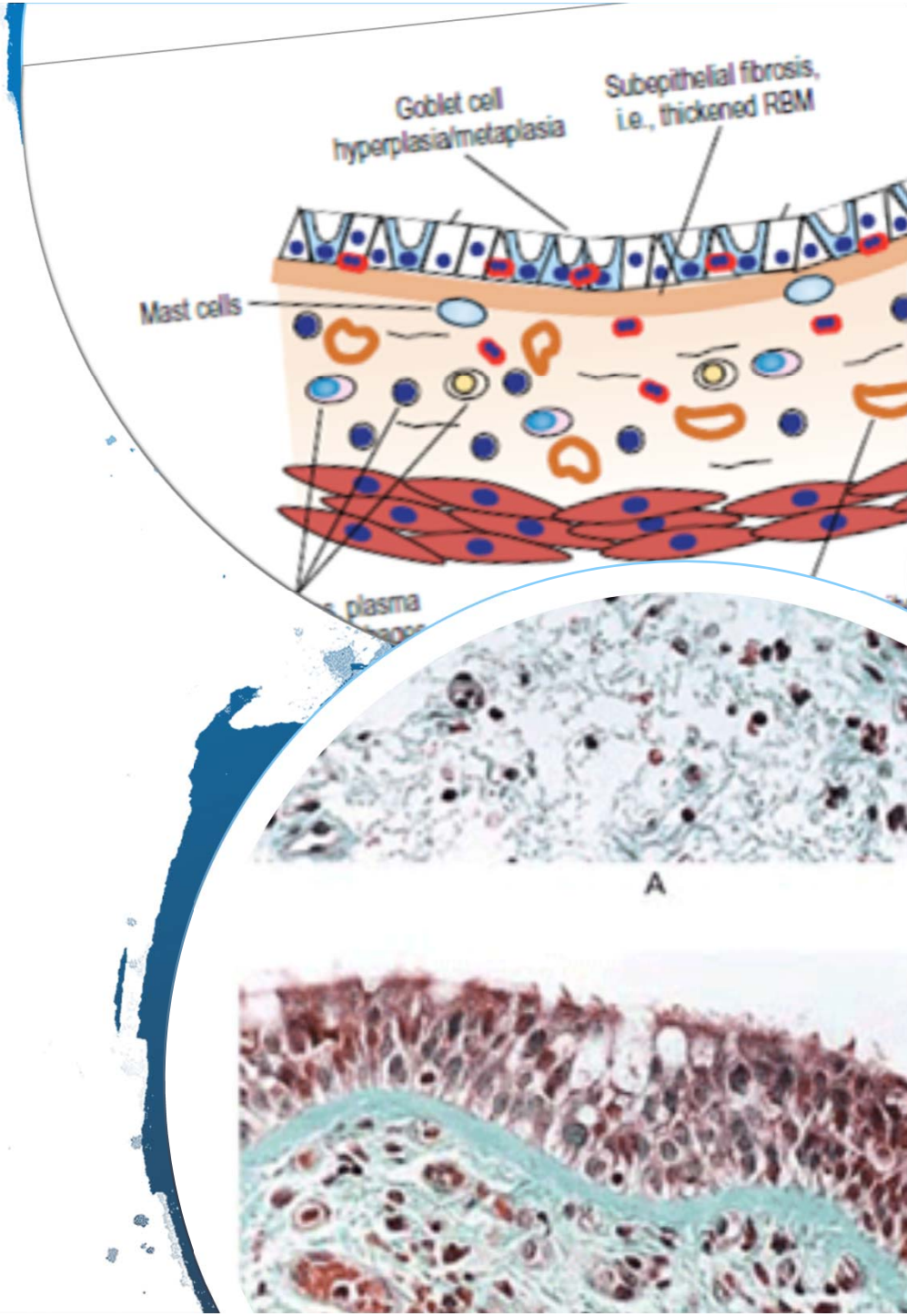
Recruitment and accumulation of
eosinophils, mast cells, lymphocytes

<u>Resulting structural changes</u>:

