



2022 Association of Asthma Educators
Conference

Pharmacology Pre-Conference

Management of Severe Asthma
Including Biologics and Bronchial Thermoplasty

Chattanooga, TN

August 4, 2022

10:45 a.m. – 11:30 a.m.

Management of Severe Asthma Including Biologics and Bronchial Thermoplasty

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Pfizer – speaker

No conflict

Objective

1. Understand the role of systematic assessment in the management of severe asthma.
2. Discuss how to assess the selection and effectiveness of biologics.
3. Review recommendations of bronchial thermoplasty by the 2020 National Asthma Education and Prevention Program.

Severe Asthma



Severe Asthma

Challenging to assess and control, due to heterogeneity of disease, complexity of diagnosis, and impact of comorbidities¹

Severe asthma affects approximately 5% - 10% of patients ^{1,2}

Responsible for a large component of the overall disease burden and results in about half of direct asthma-related costs¹

Fleming I, Heaney L. *Front. Pediatr* 7:389.

Cote A, Godbout K, Boulet LP. *Biochem Pharmacol* 2020 Sep;179:114112.

Severe Asthma

“Severe asthma is defined as asthma that remains uncontrolled despite optimized treatment with high dose inhaled corticosteroid/long-acting beta agonist (ICS/LABA) to prevent asthma from becoming uncontrolled.

Severe asthma persistent problems with adherence or comorbidities such as chronic rhinosinusitis or obesity, as there are very different treatment implications compared with if asthma is relatively refractory to high dose (ICS/LABA or even oral corticosteroids.”





Severe Asthma

- Cardinal feature is airflow obstruction leads to frequent symptoms requiring higher levels of controller therapy
- Severe asthma is associated with significant morbidity
- Challenging to assess and control due to heterogeneity of disease
- Complexity of diagnosis
- Impact of comorbidities



Accurate Asthma Diagnosis

Diagnostic confirmation of asthma can be challenging among individuals with severe asthma



Accurate Asthma Diagnosis

- Symptoms of intermittent dyspnea, wheezing, and cough are classically associated with asthma, but these are nonspecific and presentation with atypical asthma symptoms such as cough is common
- Asthma should be considered whether classical symptoms are present or not, and evaluation for other non-asthma diagnoses is warranted, even when patients present with classical symptoms
- Both under- and over-diagnosis are widespread and lead to significant risks to patients
- Diagnosis of asthma is based on clinical findings, objective measurements, such as reversible airflow obstruction, can be used to support a diagnosis

GINA 2022:

Poor Symptom Control and/or Exacerbation Despite Treatment

| | |
|----------|---|
| Watch | Watch patient using their inhaler. Discuss adherence and barriers to use |
| Confirm | Confirm the diagnosis of asthma |
| Remove | If possible, remove potential risk factors. Assess and manage comorbidities |
| Consider | Consider treatment step-up |
| Refer | Refer to a specialist or severe asthma clinic |

Assessment of Asthma and Related Conditions

Investigate and manage difficult-to-treat asthma in adults and adolescents

Consider referring to specialist or severe asthma clinic at any stage



1 Confirm the diagnosis
(asthma/differential diagnoses)

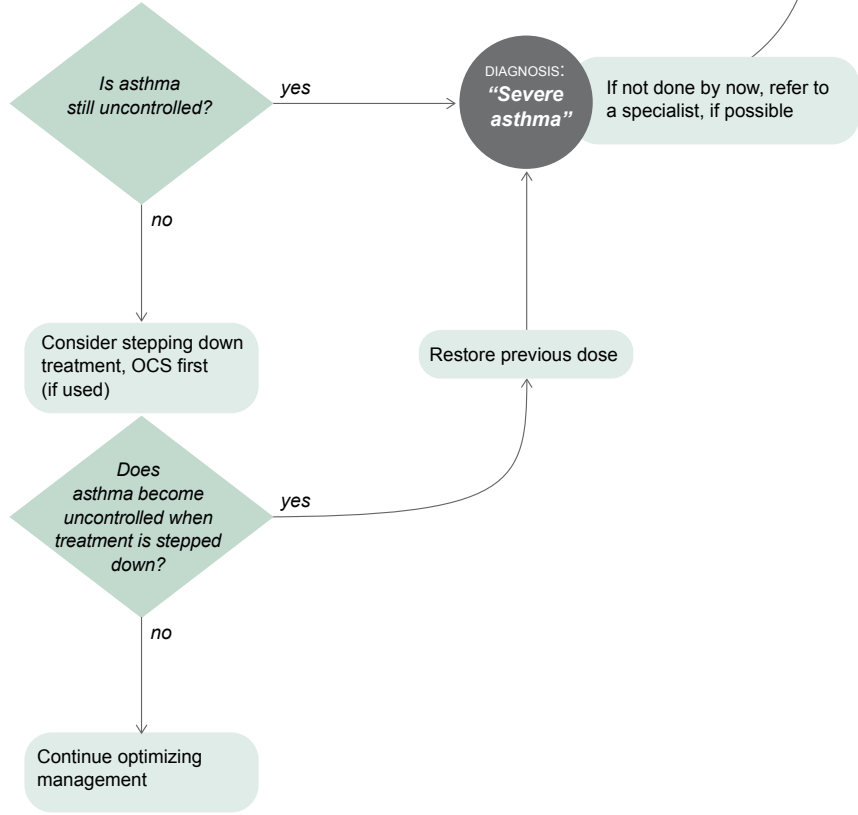
2 Look for factors contributing to symptoms, exacerbations and poor quality of life:

- Incorrect inhaler technique
- Suboptimal adherence
- Comorbidities including obesity, GERD, chronic rhinosinusitis, OSA
- Modifiable risk factors and triggers at home or work, including smoking, environmental exposures, allergen exposure (if sensitized); medications such as beta-blockers and NSAIDs
- Overuse of SABA relievers
- Medication side effects
- Anxiety, depression and social difficulties

