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What's New in EoE, Esophageal String Test and more!

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Gastrointestinal Eosinophilic Diseases Program



What's New in EoE, Esophageal String Test and more!

Objectives:

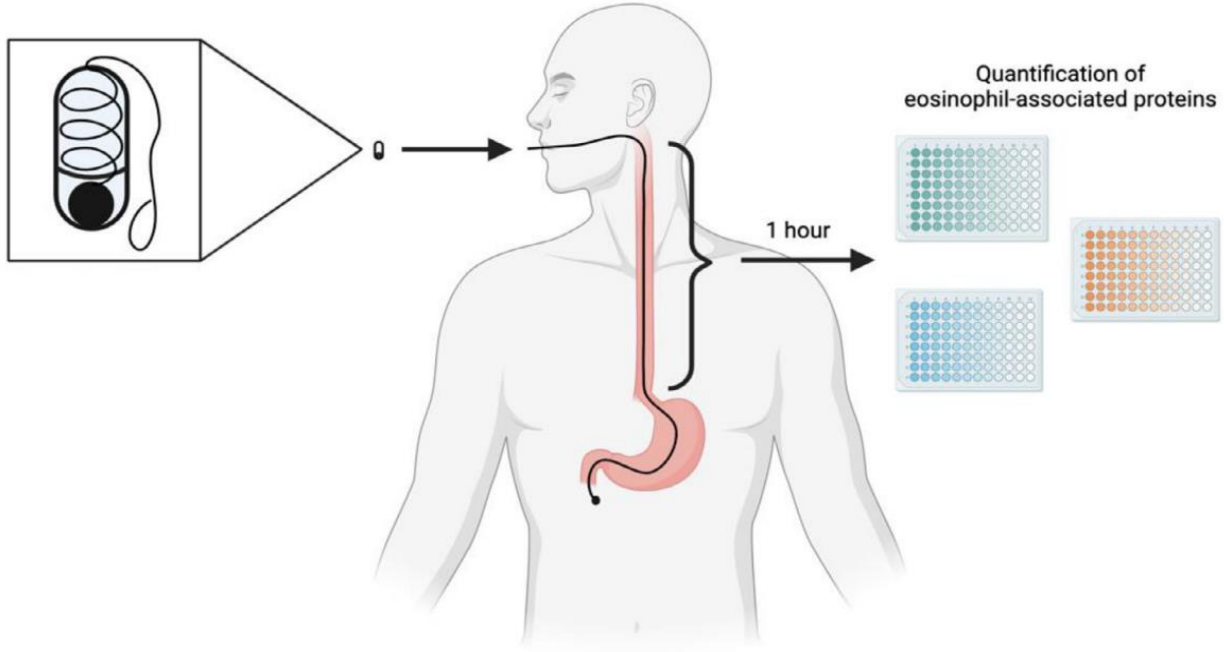
1. Review the clinical use of the Esophageal String Test (EST)
2. Discuss Implementation of EST into clinical practice
3. Provide updates and new Therapies in EoE

History of the Device

- Back in the 1970s, it was designed to identify small intestinal infections
- String would go down to small bowel and be evaluated for intestinal parasites
- Furuta et al developed to esophageal string test
- 41 children with active EoE (n=14), EoE in remission (n=8), gastro-oesophageal reflux disease (n=4) and controls with normal oesophagus (n=15).
- EST measurement of eosinophil-derived protein biomarkers significantly distinguished between children with active EoE, treated EoE in remission, gastro-oesophageal reflux disease and normal oesophagus.
- This had dwell time of 16 hours and was compared to endoscopy

Ackerman et al. Am J Gastroenterol, 2019.

Esophageal String Test



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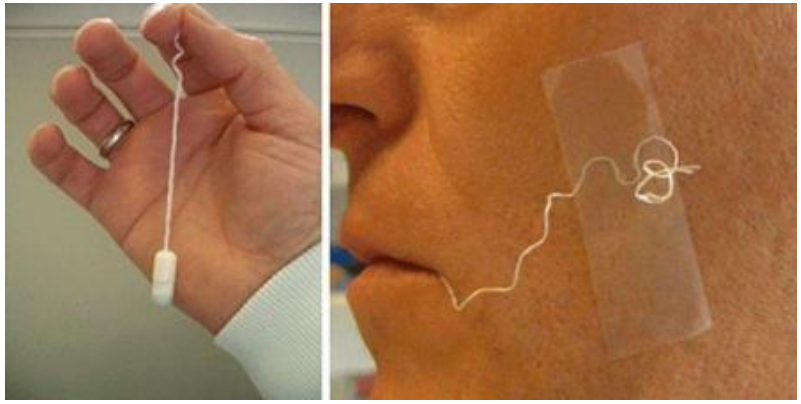
McGowan et al. Ann Allergy Asthma Immunol 2022.