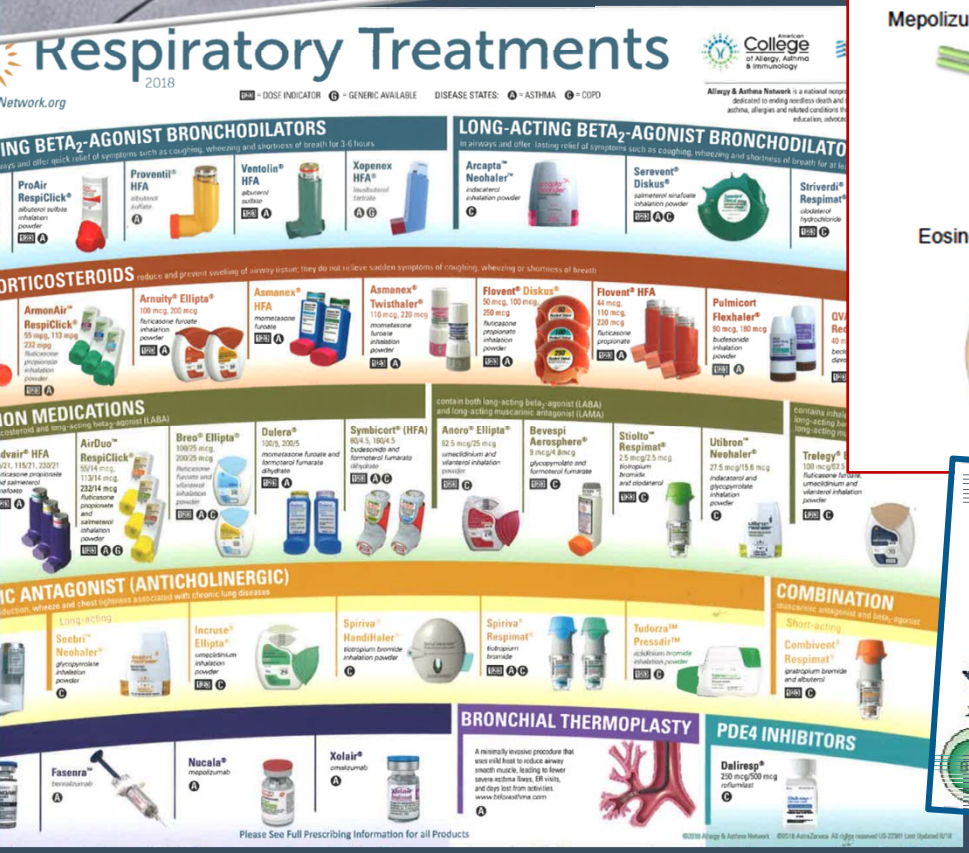
Goblet cell hyperplasia

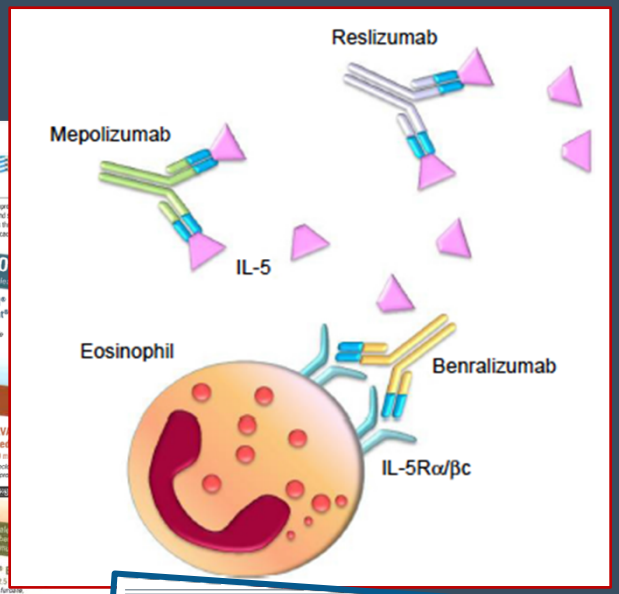
Thickening of basement membrane

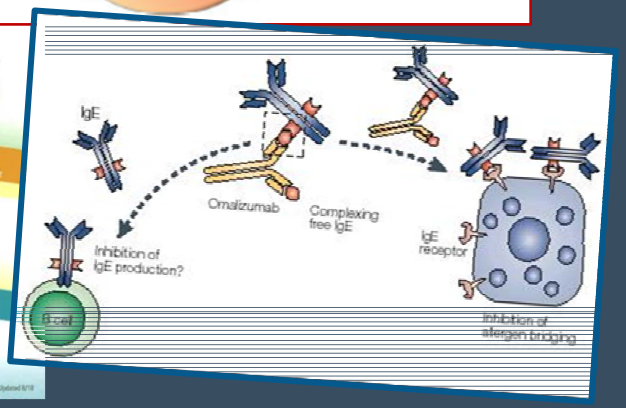
Increased vascularity

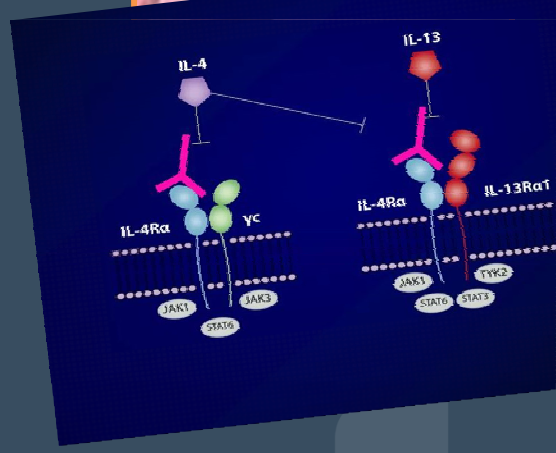


To now a selection of therapies to a more personalized care









Palaia 2016: Therapuetics and Clinical Risk Mgt

Case 1- 62 M severe asthma

tially seen at age 53 in 2011
 yrs hx of asthma, nonsmoker
ednisone only controls it
On MTX weekly
E: osteoporosis, neuropathy

uled out ABPA
ptimized regimen
onch with 33% lymphs
m mm hypertrophy, goblet cells, eos

nderwent BT did much better

Case 1- 62 M comes back

tially seen at age 53 in 2011
yrs hx of asthma, nonsmoker
ednisone only controls it
On MTX weekly
E: osteoporosis, neuropathy

uled out ABPA
ptimized regimen
onch with 33% lymphs
m mm hypertrophy, goblet cells, eos

nderwent BT did much better

Worsened again with symptoms

Never really got off prednisone after BT

Over months, weaned off prednisone

Continued ICS/LABA, stopped zileuton

Spirometry 80% without sig BDR

Case 1-what would you do next?

1) Start a biologic therapy
2) Review symptoms and reassess
3) Repeat thermoplasty (it worked before)
4) Chronic oral steroid therapy