3 Optimize management, including:

- Asthma education
- Optimize treatment (e.g. check and correct inhaler technique and adherence; switch to ICS-formoterol maintenance and reliever therapy, if available)
- Consider non-pharmacological interventions (e.g. smoking cessation, exercise, weight loss, mucus clearance, influenza and COVID-19 vaccination)
- Treat comorbidities and modifiable risk factors
- Consider non-biologic add-on therapy (e.g. LABA, LAMA, LM/LTRA, if not used)
- Consider trial of high dose ICS-LABA, if not used

4 Review response after ~3-6 months



Assess and treat severe asthma phenotypes

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities, non-pharmacologic strategies)

5 Investigate further and provide patient support → **6 Assess the severe asthma phenotype** → **7 Consider other treatments**

- 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; DEXA scan
 - Skin prick testing or specific IgE for relevant allergens, if not already done
 - Consider screening for adrenal insufficiency in patients taking maintenance OCS or high dose ICS
 - If blood eosinophils $\geq 300/\mu\text{l}$, look for and treat non-asthma causes, including parasites (e.g. Strongyloides serology, or stool examination)
 - If hypereosinophilia e.g. $\geq 1500/\mu\text{l}$, consider causes such as EGPA
 - 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)

Could patient have Type 2 airway inflammation?

yes

- Type 2 inflammation**
- Blood eosinophils $\geq 150/\mu\text{l}$ and/or
 - FeNO ≥ 20 ppb and/or
 - Sputum eosinophils $\geq 2\%$, and/or
 - Asthma is clinically allergen-driven
(Repeat blood eosinophils and FeNO up to 3x, at least 1-2 weeks after OCS or on lowest possible OCS dose)

no

Note: these are **not** the criteria for add-on biologic therapy (see 8)

- Type 2 airway inflammation**
- Consider adherence tests
 - Consider increasing the ICS dose for 3-6 months
 - Consider add-on non-biologic treatment for specific Type 2 clinical phenotypes, e.g. AERD, ABPA, chronic rhinosinusitis, nasal polyposis, atopic dermatitis

- No evidence of Type 2 airway 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 trial of add-on treatments (if available and not already tried)
 - LAMA
 - Low dose azithromycin
 - Anti-IL4R* if taking maintenance OCS
 - Anti-TSLP* (but insufficient evidence in patients on maintenance OCS)
 - As last resort, consider add-on low dose OCS, but implement strategies to minimize side-effects
 - Consider bronchial thermoplasty (+ registry)
 - Stop ineffective add-on therapies

Is add-on Type 2 biologic therapy available/affordable?

yes

- If add-on Type 2-targeted biologic therapy is NOT available/affordable**
- Consider higher dose ICS, if not used
 - Consider other add-on therapy (e.g. LAMA, LM/LTRA, low dose azithromycin)
 - As last resort, consider add-on low dose OCS, but implement strategies to minimize side-effects
 - Stop ineffective add-on therapies

no

Go to section 10

Not currently eligible for T2-targeted biologic therapy

Go to section 10

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

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities, non-pharmacologic strategies)

8 Consider add-on biologic Type 2-targeted treatments

- Consider add-on Type 2-targeted biologic therapy for patients with exacerbations or poor symptom control on high dose ICS-LABA, who have evidence of Type 2 inflammation*
- Consider **local payer eligibility criteria***, **comorbidities** 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?

Eligibility

Anti-IgE (omalizumab)

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

Anti-IL5 / Anti-IL5R (benralizumab, mepolizumab, reslizumab)

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

- Exacerbations in last year
- Blood eosinophils, e.g. $\geq 150/\mu\text{l}$ or $\geq 300/\mu\text{l}$

Anti-IL4R (dupilumab)

Is the patient eligible for **anti-IL4R** for severe eosinophilic/Type 2 asthma?*

- Exacerbations in last year
- Blood eosinophils ≥ 150 and $\leq 1500/\mu\text{l}$, or FeNO ≥ 25 ppb, or taking maintenance OCS

Anti-TSLP (tezepelumab)

Is the patient eligible for **anti-TSLP** for severe asthma?*

- Exacerbations in last year

Predictors of asthma response

- What factors may predict good asthma response to anti-IgE?
- Blood eosinophils $\geq 260/\mu\text{l}$ ++
 - FeNO ≥ 20 ppb +
 - Allergen-driven symptoms +
 - Childhood-onset asthma +

- What factors may predict good asthma response to anti-IL5/5R?
- Higher blood eosinophils +++
 - More exacerbations in previous year +++
 - Adult-onset of asthma ++
 - Nasal polyposis ++

- What factors may predict good asthma response to anti-IL4R?
- Higher blood eosinophils +++
 - Higher FeNO +++

- What factors may predict good asthma response to anti-TSLP?
- Higher blood eosinophils +++
 - Higher FeNO +++

Choose one if eligible*; trial for at least 4 months and assess response

Extend trial to 6-12 months*

Good asthma response?*

yes
Good response to T2-targeted therapy

STOP add-on

Consider switching to a different Type 2-targeted therapy, if eligible*

Little/no response to T2-targeted therapy

Eligible for none? Return to section 7

No evidence of Type 2 airway inflammation

No evidence of Type 2 airway inflammation. Go to section 10

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

Monitor / Manage severe asthma treatment

Continue to optimize management

9 Review response

- Asthma: symptom control, exacerbations, lung function
- Type 2 comorbidities e.g. nasal polyposis, atopic dermatitis
- Medications: treatment intensity, side-effects, affordability
- Patient satisfaction