Esophageal String Test

- 134 subjects, age 7-55 years
- Esophageal dwell time of 1 hour and subjects underwent endoscopy
- Eosinophil-associated protein levels were compared between EST effluents and esophageal biopsy extracts



Ackerman et al. Am J Gastroenterol, 2019.

Esophageal String Test

- EST captures eosinophil-associated biomarkers
- The combination of Eotaxin 3 with MBP-1 improved sensitivity/specificity for distinguishing active EoE from inactive EoE and normal patient controls

Table 2. Outcome measures for the EST (string) compared to biopsy for the 2 biomarker model[a] for all subjects[b] (active EoE[c], inactive EoE[d], and normal esophagus)

Predictors Eot3 +	Probability level	Sensitivity	Specificity	Positive predicative value	Negative predicative value	ROC AUC[e]
MBP1						
String	0.46833	0.72	0.89	0.86	0.76	0.86
Biopsy	0.52499	0.76	0.93	0.92	0.79	0.90

Furuta et al. Gut, 2013.
Ackerman et al. Am J Gastroenterol, 2019.

Esophageal String Test

- EST is 90 cm nylon string attached to a weight gelatin capsule (size of a jelly bean)
- EST is in place for 1 hour, string removed and esophageal segment measured for eosinophil associated proteins.
- Biomarkers (Major Basic Protein and Eotaxin-3) correlate with peak eosinophil count and endoscopic visual scoring and can distinguish active from inactive EoE and controls

The 1-hour EST distinguishes active from inactive EoE in children and adults and can facilitate monitoring of disease activity in a safe and minimally invasive fashion

Indications and Contraindications

- Clinical use of EST
  - The EST is FDA approved for follow up of EoE
- Contraindications:
  - **Allergy to Gelatin**
  - Unable to swallow pill
  - Esophageal stricture

Table 4. Subject satisfaction survey

Question	Pediatric subject	Parent	Adult subject
Willing to repeat EST?			
Yes	45/46 (98%)	42/44 (95.5%)	11/12 (92%)
No	1/46 (2%)	2/44 (4.5%)	1/12 (8%)
No response	4	6	1
Prefer EST or endoscopy if subject needed another evaluation?			
EST	32/43 (74.4%)	32/43 (74.4%)	9/12 (75%)
Endoscopy	7/43 (16.3%)	5/43 (11.6%)	3/12 (25%)
Neither	4/43 (9.3%)	6/43 (14%)	0/12 (0%)
No response	7	7	1
Prefer EST or endoscopy if EST could provide similar information?			
EST	39/45 (87%)	41/43 (95%)	12/13 (92%)
Endoscopy	5/45 (11%)	0/43 (0%)	1/13 (8%)
Neither	1/45 (2%)	2/43 (5%)	0 (0%)
No response	5	7	0

EST, esophageal string test.



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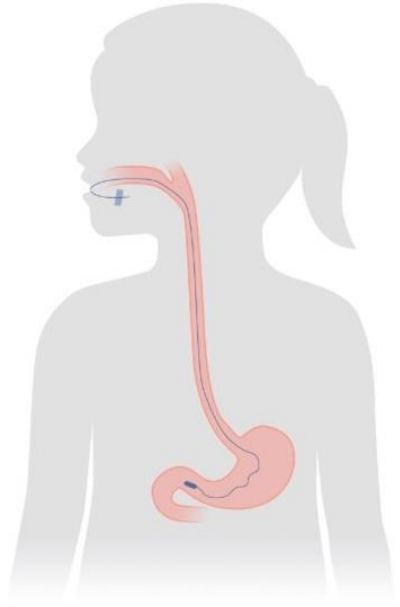
When to consider EST

- Consider string test for:
  - Follow up assessment of EoE
    - Initiation or changes in therapy
    - Increase or decrease in therapy
    - Removal or addition of foods
  - Assess if they need dosing change or have outgrown medication dose
    - Ie: well controlled on Flovent 110 mcg 2 puffs BID, but have they outgrown this dose and need Flovent 220 mcg 2 puffs BID?
  - Routine surveillance
    - Ie: well controlled on Flovent 110 mcg 2 puffs BID and need routine surveillance

Esophageal String Test



Esophageal String (E-String) Test: 23A-054Y0002

Status: **Final result**

0 Result Notes

Component	Ref Range & Units	
EoEScore(TM)	<0.530 Probability	1.000 ^

EoE Score & interpretation	
<0.530	Low likelihood active EoE
>0.530	High likelihood active EoE

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Data from 1st year of EST implementation at CHCO in GEDP

- 51 ESTs ordered, 45 ETS attempted, 39 ESTs were successful (87% successful completion rate) in 31 patients
  - 6 did not attempt due to insurance denials (n=4), prohibitive out of pocket cost (n=1),family chose to do TNE instead (n=1)
  - 46% Male / 54% Female
  - Mean age: 12 years old (range: 6–20 years old)
- Adverse events during the EST included vomiting (n = 3), swallowed the EST whole including the string (n=1)
  - These four patients were ultimately able to complete EST on a second attempt at the same visit.

