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Supplementary Table 1. Local and systemic causes of esophageal eosinophilia to rule out before diagnosing EoE

Condition	Diagnostic clues
Eosinophilic gastroenteritis	Gastrointestinal symptoms + eosinophilic infiltration in stomach and/or duodenum
Crohn's disease	Extraesophageal symptoms, inflammation and imaging
Infection (e.g., parasites)	Extraesophageal symptoms + serum and/or stool tests
Achalasia	Regurgitation + esophageal manometry
Hypereosinophilic syndrome	Peripheral blood eosinophils $>1.5 \times 10^9/L$ + eosinophil-mediated organ damage and/or dysfunction (cardiac, neurologic, skin, pulmonary or gastrointestinal disease)
Drug hypersensitivity	Rash, fever, lymphadenopathy and multiorgan involvement Resolution upon drug discontinuation
Vasculitis Pemphigoid Connective tissue disorder Graft-versus-host disease	Clinical and histological context Systemic involvement

Supplementary Table 2. EoEHSS definitions of the 8 esophageal biopsy features evaluated in this study and the 4 point scores that expressed the degree of abnormality (grade score) or the extent of pathology (stage score).

Histological feature	Grade	Stage
<p>A. Eosinophilic inflammation (EI): Intraepithelial eosinophils are not normally found in esophageal biopsies; therefore any intraepithelial eosinophils were considered abnormal. Grade score for eosinophilic inflammation was based on the quantity of eosinophils in the most inflamed high power field (HPF) (peak eosinophil count, PEC).</p>	<p>0 = intraepithelial eosinophils not present</p> <p>1 = PEC <15/HPF</p> <p>2 = PEC 15-59/HPF</p> <p>3 = PEC >60/HPF</p>	<p>0 = intraepithelial eosinophils 0-14/HPF,</p> <p>1 = PEC \geq15/HPF in <33% of HPFs</p> <p>2 = PEC \geq15/HPF in 33-66% of HPFs</p> <p>3 = PEC \geq15/HPF in >66% of HPFs</p>
<p>B. Epithelial basal zone: The basal zone of esophageal squamous epithelium is composed of closely packed small cells and normally occupies \leq 15% of the total</p>	<p>0 = BZH not present</p>	<p>0= BZH not present</p>

<p>epithelial thickness. The upper limit of the basal zone was defined as the level at which basal epithelial cell nuclei were separated by a distance equal to or greater than the diameter of a basal cell nucleus.</p>	<p>1 = basal zone occupies >15% but <33% of total epithelial thickness</p> <p>2 = basal zone occupies 33-66% of total epithelial thickness</p> <p>3 = basal zone occupies >66% of total epithelial thickness</p>	<p>1 = BZH (any grade >0) in <33% of epithelium</p> <p>2 = BZH (any grade >0) in 33-66% of epithelium</p> <p>3 = BZH (any grade >0) in >66% of epithelium</p>
<p>C. Eosinophil abscess (EA): intraepithelial eosinophil group or aggregate in which eosinophils form solid masses and the epithelial architecture is disrupted so that adjacent eosinophils are not separated by intervening epithelial tissue</p>	<p>0 = groups or aggregates of eosinophils not present</p> <p>1 = group of 4-9 eosinophils</p>	<p>0 = groups or aggregates of eosinophils not present</p> <p>1 = EA (any grade >0)</p>

	<p>2 = group of 10-20 eosinophils</p> <p>3 = group of >20 eosinophils</p>	<p>in <33% of epithelium</p> <p>2 = EA (any grade >0) in 33-66% of epithelium</p> <p>3 = EA (any grade >0) in > 66% of epithelium</p>
<p>D. Eosinophil surface layering (SL): linear alignment of at least 3 eosinophils in the upper third of the epithelium parallel to the lumen. Grade score for SL was based on the number of eosinophils forming the layer</p>	<p>0 = absent SL (fewer than 3 aligned eosinophils)</p> <p>1 = SL of 3-4 eosinophils</p> <p>2 = SL of 5-10 eosinophils</p> <p>3 = SL of >10</p>	<p>0 = absent SL</p> <p>1 = SL (any grade >0) in <33% of epithelium</p> <p>2 = SL (any grade >0) in 33-66% of epithelium</p> <p>3 = SL (any grade >0)</p>