Case 1

Revisited diagnosis, GERD uncontrolled

Sinus treatment optimized

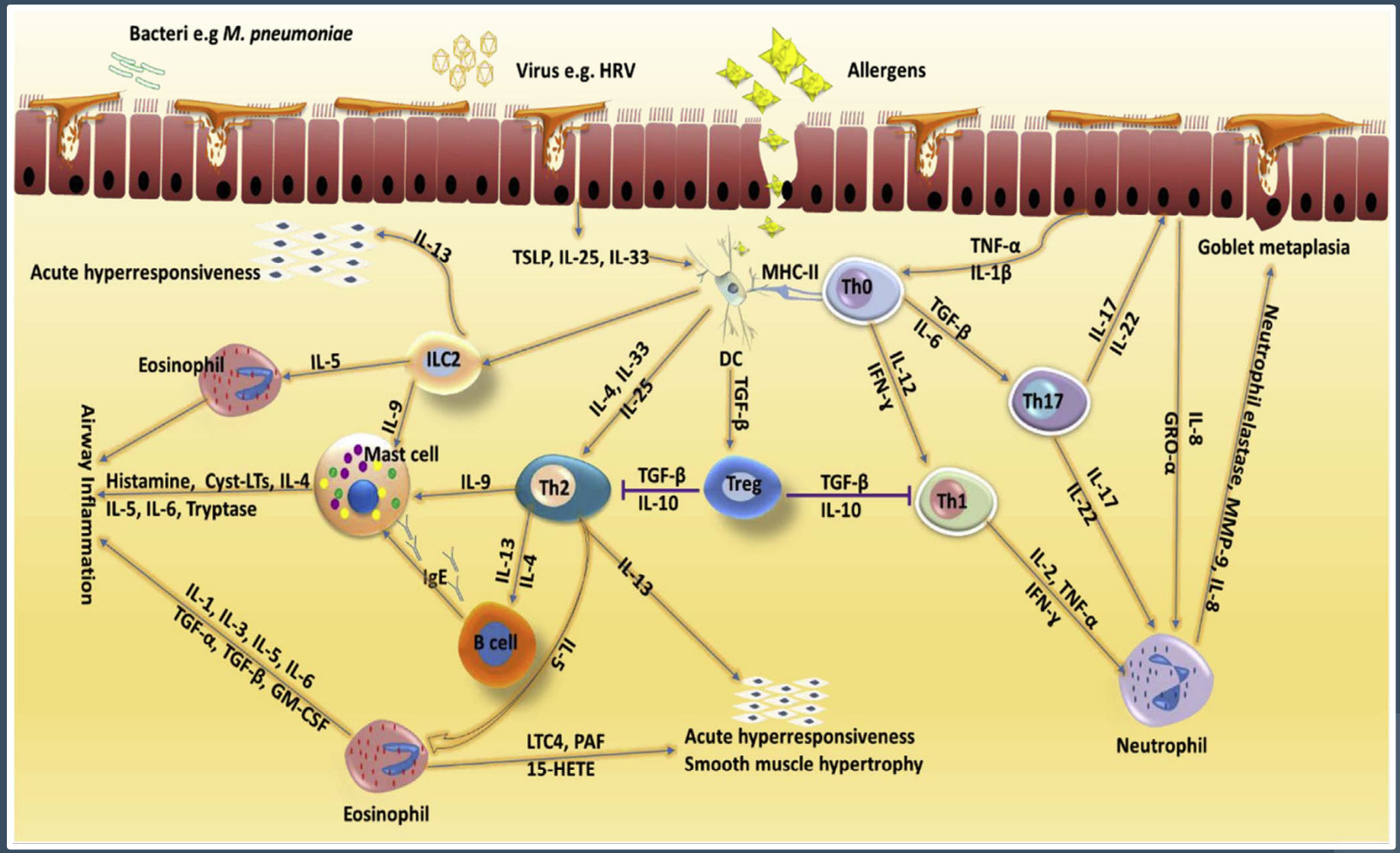
While off steroids, CBC diff obtained

Started mepolizumab

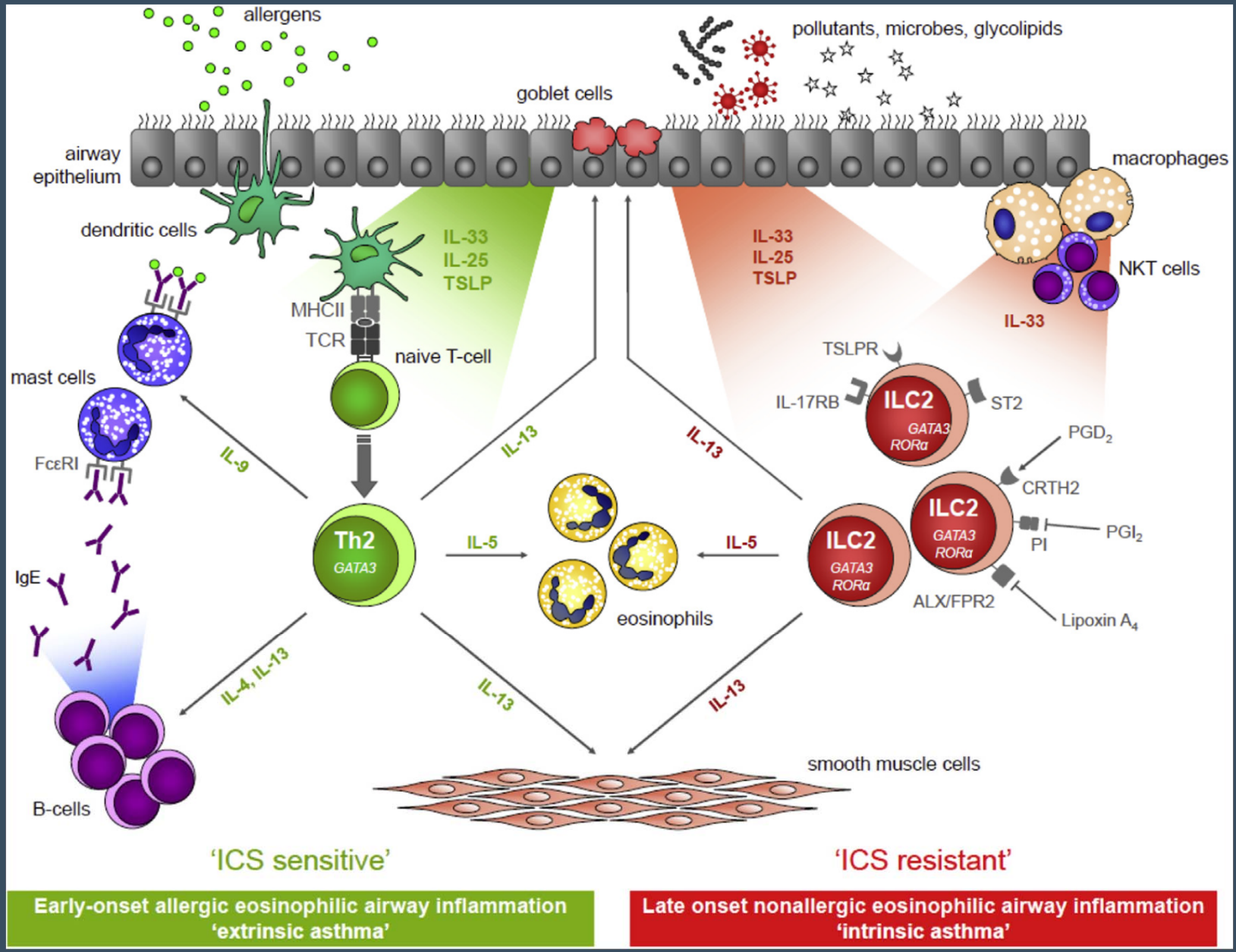
Significantly better ACT = 20

off steroids ‘I have my life back’

Biologics for Asthma



Sulaiman 2016: Pulm Pharmacol and Ther



Bel E, ten Brinke A; Chest 2017; 152

What makes severe asthma different?

Severe asthma:

- Asthma that requires tx with high dose ICS + second controller and/o systemic corticosteroids to prevent it from becoming 'uncontrolled' or that remains 'uncontrolled' despite this therapy.

- Uncontrolled asthma: poor sx control, freq severe exacerbation (>=2 bursts of systemic CS in past yr,) exacerbations-1 hosp, ICU or mech vent in prior yr; FEV1< 80%

Relatively large proportion of resource expenditure although only 10% prevalence

ERS/ATS CP guidelines Severe Asth

evere Asthma: From phenotypes to endotype

Phenotype

Observable characteristics

Airflow limitation, age, eosinophilic, etc.

Hereditary, early onset allergic asthma

Poorly reversible, very severe, neutrophilic asthma

Late onset eosinophilic asthma

Late onset, symptom dominant obese minimal inflammation

Endotype

- Subtype of a condition defined by distinct functional or pathophysiol mechanism
- Biomarker, genetic element or pathobiology, stable over time wh has a robust response to therapy

Wenzel Clin Exp Allergy 2012

Evolving Endotypes for Asthma

	Natural Hx	Clinical	Genetics/ Pathobiology	Biomarkers	Tx Response
Severe early onset allergic	Childhood/ progressive	Allergic disease	Th2, eos?	Hi Exhaled NO, IgE	Steroids, Th2 blockers
Late onset, persistently eosinophiic	Adult onset	Sinusitis, polyps, AERD Steroid refractory	Leukotriene pthway	Blood/pulm eos despite GC, csLT, IL-5	Anti-IL5, Th2 modifiers
ABPM	Usu adult onset, persistent	Cough, mucus, central b'ectasis	CFTR? Blood/lung eos	Fungus specific IgE and IgG	Steroids, antifungal, anti-IgE
Obese-female	Very late onset	Enhanced sx, less obstrn, hormonal		Adipokines	Weight loss, not steroid responsive
Neutrophilic	Exposures, pollution, viral	Fixed airway obstn	Neutrophilic, ? innate immune activation	BAL or sputum neutrophils, Th17, IL-18	Macrolides

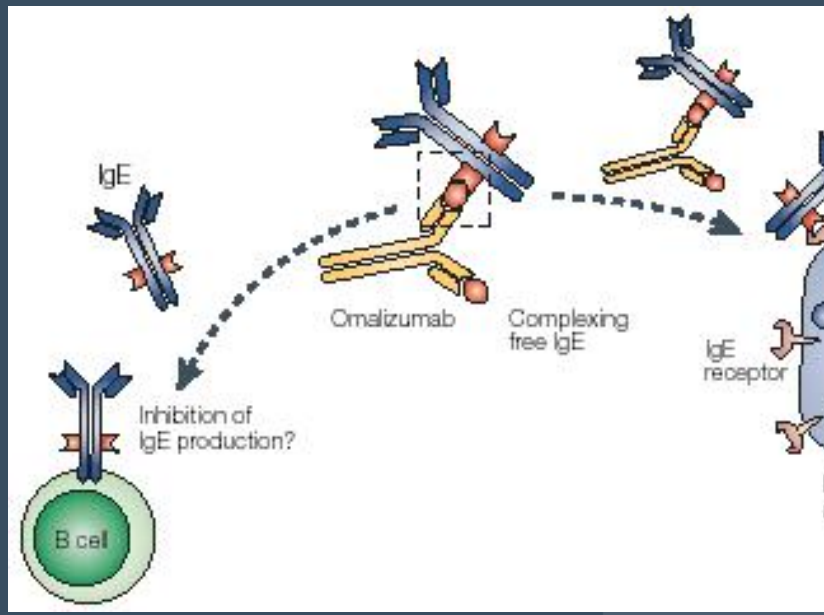
Omalizumab
Severe atopic, steroid dependent asthma

Anti IgE Ab: Omalizumab - 2003

neutralization therapy

Reduced exacerbation rate, risk of hospitalization

- IgE 30-700 IU/mL
- Recombinant mAb down-regulates IgE receptors, blunting allergic reaction



Humber M, Busse W, Hanania et al. JACI 2

Partner with allergist

- Severe asthma
  - Pheno-endotype with IgE and skin test/RAST
  - Optimize management
- Control other factors
  - Comorbidities
- Consider Omalizumab and refer for AIT
  - Counsel patients-disease modifying approach

Omalizumab with AIT

Omalizumab pretreatment

↑ safety and tolerability of cluster and rush immunotherapy schedu
n pts with moderate persistent asthma and AR

More effective together than with AIT alone

mproved symptoms load and asthma control

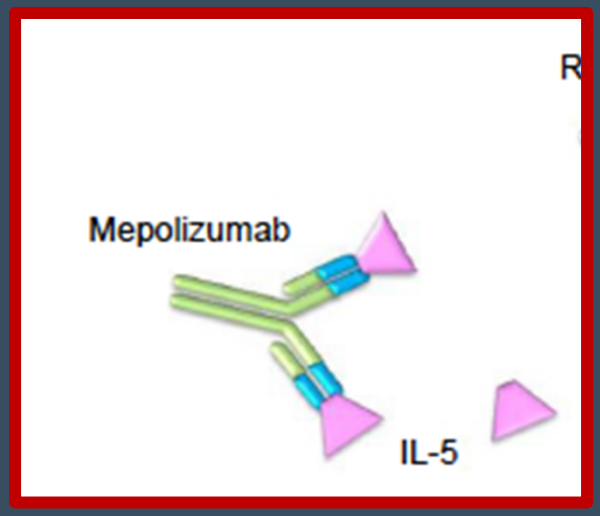
Adding Omalizumab tx to birch and grass AIT resulted in less rescue me
use and sx days c/w Omalizumab or AIT alone

Reduce rate of systemic reactions

Kopp JACI 2002, Kuehr JACI 2002

epolizumab- mAb directly binds IL-5

Approved 2015 for ≥12 yr and older
- 100 mg every 4 weeks
- self administration syringe July 2019



Reduces exacerbation rate (by ~ 50%)

