

North Carolina Society of Gastroenterology 2026 Annual Meeting



Eosinophilic Esophagitis in Focus What's Coming Next in the Therapeutic Pipeline

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DISCLOSURES

Steering Committee: TargetRWE

Health Sciences Advisory Council: APFED

OBJECTIVES

Review a guideline-based approach to care in EoE

Discuss the results of recent clinical trials

Learn about upcoming and ongoing studies in EoE

CASE

37 yo man presented to the ER with acute onset substernal chest pain in the middle of a meal. He has had dysphagia for several years and usually forces things up when they get stuck, but this episode lasted several hours.

Past medical history notable for asthma as a child (“I grew out of it”) and seasonal allergies (“much worse since moving to NC”). He is a pilot and frequently away from home.

CASE

He is not taking any medication and lives with his wife who has celiac disease (“we have a gluten-free house”).

EGD is performed and a food bolus is removed. Underlying this area is significant erosive change in the distal esophagus with a suspected stricture. A total of 6 biopsies were obtained and pathology demonstrates >15 eos/hpf in two separately sampled locations.

What treatment might you choose?

TREATMENT OPTIONS

- High dose daily Proton Pump Inhibitor
- High dose BID Proton Pump Inhibitor
- Swallowed topical steroid
- Biologic therapy
- Structured elimination diet
- Dilate and observe the course

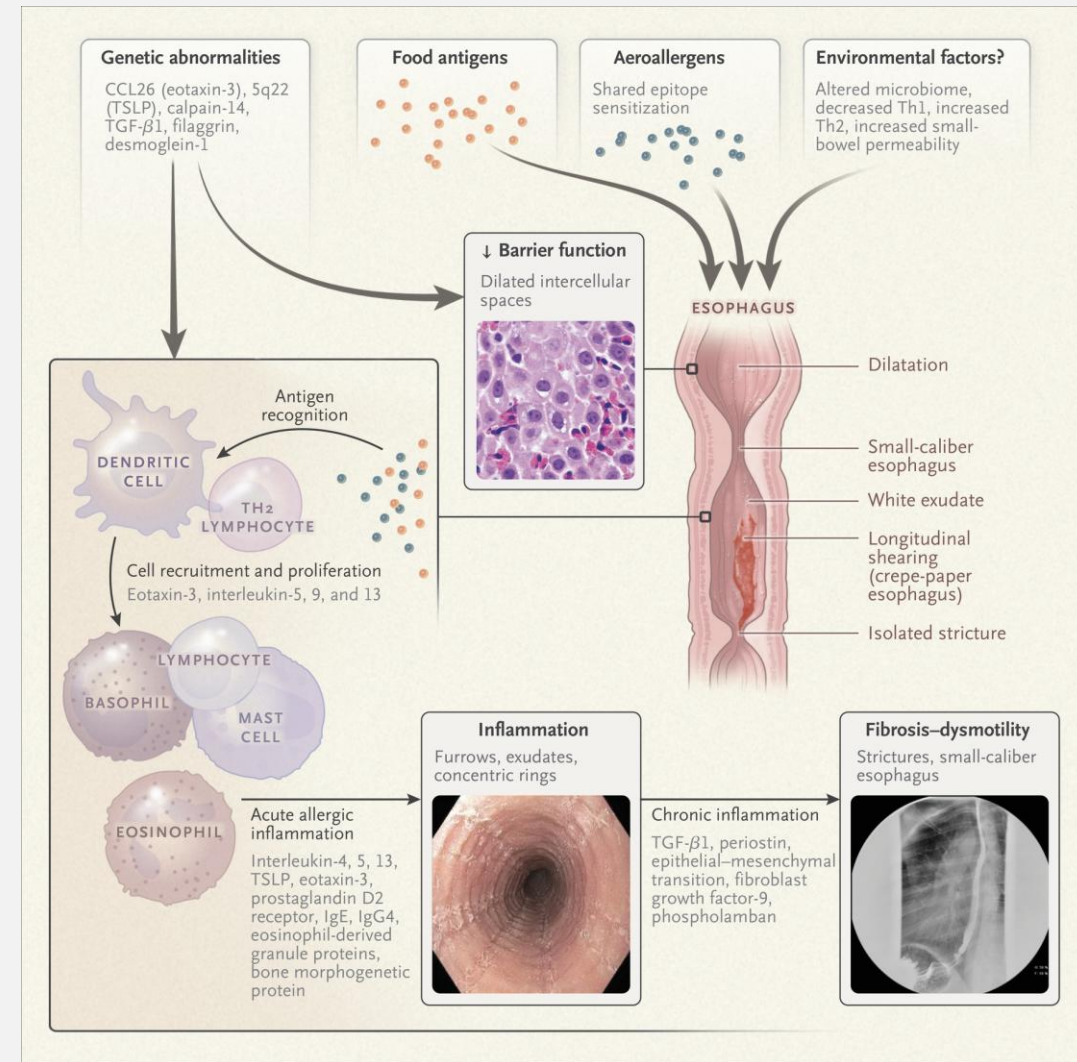


TRADEOFFS TO CONSIDER

- Concomitant allergic history
- Adherence considerations given his travel requirements
- Experience with diet-based treatment
- Stricture in need of dilation

