

# Biologic Therapy is the Preferred Treatment for AERD

AAIFNC Journal Club

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# Disclosures

- I have no relevant financial relationships to disclose

## 3 Reasons why Biologic Therapy is Preferred for AERD

1. Biologic therapy is **more clinically effective** than AD
2. Biologic therapy is **safer** than AD
3. Biologic therapy is **better tolerated** than AD

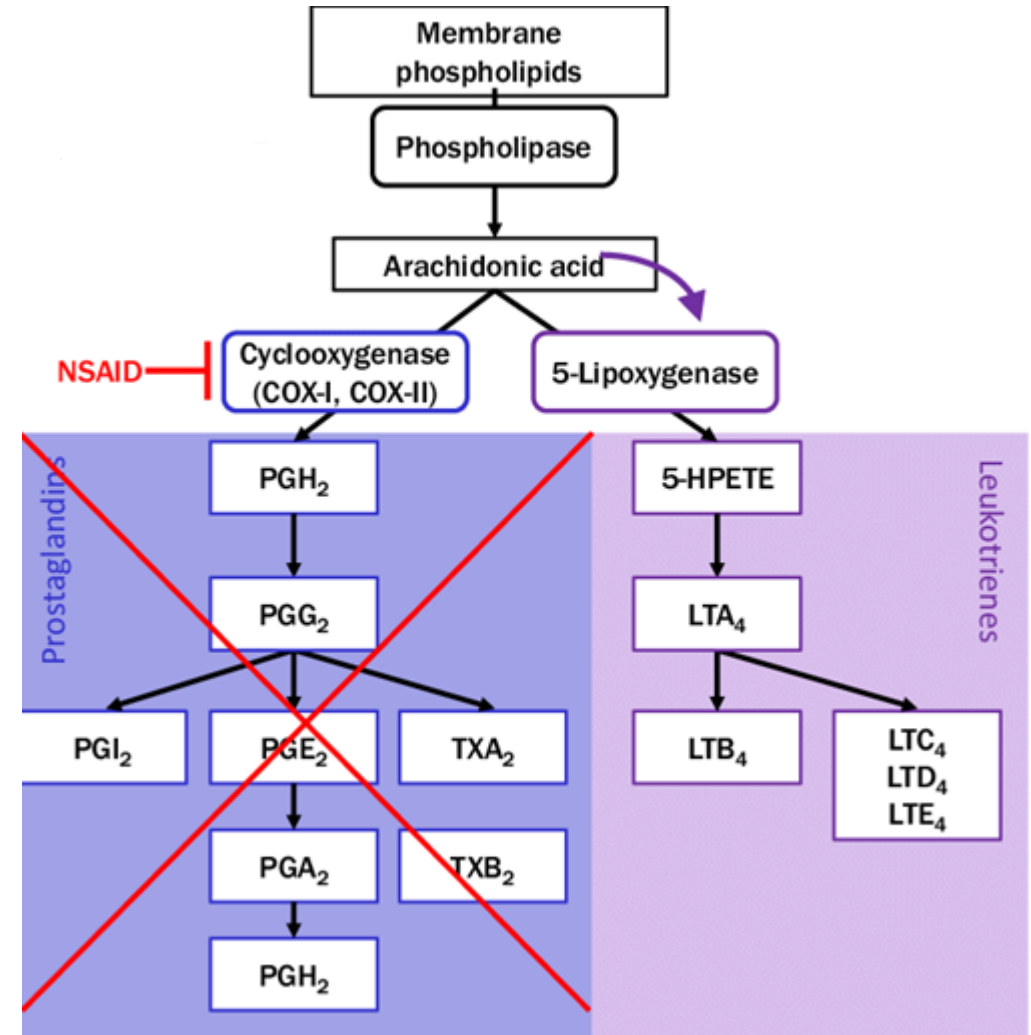
# Brief Review AERD

## Samter's Triad

- Asthma
- CRS with Nasal Polyps
- Upper and lower respiratory symptoms with NSAID

# Brief Review AERD

- Asthma
  - 7-10% adult asthma have AERD (>1.4M USA)
  - 14-15% of severe asthma have AERD
- CRS with Nasal Polyps
  - 30% adults with nasal polyps and asthma have AERD
- Upper and lower respiratory symptoms with NSAID
  - NSAID reactions with AERD are not IgE mediated
  - NSAID reactions are mediated by COX-1 inhibition
  - Dysregulation/Overproduction leukotrienes leading to increased infiltration of immune effectors