Data from 1st year of EST implementation at CHCO in GEDP

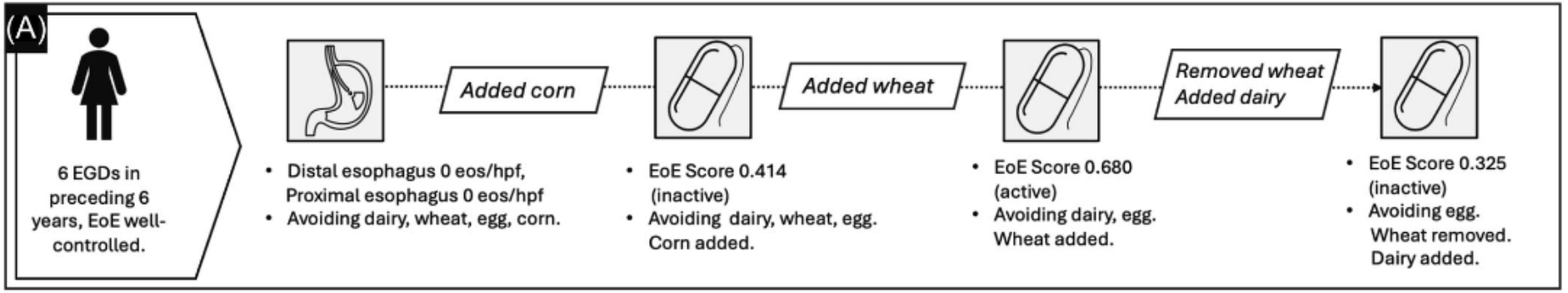
- Patients who failed to complete EST (n=6)
  - Age 7-12
  - Reasons: Patients were unable to swallow the pill (n = 5) and vomiting (n = 1)
- Number of ESTs within 1 year
  - 26 patients underwent 1 EST
  - 2 patients underwent 2 ESTs
  - 3 patients underwent 3 ESTs
- Average time spent in the clinic for EST was 129 min, range: 100–222 min
- Insurance types included
  - Private 80.7% (n = 25), Medicaid 16.1% (n = 5), TRICARE 3.2% (n = 1)

Esophageal String Test and Management Decisions

	Abnormal EST results, $n = 15$	Normal EST results, $n = 24$	p Value[a]
Average EoE score: mean (SD)	0.80 (0.13)	0.37 (0.08)	< 0.0001
Treatment changes: *n* (%)			
Escalations	4 (27%)		
Increased medication dose	4 (27%)	0	0.016
Started new medication	5 (33%)	0	0.005
Removed food	2 (13%)	0	
Further evaluation with endoscopy	2 (13%)	0	ns
Continued current therapy	1 (7%)	16 (67%)	0.0002
De-escalations			
Added food	1 (7%)	6 (25%)	ns
Decreased medication dose	0	2 (8%)	ns
Total number of endoscopies these patients underwent during this period: *n*			
EGD	6	5	ns
TNE	0	5	ns

Quinn, Andrews, Bauer, Nguyen. JPGN, 2024.

Clinical Scenarios- multiple EST in 1 year



Quinn, Andrews, Bauer, Nguyen. JPGN, 2024.

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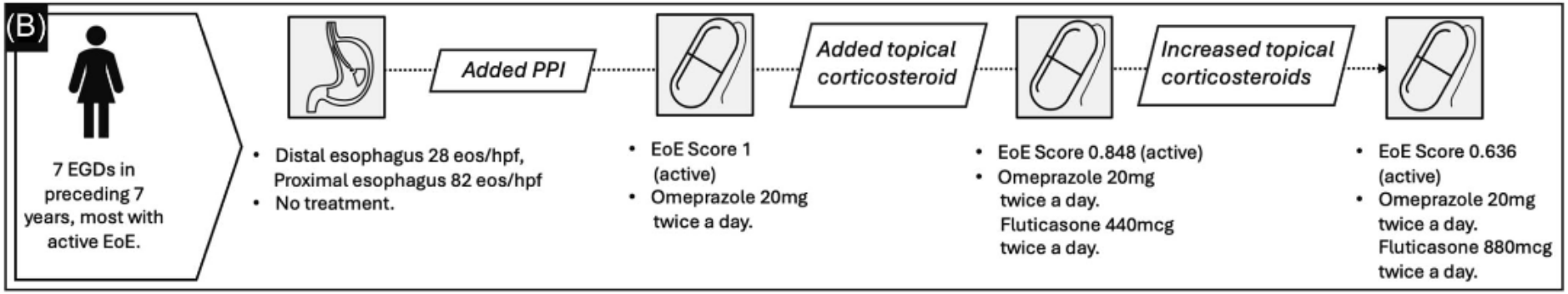

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Quinn, Andrews, Bauer, Nguyen. JPGN, 2024.