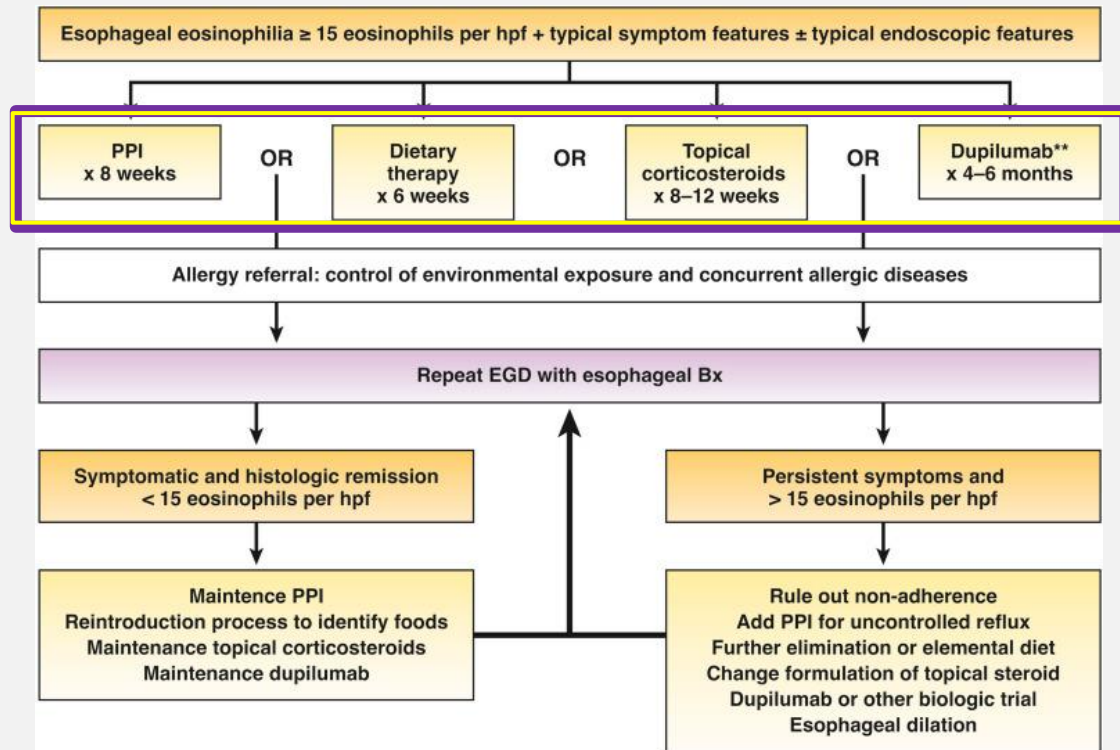
EoE Background and Conceptual Model

CLINICOPATHOLOGIC DISORDER

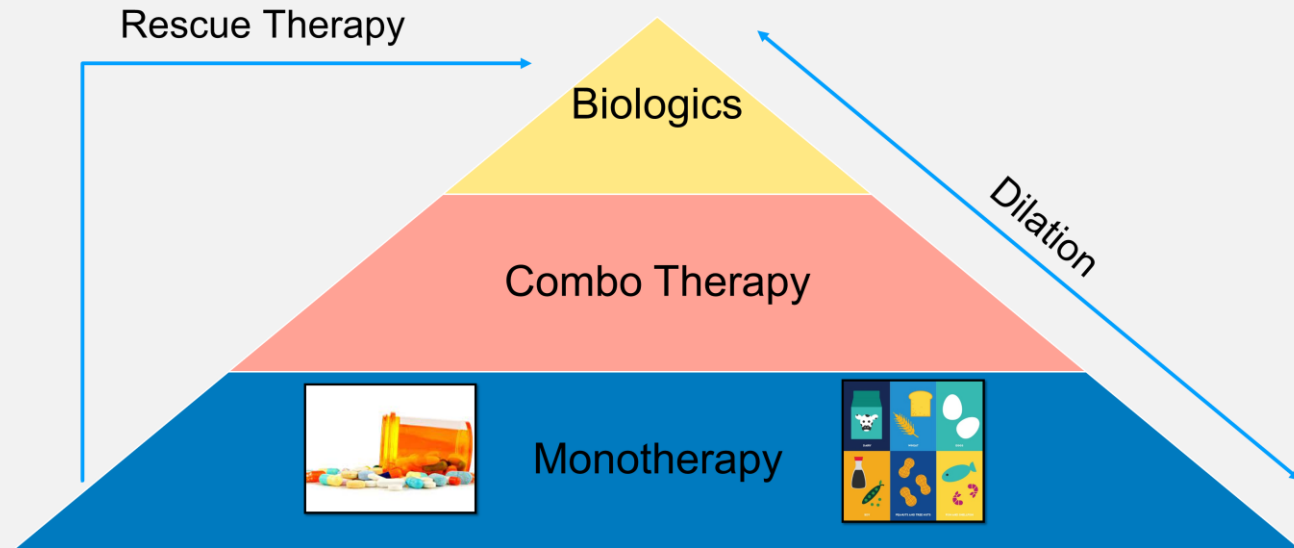


TREATMENT APPROACH

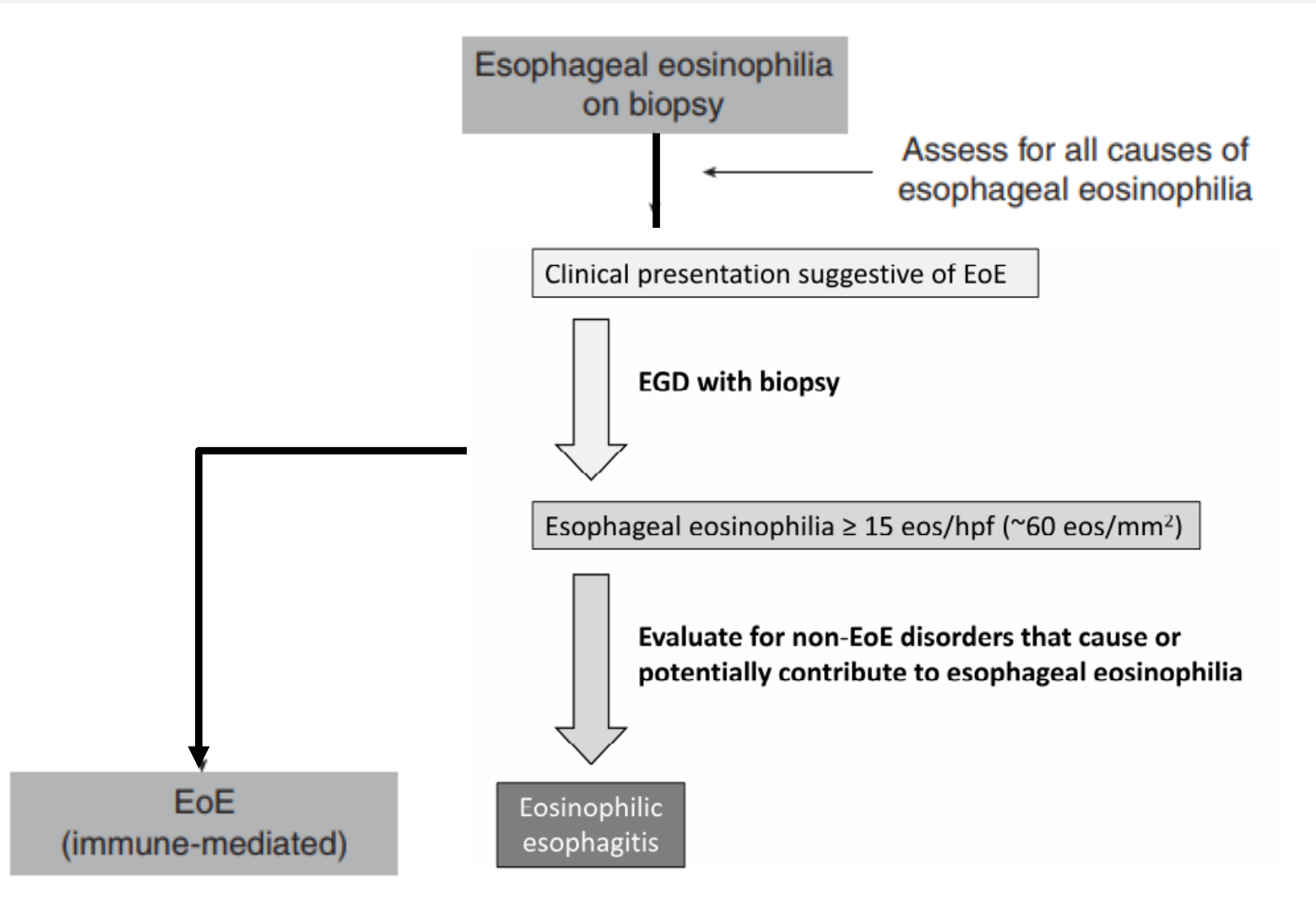
“MENU”



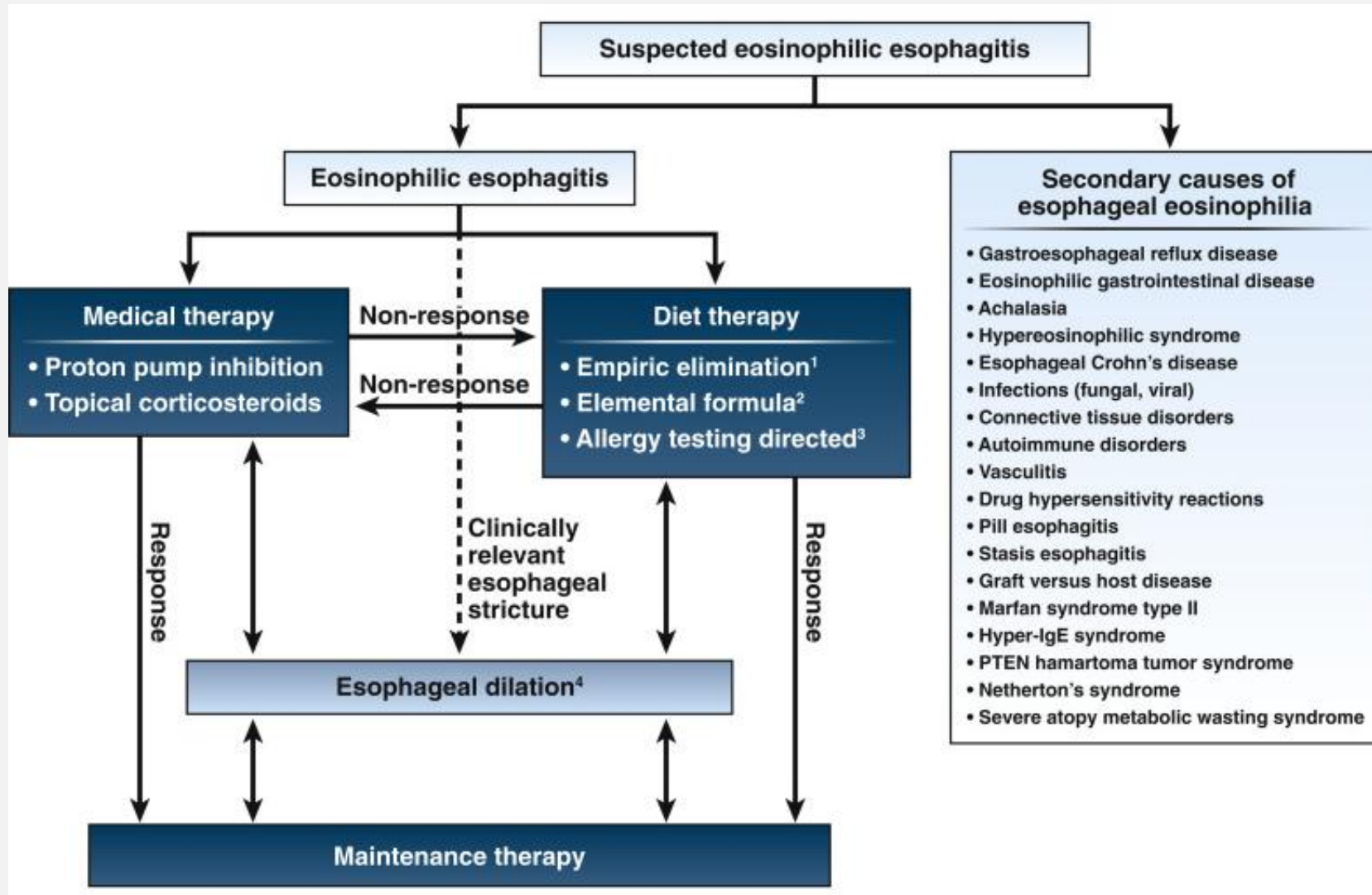
“PYRAMID”



AGREE CONSENSUS

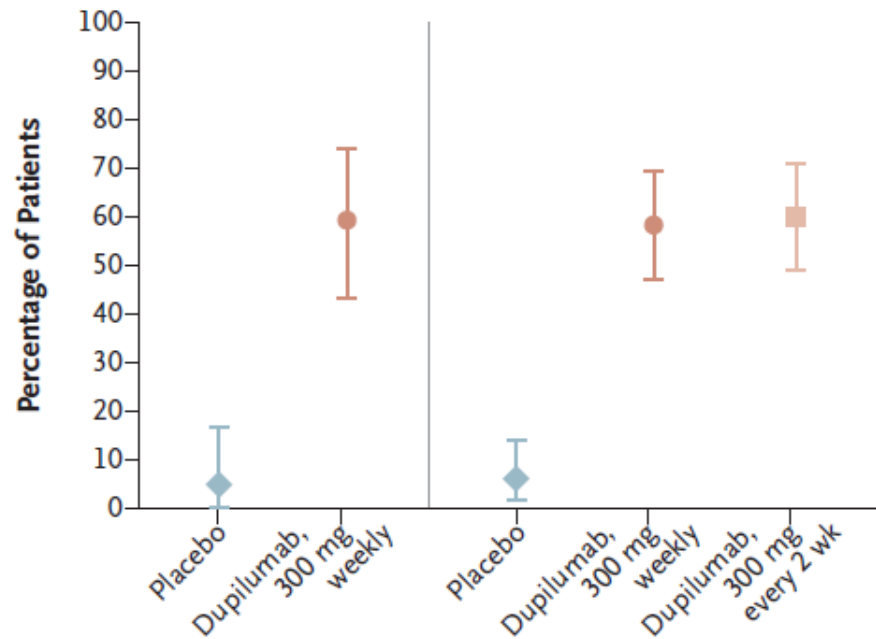


TREATMENT APPROACH



BIOLOGIC THERAPY - Dupilumab

A Histologic Remission at Wk 24 in Parts A and B



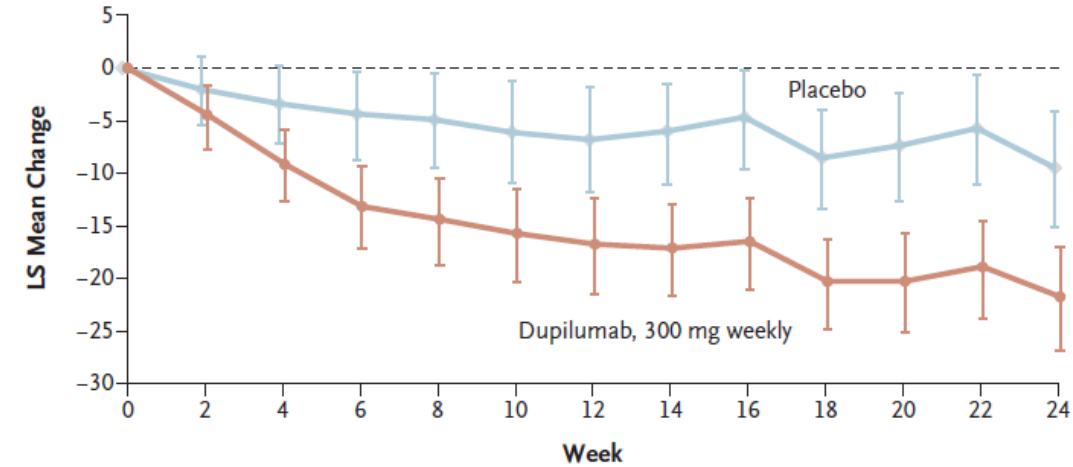
Part A, Wk 24

Part B, Wk 24

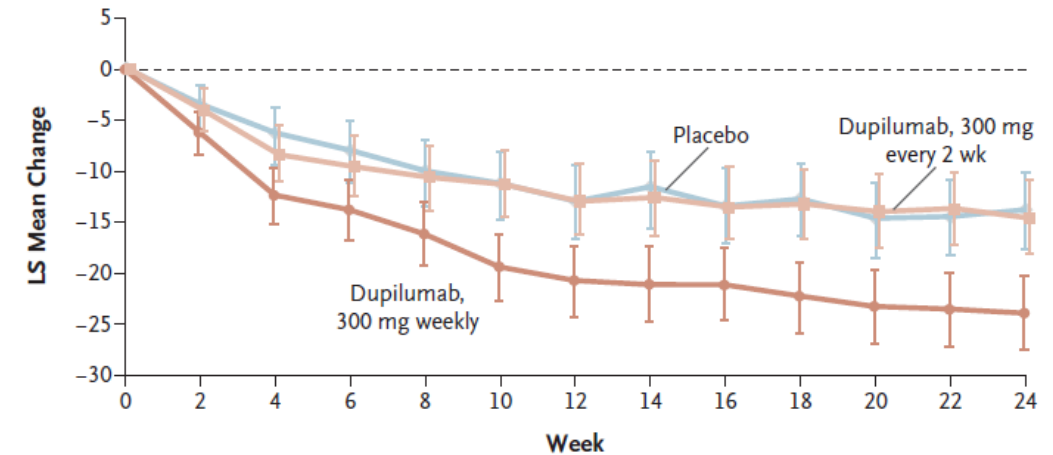
**No. of Patients
No. of Patients
with Response (%)**