If good response to Type 2-targeted therapy

- Re-evaluate the patient every 3-6 months*
- For **oral treatments**: consider decreasing/stopping OCS first (and check for adrenal insufficiency), then stopping other add-on medication
- For **inhaled treatments**: consider decreasing after 3-6 months; continue at least moderate dose ICS-LABA
- Re-evaluate need for ongoing biologic therapy
- Order of reduction of treatments based on observed benefit, potential side-effects, cost and patient preference

yes →

If no good response to Type 2-targeted therapy

- Stop the biologic therapy
- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects, emotional support
- Consider high resolution chest CT (if not done)
- Reassess phenotype and treatment options
 - Induced sputum (if available)
 - Consider add-on low dose azithromycin
 - Consider bronchoscopy for alternative/additional diagnoses
 - As last resort, consider add-on low dose OCS, but implement strategies to minimize side-effects
 - Consider bronchial thermoplasty (+ registry)
- Stop ineffective add-on therapies
- Do not stop ICS

no →

No evidence of Type 2 airway inflammation. Go to section 10

10 Continue to optimize management as in section 3, including:

- Inhaler technique
- Adherence
- Comorbidity management
- Non-pharmacologic strategies
- Patients' social/emotional needs
- Two-way communication with GP for ongoing care

Notes:

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

Accurate Asthma Diagnosis


- Obtain a thorough history
 - identifying common triggers
 - Work/school exposures
 - personal history of wheezing
 - symptoms with exercise
 - family history of asthma symptoms

Evaluation in patients > 5 years of age should include spirometry with evaluation for a bronchodilator response and in patients without airflow obstruction consideration of bronchoprovocation testing

Accurate Asthma Diagnosis

Further testing:

- measurement of exhaled fractional excretion of nitric oxide
 - CBC count with differential to evaluate for eosinophilia
 - serum IgE levels
 - allergy testing to environmental allergens
-
- In cases of persistent or severe asthma consider chest radiograph and/or chest CT scan



Comorbidities and Severe Asthma

- Allergic rhinitis/Chronic rhinosinusitis
 - Vocal cord dysfunction (VCD)
 - Sleep apnea
 - COPD
 - Bronchiectasis
 - Obesity
 - Psychiatric conditions/Anxiety/depression
 - GERD
 - Cardiovascular and metabolic disorder
 - Allergic bronchopulmonary aspergillosis (ABPA)
 - COPD
-

Comorbidities and Associated Conditions with Severe Asthma

Vocal cord dysfunction

Dysfunctional breathing

Rhinosinusitis

Nasal polyps

Obstructive sleep apnea

Gastroesophageal disease

Anxiety/Depression

Obesity/overweight

Corticosteroid side effects:

osteoporosis, obesity, diabetes


Chronic obstructive pulmonary
disease

Bronchopulmonary aspergillosis

Bronchiectasis

Eosinophilic conditions

eosinophilic granulomatosis
bronchopulmonary aspergillosis
hyper-eosinophilic syndrome



Severe asthma is a
heterogeneous disease
encompassing different
phenotypes and endotypes

Heialy SA, Ramakrishnan R, Hamid Q. J Allergy Clin Immunol 2022;149:455-65

Severe Asthma: What is Phenotyping?

Accurately and easily characterize an individual's severe asthma and assign a "phenotype" for the application of personalized therapeutic approaches → precision medicine

Refine phenotyping to measure or make inferences about basic pathophysiologic and biologic mechanisms → endotypes that underlie the disease and ultimately guide therapy


GOAL:

Derive clinical phenotypes that clearly translate to biological endotypes for the purpose of efficient and therapeutic precision pharmacological treatment

Carr T, Zeki A, Kraft M. AJRCCM Jan 2018

Kuruvilla ME, Lee FE, Lee GB. Clin Rev Allergy Immunol. 2019 Apr;56(2):219-233.

Phenotypes



Observable characteristics that result from a combination of hereditary and environmental influences

- Allergic asthma
- Non-allergic asthma
- Adult-onset asthma
- Aspirin-exacerbated respiratory disease
- Asthma predictive index-positive (preschool wheezer)
- Exercise-induced asthma
- Asthma with obesity
- Persistent airflow limitation



Phenotypes

- Phenotyping can be incorporated into clinical practice and can be used to guide advanced biological therapies that target specific molecules and inflammatory pathways that contribute to asthma pathogenesis
- Phenotypes of asthma have been identified according to causal or triggering factors, such as allergen-induced or aspirin-induced, to the type of airflow obstruction, to the severity and response to treatments, to radiological findings, and to the nature of airway inflammation

Carr TF, Zeki AA, Kraft M. Am J Respir Crit Care Med 2018 ;197, 1, 22–37,

Fajt M. Wenzel SE. J Allergy Clin Immunol 2015;135:299-310.

Global Initiative for Asthma. 2022. www.ginasthma.org

Kuruvilla ME, Lee FEH, Lee GB Clin Rev Allergy Immunol. 2019 Apr; 56(2): 219–233.

Endotype

Asthma endotypes describe these distinct pathophysiologic mechanisms at a cellular and molecular level

Specific biological mechanism that causes those observed properties of any given phenotype

Carr TF, Zeki AA, Kraft M. Am J Respir Crit Care Med 2018 ;197, 1, 22–37,

Fajt M. Wenzel SE. J Allergy Clin Immunol 2015;135:299-310.