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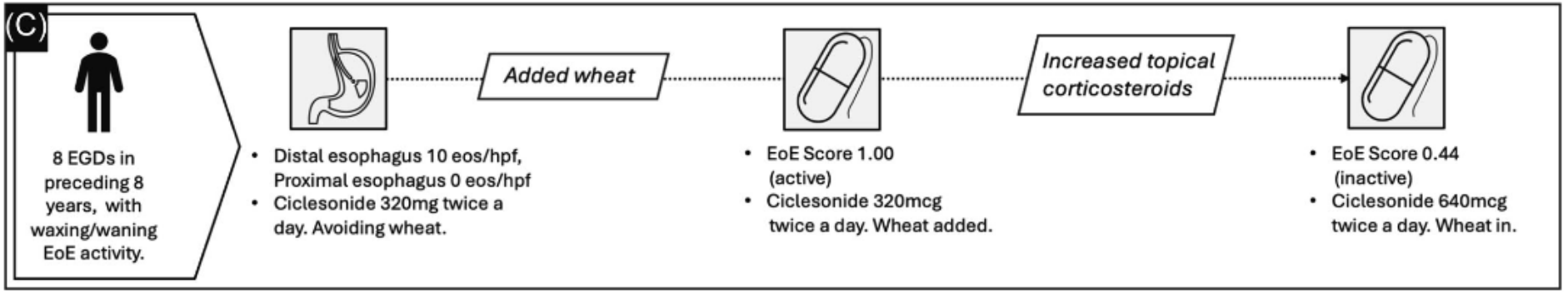

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Quinn, Andrews, Bauer, Nguyen. JPGN, 2024.

EST: Implementation in Practice

How much does it cost ?

- There is no cost for the EnteroTracker collection kit. Return shipping to EnteroTrack Labs is also pre-paid.

Is there a specialized billing code for the procedure ? How will clinics get paid ?

- Currently, there is no specialized procedure code for the collection. Clinics typically use a combination of E/M codes (level 4 or level 5), frequently with a code -25 modifier, **and a modest out of pocket fee of about $250 to cover clinic and personnel costs for administering the collection**.

EST: Implementation in Practice

Will EnteroTrack charge for the assay ?

- Yes, EnteroTrack Labs will charge the patient's insurance for the assay using an approved lab analysis code.
- **For cases of incomplete insurance payment, EnteroTrack will balance bill the patient to a maximum of $122.** Therefore, EnteroTrack will not charge patients more than $122 in out-of-pocket costs.

EST; Implementation in Practice

Is there a minimum order ?

- Yes, we ask that clinics commit to performing a minimum of 5 tests per month.

Will EnteroTrack train staff on sample collection ?

- Yes, EnteroTrack will set up in-service visits to train staff

Is dry ice required for shipping the sample ?

- No dry ice is needed. One component of the kit requires refrigeration

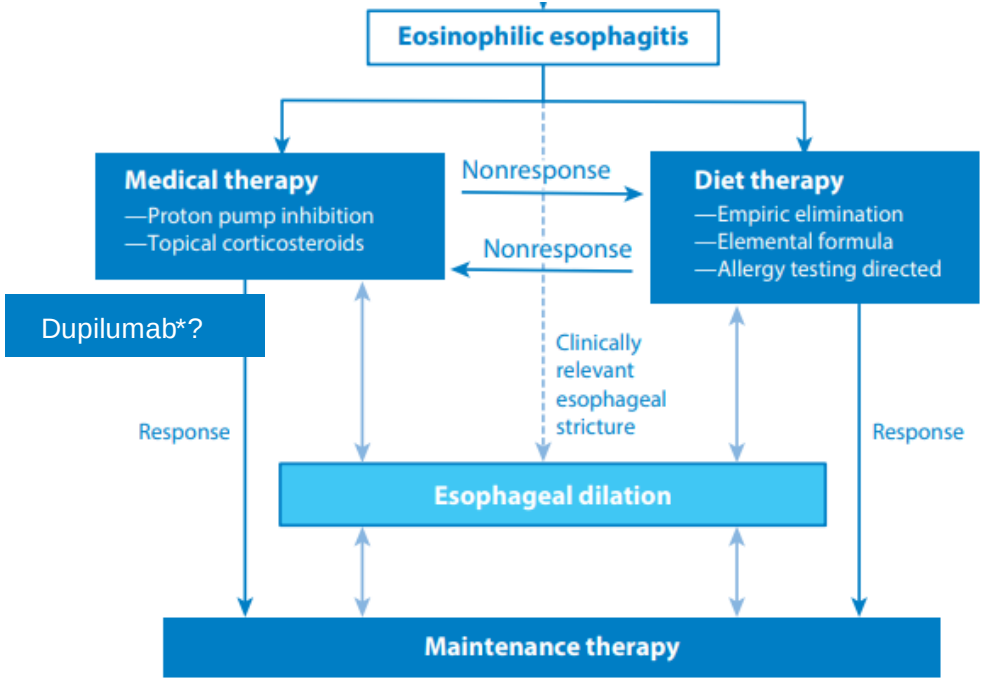
Who should I contact ?