Placebo	Dupilumab, 300 mg weekly	Placebo	Dupilumab, 300 mg weekly	Dupilumab, 300 mg every 2 wk
39	42	79	80	81
2 (5)	25 (60)	5 (6)	47 (59)	49 (60)

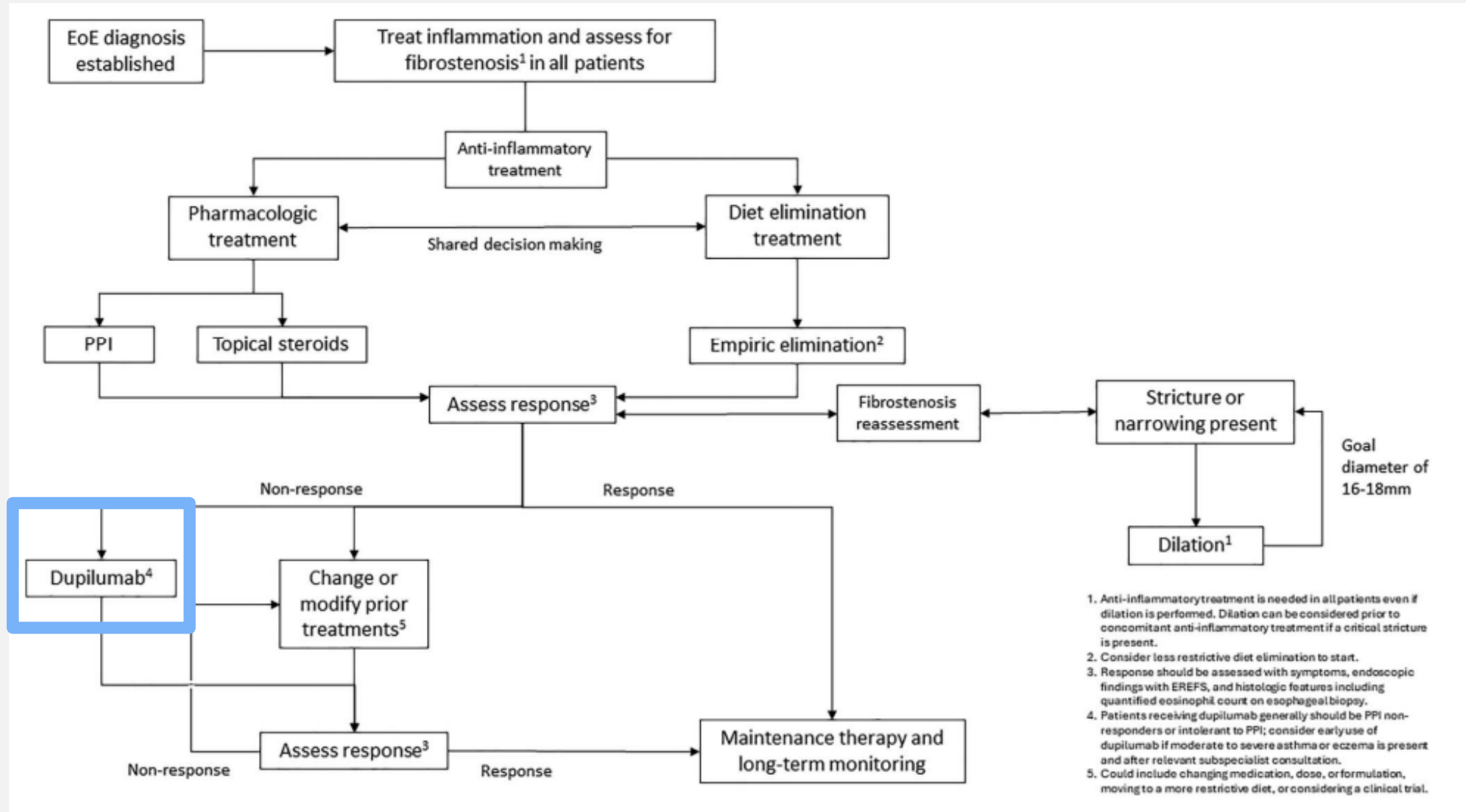
A Change from Baseline in DSQ Score in Part A



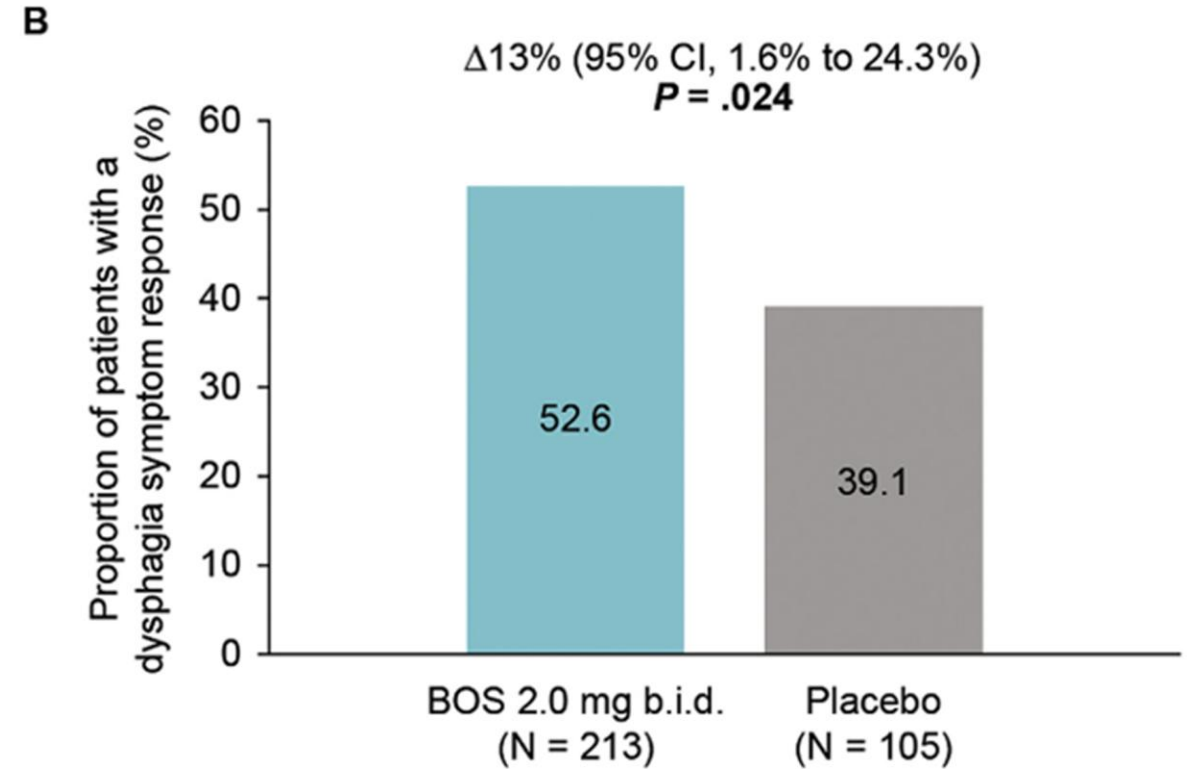
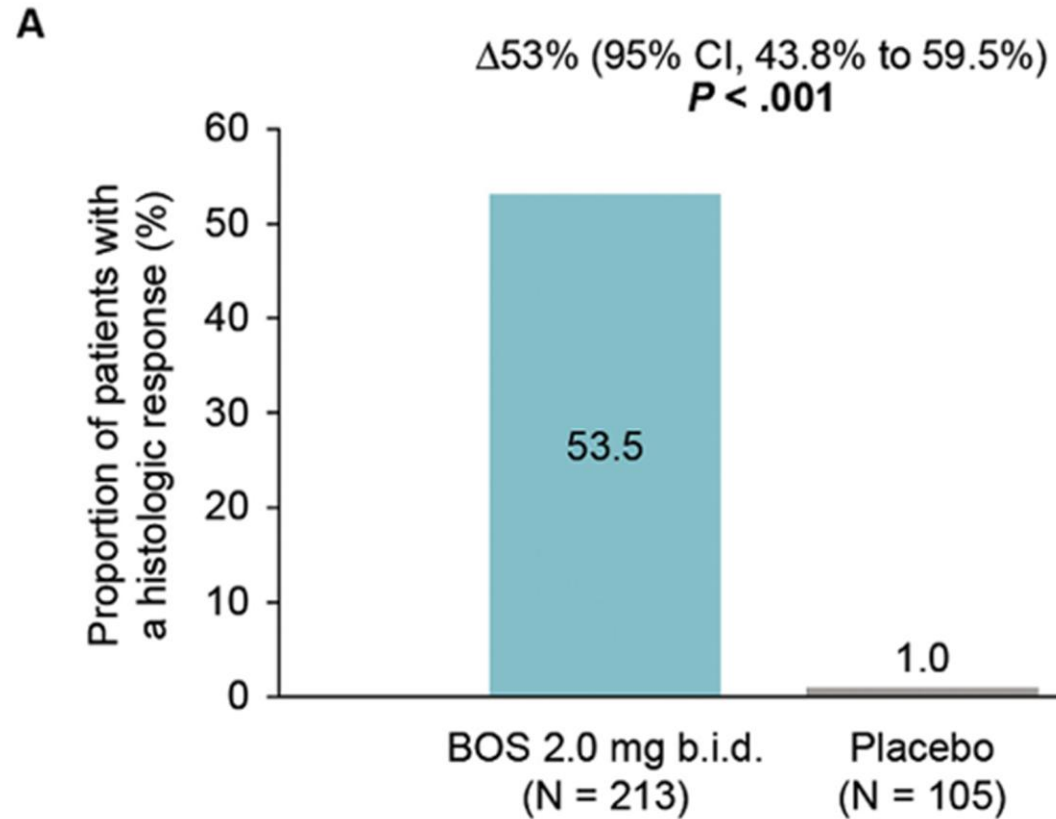
B Change from Baseline in DSQ Score in Part B