Global Initiative for Asthma. 2022. www.ginasthma.org

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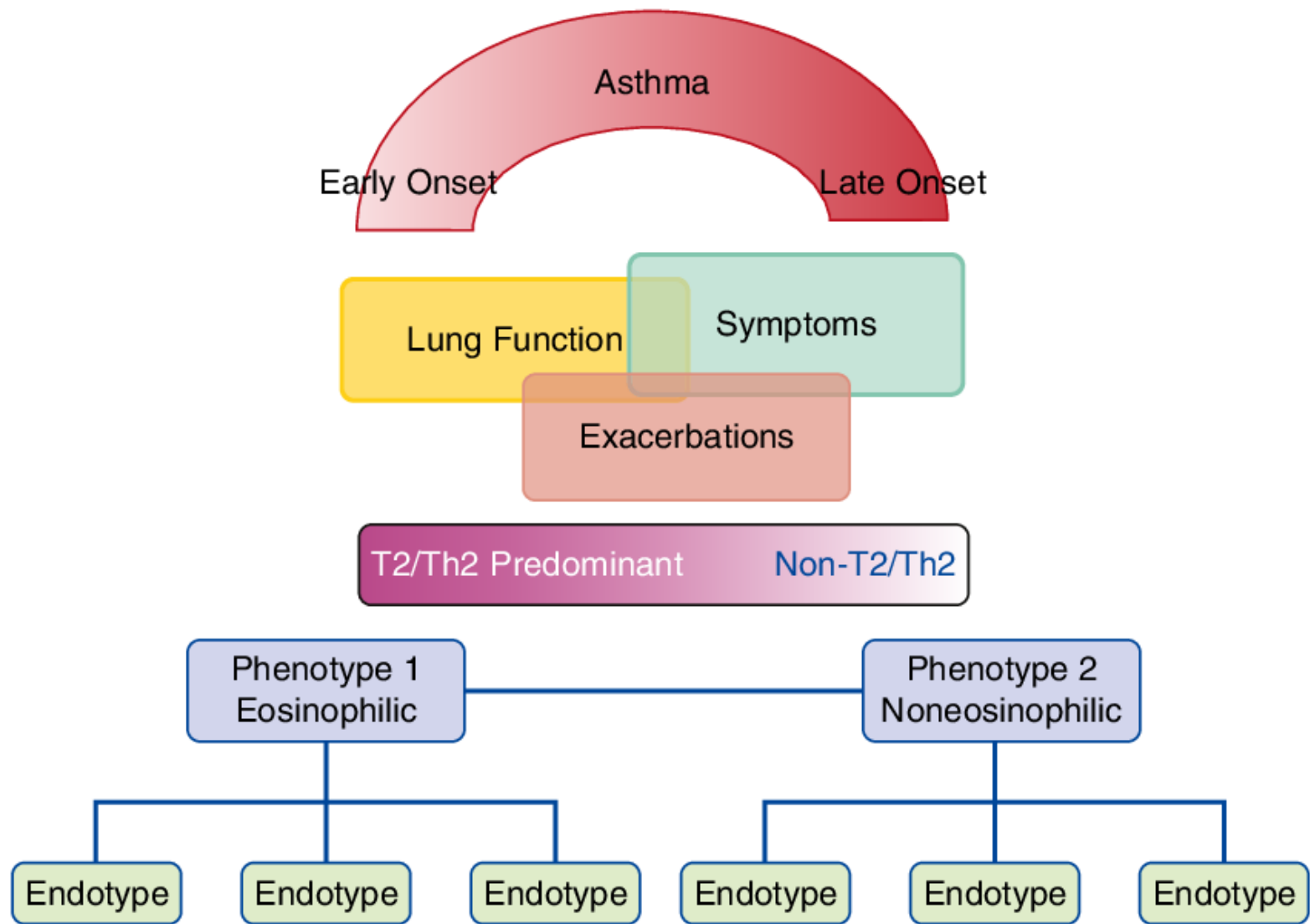


Figure 1. Schematic representation of asthma and the spectrum of inflammation type and endotype.

Clinical Phenotypes of Severe Asthma

- Severe asthma is a complex chronic disease which is reinforced by several phenotypes and impacted by various co-morbidities and risk factors*
- various clinical phenotypes with diverse molecular mechanisms that may be driving these different phenotypes
- Optimizing individualized treatment for severe asthma will require determining the asthma sub-phenotypes and endotypes, and the underlying molecular mechanisms responsible for those traits

Severe Asthma Endotypes

Severe asthma endotypes are broadly classified into:

TH2-high (eosinophilic)

TH2-low (noneosinophilic)

Based on the mechanisms driving the different inflammatory profiles

Common Features of T2-High and T-2 Low Asthma

| Feature | T2-High | T-2 Low |
|--------------------------------------|------------------------------------|------------------------------------|
| Age of onset | Earlier onset | Later onset |
| Symptoms | May be significant | May be significant |
| Life-threatening exacerbations | More exacerbations | Fewer exacerbations |
| Obesity/metabolic dysfunction | May be present | Often present |
| Lung function | More obstruction | Less obstruction |
| Short-acting bronchodilator response | More responsive | Less responsive |
| Allergic sensitization | Present | Absent |
| FeNO | Normal to elevated | Low to normal |
| Airway eosinophilia | Present | Absent |
| Airway Neutrophilia | May be present | May be present |
| Medication requirements | More responsive to corticosteroids | Less responsive to corticosteroids |



Asthma Pathogenesis

Characterized by two
major endotypes

- T2-high
 - increased eosinophilic airway inflammation
 - T2-low
 - endotype presenting with either neutrophilic or paucigranulocytic airway inflammation
 - greater resistance to steroids
-