- Please send an e-mail to info@enterotrack.com if you are interested in the test.

New Treatments/Recommendations in EoE

- Budesonide oral suspension (Eohilia)
- Dupilumab
- Monitoring recommendations in EoE

Approach to EoE Management



- Management strategies include drugs, diet elimination, and esophageal dilation
  - Drugs and diet reduce EoE-associated inflammation; dilation targets esophageal strictures and narrowing
- Treatment choice driven by patient preference, clinical features, and cost

*Guidelines were released before FDA-approved treatment became available.

Eosinophilic Esophagitis. American Academy of Allergy Asthma & Immunology. Revised May 1, 2023. Accessed August 2022. https://www.aaaai.org/Conditions-Treatments/related-conditions/eosinophilic-esophagitis
Katzka DA. *Ann Intern Med*. 2020;172:ITC65-ITC80; Cotton CC, et al. *Dig Dis Sci*. 2019; 64:1401–1408.

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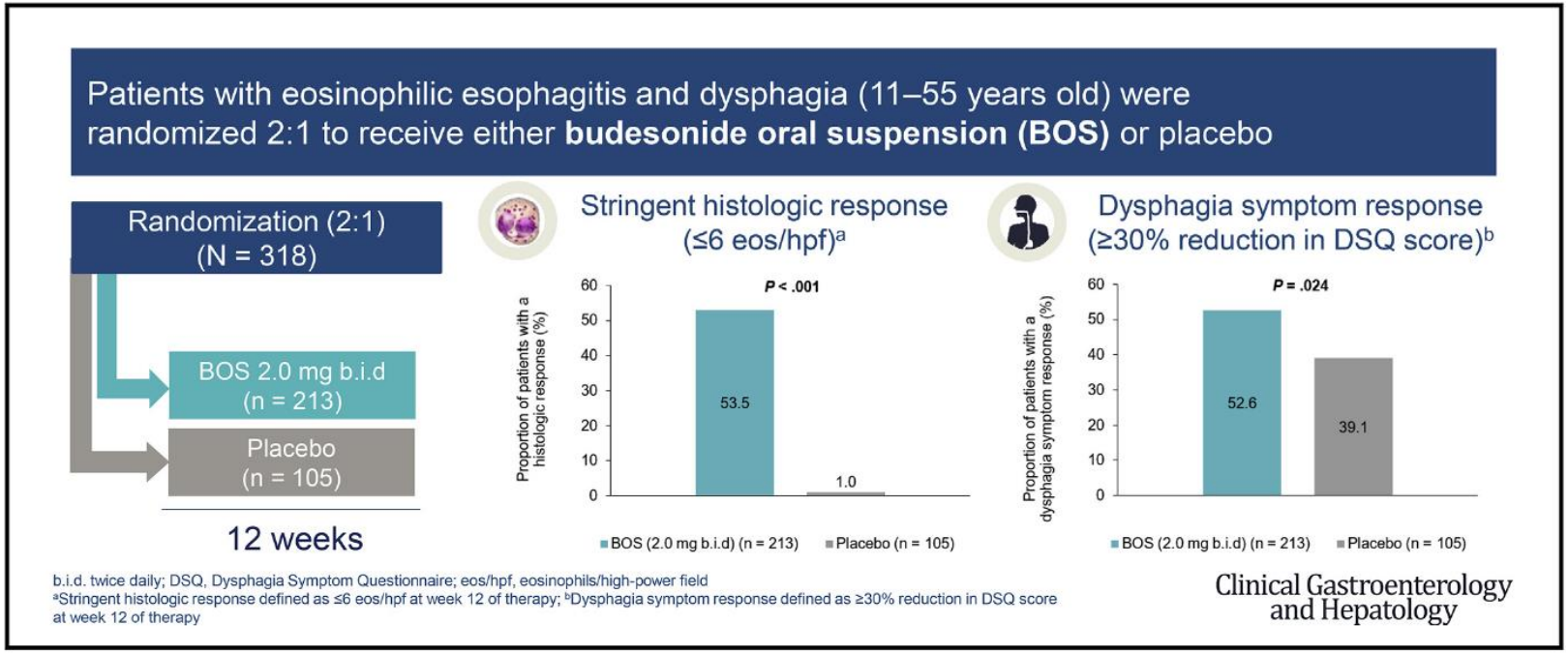
Barriers to swallowed topical corticosteroid therapy

- Strong recommendation in treatment of EoE
- Prior to 2024, no FDA approved therapy
- Off label use of asthma formulations
- Not designed for esophageal delivery
    - Suboptimal delivery may fail to control
- Patients frequently encounter difficulties obtaining insurance coverage for off-label medications

Hirano et al. Gastroenterolgy. 2020
Hirano et al. Clin Gastroenterol Hepatol 2017
Schupack et al. Dig Dis Sci 2021.

