

A scenic view of a rocky coastline with turquoise water and a large tree in the foreground. The text is overlaid on the left side of the image.

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University of California
San Francisco

Updates in Eosinophilic Esophagitis

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Disclosures

- Phathom Pharmaceuticals

Objectives

- Discuss **epidemiology** of eosinophilic esophagitis (EoE)
- Review **clinical presentation** as it relates to **pathogenesis** of EoE
- Assess various **treatment options** for EoE
- Highlight **'treat to target'** approach

Eosinophilic Esophagitis (EoE): Overview

- Increasingly recognized as a clinical entity
 - First case described in the mid 90s
- Incidence:
 - Adults - 7.7/100,000 per year
 - Children – 6.6/100,000 per year
- Healthcare costs: \$500 – \$947 million/year

EoE: Epidemiology

- Male:Female 3:1
- Biphasic age at presentation
 - Children age 6-10
 - Adults age 30-40
- Association with other atopic conditions
- Family history:
 - In monozygotic twins, proband concordance: 58%

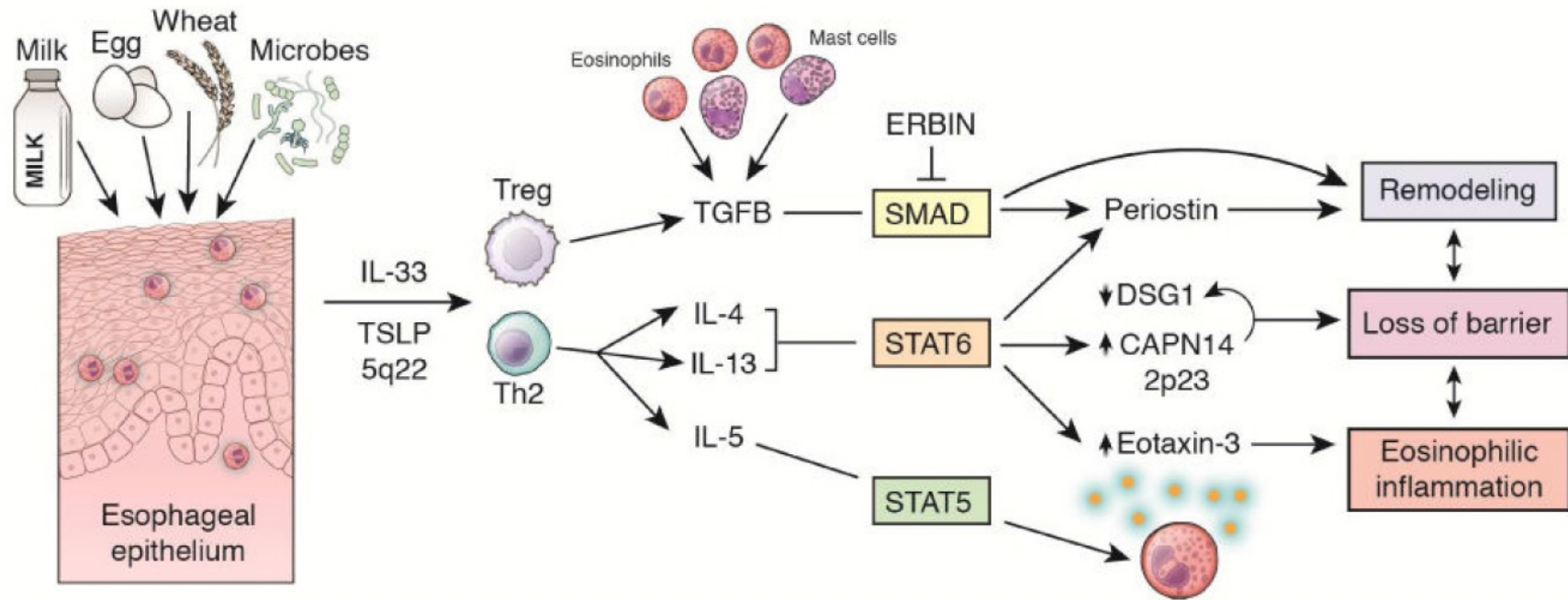
EoE: Clinical Presentation

Table 1

Most common presenting symptoms of eosinophilic esophagitis by age

Age	Infants/Younger Children	Older Children/Adolescents	Adults
Symptoms	Feeding refusal Delayed feeding skills Textural preferences Vomiting chronic nausea/abdominal pain Regurgitation Irritability	Preference for soft/ liquid diet Heartburn Abdominal pain Vomiting Dysphagia/choking/ food sticking Fear/anxiety with meal Food impaction	Dysphagia Chest/upper abdominal pain Heartburn