Strategies for Management of Severe Asthma

Oral Corticosteroids

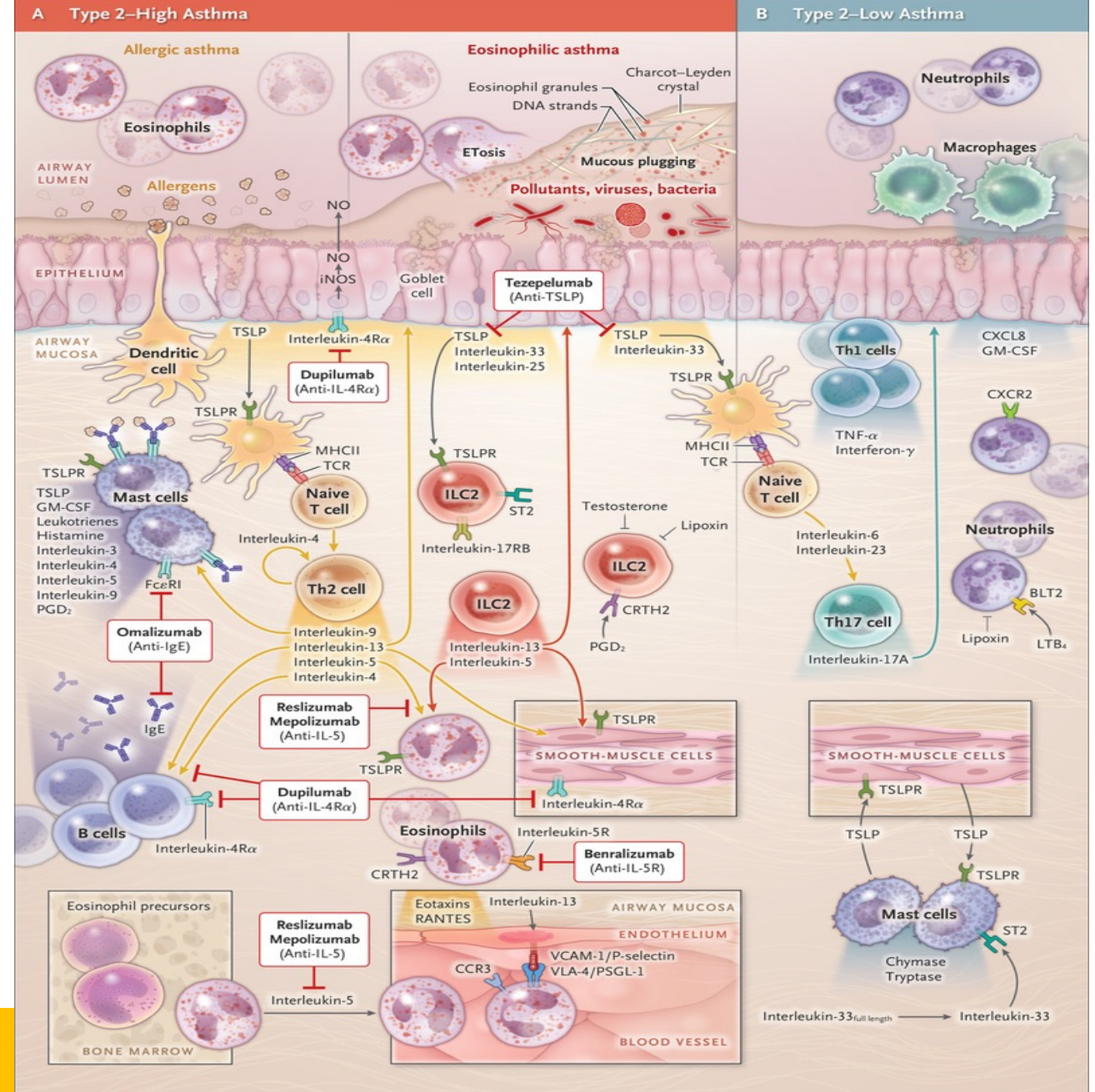
- Corticosteroids elicit potent anti-inflammatory responses from several different cell types that can dramatically alter asthma symptoms
- Most patients respond to systemic corticosteroid therapy at high doses
- Short-term and long-term adverse effects of corticosteroid therapy often complicate their chronic use in severe asthma

Biologic Therapies

- Used for patients who continue to have symptoms despite use of standard daily controller medications
- Biologic therapies target type 2 inflammatory pathways that are central to exacerbation pathogenesis in asthma
- All biologic therapies have been shown to reduce exacerbation frequency in controlled trials
- Elevated blood eosinophil counts \pm FeNO are associated with greater clinical efficacy with all the asthma biologics

Immunomodulatory Biologic Agents Approved for Use in Asthma

- Xolair (omalizumab)
- Nucala (mepolizumab)
- Cinqair (reslizumab)
- Fasenra (benralizumab)
- Dupixent (dupilumab)
- Tezspire (tezepelumab-ekko)





Selection and Effectiveness: How do we decide?

*Before addition of a biologic, clinic evaluation must include:

- Properly classify asthma severity
 - Identifying causes of poor asthma control
 - Addressing poor adherence
-

How do we decide which biologic therapy is best for our patient severe asthma?

Biologic Therapy: Selection and Effectiveness



Biologic Therapy: Selection and Effectiveness

- Head-to-head comparative studies of the biologics are not currently available to guide the selection of biologics for individual patients
- Choosing between the various IL-5 antagonists is difficult, as their effects on various clinical end points have proven to be similar
- Biologic therapeutics are expensive and sometimes can be challenging for insurance coverage