2025 ACG GUIDELINE

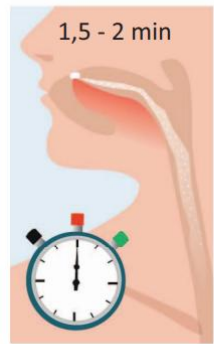


SWALLOWED STEROIDS

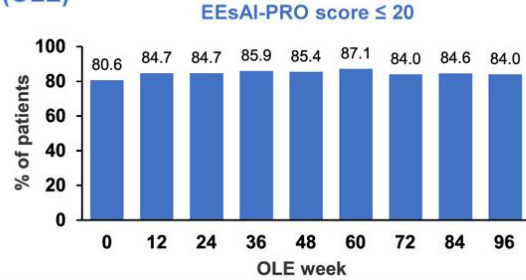


SWALLOWED STEROIDS

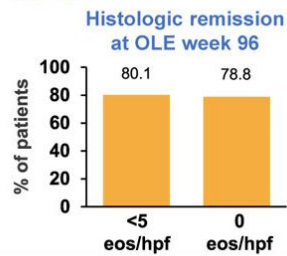
BUDESONIDE ORODISPERSIBLE



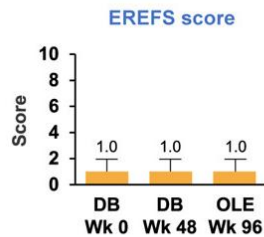
Clinical remission: 96 weeks (OLE)



Histology: Week 96 (OLE)



EREFS: 144 weeks (DB+OLE)



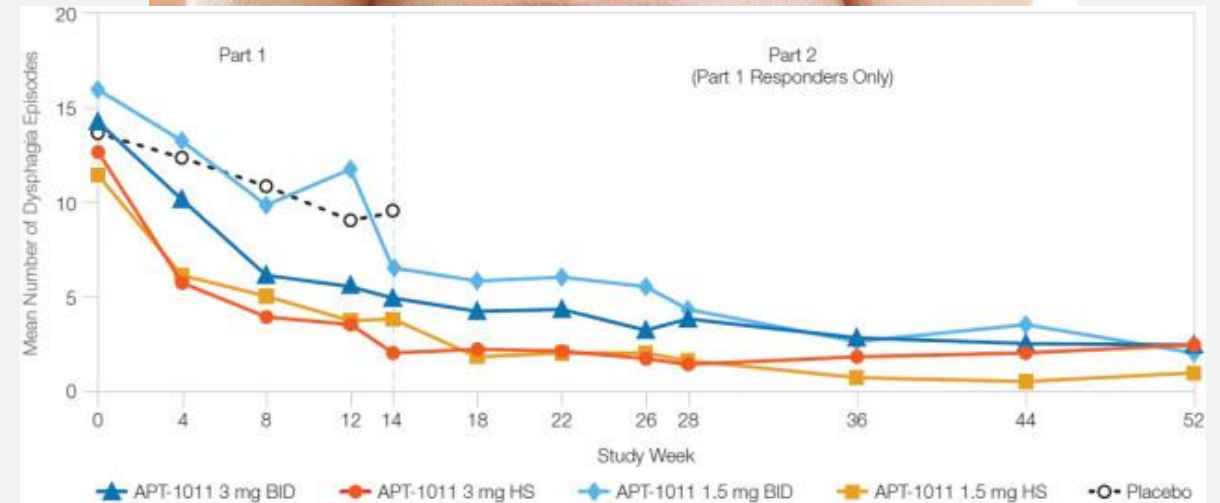
le tablet with

odies*
a production

of the tablet
de into saliva

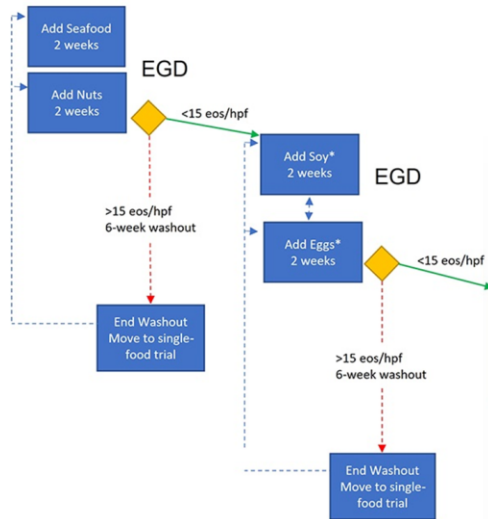
in enhanced
mucosa

FLUTICASONE ORALLY DISINTEGRATING



ELIMINATION DIET

Weeks
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18



	1FED (n=67)	6FED (n=62)	Percentage point difference*	p value
<15 eos/hpft	23 (34%; 23 to 46)	25 (40%; 28 to 53)	6% (-11 to 23)	0.58
≤ 10 eos/hpft	20 (30%; 19 to 41)	23 (37%; 25 to 49)	7% (-9 to 24)	0.46
≤ 6 eos/hpft	12 (18%; 9 to 27)	20 (32%; 21 to 44)	14% (-0 to 29)	0.069
≤ 1 eos/hpft	4 (6%; 0 to 12)	12 (19%; 10 to 29)	13% (2 to 25)	0.031

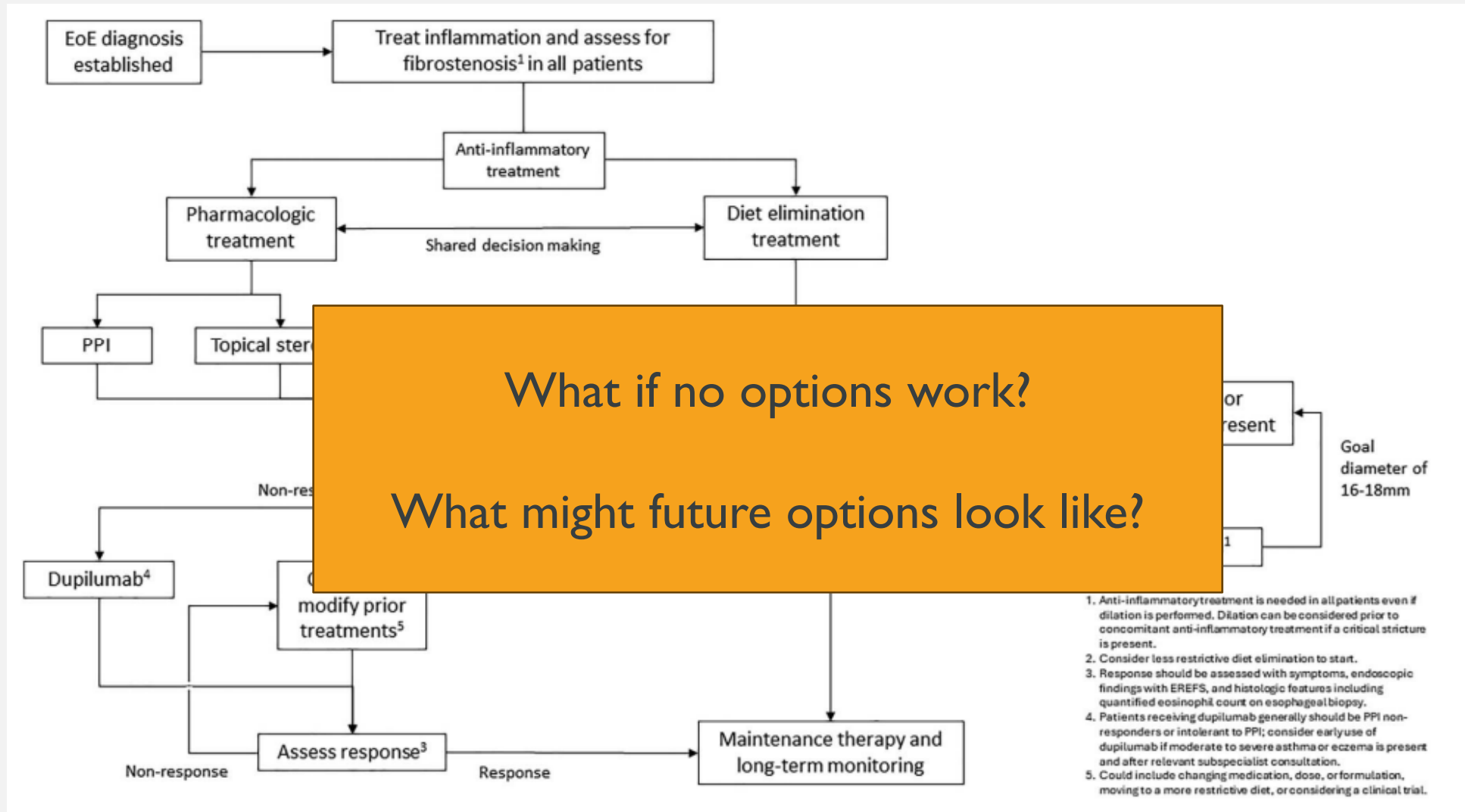
- Withdrew Study or Refused Consent (5)
- Lost to Follow up (3)
- Attempted 1FED, but unable to tolerate (3)
- Active IBD (1)
- Type 1 Diabetes, unable to tolerate milk substitutes (1)

(N=20)
(≥ 15 /hpf)