EoE: Pathogenesis



EoE: Making the Diagnosis

- AGREE group consensus
- Diagnosis:
 - 1) Clinical symptoms of esophageal dysfunction
 - 2) Esophageal eosinophilic count >15 eos/hpf
 - 3) Exclusion of other causes of esophageal eosinophilia

EoE: Treatment options

- PPI use
- Topical steroids
- Dietary interventions
- Dupilumab

EoE: Proton Pump Inhibitors

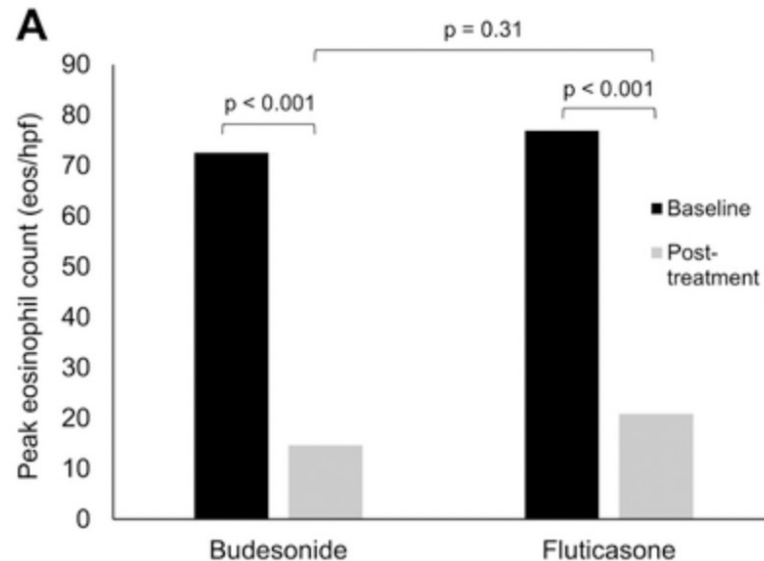
- PPI use *off label
 - No longer required for diagnosis of EoE
 - Traditionally tried at higher dosages than GERD
 - Overall effectiveness for histologic response: 42% vs 13% placebo
 - PPIs have anti-inflammatory effects in addition to acid suppression

EoE: Topical corticosteroids

- Topical corticosteroids *off label
 - Fluticasone metered dose inhaler
 - Budesonide slurry
 - ~~Budesonide oral suspension~~
 - Fluticasone oral disintegrating tablet: phase 3
 - Budesonide orodispersible tablet
- 8 total RCTs in children and adults:
 - Histologic response 65% vs 13% in placebo

EoE: Topical corticosteroids

- Topical corticosteroids *off label
 - Fluticasone inhaler vs Budesonide slurry



EoE: Topical corticosteroids

- Adverse effects
 - Esophageal candidiasis
 - Adrenal suppression
 - Other less common side effects: cataracts, osteoporosis

EoE: Dietary interventions

- Three basic categories:
 - 1) allergy based diet
 - 2) elemental diet
 - 3) elimination diet
 - 6-food: dairy, wheat, eggs, soy, nuts, shellfish/seafood
 - 4-food: dairy, wheat, eggs, soy
 - 2-food: dairy, wheat