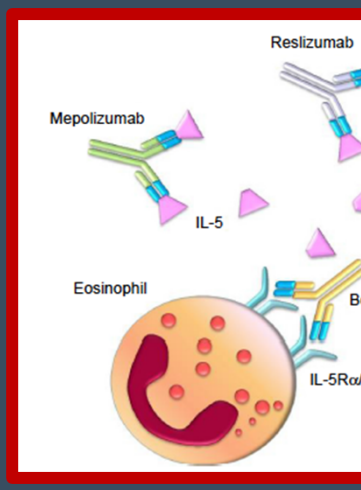
Reduces sputum and blood eosinophils

mproves asthma control

Glucocorticoid-sparing effect (2.39 more likely with tx)

Pavord D. et al. Lancet 380 2012; Ortega H et al. NEJM 2014; Bel et al NEJ

nti-IL5 Reslizumab- mAb



proved in 2016

ight-based IV

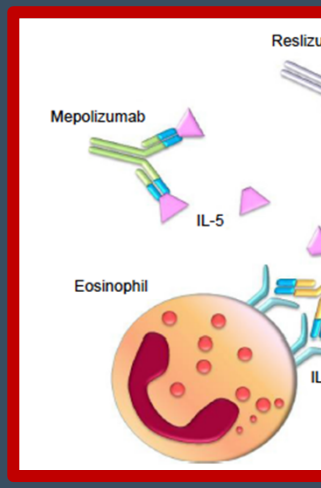
- Best response with high eosinophils and nasal polyps
- Subgroup with > 400 eos/uL:
  - significant mean FEV_1 increase 270 mL vs. placebo)

ibits IL-5 from binding to IL-5 receptor on eosinophils

duces frequency of asthma exacerbations

Castro M, et al. Lancet Respir Med. 2015

Benralizumab (Anti-IL 5 receptor α mAb)



proved in 2017

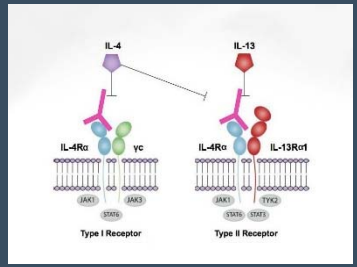
- Reduction in exacerbations by 51%
- Increased lung function, improved symptom control
- Oral steroid-sparing effect-reduces OCS on avg by 75% and total discontinuation in 52%
- Reduced hospitalization by 60%

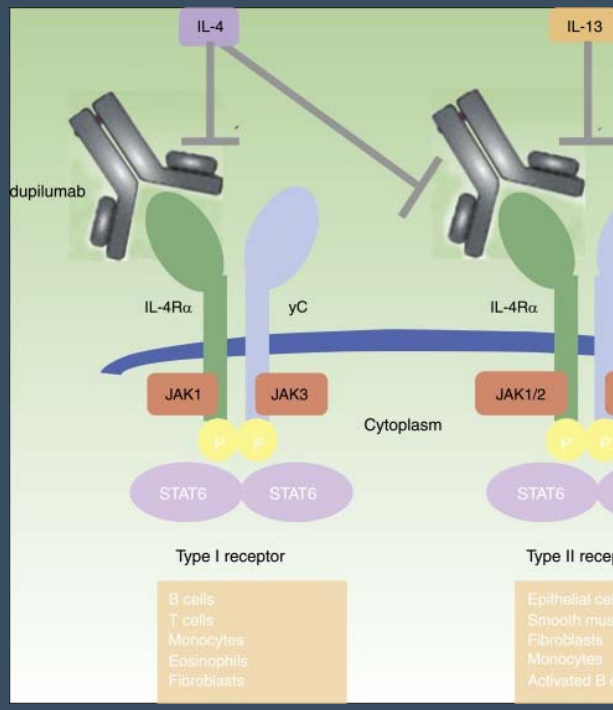
Palaia 2016: Therapuetics and Cl

gets IL 5 receptor α results in apoptosis of eos and sophils via Ab-dependent cytotoxicity

FitzGerald JM, et al Lancet. 2016.

Dupilumab
(Anti IL-4 R α / IL-13)





Sciencec

- Approved 2017 now mod-sev asthma
- Inhibits IL-4 and IL-13 signaling
- Initial indication: atopic dermatitis
- Newer Indications ages ≥ 12:
  - severe eosinophilic asthma
  - nasal polyposis
- Asthma: better control (reduced exacerbation by 50-70%)
  - Improved lung function (29-33%), steroid sparing (off OCS in 50%)
- Dosing variable:
  - Loading dose 600mg then 300 mg q 2 weeks or 200 mg q 2 weeks SQ

Wenzel et al. Lancet 2016; Castro et al NE

logic therapy-Biomarkers for guidance
dict efficacy?