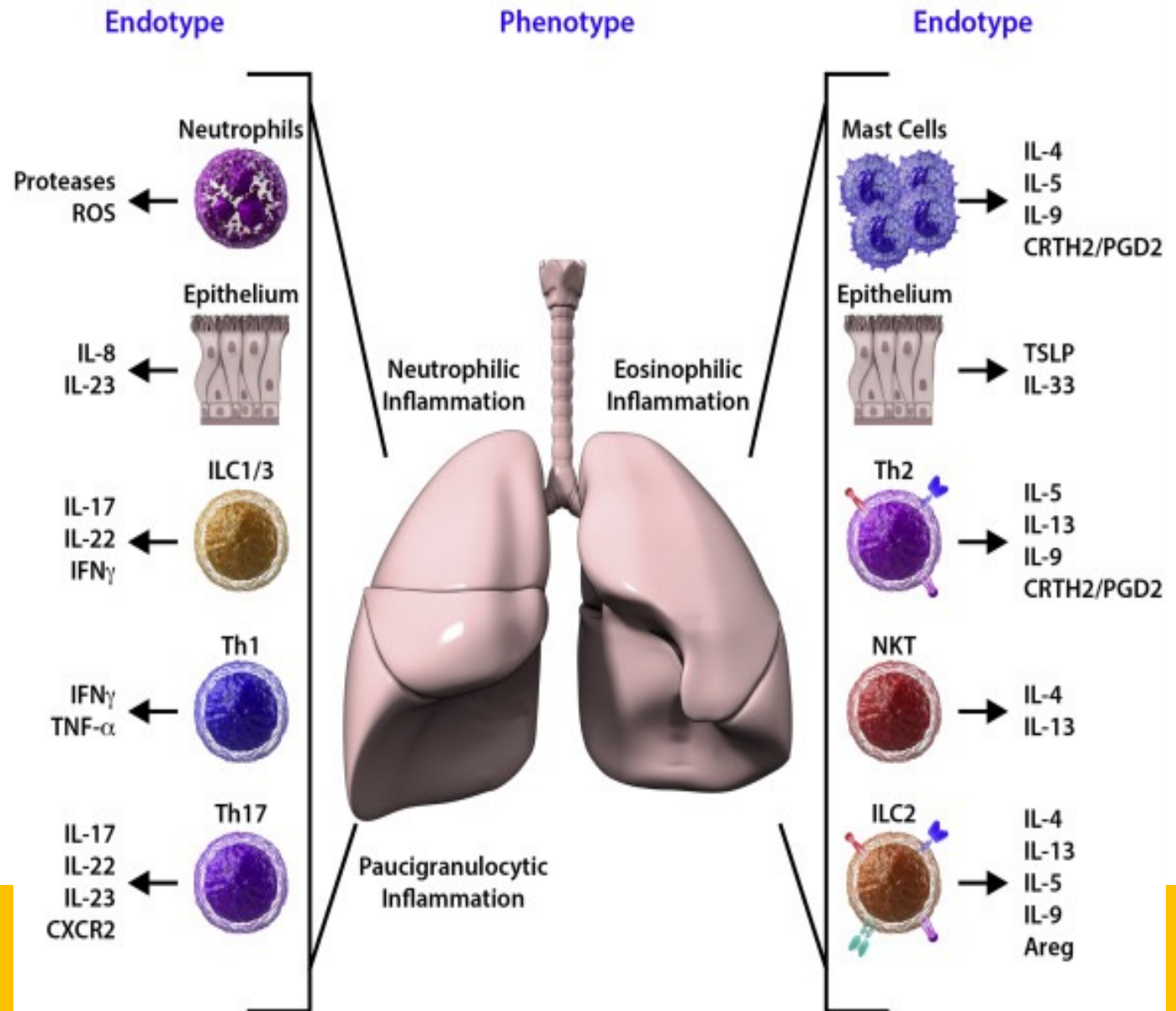
**The emergence of biologics
has revolutionized the
treatment of patients with
severe asthma**

Think with the end in mind:

Primary outcome improved by T2 biologics is the prevention of asthma exacerbations

T2 Low Asthma

T2 High Asthma



T-2 High or T-2 Low Airway Inflammation?

- T2-high asthma encompasses both allergic and nonallergic eosinophilic asthma.
- Sputum and blood absolute eosinophil counts (AECs), serum IgE, FeNO, and serum periostin are all important biomarkers of T2 inflammation that can help predict response to biologics
- Currently, there is no approved biologic for T2-low asthma

Biologic Therapy

| Class | Name | Age | Asthma indication | Other indications |
|-----------|-------------------|-----------|---|---|
| Anti-IgE | Omalizumab (SC) | ≥6 years | Severe allergic asthma | Nasal polyposis, chronic spontaneous urticaria |
| Anti-IL5 | Mepolizumab (SC) | ≥6 years | Severe eosinophilic/Type 2 asthma | Mepolizumab: EGPA, CRSwNP, hypereosinophilic syndrome |
| | Reslizumab (IV) | ≥18 years | | |
| Anti-IL5R | Benralizumab (SC) | ≥12 years | | |
| Anti-IL4R | Dupilumab (SC) | ≥6 years | Severe eosinophilic/Type 2 asthma, or maintenance OCS | Moderate-severe atopic dermatitis, CRSwNP |
| Anti-TSLP | Tezepelumab (SC) | ≥12 years | Severe asthma | |

Biologic Therapy:

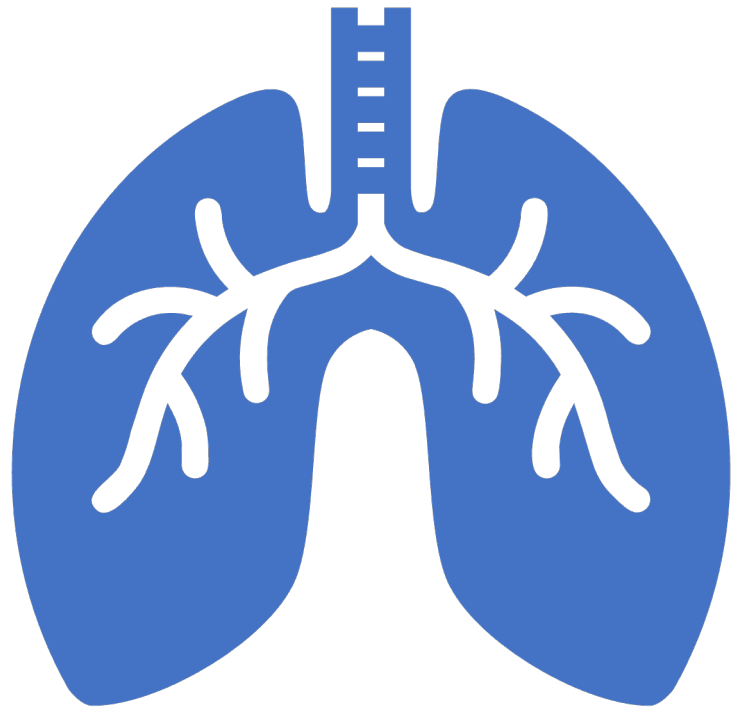
- Phenotyping for T2 inflammation with basic biomarkers determinations should be made
 - measures of peripheral blood eosinophil (EOS) values (!150 cells/mL)
 - FeNO (20 ppb)
 - IgE levels
 - Allergen-specific sensitization by either skin test or serologic testing
 - Exceptional documentation