EoE: Dietary interventions

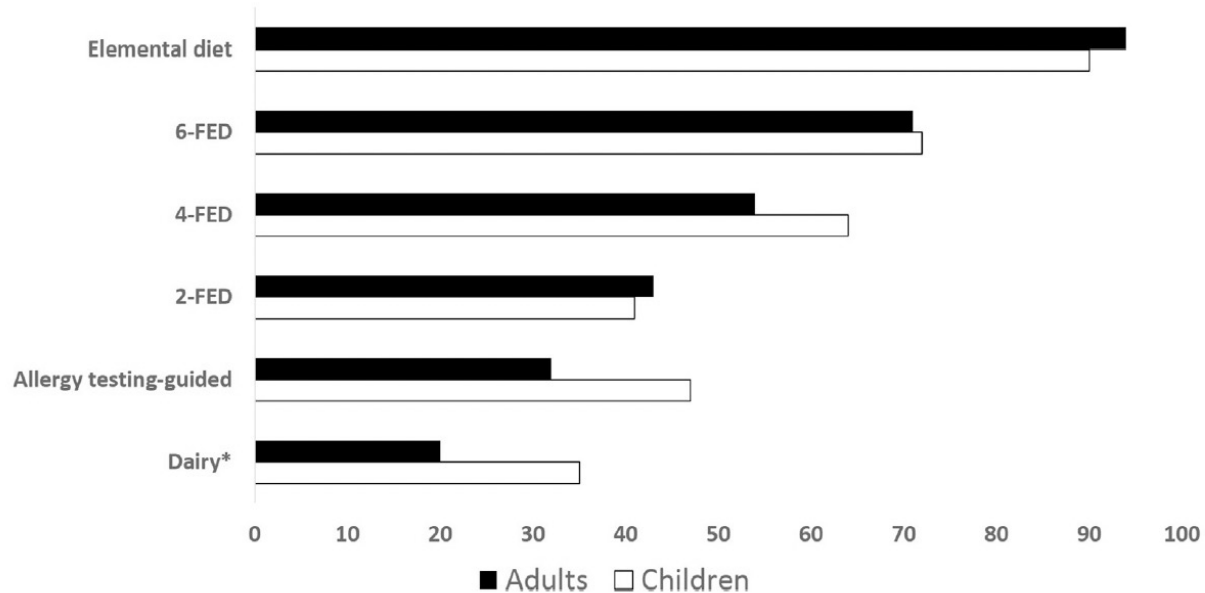


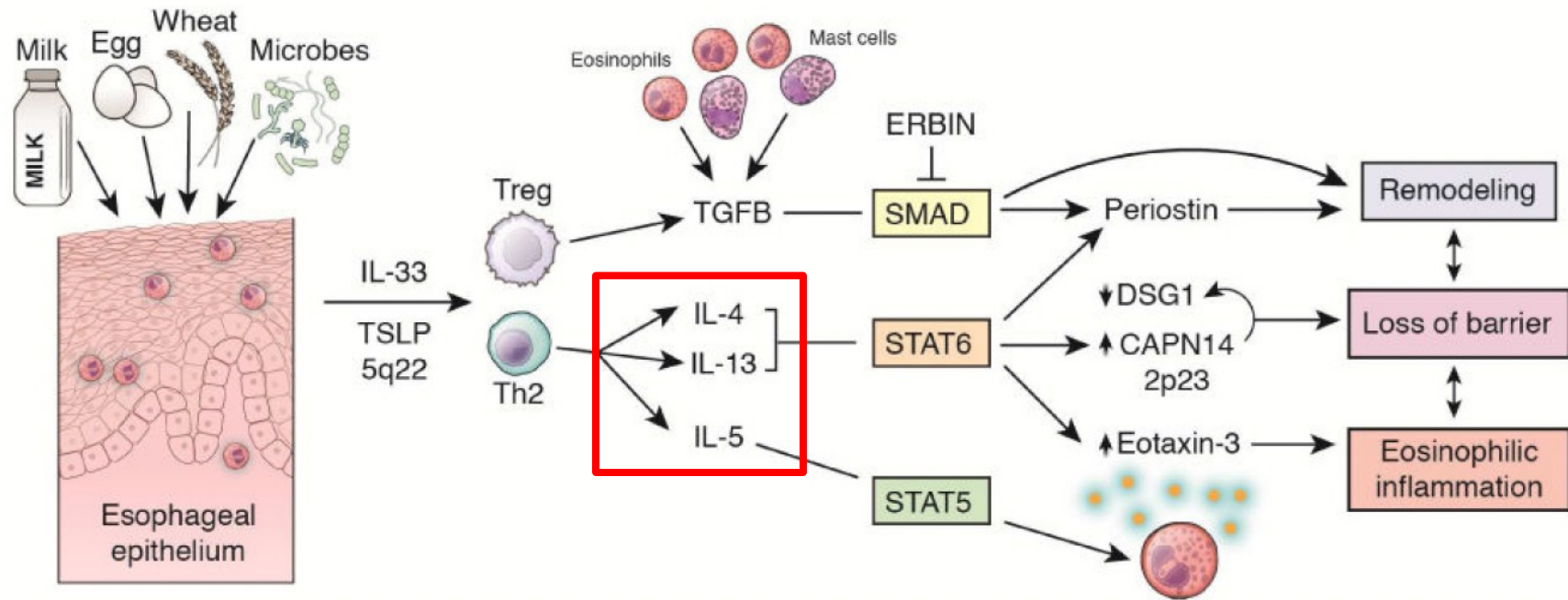
FIG 1. Histologic remission rates broken down by age group and shown by different modalities of dietary therapy (elemental diet, empiric elimination diet, and allergy testing-guided elimination diet) for EoE. *Indirect data from prospective studies on 4-FEDs and 2-FEDs. Efficacy of milk elimination diets in children ranges from 33% to 56%.

EoE: Six-food vs one-food elimination diet

- Randomized, multicenter study of one (milk) vs six food elimination diet (n = 129, age 18-60)
- Nearly identical proportion of patients in histologic, clinical, endoscopic remission in both study arms over 6-week study period