	eosinophils	in >66% of epithelium.
E. Dilated intercellular spaces (DIS): circumferential paracellular spaces in esophageal squamous epithelium that exhibit intercellular bridges. Grade score of DIS was based on the degree of magnification required to see the intercellular bridges	<p>0 = DIS not seen at any magnification</p> <p>1 = intercellular bridges in DIS visible at 400X magnification only</p> <p>2 = intercellular bridges in DIS visible at 200X magnification</p> <p>3 = intercellular bridges in DIS visible at 100X magnification or lower</p>	<p>0 = DIS not seen at any magnification</p> <p>1 = DIS (any grade >0) in <33% of epithelium</p> <p>2 = DIS (any grade >0) in 33-66% of epithelium</p> <p>3 = DIS (any grade >0) in >66% of epithelium</p>
F. Surface epithelial alteration (SEA): altered tinctorial properties of surface	0 = SEA not present	0 = SEA not present

<p>epithelium that manifest as increased (darker red) staining of surface epithelial cells, with or without associated eosinophil infiltrate.</p> <p>Grade score for SEA was based on the amount of eosinophil infiltration in altered surface epithelium</p>	<p>1= SEA without eosinophils</p> <p>2 = SEA with any eosinophils</p> <p>3 = shed altered surface epithelium admixed with numerous eosinophils consistent with exudate</p>	<p>1 = SEA (any grade >0) in <33% of epithelium</p> <p>2 = SEA (any grade >0) in 33-66% of epithelium</p> <p>3 = SEA (any grade >0) in >66% of epithelium</p>
<p>G. Dyskeratotic epithelial cells (DEC): individual cells with deeply eosinophilic cytoplasm and round small hyperchromatic nuclei. Grade score for DEC was based on the quantity of dyskeratotic cells</p>	<p>0 = DEC not present</p> <p>1 = 1 DEC/HPF</p> <p>2 = 2-5 DEC/HPF</p> <p>3 = >5 DEC/HPF</p>	<p>0 = DEC not present</p> <p>1 = DEC (any grade >0) in <33% of epithelium</p> <p>2 = DEC (any grade >0) in 33-66% of</p>

		epithelium 3 = DEC (any grade >0) in >66% of epithelium
H. Lamina propria fibrosis (LPF): thickened connective tissue fibers in the lamina propria. Lamina propria fibers that were arranged singly and had a diameter smaller than a basal layer nucleus were considered normal, fibers that were cohesive without increased diameter were considered abnormal, as were fibers with a diameter equal to or greater than a basal layer cell nucleus. Grade score for lamina propria fibrosis was based on the degree of fiber thickening	0 = LPF not present 1 = fibers are cohesive and interfiber spaces cannot be demarcated 2 = fiber diameter equals the diameter of a basal cell nucleus 3 = fiber diameter exceeds the diameter of a basal cell nucleus	0 = LPF not present 1 = LPF (any grade >0) in <33% of lamina propria 2 = LPF (any grade >0) in 33-66% of lamina propria 3 = LPF (any grade >0) in >66% of lamina propria

The maximum possible grade or stage score for each biopsy was 24. The final score was the ratio of the sum of the assigned scores for each feature evaluated divided by the maximum possible score for that biopsy. For example, if all 8 features had maximum grade and stage scores of 3, the final score for both grade and stage would be $24/24 = 1$. If a feature was not evaluated, the maximum possible score was reduced by 3. Most maximum possible score reductions occurred because lamina propria was not present; if all other features were evaluable, the maximum possible score for a biopsy lacking lamina propria was reduced from 24 to 21 because 7 instead of 8 features were evaluated.

Supplementary Table 3. Evidence for Statements 23 (Effectiveness of proton pump inhibitor drugs for induction of histological remission EoE patients).

Studies	Quality assessment					Summary of findings				Comments
	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations ^a	Quality of evidence	Effectiveness rate	95% CI	Comparator	
Proton pump inhibitor drugs for achieving histologic remission in EoE (importance of outcome: critical for decision making)										
Efficacy: Proportion of patients with <15 eos/hpf after therapy.										
1 SR (25 observational studies & 2 RCT) ²¹⁵	moderate ^b	moderate	none	none	Different drug, doses and duration	⊕⊕⊕⊖ Moderate	50.46 %	42.2 – 58.71	NA	17 studies included adult patients; 11 included pediatric patients
Symptomatic improvement after proton pump inhibitor drugs (importance of outcome: critical for decision making)										
1 SR (24 observational studies & 1 RCT) ²¹⁵	moderate ^b	high	none	moderate	Different drug, doses and duration.	⊕⊖⊖⊖ Very Low	60.8 %	48.38 – 72.2	NA	15 studies included adult patients; 11 included pediatric patients. No validated instruments were used to assess symptoms

^aIncluding publication bias.