# AERD: Disease of Reduced Quality of Life

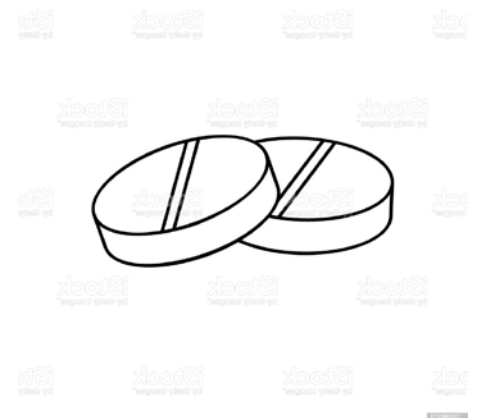
- Frequent clinical and surgical interventions
- Increased sleep dysfunction, reduced productive, and increased risk of depression
- Chronic nasal symptoms and decreased sense of smell – *loss of enjoyment of food and eating*

# What would be the ideal treatment for AERD?

- Effective
- Safe
- Well tolerated

# Option 1

- Schedule Sinus Surgery at hospital or surgical center
- Schedule AD 3-6 weeks after Surgery at specialized center
- By definition, have a reaction during AD
- Take 2 pills every day for at least 6 months and 1-2 pills every day uninterrupted





# Option 2

- Subcutaneous injection every two weeks at home



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# Multiple Biologics for AERD

- **Anti-IL-4/13: Dupilumab**
- Anti-IgE: Omalizumab
- Anti-IL-5: Mepolizumab, Reslizumab

1. Biologic therapy is more clinically effective than AD

- Better control of asthma
- Fewer surgeries

1. Biologic therapy is more clinically effective than AD

Why is asthma critical in AERD?

- 2015 Study *Respiratory Medicine* of 201 AERD patients
  - Poorly controlled asthma 91 (45%)
  - Partially controlled asthma 69 (34%)
  - 79% have either poorly or only partially controlled asthma

1. Biologic therapy is more clinically effective than AD

Dupixent is more effective than AD for asthma control in AERD

- Probability of asthma exacerbation (2021 analysis)
  - Standard medical therapy - 20%
  - AD - 16%
  - Dupilumab - 6%
- RCT AD 25 patients (JACI) - 48% noted improved asthma with AD

1. Biologic therapy is more clinically effective than AD

- Dupixent therapy is more effective at reducing surgery than AD

2021 Analysis Revision Surgery

- AD arm 6.45%
- Dupilumab 1.56%

1. Biologic therapy is more clinically effective than AD

Dupixent therapy has also demonstrated efficacy

- Sino-nasal symptoms and SNOT-22 scores (SINUS 24/52 Trial in 2019)
- Reduced corticosteroid bursts (2021, Wangberg)
- Reduced median antibiotic courses for respiratory disease (2021, Wangberg)
- UPenn Smell Identification score (2019, Laidlaw)



1. Biologic therapy is more clinically effective than AD

1. Better at controlling asthma
2. Better at reducing surgical interventions
3. Also improves sino-nasal symptoms and reduces corticosteroid/antibiotic need

## 3 Reasons why Biologic Therapy is Preferred for AERD

1. Biologic therapy is **more clinically effective** than AD
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## 2. Biologic therapy is safer than AD

- Short term
- Long term

## 2. Biologic therapy is safer than AD

- Short term effect
  - Anaphylaxis: Dupilumab had 1 anaphylaxis episode in the pivotal trials
  - AD 2021 long term study found 0.92% rate of anaphylaxis
- Long term effects
  - Nasopharyngitis
  - Injection site reaction
  - Conjunctivitis (more frequent atopic dermatitis patients)

Adverse Reaction	DUPIXENT 200 mg Q2W + SOC n=779 n (%)	DUPIXENT 300 mg Q2W + SOC n=788 n (%)
Injection site reactions <sup>a</sup>	111 (14)	144 (18)
Oropharyngeal pain	13 (2)	19 (2)

## 2. Biologic therapy is safer than AD

Contrast: expect reaction with AD

- Study of 167 consecutive AD - 23 (13.7%) were classified as severe
  - FEV1 drop >30%
    - FEV1 decline >20% observed in 37% of patients with AERD
  - GI reaction
    - 10-30% develop systemic GI symptoms (n/v/d) - treatment or prevention of this side effect is not easy
  - IM Epi
  - 3 more doses of Beta agonist
- Rare but important side effects
  - Laryngeal spasms – specialized centers
  - Coronary artery vasospasm
  - Acute pancreatitis (JACI 2012, JACI 2013)
- **Of note: history of severe reactions to NSAID is not predictive of reaction severity during office challenge**