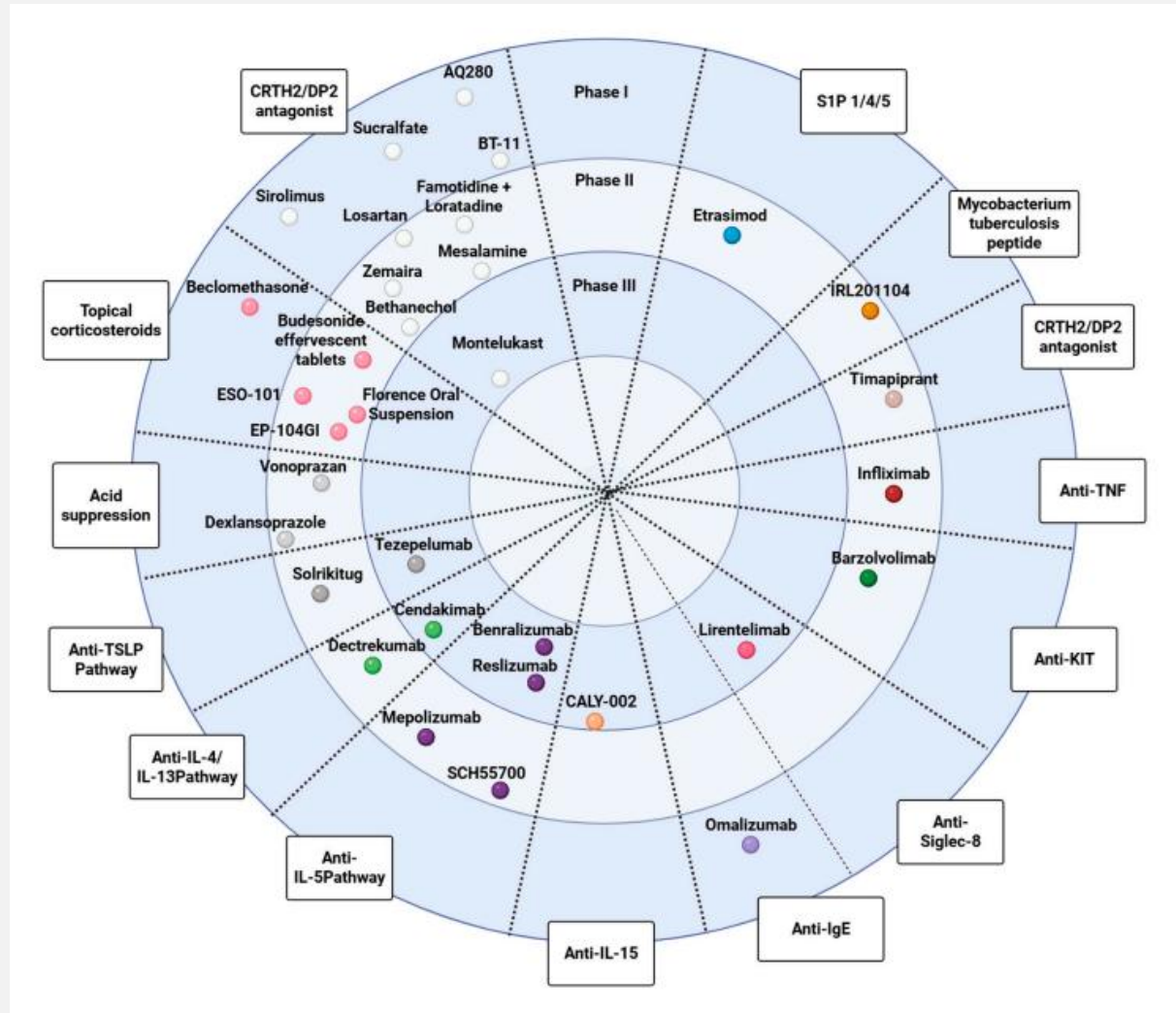
6FED Approach
54% success in adults

1-FED Approach
51% success in children

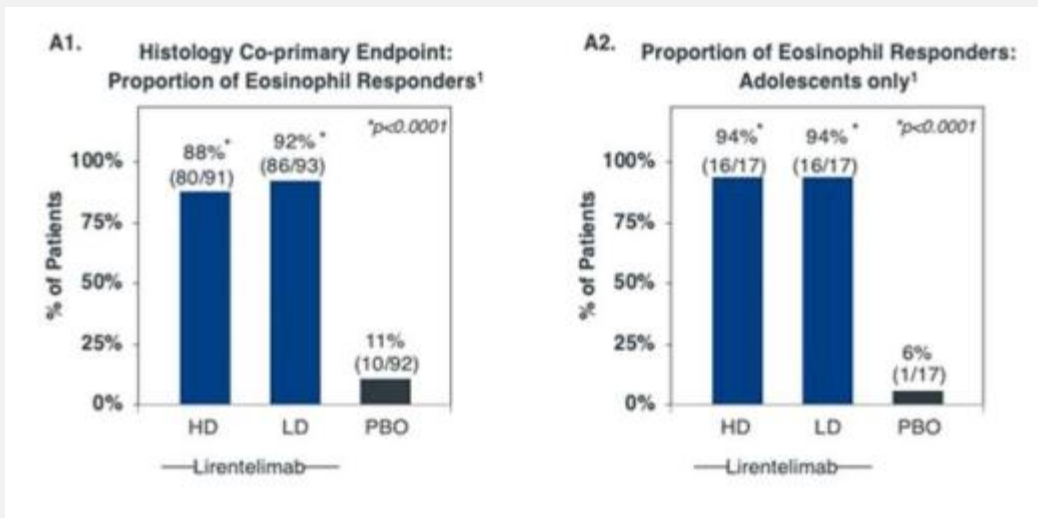
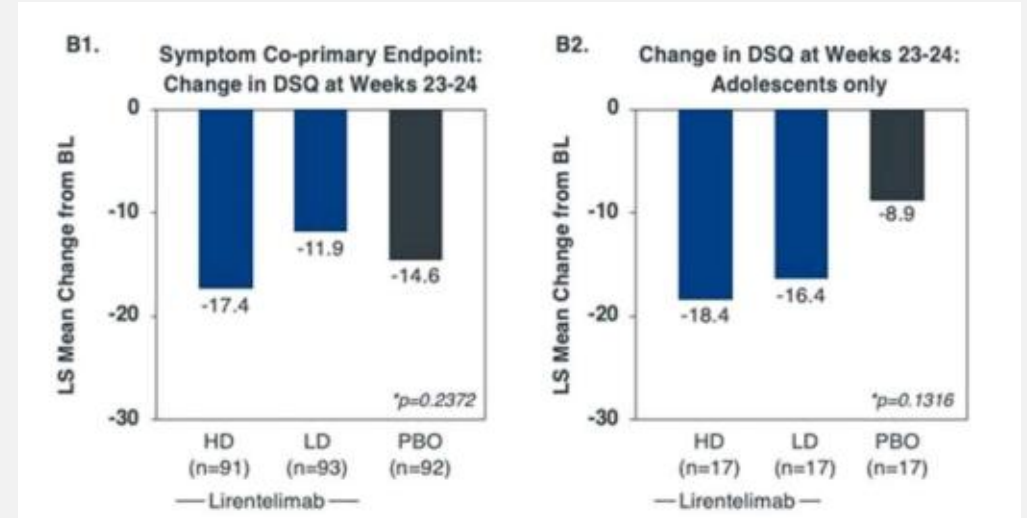
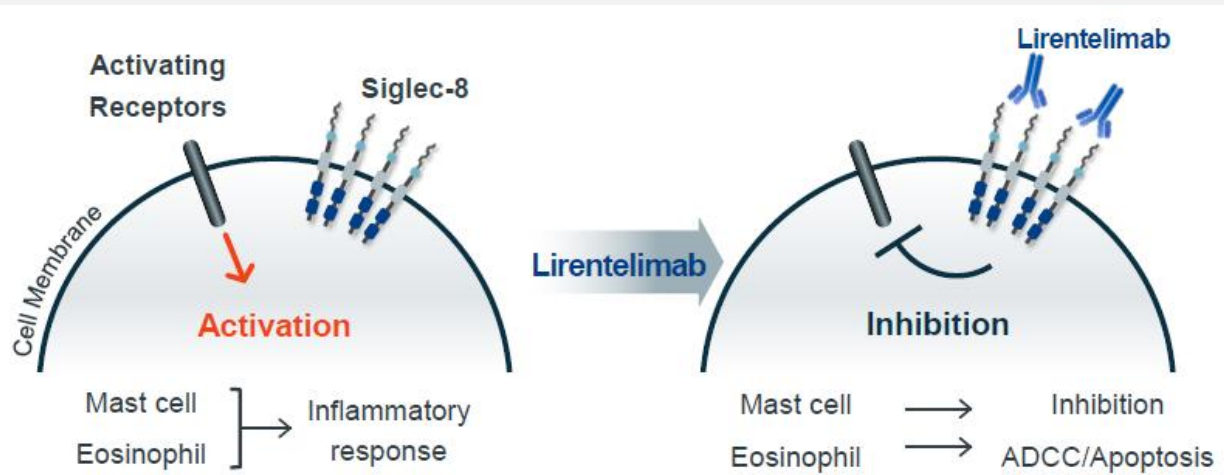
2025 EOE GUIDELINE



THERAPEUTIC PIPELINE



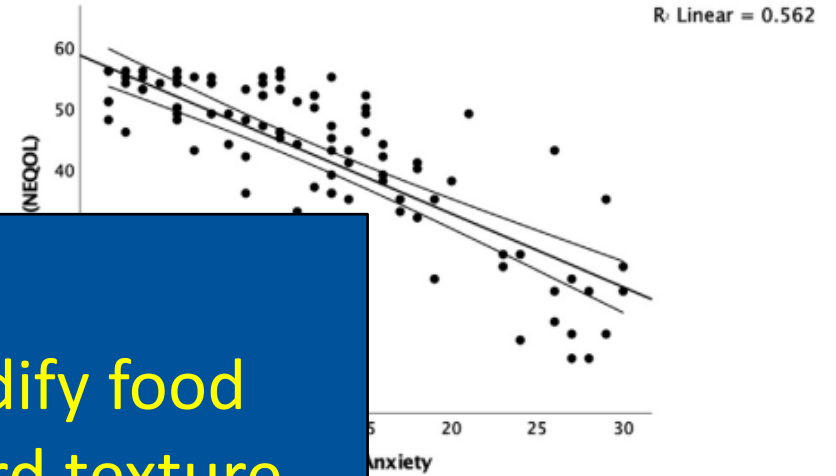
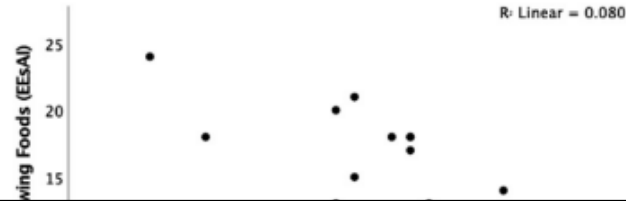
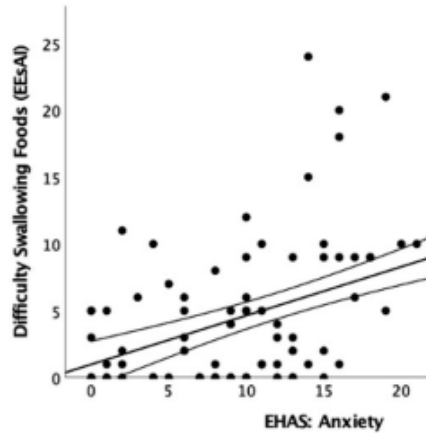
DEVELOPMENT OBSTACLES - lirentelimab