^bMainly due to lack of blinding.

Supplementary Table 4. Evidence for Statement 26 (Topical corticosteroids are effective for induction of histological remission in both pediatric and adult EoE patients)

Studies	Quality assessment					Other considerations ^a	Quality of evidence	Overall quality of evidence	Summary of findings			Comments
	Risk of bias	Inconsistency	Indirectness	Imprecision	Steroid therapy				Comparator (placebo)	Relative effect (95% CI)		
Disease remission after topic steroid therapy (importance of outcome: critical for decision making)												
Efficacy of topical steroids versus placebo in inducing complete histologic remission in EoE patients							⊕⊕⊕∅ Moderate					Remission criteria varied among individual studies
1 SR (5 RCTs) ²²⁸	none	none	none	serious ^b	Different drugs and doses ^c	⊕⊕⊕∅ Moderate		56/95	3/66	OR 20.81 (7.03 – 61.63)		
1 SR (7 RCT) ²²⁷	none	none	none	serious ^b	Different drugs and doses ^c	⊕⊕⊕∅ Moderate		92/141	4/117	OR 33.89 (13.35 – 86.04)		
Efficacy of swallowed fluticasone propionate versus placebo in inducing complete histologic remission in EoE patients							⊕⊕∅∅ Low					Remission criteria varied among individual studies
1 SR (3 RCTs) ²²⁸	none	none	none	serious ^b	Different doses ^c	⊕⊕∅∅ Low		38/62	1/39	OR 25.12 (1.07 – 93.44)		
Efficacy of swallowed budesonide versus placebo in inducing complete histologic remission in EoE patients							⊕⊕∅∅ Low					Remission criteria varied among individual studies
1 SR (2 RCTs) ²²⁸	none	none	none	serious ^b	Different doses ^c	⊕⊕∅∅ Low		18/33	2/27	OR 17.17 (3.66 – 80.40)		
Disease improvement after topic steroid therapy (importance of outcome: critical for decision making)												
Efficacy of topical steroids versus placebo in inducing partial histologic remission in EoE patients							⊕⊕⊕∅ Moderate					Remission criteria varied among individual studies
1 SR (5 RCTs) ²²⁸	none	moderate	none	serious ^b	Different drugs and doses ^c	⊕⊕⊕∅ Moderate		95/77	66/9	OR 32.20 (6.82 – 152.04)		
Peak eosinophil count change after therapy with topic steroids compared to placebo							⊕⊕⊕∅ Moderate					
1 SR (5 RCTs) ²²⁹	none	moderate	none	serious ^b	Different drugs and doses ^c	⊕⊕⊕∅ Moderate		92 ^e	66 ^e	WMD ^g -37.2 (- 56.8, -18.5)		
1 SR (5 RCTs) ²²⁶	none	high	none	serious ^b	Different drugs and doses ^c	⊕⊕∅∅ Low		-130.1 ^f	-9.2 ^f	WMD ^g -60.74 (-89.44, -32.04)		
Symptomatic improvement after topic steroid therapy (importance of outcome: critical for decision making)												
Efficacy of topical steroids versus placebo in achieving symptomatic improvement in EoE patients							⊕⊕∅∅ Low					No validated instruments were used to assess symptoms ^d
1 SR (4 RCTs) ²²⁸	moderate	moderate	none	serious ^b	Different drugs and doses ^c	⊕⊕∅∅ Low		43/68	20/51	OR 2.72 (0.90 – 8.23)		
1 SR (7 RCT) ²²⁷	moderate	moderate	none	serious ^b	Different drugs and doses ^c	⊕⊕∅∅ Low		73/122	37/98	OR 3.12 (1.44 – 6.75)		
Efficacy of Topic steroid therapy in adults with EoE (importance of outcome: critical for decision making)												