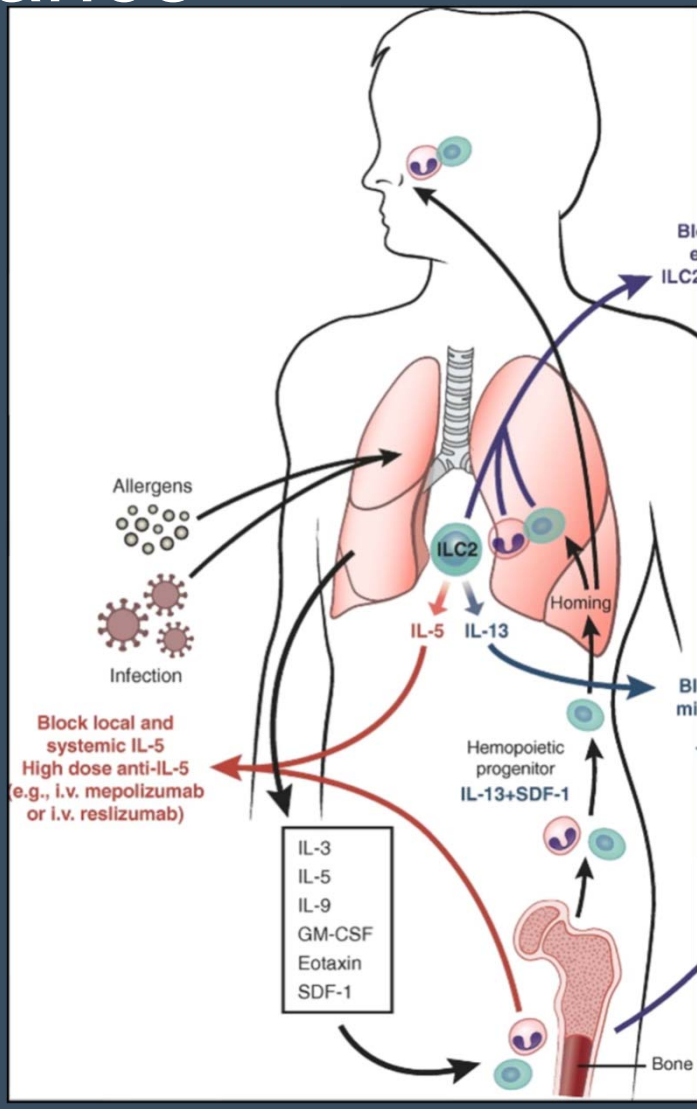
Omalizumab - high eos, high FeNO

Mepolizumab - eos ≥ 300 cells/uL

Reslizumab - eos ≥ 400 cells/uL

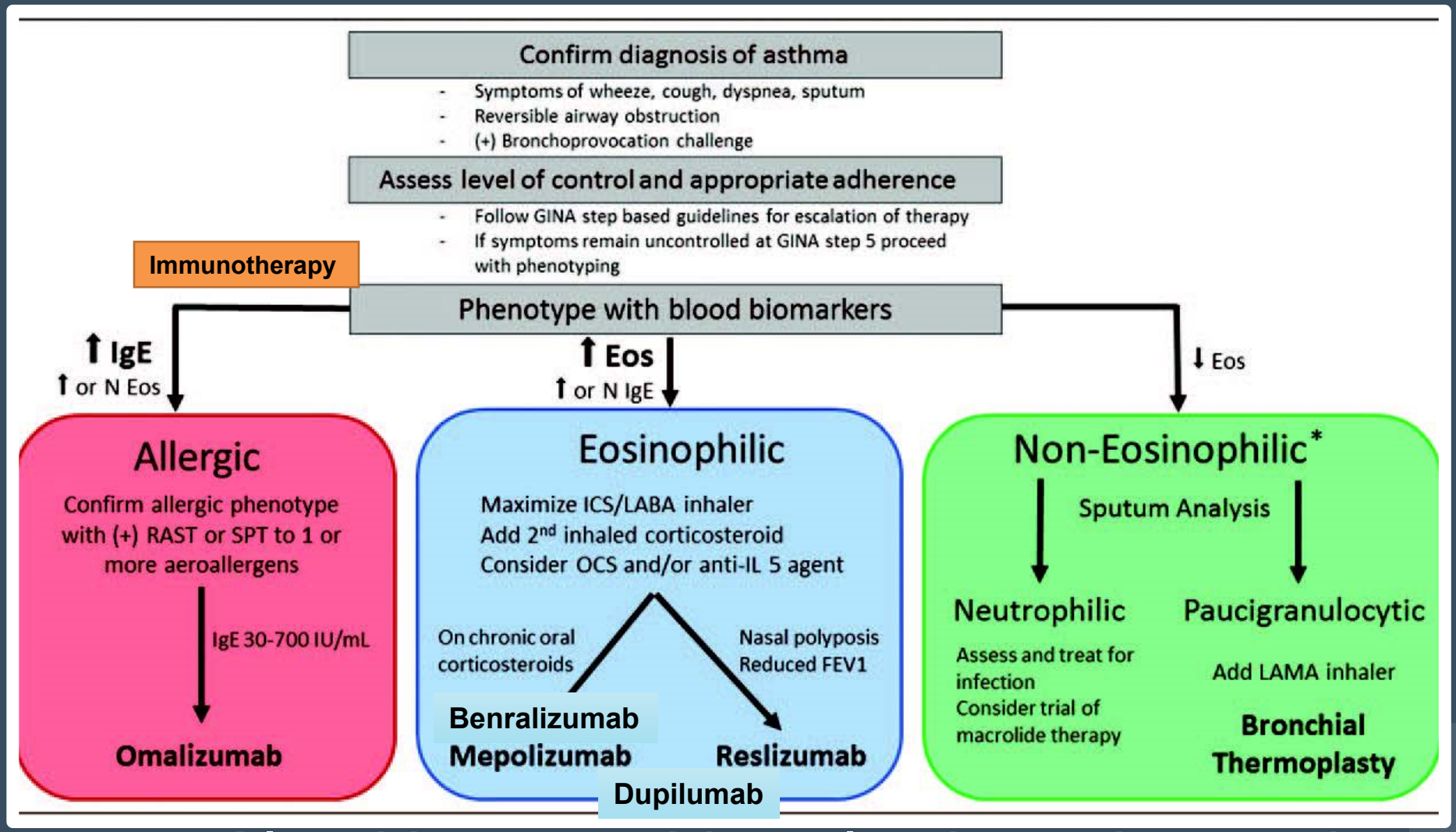
Benralizumab - any eos

Dupilumab - eos ≥ 300 cells/uL



McGregor Am J Respir Crit Care Med, 20

How does everything fit in?



Algorithm to guide selection advanced therapies for (severe) asthma

Adapted from Oberle Current Opinion Pulm Med 20

Case 2: Path to success(?)

54 M longstanding patient
- Developed asthma worsening in 2012, initial FEV_1 best was 78%
- Mucus production/thick
- Variable adherence
- + atopic with + eos
- Chronic sinusitis

Ratio 57%, FEV_1 62% *(proven BDR in past)*
- Optimized management and treated GERD

At FU, FEV_1 remained at 53% and ACT = 12
- Added nebulized medications + LAMA therapy

Case 2: Path to success(?)

54 M longstanding patient
- Developed asthma worsening in 2012
- Mucus production/thick
- Variable adherence
- + atopic with + eos
- Chronic sinusitis

STILL NOT BETTE

Only prednisone h

Ratio 57%, FEV_1 62% *(proven BDR in past)*
- Optimized management and treated GERD

FEV_1 stayed at 53% and ACT = 12 *and then as low as 40%*
- Added nebulized medications + LAMA therapy

What would you do next?

1) Bronchoscopy to evaluate severe asthma
2) CT chest
3) Initiate Omalizumab therapy
4) Evaluate for sinus surgery

How we got to 65%

CT chest progressive worse from prior:

- diffuse central/periph bronchial wall thickening, mucoid impactions, G

Agreed to omalizumab → duration of stability

- 1 yr later, unsatisfactory results, started benralizumab

Stagnant lung function (low) at 35-40%

- Bronch no sig eos (benra) but PMNs 53 - PCR mycoplasma/chlamyc neg
- EBBx: BM thickening, smooth muscle hypertrophy
- possible ABPA/SAFS – added vori did better, however d/c'd (↑d LFTs

After 8 doses of benralizumab switched to dupilumab

- Hx of nasal polyposis and chronic rhinosinusitis

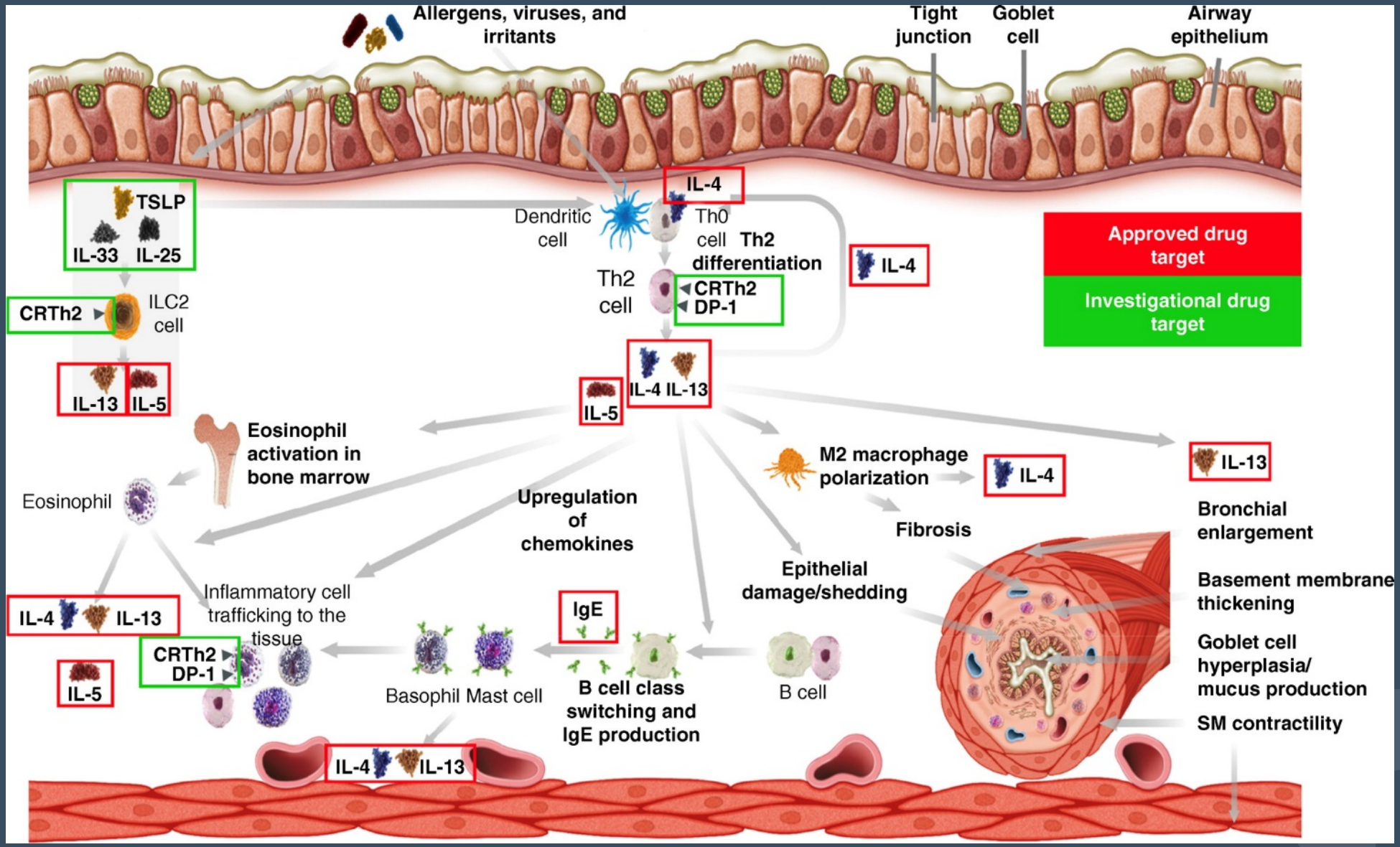
Emerging therapies

Target receptors

- Toll-like receptor activator
- Chemoattractant receptor homologous molecule on TH2 (CRTH2)
- Proteinase-activated receptor 2 (PAR-2)
- Calcium sensing receptor (CaSR) antagonism
- H4 receptor antagonism