➔ Consider one-food elimination diet to start

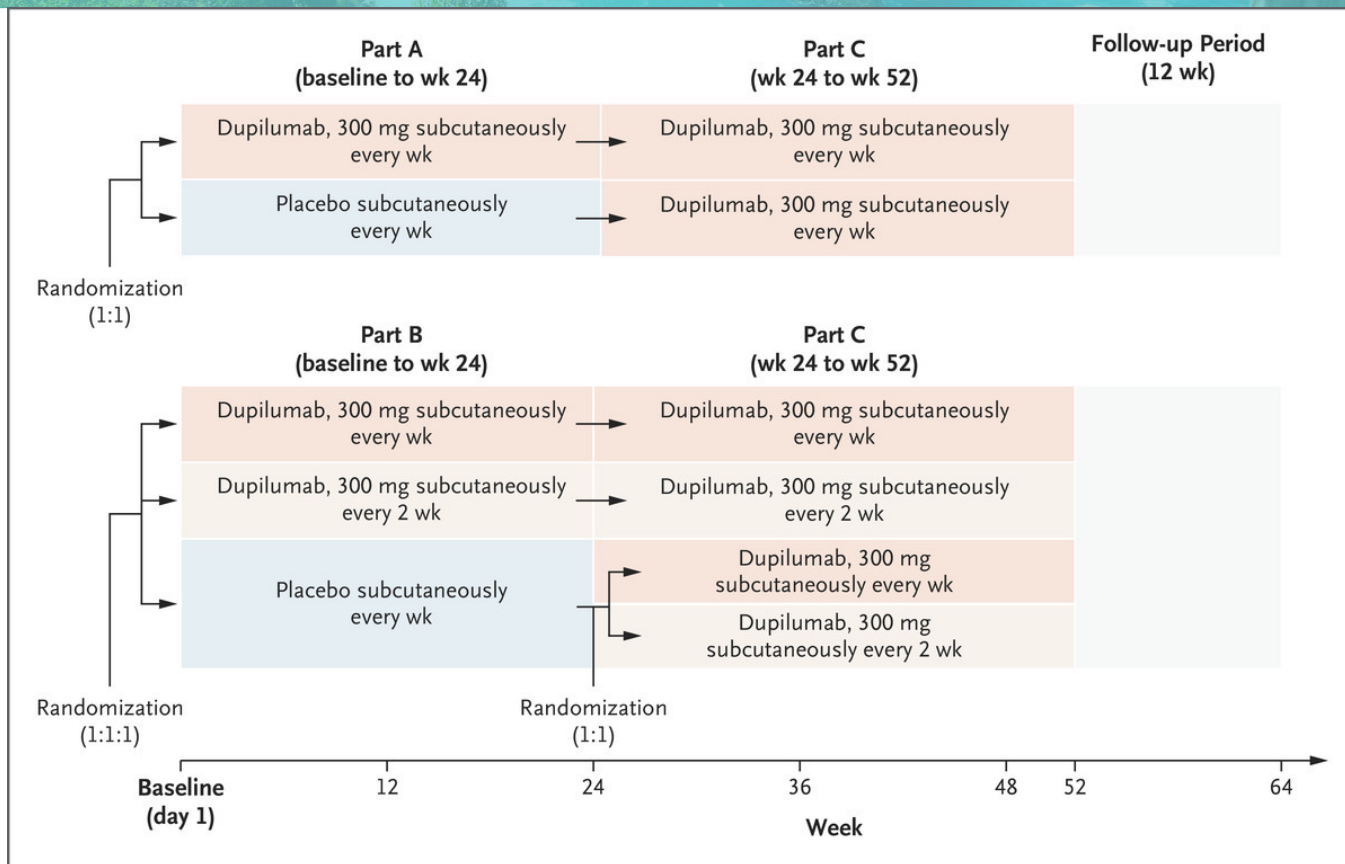
EoE: Targeting other therapies



EoE: Dupilumab

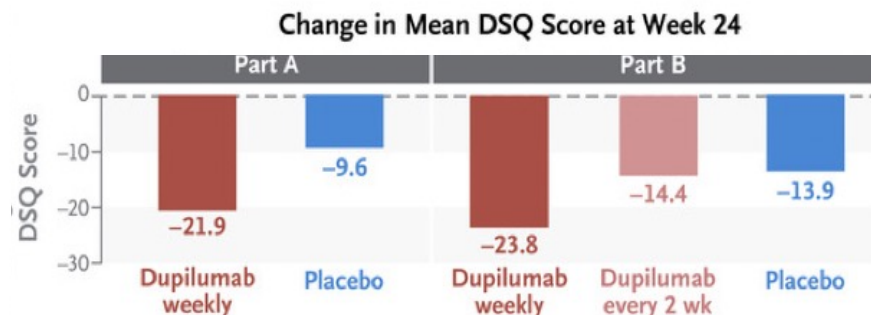
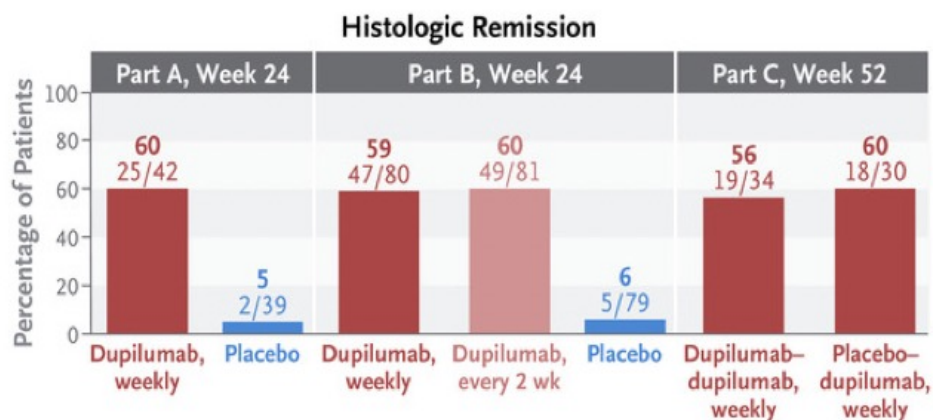
- Human monoclonal IgG4 antibody
 - Inhibits IL-13 and IL-4 signaling by binding to IL-4R α
- **First FDA approved drug** for EoE as of May 2022
 - Previously approved for asthma, atopic dermatitis, nasal polyposis
- Bioavailability: 60-65%
- Time to peak: 1 week