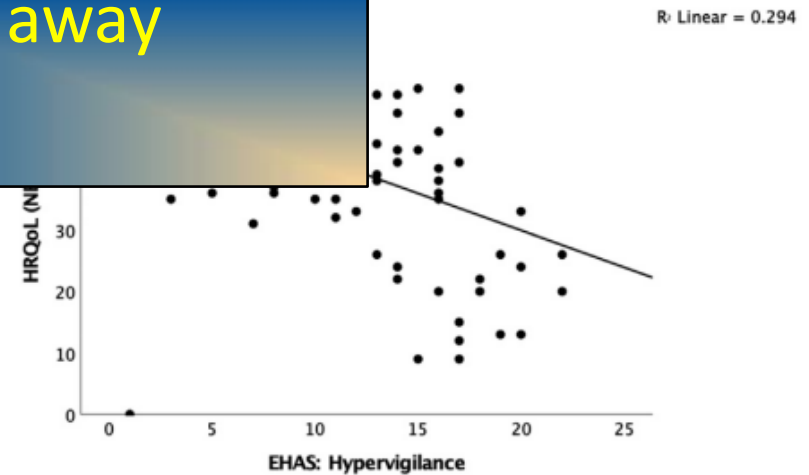
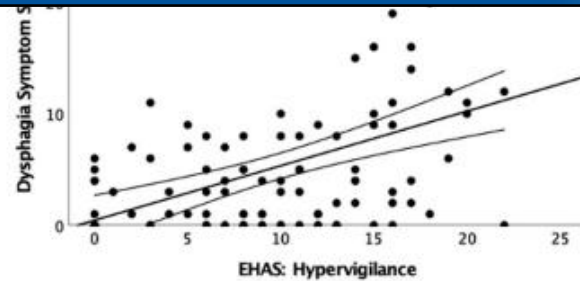
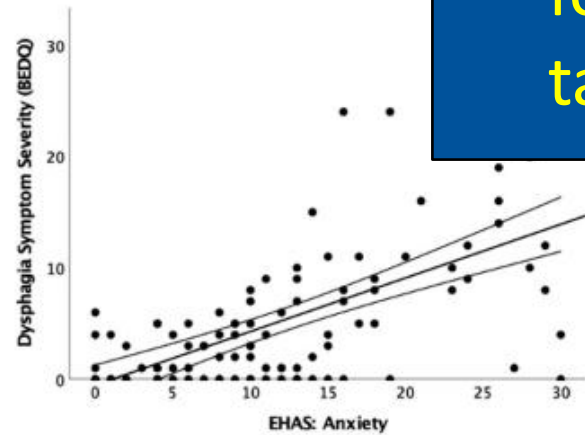
Why did this and other drugs fail to meet endpoints?

- Allergic or environmental trigger for EoE remains present
- An esophageal barrier defect remains present
- Other inflammatory pathways still unopposed
- Eosinophils are a marker of disease, but not the only contributor to disease

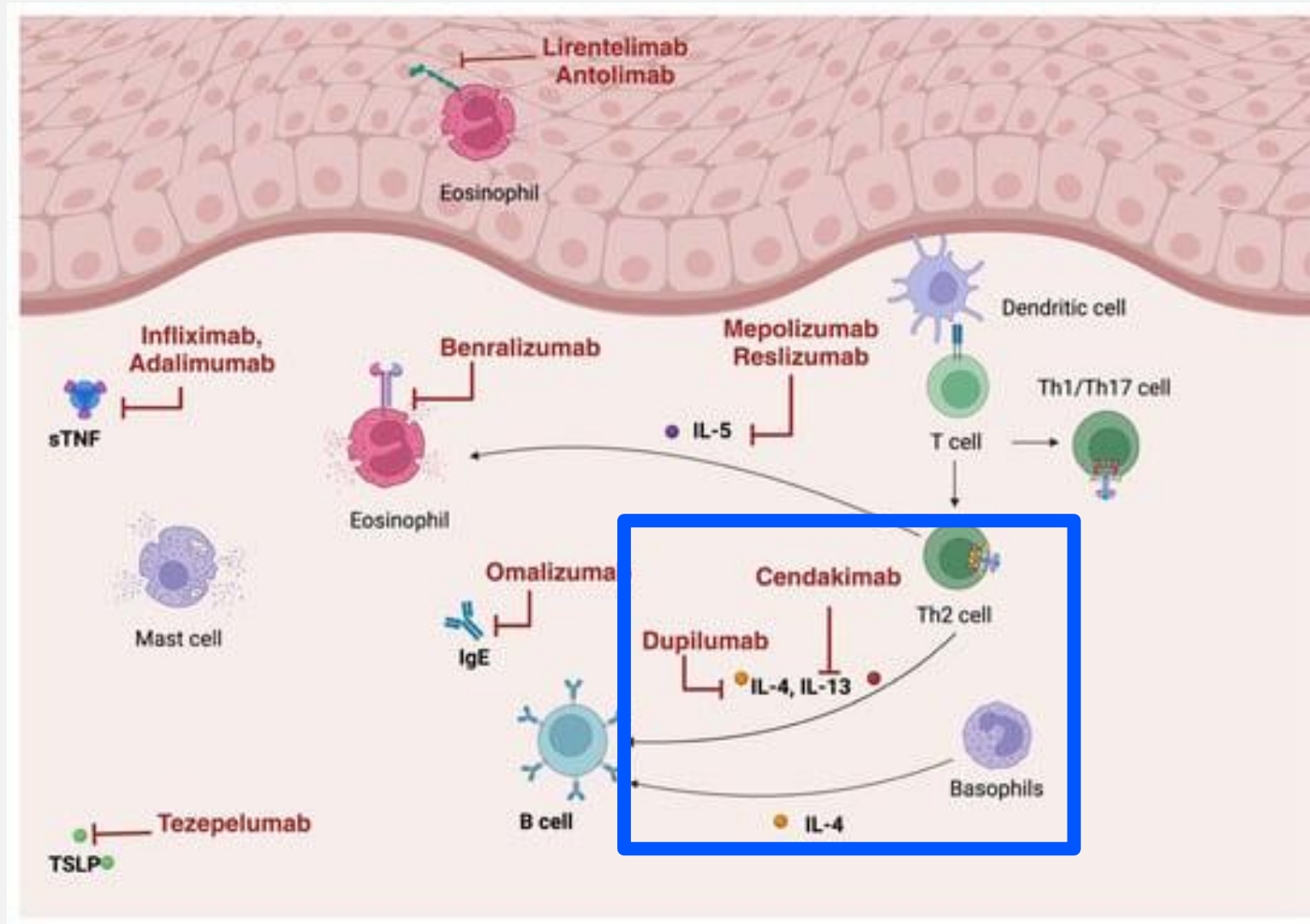
EOE TREATMENT ENDPOINTS



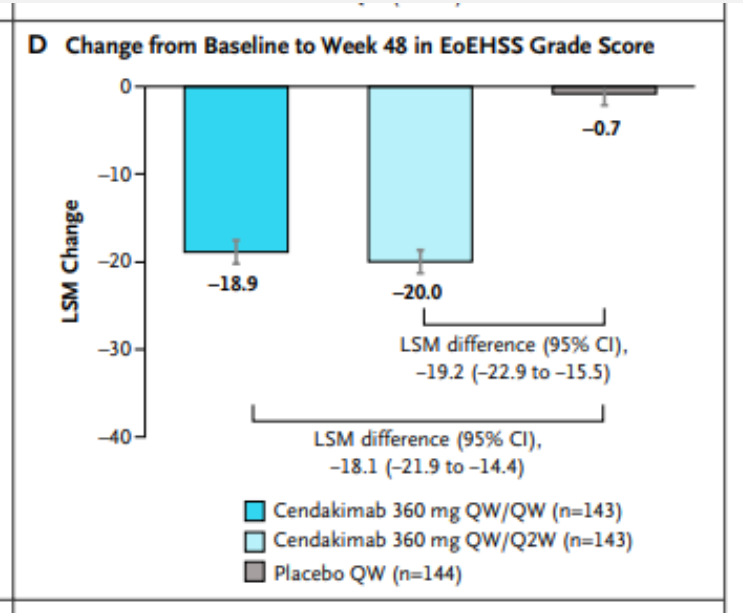
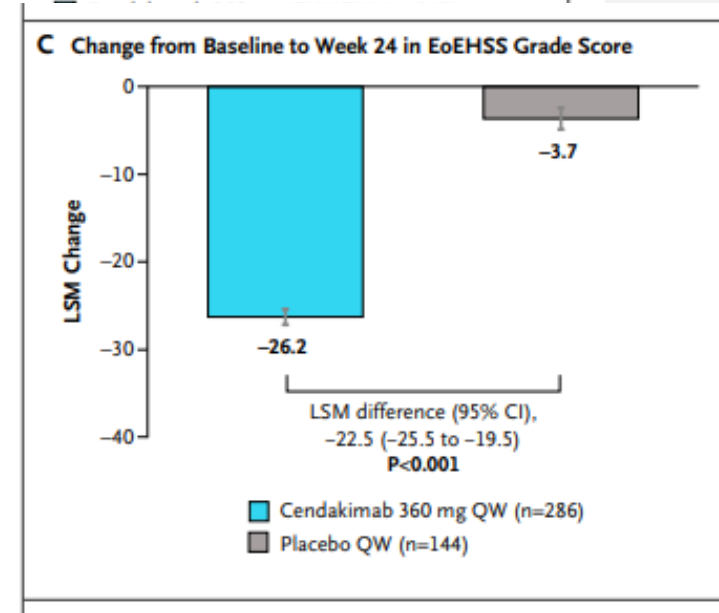
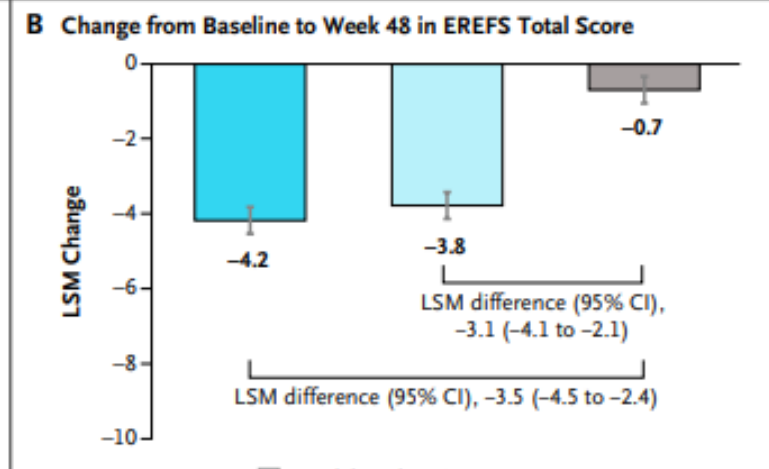
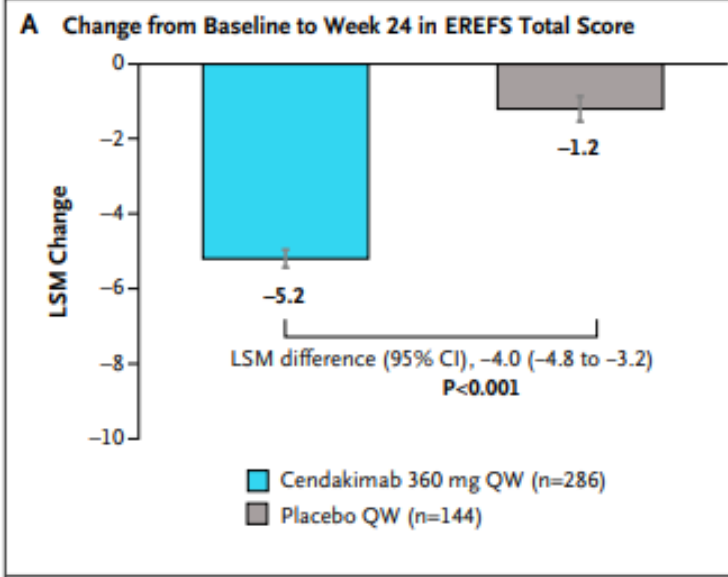
IMPACT Behaviors
Imbibe fluids with meals, **Modify food**
Prolong meal times, Avoid hard texture
foods, Chew excessively, Turn away
tablets/pills