Budesonide Oral Suspension

Recently FDA-approved for people 11 years and older with EoE



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Clin Gastroenterol Hepatol. 2022 Mar;20(3):525-534.e10. Dellon ES, et al. *Gastroenterology*. 2017 Mar;152(4):776-786.e5. EOHILIA. Prescribing Information. Takeda Pharmaceuticals. Accessed February 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/213976s000lbl.pdf

Clinical Considerations

- Does NOT require mixing
- Insurance coverage barriers beyond 12 weeks of use?
- Adrenal insufficiency risk with longer use (2mg bid is higher end of dosing)?
- Long term Use in adolescents (12% of studied population was <18yo)?
- Limited flexibility of dosing

Clinical Use

The three-step overview for taking EOHILIA:

This is not all the information you need to know. Please refer to the Instructions for Use for complete information on how to take EOHILIA. Do not take with food or liquid.

1. **Shake & snip:** Shake the stick pack for at least 10 seconds before opening. Using scissors, cut along the dotted line straight across the top of the stick pack.

2. **Squeeze & swallow:** Take EOHILIA by squeezing the stick pack from the bottom to the top directly into the mouth. Repeat 2 to 3 times until all medicine is taken. Swallow all the EOHILIA suspension. Discard the empty stick pack in the household trash.

3. **Rinse & spit:** Do not eat or drink for 30 minutes after taking EOHILIA. After 30 minutes, rinse your mouth with water and spit out the contents without swallowing.

Do not mix EOHILIA with food or liquid. Avoid drinking grapefruit juice during treatment with EOHILIA. Do not eat or drink when taking EOHILIA and for at least 30 minutes after taking EOHILIA.



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EoE Topical Steroid Dosages Based On Age

	Years of Age	Years of Age	Years of Age	Starting Dosage
Medication	1-5	6-11	12 and older	All
Fluticasone (Flovent)	44 mcg	110 mcg	220 mcg	2 puffs swallowed twice a day. Order one inhaler per
Budesonide (Pulmicort)	0.25mg/2ml	0.5mg/2ml	1mg per dose (2 respules of 0.5mg, doubling Splenda or Nutra)	1 respule twice a day mixed with 5 packets Splenda or ½ teaspoon Nutra.
Ciclesonide (Alvesco)	80 mcg	80 mcg	160 mcg	2 puffs swallowed twice a day. Order two inhalers per month.
Beclomethasone Dipropionate (QVAR)	40 mcg	40 mcg	80 mcg	2 puffs swallowed twice a day. Order one inhaler per month.

Budesonide 2mg bid ≈ Fluticasone MDI 220mcg 4 puffs bid

Table 2. Summary of TEAEs by Treatment Group, and by System Organ Class, Preferred Term, and Treatment Group (Safety Set)

Category	BOS 2.0 mg Twice Daily (n = 213)	Placebo (n = 105)	Total (N = 318)
Infections and infestations			
Nasopharyngitis	11 (5.2)	4 (3.8)	15 (4.7)
Sinusitis	9 (4.2)	3 (2.9)	12 (3.8)
Esophageal candidiasis	8 (3.8)	2 (1.9)	10 (3.1)
Oral candidiasis	8 (3.8)	0 (0.0)	8 (2.5)
Gastrointestinal disorders			
Nausea	6 (2.8)	3 (2.9)	9 (2.8)
Vomiting	4 (1.9)	4 (3.8)	8 (2.5)
Investigations			
ACTH stimulation test abnormal	6 (2.8)	3 (2.9)	9 (2.8)
Respiratory, thoracic, and mediastinal disorders			
Cough	6 (2.8)	3 (2.9)	9 (2.8)
Skin and subcutaneous tissue disorders			
Acne	5 (2.3)	3 (2.9)	8 (2.5)
Nervous system disorders			
Headache	7 (3.3)	1 (1.0)	8 (2.5)