Transcription Factors

- Biologics
  - Anti-IL5, 13, IL4Rα
  - Anti-IL17
  - Anti-TNF
  - Anti-TSLP
- Enzymatic Targets
  - Rho-kinase inhibitor
  - PDE4 Inhibitor (roflumilast)
  - iNOS and arginase inhibitor



Am J Respir Crit Care Med, 2019
https://www.atsjournals.org/doi/abs/10.1164/rccm.201810-1944CI

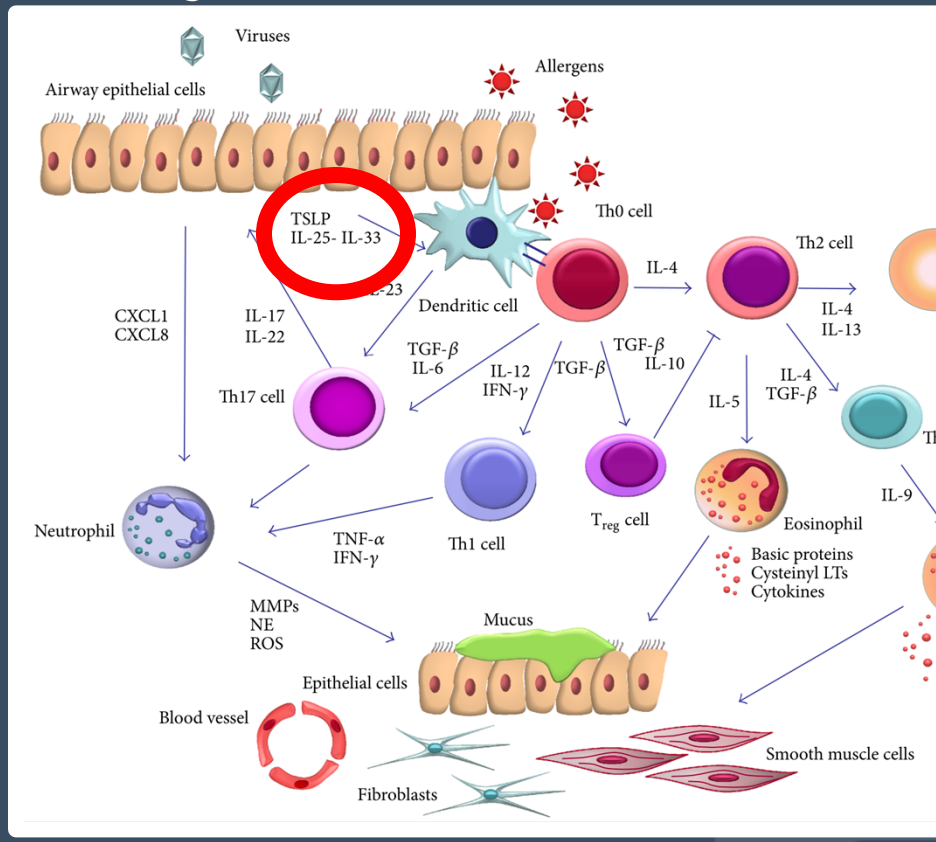
Tezepelumab (anti-TSLP) Targets upstream cytokine

Anti-TSLP

- Expression higher in asthma airways
- IgG2 mAB, binds prevents interaction with TSLP complex → increased cytokines Th2 cells

Tx demonstrated lower rates asthma exacerbation, regardless baseline eos counts, Th2 status

- Substantial decreases in eos and FeNO
- influencing more than a single downstream pathway
- Phase 3 trials underway



Courtesy of Mark Aronica

Corren et al NEJM 2017

Guidelines

EPR4

ERS/ATS

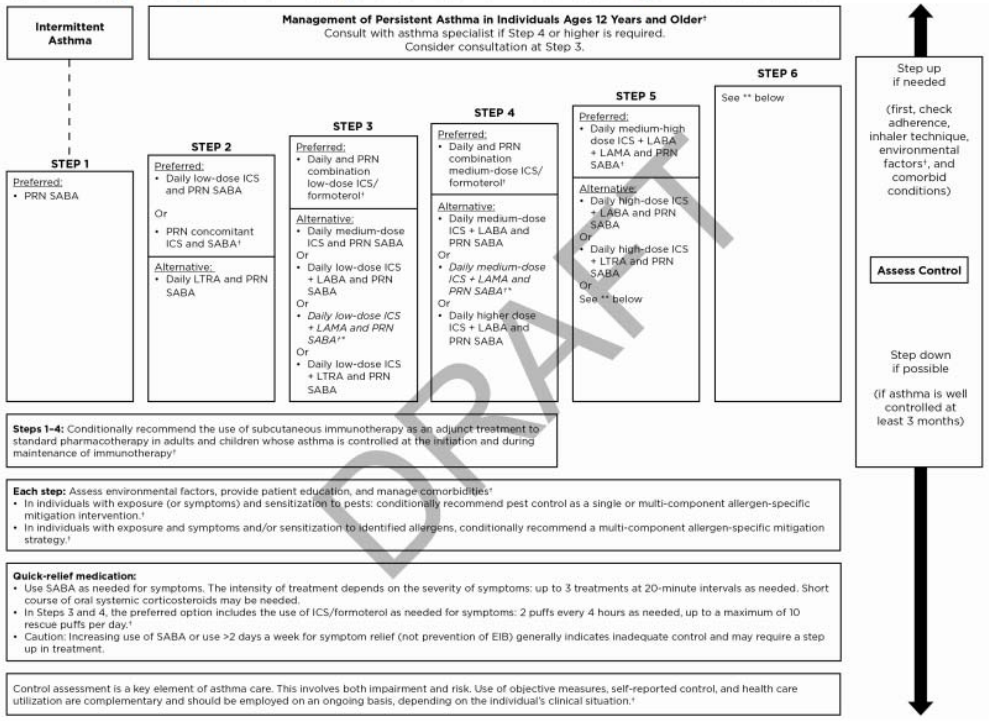
GINA

Consensus / Workshop documents

NHLBI/EPR4

Did not specifically have recommendations on biolog therapy (IgE/IL-5)
Suggested reference: ERS/ATS

467 **Figure iii Stepwise Approach for Management of Asthma in Individuals Ages 12 Years and Older**



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Notes for Individuals Ages 12+ Years Diagram

- Abbreviations: ICS, inhaled corticosteroid; LABA, inhaled long-acting beta2-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta2-agonist; EIB, exercise-induced bronchoconstriction; PRN, as needed
- † = Updated based on the 2020 guidelines.
- ‡ - The term "pests" in the diagram refers to mice and cockroaches. These were specifically examined in the evidence reviewed.
- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- Review the Integration of the New Recommendations into Asthma Care section of the guideline for guidance on how to use the diagram.
- Where formoterol is specified in the steps, it is because the evidence is based on studies specific to formoterol.
- If there is uncertainty in choosing, monitoring, or adjusting anti-inflammatory therapies based on history, clinical findings and spirometry, FeNO measurement is conditionally recommended as part of an ongoing asthma monitoring and management strategy that includes frequent assessments.
- Bronchial thermoplasty was evaluated in Step 6. The outcome was a conditional recommendation against the therapy.
- **The evidence-based reviews that informed the GRADE methodology employed in this report did not include studies that examined the role of anti-IgE or more recently FDA-approved biologics (anti-IL5, anti-IL5R, anti-IL4/IL13). Thus, this report does not contain specific recommendations for the use of biologics in asthma in Steps 5 and 6. Readers are referred to a recently released guideline on the management of severe asthma that also used GRADE methodology for further information (Holguin F, Cardet JC, Chung KF, et al. Management of Severe Asthma: a European Respiratory Society/American Thoracic Society Guideline. Eur Respir J 2019; in press [https://doi.org/10.1183/13993003.00588-2019]).