EoE: Dupilumab, Phase 3 Study Design



EoE: Dupilumab, Phase 3 Results

- Primary endpoints:
 - Histologic remission: peak eosinophilic count ≤ 6 eos/hpf
 - Absolute change from baseline in DSQ



EoE: Dupilumab, Phase 3 Adverse Events

Incidence of Adverse Events at Week 24

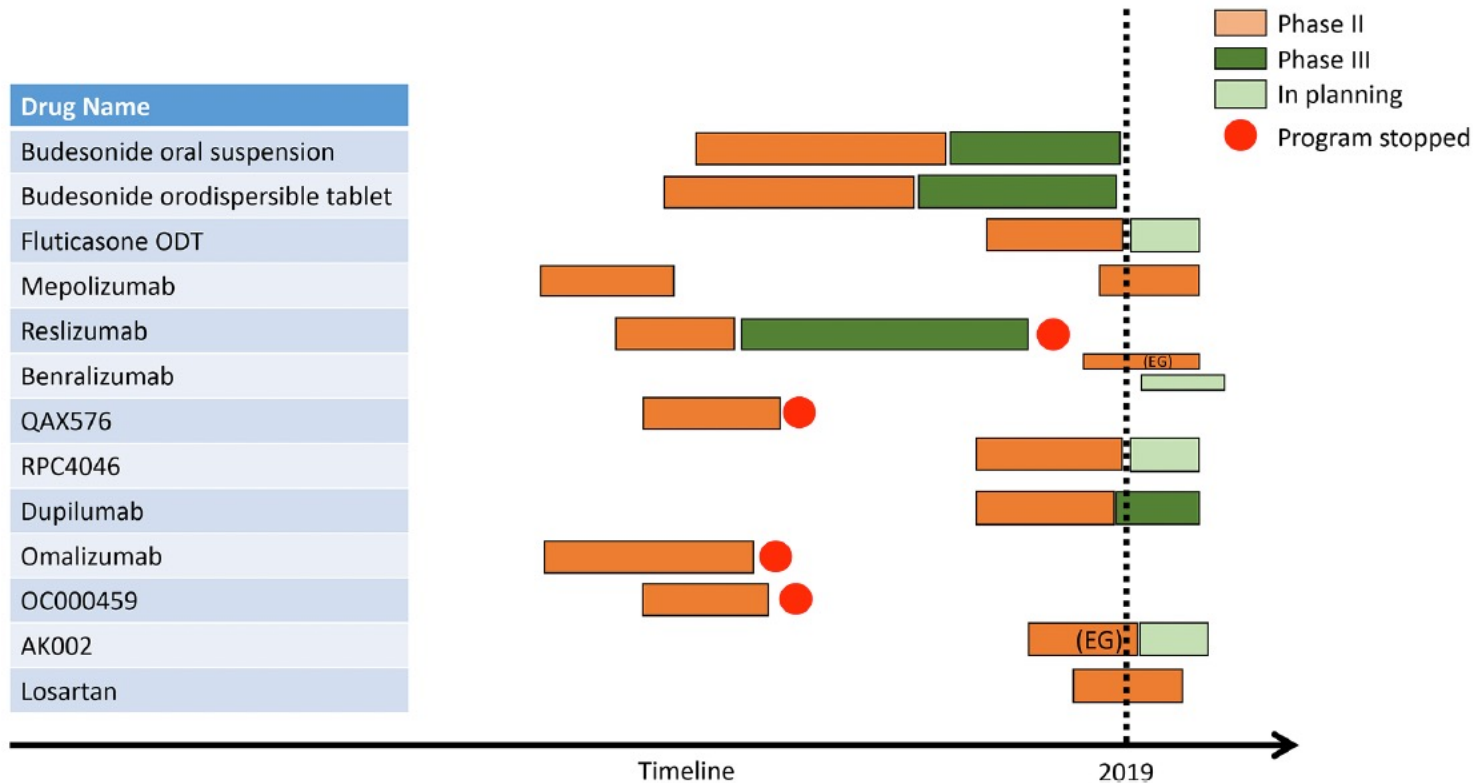
Adverse Event	Part A		Part B		
	Dupilumab, weekly (N=42)	Placebo (N=39)	Dupilumab, weekly (N=80)	Dupilumab, every 2 wk (N=81)	Placebo (N=78)
	<i>no. of patients (%)</i>				
Death	0	0	0	0	0
Any adverse event	36 (86)	32 (82)	67 (84)	63 (78)	55 (71)
Serious adverse event	2 (5)	0	5 (6)	1 (1)	1 (1)