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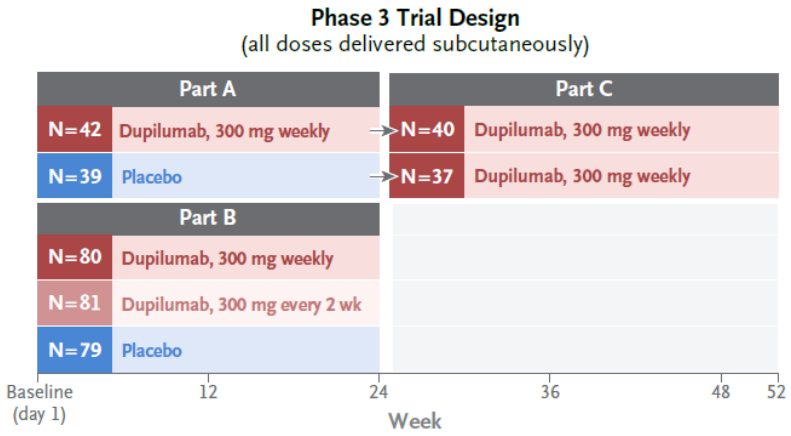
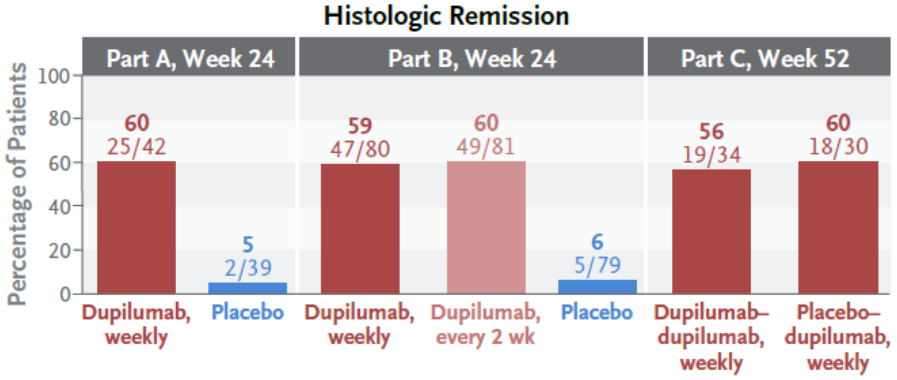
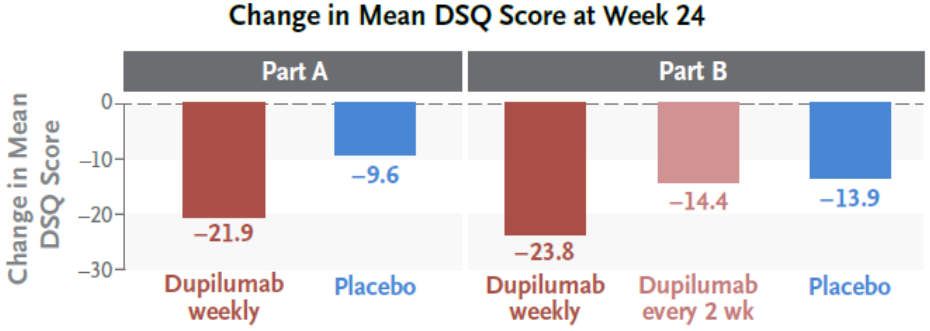
Dupilumab Phase 3 Results in EoE Patients ≥12 Years of Age







*The FDA has approved dupilumab for children aged 1 year and older, weighing at least 15 kg, based on the Phase 3 EoE KIDS trial (Part A and Part B) .

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Dellon ES et al. DOI: 10.1056/NEJMoa2205982

Dupilumab Phase 3 Results in EoE Patients 1-11 Years of Age

Table 2. Primary and Secondary End Points in Part A of the Trial (Full Analysis Population).

End Point	Placebo (N=34)	HE Dupilumab (N=37)	LE Dupilumab* (N=31)
Primary end point			
Peak esophageal intraepithelial eosinophil count of ≤6 per high-power field — no. (%)†	1 (3)	25 (68)	18 (58)
Absolute difference in percentage vs. placebo (95% CI) — percentage points	—	65 (48 to 81)	55 (37 to 73)
P value	—	<0.001	<0.001
Secondary end points			
Peak esophageal intraepithelial eosinophil count of <15 per high-power field			
No. of patients (%)	1 (3)	31 (84)	21 (68)
Absolute difference in percentage vs. placebo (95% CI) — percentage points	—	81 (68 to 94)	65 (48 to 83)
P value	—	<0.001	ND

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Chehade et al. NEJM 2024

Criteria to Consider Initiating Dupilumab

Clinical Scenarios Suggesting the Use of Dupilumab for Eosinophilic Esophagitis

Contexts Where First Line Use Should Be Considered

- Patients with multiple comorbid atopic conditions that include
  - Moderate, persistent, or difficult to control asthma
  - Moderate, persistent, or difficult to control atopic dermatitis
  - Difficult to control chronic sinusitis with nasal polyps
- Patients with a strong preference to avoid dietary restriction or topical swallowed steroids

Context when dupilumab can be considered as step up therapy

- Eosinophilic Esophagitis that is difficult to treat
- Patients with failure to thrive, poor growth or significant weight loss due to EoE
- Patient with frequent use of rescue therapies
  - Oral systemic steroids
  - Esophageal dilations
- Patients with severe diet restriction or requiring amino acid formula
- Patients with clinically significant esophageal strictures or narrow caliber esophagus
- Patients refractory to current therapy
  - Due to continued symptoms
  - Due to persistent abnormal esophageal inflammation
  - Due to adverse effects of current therapy
  - Due to intolerance of current therapy
  - Due to inability to adhere to current therapy
- Patients with adverse effects to current therapy

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Aceves S, et al. *Ann Allergy Asthma Immunol*. 2023 Mar;130(3):371-378.