Take Home Message

- Recognize eosinophilic airway inflammation is a treatable trait and has allowed for the emergence of biologic therapy
- Clinical indicators:
 - are easily measured
 - provide shared decision making with our patients
 - helps us decide if the biologic should be continued or if a switch to alternate treatment

Evaluate Factors Contributing to Poor Asthma Control

- Incorrect inhaler technique
- Suboptimal adherence
- Comorbidities: GERD, obesity, chronic rhinosinusitis, OSA
- Modifiable risk factors and triggers
 - Smoking, environmental exposures, allergen exposures, medications beta-blocker or NSAIDs
- Overuse of SABA relievers
- Medication side effects
- Anxiety, depression and social difficulties



Bronchial Thermoplasty (BT)

Bronchothermoplasty

Device-based treatment for patients ≥ 18 years of age
with severe asthma poorly controlled
with inhaled corticosteroids
and long-acting beta-agonists

What clinicians should discuss with their patients about BT

- BT may reduce severe asthma exacerbations compared with standard care after treatment
- Benefits could last 5 years or more, only limited data demonstrate that this treatment improves long-term asthma outcomes
- Risks:
 - worsening of asthma
 - respiratory infections
 - Hemoptysis
 - bronchiectasis
 - pulmonary artery complications
 - severe, delayed-onset complications could occur that have not yet been recognized because of the small numbers of individuals who have undergone the procedure

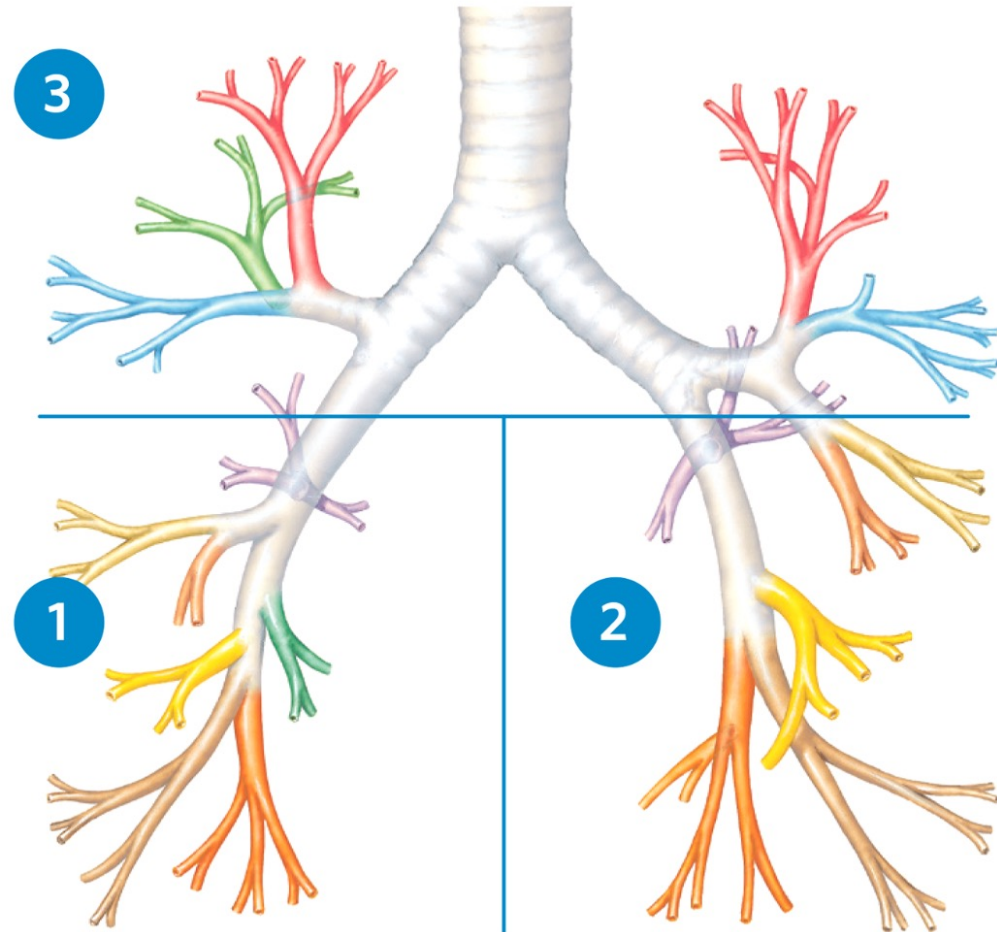
Bronchial Thermoplasty (BT)

- Bronchial Thermoplasty (BT) is a minimally invasive and safe outpatient procedure for the treatment of severe asthma in adults
- BT is for patients with severe asthma ≥ 18 years old who are on inhaled corticosteroids and long-acting beta₂ agonists but still experience asthma symptoms and/or risk of future exacerbations
- BT is a clinically proven non-drug therapy for patients with severe asthma, with benefits demonstrated out to 5 years

Identifying BT Candidates

- Asthma exacerbations requiring oral corticosteroids
- ER, urgent care, or unscheduled office visits in the past 12 months
- Use of rescue inhaler > 2x per week
- Physical or activity limitations due to asthma

