



Navigating Asthma Control

A Severe Asthma Roadmap



MOUNT SINAI - NATIONAL JEWISH HEALTH

Respiratory Institute



Evaluate Adherence and Optimize Inhaler Technique

- Use shared-decision making approach to select treatment
- Choose best device for patient and individualize education
- Assess barriers to proper medication use
- Assess knowledge and attitudes about medication
- Educate patient about strategies to reduce side effects
- Check and correct inhaler technique at each visit

DOES THE PATIENT HAVE ASTHMA?

- **Confirm** variable airflow limitation: review/repeat pulmonary function tests with bronchodilator
- **Consider** methacholine or exercise challenge tests if spirometry inconclusive and clinical response to treatment is absent or limited
- **Exclude** other conditions (eg, airway tumor, foreign body, COPD, bronchiectasis, vocal cord dysfunction, CF, aspiration)



Treat other pulmonary conditions if misdiagnosed



EVALUATE COMORBIDITIES AND COMPLICATING FACTORS

Diagnose and manage comorbidities

- Rhinosinusitis/nasal polyps
- Gastroesophageal reflux
- Obstructive sleep apnea
- Vocal cord dysfunction
- Allergic bronchopulmonary aspergillosis
- Eosinophilic granulomatosis with polyangiitis
- Obesity
- Psychological factors (personality, depression, anxiety)
- Drug side effects aspirin, NSAIDs, beta-blockers, ACE inhibitors
- Aspiration

Address environmental factors

- Allergen exposures (indoor, outdoor, pets)
- Occupational exposures
- Respiratory infections (eg, viruses)
- Second-hand cigarette smoke
- Traffic-related pollution
- Respiratory irritants

Asthma education and health maintenance



eating healthy
vaccination
smoking cessation
exercise

Consider safety and potential effects of long-term oral corticosteroids (OCS)

1. Counsel patients about long term effects of OCS
2. Optimize chronic OCS dose (establish current dose is truly needed)
3. Use objective criteria to control taper (PEF, symptoms score, SABA use)
4. Counsel patients regarding symptoms of adrenal insufficiency and steroid withdrawal ("go slow when low")
5. Manage steroid related adverse effects



CONSIDER ADDING A NON-BIOLOGIC THERAPY

- Tiotropium
- Leukotriene modifier
- Theophylline
- Macrolide antibiotic
- Oral corticosteroid (short course)



DETERMINE INFLAMMATORY PHENOTYPE/ ENDOTYPE FOR PERSONALIZED TREATMENT SELECTION

- Start with non-invasive testing (allergy testing, IgE level, blood eosinophil count and FeNO* level)
*Fractional nitric oxide concentration in exhaled breath.
- If poor response to therapy continues, consider induced sputum differential for eosinophil and neutrophil counts and/or bronchoscopy with endobronchial biopsy and BAL

IS ASTHMA STILL UNCONTROLLED, DESPITE TREATMENT WITH HIGH-DOSE ICS + LABA AND A NON-BIOLOGIC ADD-ON THERAPY?



Consider referring patient to an asthma specialist

Close follow-up.
Reduce treatment intensity after at least 3–6 months of stable, good control



Non-Type 2

Neutrophilic airway inflammation or Pauicgranulocytic

Biomarkers

- No T2 biomarkers
- Blood eosinophil <150 μ L AND
- FeNO < 20 ppb AND
- Sputum or BAL eosinophil < 2%

OR

If sputum BAL neutrophils also < 40-60% = pauciinflammatory

Associated Phenotypes

- Obesity
- Smoking History
- Infections
- Lack of response to corticosteroids

Treatment

- Weight loss
- Bariatric surgery
- Macrolide antibiotics
- Bronchial Thermoplasty
- Secretion clearance
- Pulmonary rehabilitation

† Consider experimental therapy from clinical trials with Anti-TSLP, Anti-IL-6, Anti-IL-17 or other drugs in development.



Type 2

IL-4, IL-5, IL-13 or IgE mediated inflammation with high eosinophils or FeNO

Biomarkers

- Blood eosinophils > 150 μ L
- FeNO > 20 ppb
- Sputum or BAL eosinophils > 2%
- Elevated IgE

Associated Phenotypes

- Early age onset
- History of allergies
- Chronic Rhinosinusitis/Nasal Polyps

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References

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Type 2 patients with:

Allergic Eosinophilic Asthma

Allergic Noneosinophilic Asthma

Eosinophilic Asthma who:

- Are nonallergic OR
- Do not respond to anti-IgE treatment OR
- Are out of dosing range for anti-IgE treatment

OCS Dependence

Considerations for Related Type 2 Phenotypes

- Atopic Dermatitis Anti-IL-4Ra/13 Dupilumab
- Chronic Idiopathic Urticaria Anti-IgE Omalizumab
- Chronic Rhinosinusitis and Nasal Polyps Anti-IL-4Ra/13 Dupilumab*

Consider patient preference factors related to route/frequency/location of administration and cost.

Select Add-on Biologic Therapy

Allergic Eosinophilic Asthma	Anti-IgE	Omalizumab
	Anti-IL-5	Mepolizumab, Reslizumab
Allergic Noneosinophilic Asthma	Anti-IL-5Ra	Benralizumab
	Anti-IL-4Ra/13	Dupilumab
Eosinophilic Asthma who: • Are nonallergic OR • Do not respond to anti-IgE treatment OR • Are out of dosing range for anti-IgE treatment	Anti-IL-5	Mepolizumab, Reslizumab
	Anti-IL-5Ra	Benralizumab
OCS Dependence	Anti-IL-4Ra/13	Dupilumab*
	*While Dupilumab has the FDA indication for OCS dependence, both Mepolizumab and Benralizumab have shown efficacy.	