- Adverse reactions:
 - Injection site reaction / URIs / Arthralgias / Herpes viral infections

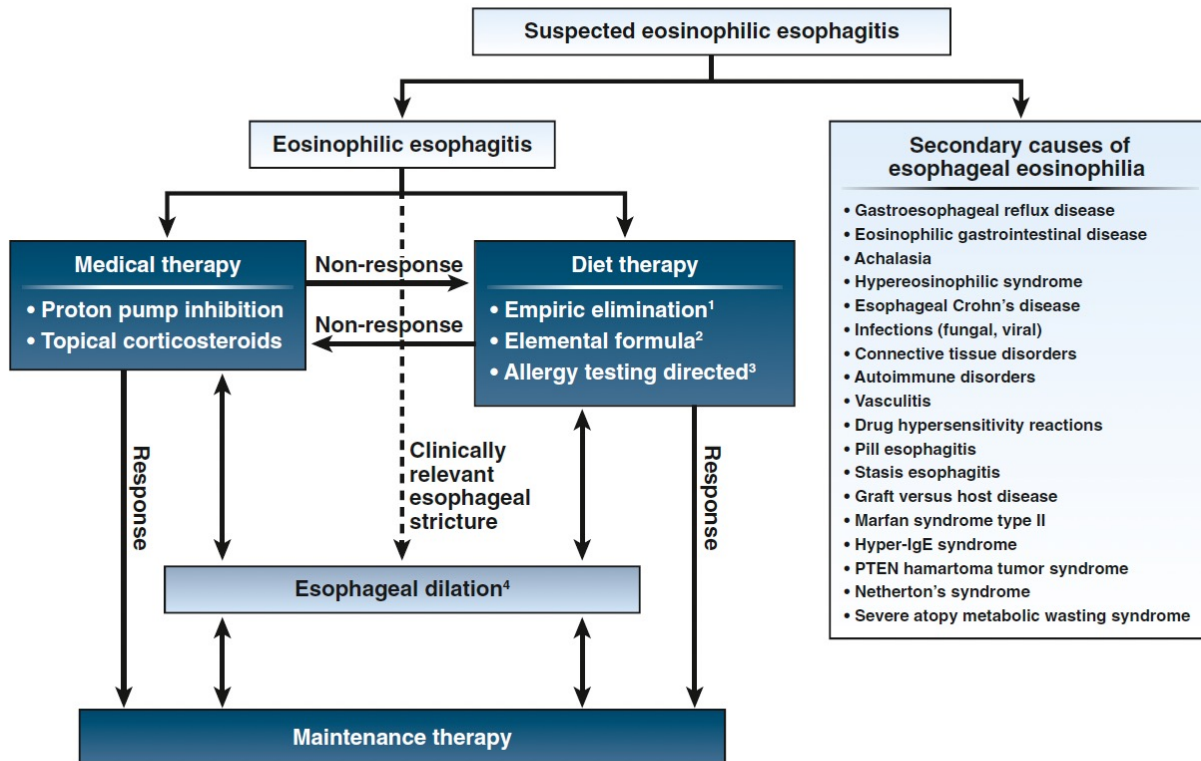
EoE: So who should get Dupilumab?