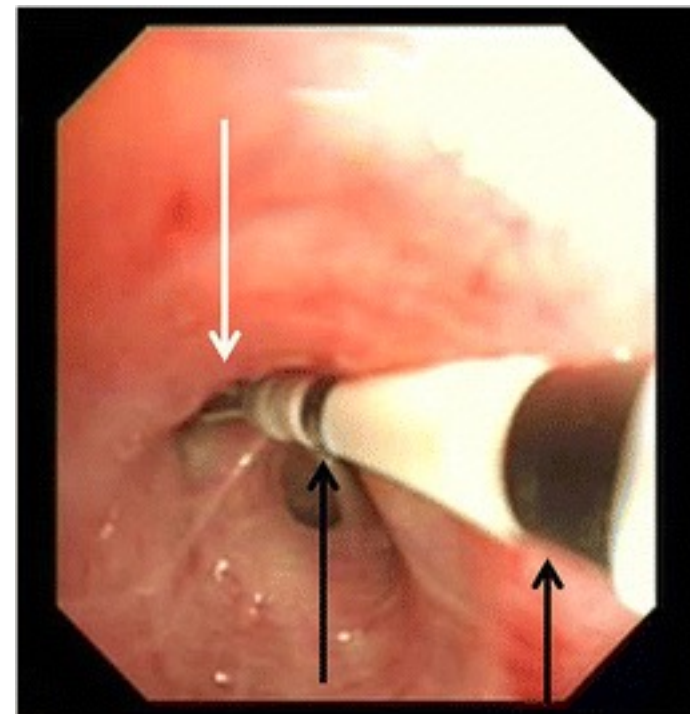
BT IS DONE IN 3 SESSIONS



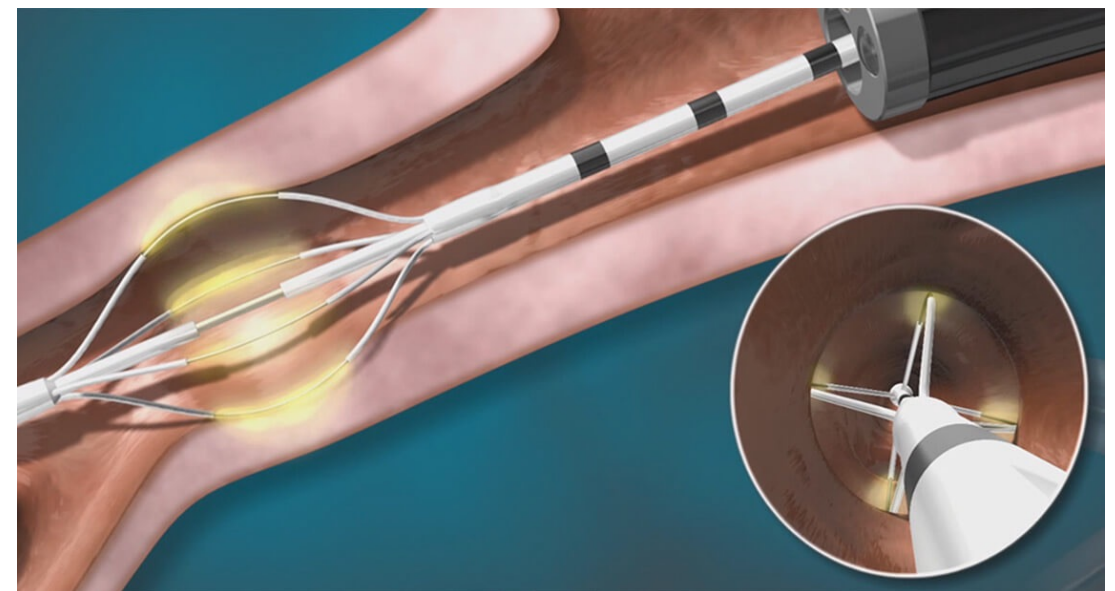
The Alair® Bronchial Thermoplasty System by Asthmatx®



Eurekalert.org



Researchgate.net



VITAL Innovation

2020 Focused Updates to the Asthma Management Guidelines

- Expert Panel conditionally recommends against BT in individuals aged 18 years and older with persistent asthma because of the small benefit to risk ratio and uncertain outcomes
- BT should not be used in individuals with low lung function (FEV1 that is <50% or 60% predicted) and life-threatening asthma

2020 Focused Updates to the Asthma Management Guidelines

- For individuals who decide to undergo BT, an experienced specialist (eg, pulmonologist with training in BT administration) should provide this treatment in a center that has appropriate expertise
- Clinicians should optimize asthma treatment and address comorbidities, and they should assess and optimize adherence to existing therapy, before considering BT

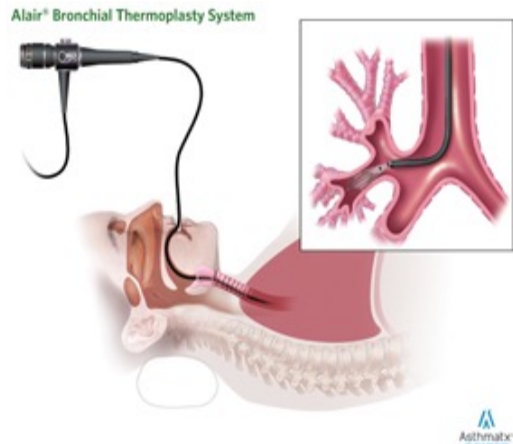
Bronchial Thermoplasty (BT)

- Recommendation 19:
 - In individuals ages 18 years and older with persistent asthma, the Expert Panel conditionally recommends against bronchial thermoplasty.

Conditional recommendation, low certainty of evidence

- Individuals ages 18 years and older with persistent asthma

who place a low value on harms (i.e., short-term worsening of symptoms and unknown long-term side effects) and a high value on potential benefits (i.e., improvement in quality of life and a small reduction in number of exacerbations) might consider BT



Uab.edu

Take Home Message

Systematic assessment of severe asthma

- Confirmation of asthma diagnosis:
 - Lung function → Bronchial provocation test
- Exclude other conditions masquerading as asthma
- Assess severity of disease:
 - Poor symptom control, airflow obstruction, frequent exacerbations, life-threatening severe exacerbations
- Optimization of treatment according to national guidelines
- Assess adherence to therapy
- Adaptation and using individualized self-management plans
- Identification and avoidance of trigger factors
- Assessment and management of comorbidities
- Phenotyping according to clinic-physiologic inflammatory parameters

*thank
you*

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