MECHANISTIC PIPELINE



DEVELOPED, NOT APPROVED- cendakimab



IMMUNOLOGIC RE-TRAINING

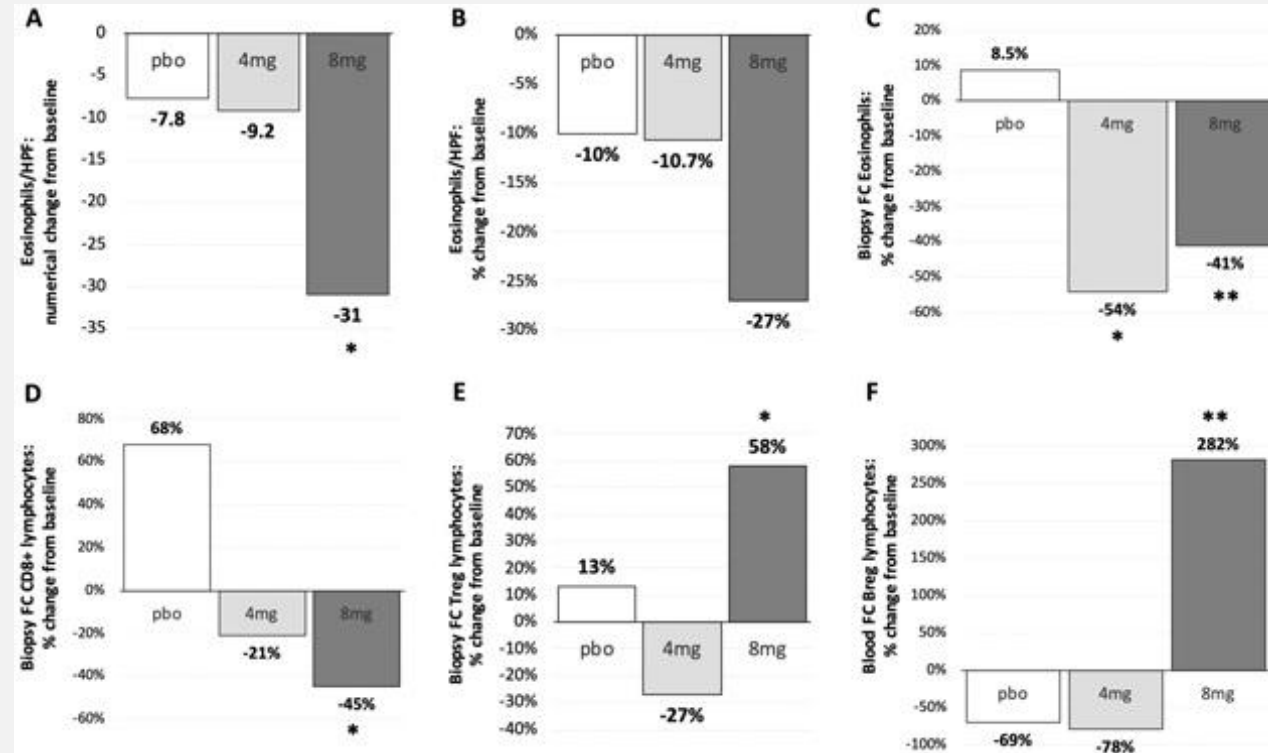
IRL200104

Novel immunomodulatory peptide, derived from mTB chaperonin protein that may induce anti-inflammatory milieu

Phase 2A study of IV injection with 4 week follow-up

Improvements in esophageal histology and increase in regulatory lymphocytes

PHASE 2A RESULTS



NOVEL STEROID FORMULATION

EP-104GI

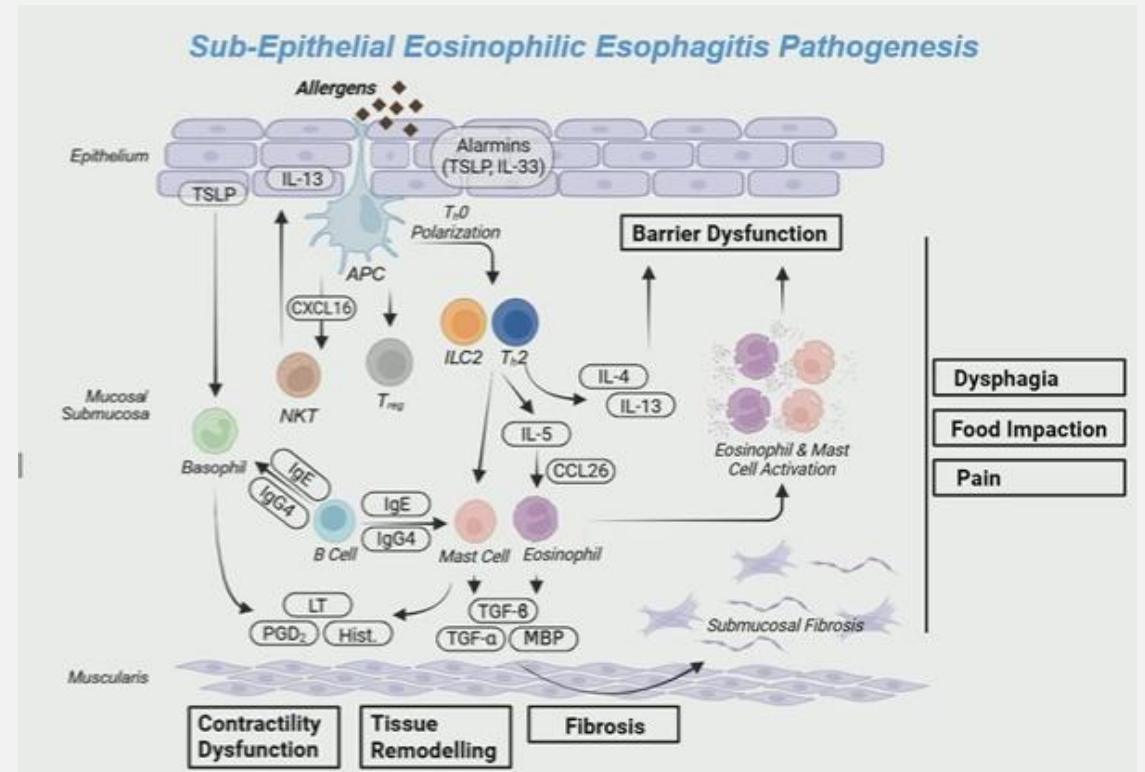
Submucosally active, long-acting formulation of fluticasone

Endoscopically administered in the submucosal space

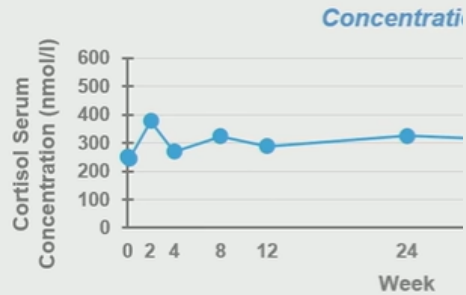
Long-term diffusion of anti-inflammatory activity

Phase 1b/2 (n=18) assessed histologic changes and symptoms up to 52 weeks

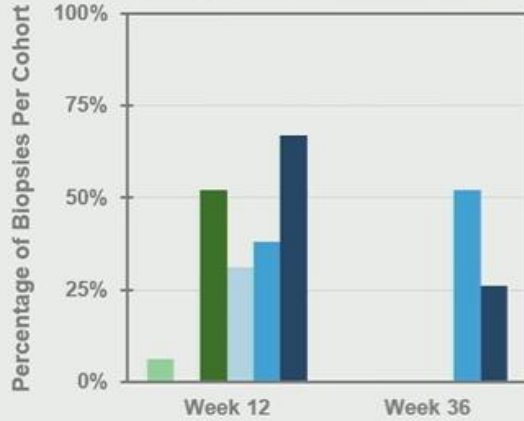
SUBEPITHELIAL INFLAMMATION



NOVEL STEROID FORMULATION



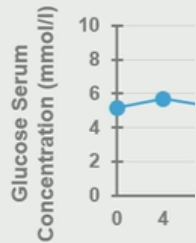
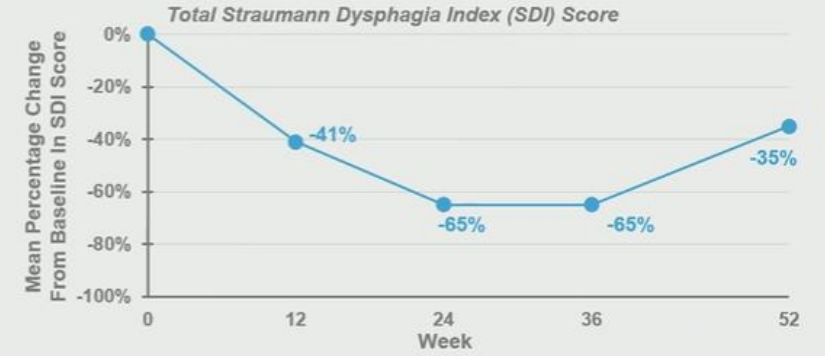
Mean Percentage of Esophageal Biopsies With Peak Eosinophil Count $\leq 6/hpf$ Following EP-104GI Administration



EP-104GI 12x4mg

Fluticasone

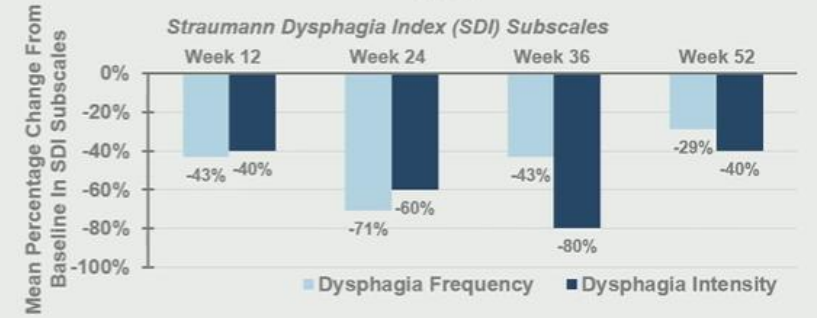
Reported Improvements In Dysphagia Following 12x4mg EP-104GI Administration



Mean Relative Change In Eosinophilic Esophagitis Histology Scoring System Total Score Following EP-104GI Administration



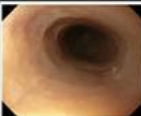


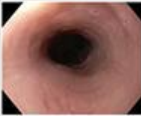
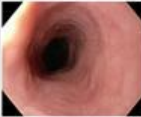
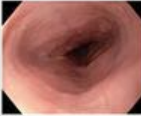
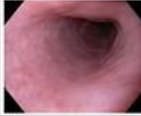