uidelines *ERS ATS*

ERS OFFICIAL DOCUMENTS
ERS/ATS GUIDELINES

Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline

TABLE 2 European Respiratory Society (ERS)/American Thoracic Society (ATS) Severe Asthma Task Force recommendations for the management of severe asthma

Question	Recommendation	Strength	Quality of evidence
1	We suggest an anti-IL-5 strategy as add-on therapy for adult patients with severe uncontrolled asthma with an eosinophilic phenotype and for those with severe corticosteroid-dependent asthma	Conditional	Low
2	We suggest that a blood eosinophil cut-point $\geqslant 150\ \mu L^{-1}$ can be used to guide anti-IL-5 initiation in adult patients with severe asthma and a history of prior asthma exacerbations	Conditional	Low
3	We suggest using a blood eosinophil cut-off $\geqslant 260\ \mu L^{-1}$ to identify adolescents (>12 years) and adults with severe allergic asthma more likely to benefit from anti-IgE treatment	Conditional	Low
	We suggest using a F_{ENO} cut-off $\geqslant 19.5$ ppb to identify adolescents (>12 years) and adults with severe allergic asthma more likely to benefit from anti-IgE treatment	Conditional	Low
4	For children, adolescents and adults with severe asthma uncontrolled despite GINA step 4–5 or NAEPP step 5 therapies, we recommend the addition of tiotropium	Strong	Moderate
5	We suggest a trial of macrolide treatment to reduce asthma exacerbations in adult asthma subjects on GINA/NAEPP step 5 therapy that remain persistently symptomatic or uncontrolled	Conditional	Low
	We suggest against the use of chronic macrolide treatment in children and adolescents with severe uncontrolled asthma	Conditional	Low
6	We suggest dupilumab as add-on therapy for adult patients with severe eosinophilic asthma and for those with severe corticosteroid-dependent asthma regardless of eosinophil levels	Conditional	Low

IL: interleukin; R: receptor; F_{ENO}: exhaled nitric oxide fraction; GINA: Global Initiative for Asthma; NAEPP: National Asthma Education and Prevention Program.

Holguin et al. ERS/ATS Severe Asthma Guideline – ERJ 2020; 55

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities)

5 Assess the **severe asthma phenotype** and factors contributing to symptoms, quality of life and exacerbations

- ***Assess the severe asthma phenotype during high dose ICS treatment*** *(or lowest possible dose of OCS)*

Type 2 inflammation	
Could patient have Type 2 airway inflammation? *Note: these are not the criteria for add-on biologic therapy (see* **6b***)*	• Blood eosinophils ≥150/µl and/or • FeNO ≥20 ppb and/or • Sputum eosinophils ≥2%, and/or • Asthma is clinically allergen-driven and/or • Need for maintenance OCS (Repeat blood eosinophils and FeNO up to 3x, on lowest possible OCS dose)

yes →
- Consider adherence tests
- Consider increasing the ICS dose for 3-6 months
- Consider AERD, ABPA, chronic rhinosinusitis, nasal polyposis, atopic dermatitis (clinical Type 2 phenotypes with specific add-on treatment)

no →

- ***Investigate for comorbidities/differential diagnoses*** *and treat/refer as appropriate*
  - Consider: CBC, CRP, IgG, IgA, IgM, IgE, fungal precipitins; CXR and/or HRCT chest; DLCO
  - Skin prick testing or specific IgE for relevant allergens, if not already done
  - Other directed testing (e.g. ANCA, CT sinuses, BNP, echocardiogram) based on clinical suspicion
- ***Consider need for social/psychological support***
- ***Involve multidisciplinary team care (if available)***
- ***Invite patient to enroll in registry (if available) or clinical trial (if appropriate)***

If no evidence of Type 2 inflammation:
- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects
- Avoid exposures (tobacco smoke, allergens, irritants)
- Consider investigations (if available and not done)
  - Sputum induction
  - High resolution chest CT
  - Bronchoscopy for alternative/additional diagnoses
- Consider add-on treatments
  - Trial of tiotropium or macrolide* (if not already tried)
  - Consider add-on low dose OCS, but implement strategies to minimize side-effects
  - Stop ineffective add-on therapies
- Consider bronchial thermoplasty (+ registry)

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities)

6b Consider *add-on biologic Type 2* targeted treatments

- Consider add-on Type 2-targeted biologic for patients with exacerbations or poor symptom control on high dose ICS-LABA, who:
  - have eosinophilic or allergic biomarkers, or
  - need maintenance OCS
- Consider **local payer eligibility criteria** and **predictors of response** when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

Which biologic is appropriate to start first?

Anti-IgE

*Is the patient eligible for **anti-IgE** for severe allergic asthma?*

- Sensitization on skin prick testing or specific IgE
- Total serum IgE and weight within dosage range
- Exacerbations in last year

no / *no*

Anti-IL5 / Anti-IL5R

*Is the patient eligible for **anti-IL5 / anti-IL5R** for severe eosinophilic asthma?*

- Exacerbations in last year
- Blood eosinophils ≥300/µl

no / *no*

Anti-IL4R

*Is the patient eligible for **anti-IL4R***

… for severe eosinophilic/Type 2 asthma?

- Exacerbations in last year
- Blood eosinophils ≥150/µl or FeNO ≥25 ppb

… or because of need for maintenance OCS?

Eligible for none?

Return to section **6a**

Check local eligibility criteria for specific biologic therapies as these may vary from those listed

pean Expert
ion
t Steps

Severe T2-high asthma in the biologics era: European experts' opinion

Ian Pavord[1], Thomas Bahmer[2], Fulvio Braido[3], Borja G. Cosío[4,5], Marc Humbert[6,7], Marco Idzko[8] and Lukasz Adamek[9]

1 Important concerns in the management of severe asthma identified at the European tory Biologics Forum

- biomarkers and phenotypes be best identified and utilised in daily clinical practice?
- CQ the right tool for monitoring the response to biologics?
- nent response assessed using the ACQ related to the effect of treatment on exacerbations?
- awareness be raised among patients and non-specialists regarding the burden of oral osteroids and the potential of new treatments available?
- steroids effective in patients having exacerbations while on biological therapies?
- ould patients start and stop taking a biologic?
- ould patients be switched from one biologic to another?

thma Control Questionnaire.

- Early access to specialt referral
- Earlier consideration of biologics
- No consensus on lengt wait time before deemi non-responder-does it l effectiveness?
- Switch if not able to red OCS use
- Biologics hope to functi as disease modifiers
- Focus on composite phenotypes/treatable tr (sx, pfts, AHR, OCS, H

et al. Eur Respir Rev 2019; 28

Practical considerations…. regardless of intervention

Essential to monitor and see the patient

- When they feel better, they may disappear
- Home administration may make monitoring more difficult

Registries help with severe asthma management

Discuss therapeutic contract:

- Continue FU
- Maintain asthma meds
- Before stopping or reducing to let us know
- Provide educn and guidelines on stopping prednisone therapy