Case Examples of Dupilumab

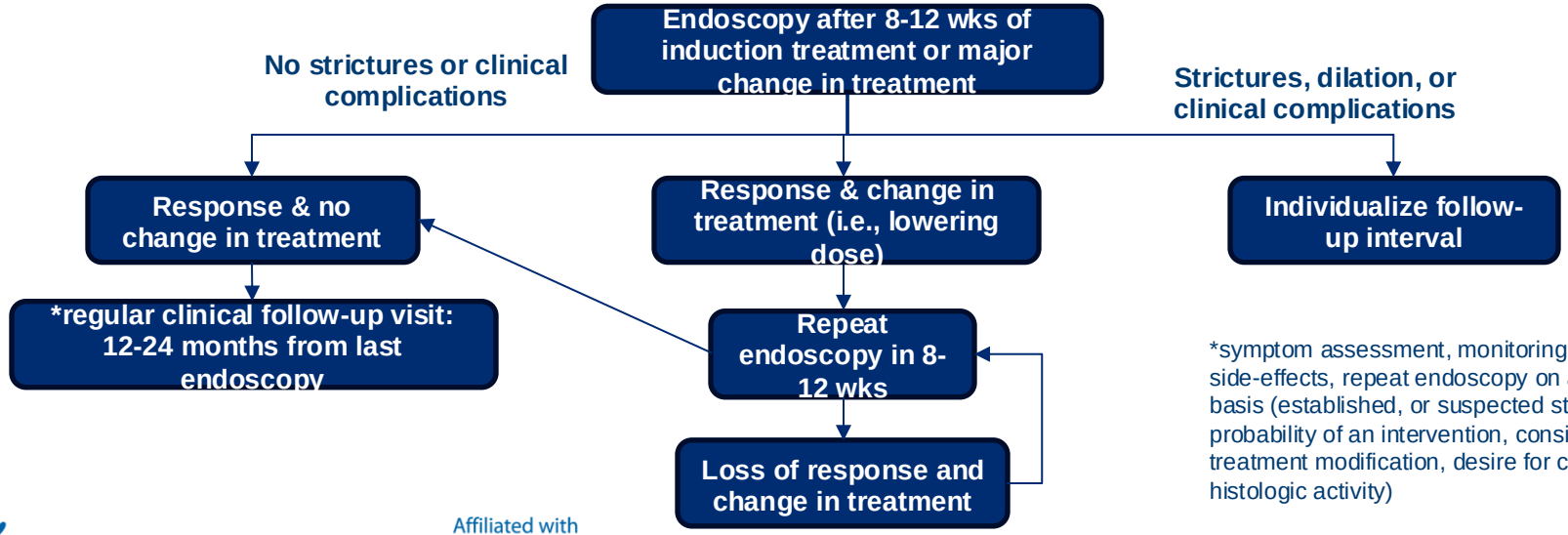
- 2yo M with failure to thrive, numerous food avoidances for IgE mediated food allergies and low AM cortisol on budesonide 0.25mg bid swallowed
- 17yo M with a history of stricture requiring repeat dilation not responsive (? compliance) to swallowed topical steroid therapy
- 12yo M whose EoE is not responsive to PPI with comorbid moderate atopic dermatitis recalcitrant to skincare
- 14yo F with EoE responsive to swallowed fluticasone but developed recurrent thrush

Clinical Considerations

- Dupilumab has less rapid onset that traditional therapies so likely need to wait longer for histological assessment
- Success in patients without atopic comorbidities?
    - 98% and 89% had coexisting atopic condition in peds and adult trials
- Dosing selection in patients with multiple comorbidities dupilumab is approved for?
- Trial of spacing out to q2 week dosing in >12yo?

Monitoring Patients with EoE in Routine Clinical Practice

A multidisciplinary, international group of EoE experts developed guidance on how to monitor patients with EoE in routine clinical practice, based on available clinical evidence and expert opinion. They published 11 statements and a proposed algorithm for monitoring patients with EoE.



*symptom assessment, monitoring of medication side-effects, repeat endoscopy on an individual basis (established, or suspected stricture and probability of an intervention, consideration of treatment modification, desire for clarification of histologic activity)

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Arnim et al. *Clin Gastroenterol Hepatol*. 2023 Sep;21(10):2526-2533.

Questions?