### 3. Biologic therapy is better tolerated than AD

- Contraindications
- Side Effects
- Discontinuation rates

### 3. Biologic therapy is better tolerated than AD

- Fewer contraindications
- Fewer side effects
- Lower discontinuation rate

### 3. Biologic therapy is better tolerated than AD

- Contraindications to Dupilumab

- Hypersensitivity to drug

- Contraindications to AD

- Poorly controlled asthma
- Gastric ulcers
- GI bleed
- Upcoming surgery
- Pregnancy
- EOE



### 3. Biologic therapy is better tolerated than AD

AD has more side effects:

- Major Complications of AD and maintenance therapy AERD (2021) – 109 patients
  - GI bleed required admission and pRBC
  - 9 patients diagnosed with gastritis after starting AD and discontinued AD
  - Most epigastric pain is gastric irritation from NSAID, some patients with GI demonstrated biopsy-proven EOE. EOE-AERD patients had greater rates of gastric irritation at follow-up visits ( $P < 0.001$ ) and of aspirin discontinuation due to gastric irritation ( $P < 0.05$ ) than the non-EOE group

Complication	n (%)
Gastritis	9 (8.2)
GI bleed	1 (0.92)
Anaphylaxis	1 (0.92)
Exacerbation of upper airway symptoms	1 (0.92)
Recurrent epistaxis	1 (0.92)
Exacerbation of lower airway symptoms	4 (3.7)
Cutaneous reaction (nummular rash)	1 (0.92)

### 3. Biologic therapy is better tolerated than AD

#### Dupilumab has lower discontinuation rate

- 2013 Study - 24 of 172 patients (14%) discontinued AD in first year due to side effects, majority epigastric
- 2021 Study – 18 of 109 patients (14.7%) discontinued aspirin therapy due to complications (**10 during AD**)
- 2020 study - 171 patients (63%) discontinuation rate (did not affect the number of perioral steroid courses - mean 7.6 year follow up)
- 2021 analysis estimates probability of discontinuing therapy in first / subsequent years
  - AD: 33% first year, 5.6% subsequent
  - Dupilumab: 11% first year, 2.1% subsequent

## 3 Reasons why Biologic Therapy is Preferred for AERD

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# Rebuttal

- One Clarification
- Is AD a cheaper than biologic?
- Conclusion

# Clarification

- AD does work and can be safe in some cases
- Biologics work better, is safer, and better tolerated

# 3 Reasons why Biologic Therapy is Preferred for AERD

1. Biologic therapy is **more clinically effective** than AD
  1. Better control of asthma, fewer exacerbations
  2. Better reduction of surgeries
2. Biologic therapy is **safer** than AD
  1. Fewer severe complications during AD
  2. Less complications in the long term
3. Biologic therapy is **better tolerated** than AD
  1. Fewer contraindicated groups
  2. Lower rates of discontinuation

# Dupilumab Cost-Effectiveness (2021 Yong)

- Dupilumab for the treatment of severe CRSwNP **was found to be cost-effective**
  - Salvage therapy under the willingness-to-pay threshold of \$150,000
  - Initial therapy for willingness-to-pay threshold of \$200,000
- Cost-effectiveness analysis was sensitive **gains in quality of life**

# Are you getting what you pay for?

- More frequent asthma exacerbations
- More frequent revision surgeries and initial surgery
- More side effects – anaphylaxis, gastritis
- More contraindicated groups – poorly controlled asthma, GI bleed, pregnant, anticoagulation, needing surgery
- More barriers to care – surgery prior to starting, specialized center to do AD, stopping prior to other needed surgical procedures



# Aspirin and USPTF: Even low dose is not without harm

## Recommendation Summary

Population	Recommendation	Grade
Adults ages 40 to 59 years with a 10% or greater 10-year cardiovascular disease (CVD) risk	The decision to initiate low-dose aspirin use for the primary prevention of CVD in adults ages 40 to 59 years who have a 10% or greater 10-year CVD risk should be an individual one. Evidence indicates that the net benefit of aspirin use in this group is small. Persons who are not at increased risk for bleeding and are willing to take low-dose aspirin daily are more likely to benefit.	C
Adults age 60 years or older	The USPSTF recommends against initiating low-dose aspirin use for the primary prevention of CVD in adults age 60 years or older.	D

# For AERD, we all want

- Fewer asthma exacerbations
- Fewer surgical interventions
- Fewer side effects – in short and long run

# Final takeaways

- **Biologics work better, in more patients**
- AERD Cohort
  - Poorly controlled asthma 91 (45%)
  - Partially controlled asthma 69 (34%)
- Majority (79%) or plurality (45%) would better benefit from biologic therapy
- **Aspirin desensitization is the past, Dupilumab is the future**

## Conclusion: 3 Reasons why Biologic Therapy is Preferred for AERD

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Thank you!

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