Leverage virtual care

ATS/ERS and European Expert Panel guidelines— switch vs. continue

dividualized decision

ase-by-case

etermine goal of therapy

omarkers/treatable traits

- Move beyond FEV_1

de effect profile

nimum 3 months; often 6-12

Flexibility of criteria*

Monitor every 3 months while initiating therapy**

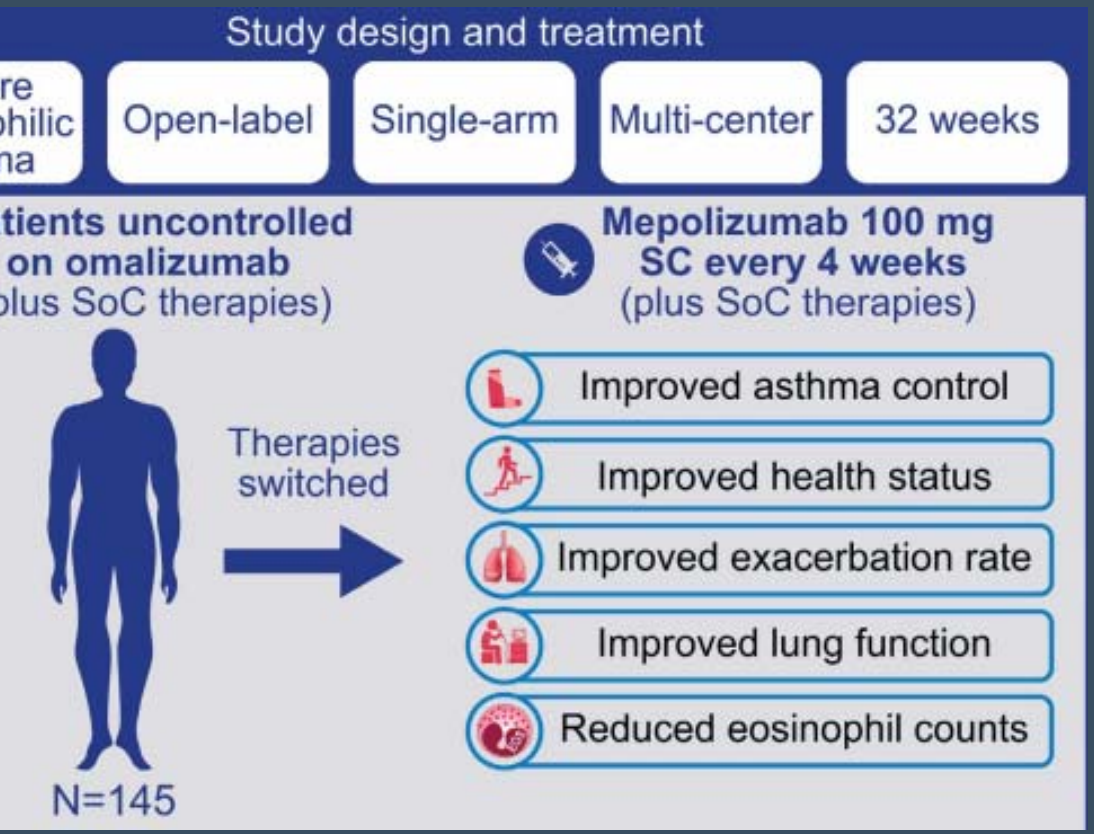
Need head-to-head

No assumption of a superior agent for any individual

**Some with fewer eos benefit*

***adherence/comorbidities reinfo*

How to switch-real world panel studies



ically important difference for improvement in asthma control questionnaire-5
orge's Respiratory Questionnaire total scores was achieved by 77% and 79%
respectively. Annualized rate of clinically significant exacerbations was
m 3.26 to 1.18 events/year. Safety and immunogenicity profiles of
ab were consistent with previous placebo-controlled trials in severe
asthma.

- Direct switch from omalizumab mepolizumab (within 2-4 wks last dose) with no adverse tolerability issues
- Also need to consider overlap biologic therapies
- No head to head trials

Chapman Allergy2019

Side effects/adverse reactions

malizumab

- Injection rxn 45%
- Resp infn 20%
- Sinusitis 16%
- HA 15%
- Pharyngitis 11%

Initial concern for malignancy, not substantiated

Systemic anaphylaxis 0.1-0.2% within 1st 3 injection and within 2 hrs administration

- Epipen

Mepolizumab

- HA 29%
- Worsening asthma 27%
- Bronchitis 21%
- Injection site rxn12%

- Well tolerate peds age
- Long term safety studies reassuring
- Shingles / zoster

Side effects/adverse reactions

Reslizumab

- Similar to placebo
- Nasopharyngitis
- Sinusitis 8%
- URI 10%
- HA 7%

Anaphylaxis 0.3% as early as 2nd dose, during or within 20 min after infusion

- Close monitoring in-office

Benralizumab

- any AE = 65-75%
- Nasopharyngitis 12-21%
- Wosening asthma 11-13%
- Hypersensitivity 3%

- No report of helminthic infections
- *? Vaccinate vs zoster?*

Case 3 – Problems below the diaphragm

55 M with severe asthma,
flares every 2 months

- Sinus disease w polyps
- FEV_1 at 58% + 12% BDR
- FeNO 136 ppb

Benralizumab without
improvement after 18 months

…

Switched to dupilumab

Case 3 – Problems below the diaphragm

55 M with severe asthma,
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- Sinus disease w polyps
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…

Switched to dupilumab

Tolerated loading
dose 600 mg

2nd dose with
profound
abdominal pain

What would you do next?

1) RUQ ultrasound
2) Bloodwork: CBC diff
3) Desensitize before next administration
4) CT abdomen

Patient: “Good to read the package insert”

Abd: *Soft tissue stranding and wall thickening predominantly involving celiac artery, short segment of the suprarenal aorta, common hepatic ry, and left gastric artery. Findings suggestive of vasculitis versus less y malignancy.*

eum WU

- ANCA neg
- Abs Eos 4200

epolizumab at higher dose indication

- EGPA

	Ref. Range	8/10/2018	9/24/2018	11/14/2018	6/4/2019
Abs Eosin	Latest Ref Range: <0.46 k/uL	1.24 (H)	0.08	<0.03	<0.03

	Ref. Range	6/4/2019 16:00	6/11/2020
c-ANCA Fluorescence	Latest Ref Range: Negative	Negative	Negative

	Ref. Range	6/4/2019 16:00	6/11/2020
p-ANCA Fluorescence	Latest Ref Range: Negative	Negative	Negative

	Ref. Range	9/29/2015	12/12/2015	7/20/2017
IgG	Latest Ref Range: 717 - 1,411 mg/dL	809	762	904

Dupilumab adverse effects

- Different mechanism
- Home administration and good safety profile
- Transient eosinophilia ≥ 3000 cells/uL from inhibition of migration from circulation to the tissues
- Consequences rare (eosinophilic pneumonia, EGPA)
- Ocular complications from lacrimal gland excretion (2-28% with conjunctivis)

ortant to have a core set of relevant asthma outco to inform guidelines

Review of 117 studies / clinical trials

117 studies, and 111 outcomes identified

Asthma control, symptom severity, some PROs

With growing number of clinical trials a core outcome set from stakeholders needed to evaluate pooled outcomes

Head-to-head comparisons are not available

- Cost, risks short term, long term
- Ongoing research and development needed b/c of gaps / non-responders

Tejwani et al. Journal of Asthma 202

COVID and asthma / biologics

No evidence asthmatics at greater risk with SARS-CoV-2,

- Prevalence of infection may be underestimated

3 pts who had exacerbation the prior week treated with systemic steroids admitted to ICU*

General consensus: *AAAAI, ACAAI, GINA, ERS, BTS*

- Continue treatment/maintenance therapy for best control
- No suggestion that immune response will be impaired with COVID
- Home administration recommended
- Continue biologics even if treatment initiated for COVID

**Bhatraju et al NEJM 2020*

Cleveland Clinic

Every life deserves world class care.

Other/combined indications

Case: 18 y/o tennis player

- 8 y/o with hx of asthma
- Symptoms pre-match SABA does not sustain sx
- Chest tightness worsening
- ncreased phlegm, muffled voice/throat
- ncreasing controller therapy doubling ICS, LTRA, ACT still at 15
- Moderately prolonged systemic steroid course resulting in Cushir
- Spiro mild obstruction with sig BDR

Recent evaluation

Worsening reflux after increasing asthma meds: ICS/LABA, LTRA, antihistamine, PPI, H2 blocker

Pursued EGD demonstrated esophageal bx with significant eosinophilia

B. PROXIMAL ESOPHAGUS, BIOPSY:
MULTIPLE SEGMENTS OF SQUAMOUS MUCOSA SHOWING DIFFUSE EPITHELIAL REPAIR AND EOSINOPHILIA.

COMMENT: No columnar epithelium is identified on Alcian Blue/PAS stain. Foci containing at least 40 eosinophils per high power field can be identified suggesting eosinophilic esophagitis over simple reflux.

C. DISTAL ESOPHAGUS, BIOPSY:
SQUAMOUS MUCOSA SHOWING PATCHY EPITHELIAL REPAIR AND EOSINOPHILIA.

COMMENT: No columnar epithelium identified on Alcian Blue/PAS stain. No Helicobacter pylori organisms identified on Giemsa stain. At least focally, greater than 40 eosinophils per high power field can be identified again suggesting eosinophilic esophagitis.