- Patients with:
 - Other atopic conditions
 - Lack of response to PPI
 - Poor response to topical steroids or elimination diets
 - Severe phenotypes
 - Patient preference

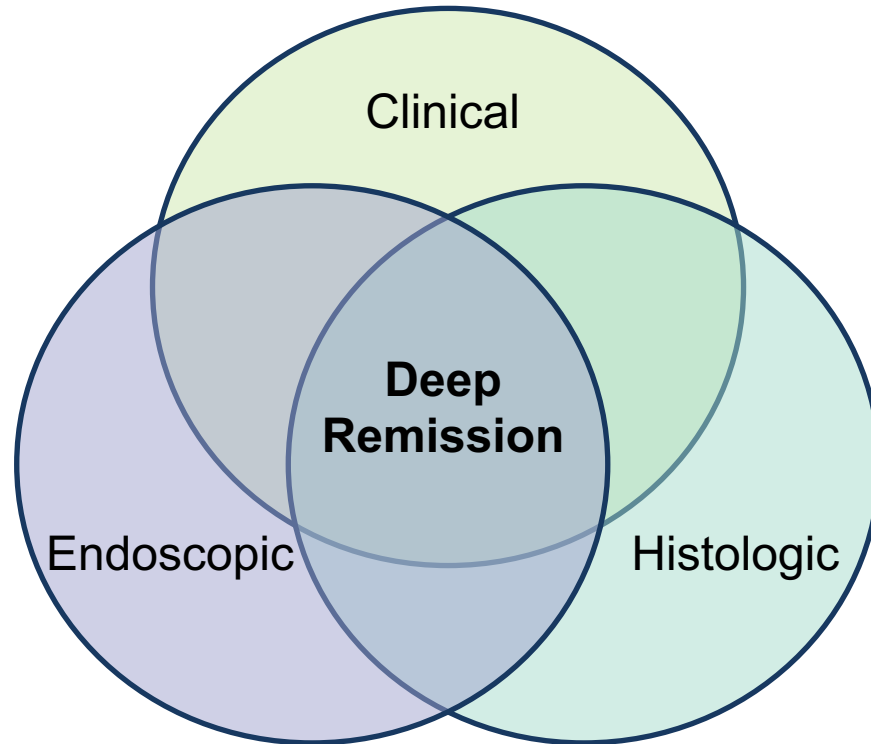
EoE: Other therapies



EoE: Approach to Therapy



EoE: Goals of Therapy



EoE: Summary

- EoE is more common in males and has bimodal age at onset
- Multiple different therapies
 - PPIs vs topical steroids vs elimination diet
 - 1st FDA approved drug: Dupilumab (in PPI refractory patients)
 - Several emerging biologics in the pipeline
- Maintenance therapy needed to prevent recurrence / progression
- Goal of therapy: deep remission

A scenic view of a coastline with a large tree in the foreground, a rocky shore, and the ocean. The image is overlaid with a semi-transparent teal filter.

Thank You!

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