52

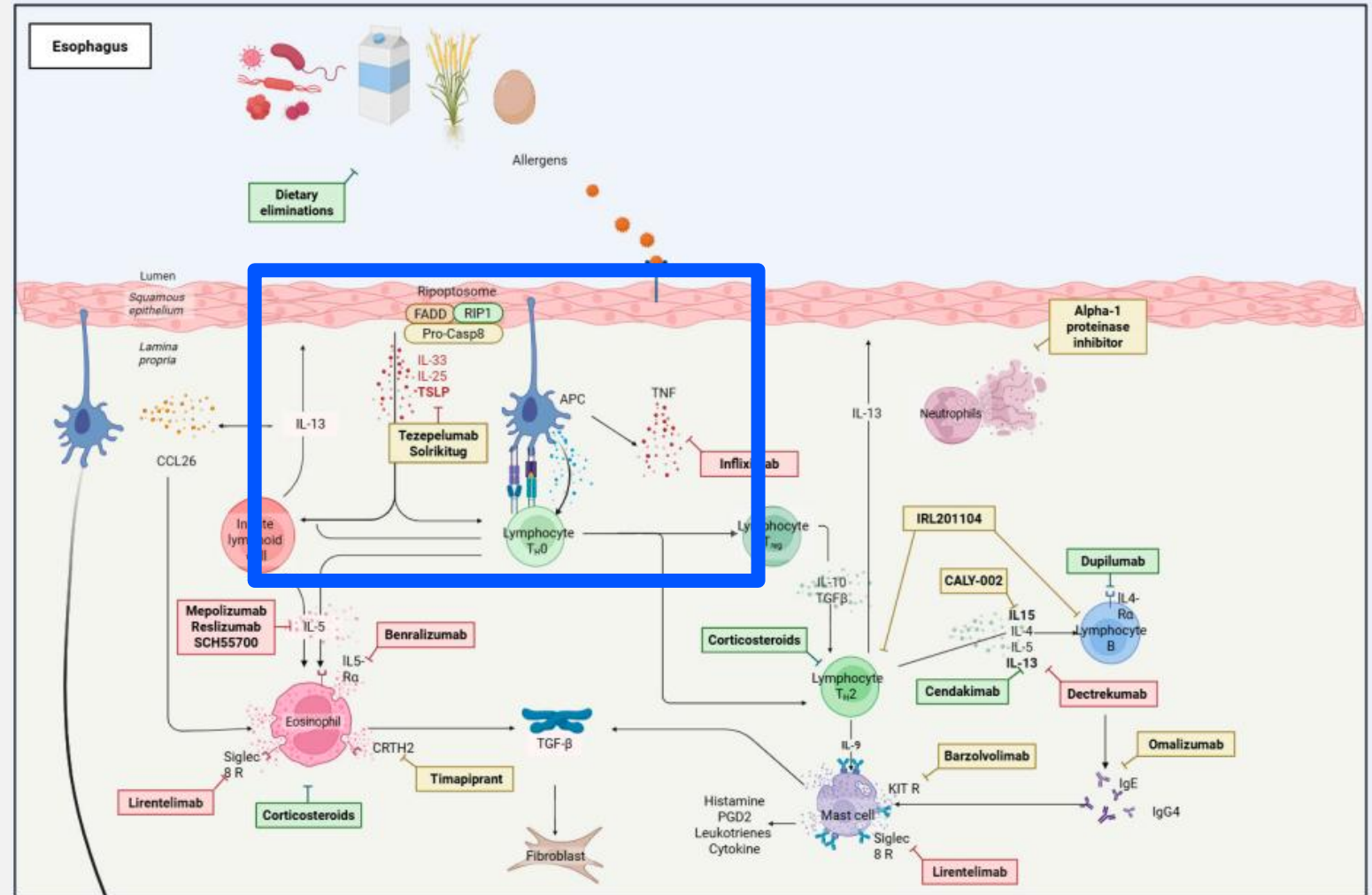


THERAPEUTIC PIPELINE

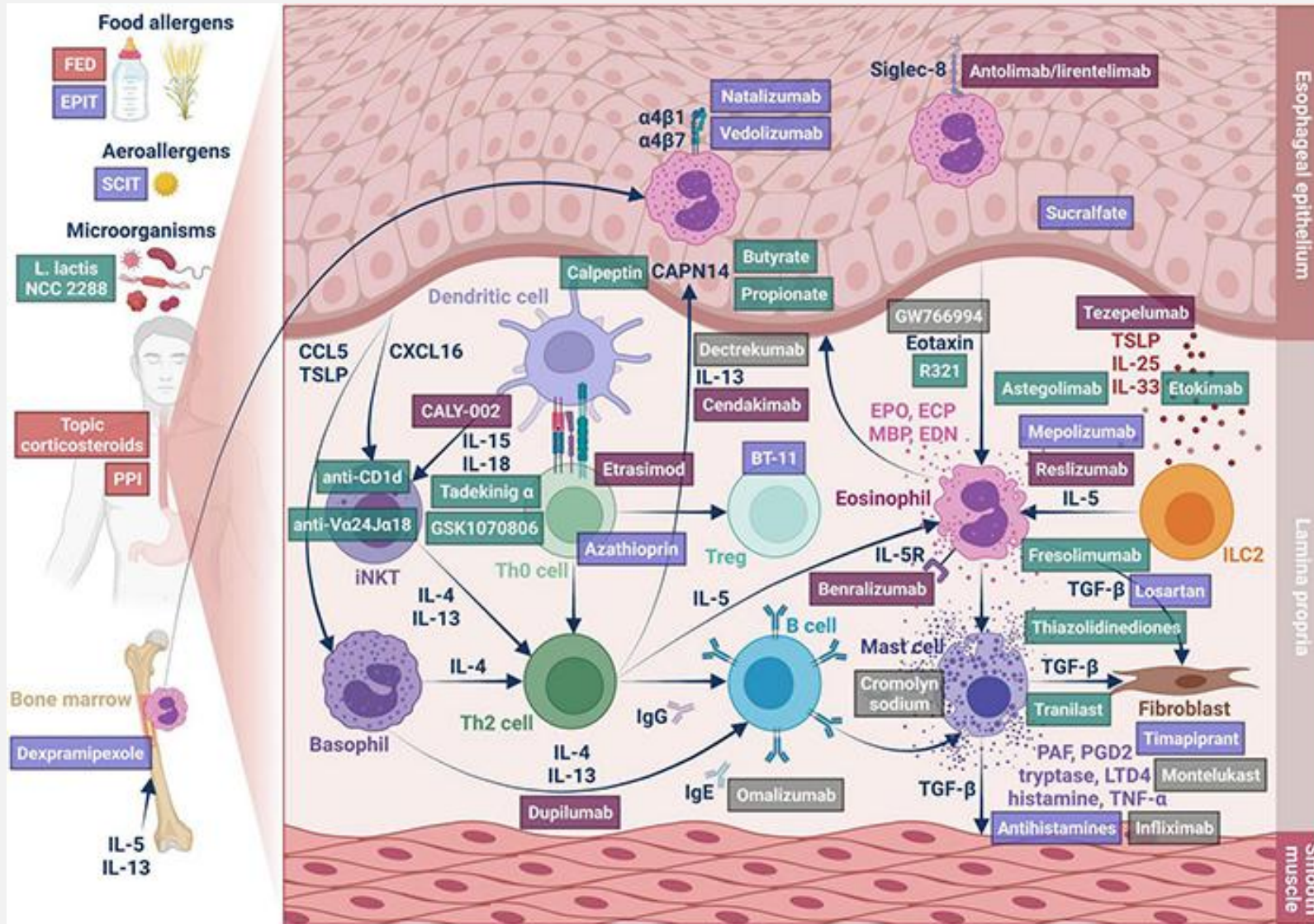
TARGET	MECHANISM	STATUS
Tezepelumab	Blocks thymic stromal lymphopoietin	Phase III study ongoing
IRL201104	Immune-regulatory protein, mTB Chaperonin 60.1	Phase IIa study completed and positive results
Etrasimod	Sphingosine 1-phosphate (S1P) receptor modulator	Phase II study completed and positive results
EP-104GI	Injectable long-acting fluticasone	Phase II results presented 2025 (ACG)
Vonoprazan	Potassium-competitive acid blocker	Phase II study planned
Barzolvolimab	Humanized Ab inhibiting KIT activation	Phase II study ongoing
Solrikitug	Blocks thymic stromal lymphopoietin	Phase II study ongoing

NOVEL BIOLOGICS - Tezepelumab

Timeline and treatment	Endoscopy	Histology
24 months prior to consultation - OVB 2mg BID x 3 months		EREFs = 5 Ex1, R1, E1, F1, S11 No dilation PEC = 140 eos/hpf HSS grade = 0.63 HSS stage = 0.54
18 months prior to consultation - SFED x 2 months		EREFs = 5 Ex1, R1, E1, F1, S8 No dilation PEC = 75 eos/hpf HSS grade = 0.63 HSS stage = 0.54
Initial consultation - Off treatment		EREFs = 5 Ex1, R1, E1, F1, S11 No dilation Crepe-paper noted PEC = 35 eos/hpf HSS grade = 0.63 HSS stage = 0.63
3 months after consultation - Mepolizumab 300 mg monthly x 3 months		EREFs = 5 Ex1, R1, E1, F1, S10 Savary to 12mm PEC = 18 eos/hpf HSS grade = 0.50 HSS stage = 0.50
12 months after consultation - Benralizumab 30mg every 8 weeks x 9 months		EREFs = 5 Ex1, R1, E1, F1, S11 Savary to 14mm PEC = 0 eos/hpf HSS grade = 0.33 HSS stage = 0.21
36 months after consultation - Benralizumab 30 mg every 8 weeks x 33 months		EREFs = 5 Ex1, R1, E1, F1, S12 Savary to 15mm PEC = 1 eos/hpf HSS grade = 0.38 HSS stage = 0.33
42 months after consultation - Tezepelumab 210 mg every 4 weeks x 6 months		EREFs = 1 Ex0, R0, E0, F0, S15 Savary to 16mm PEC = 0 eos/hpf HSS grade = 0.25 HSS stage = 0.25
48 months after consultation - Tezepelumab 210 mg every 4 weeks x 12 months		EREFs = 1 Ex0, R0, E0, F0, S17 No effect with Savary to 16mm PEC = 13 eos/hpf HSS grade = 0.25 HSS stage = 0.25



THERAPEUTIC PIPELINE



CME/MOC QUESTION

Which currently available medications is approved specifically for the management of patients with eosinophilic esophagitis?

- A. Vonoprazan
- B. Mepolizumab
- C. Tezepelumab
- D. Dupilumab**

CONCLUSIONS

EoE is a chronic allergen-mediated inflammatory condition that is rising in both incidence and prevalence

Current guideline recommendations include elimination diets and medical therapy, with two treatments specifically FDA-approved for EoE

With increasing mechanistic understanding and more clinical trials underway or planned, treatment options are expanding and likely to become increasingly complex

QUESTIONS?

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