Complete histologic remission in adults, compared to placebo						⊕⊕⊕∅ Moderate					Remission criteria varied among individual studies
1 SR (4 RCT) ²²⁶	none	moderate	none	serious ^b	Different drugs and doses ^e	⊕⊕⊕∅ Moderate	47/64	2/60	38.09 (7.49 – 193.72)		
Symptomatic improvement in adults, compared to placebo						⊕∅∅∅ Very Low					No validated instruments were used to assess symptoms ^d
1 SR (4 RCT) ²²⁶	none	moderate	none	serious ^b	Different drugs and doses ^e	⊕∅∅∅ Very Low	33/60	14/56	OR 2.78 (0.09 – 83.84)		
Efficacy of Topic steroid therapy in children with EoE (importance of outcome: critical for decision making)											
Complete histologic remission in children, compared to placebo						⊕⊕⊕∅ Moderate					Remission criteria varied among individual studies
1 SR (4 RCT) ²²⁶	none	moderate	none	serious ^b	Different drugs and doses ^e	⊕⊕⊕∅ Moderate	45/77	2/56	OR 24.58 (6.96 – 86.77)		
Symptomatic improvement in children, compared to placebo						⊕∅∅∅ Very Low					No validated instruments were used to assess symptoms ^d
1 SR (4 RCT) ²²⁶	none	moderate	none	serious ^b	Different drugs and doses ^e	⊕∅∅∅ Very Low	47/77	24/56	OR 3.12 (1.39 – 7.05)		

^aIncluding publication bias.

^bImprecision was rating down due to sample sizes of less than 400.

^cIncluded budesonide (delivered both as swallowed inhalation powder and viscous solution) and fluticasone propionate inhalation powder. Budesonide doses ranged from 1 to 2 mg daily. Fluticasone propionate doses ranged between 440 and 1760 mcg/daily, administered in one or two doses.

^dThe studies have tested improvements in symptom by using non validated instruments.

^eExpressed as average number of eosinophils in study groups after intervention.

^fExpressed as average reduction in eosinophil densities (cells per high power field) after intervention.

^gWeighted mean difference.

Supplementary Table 5. Main findings from randomized controlled trials evaluating the efficacy of topical corticosteroid therapy in inducing histologic and clinic remission of EoE.

First author, country, year of publication	Swallowed drug Delivery system Daily dosage Duration	Comparator Daily dosage Duration	Population Sample size in each arm	Histologic remission topical steroids, n (%), definition	Histologic remission comparator, n (%)	Clinical response topical steroids, measurement tool	Clinical response comparator, measurement tool
Konikoff, US, 2006 ¹	Fluticasone propionate Metered-dose inhaler 880 mcg 12 weeks	Placebo 12 weeks	Children 21/15	10/21 (47%)* <i>< 1 eos/HPF</i>	1/15 (6.7%) <i>< 1 eos/HPF</i>	Resolution of vomiting (67%)*	Resolution of vomiting (27%)
Schaefer, US, 2008 ²	Fluticasone propionate Metered-dose inhaler 880 mcg 4 weeks	Oral prednisone 1 mg/kg/day 4 weeks	Children 40/40	18/45 (45%) <i>< 1 eos/HPF</i>	26/45 (65%) <i>< 1 eos/HPF</i>	No differences	
Dohil R, US, 2010 ³	Budesonide Viscous solution 1 mg (< 5 feet tall) 2 mg (> 5 feet tall) 12 weeks	Placebo 12 weeks	Children 15/9	13/15 (86%)* <i>< 6 eos/HPF</i>	0/9 (0%) <i>< 6 eos/HPF</i>	1.2 ± 1.87 Non-validated symptom score	1.85 ± 2.67 Non-validated symptom score

Straumann, Switzerland, 2010 ⁴	Budesonide Viscous suspension 4 mg 2 weeks	Placebo 2 weeks	Adults 18/18	13/18 (72%)* < 5 eos/HPF	2/18 (11%) < 5 eos/HPF	2.22 ± 2.07* Dysphagia Symptom Score	4.72 ± 1.96 Dysphagia Symptom Score
Peterson, US, 2010 ⁵	Fluticasone propionate Metered-dose inhaler 880 mcg 8 weeks	Esomeprazole 40 mg 8 weeks	Adults 15/15	2/15 (13%) < 5 eos/HPF	4/15 (27%) < 5 eos/HPF	1.7 Non-validated dysphagia scale	2.3 Non-validated dysphagia scale
Dellon, US, 2012 ⁶	Budesonide Viscous slurry 2 mg 8 weeks	Budesonide Metered-dose inhaler 2 mg 8 weeks	Adults 11/11	7/11 (64%)* < 1 eos/HPF	3/11 (27%) < 1 eos/HPF	16 ± 17 Mayo Dysphagia Questionnaire	10 ± 12 Mayo Dysphagia Questionnaire
Alexander, US, 2012 ⁷	Fluticasone propionate Metered-dose inhaler 1760 mcg 6 weeks	Placebo 6 weeks	Adults 21/21	13/21 (62%) > 90% reduction baseline esophageal eosinophilia	0/21 (0%) > 90% reduction baseline esophageal eosinophilia	9/21 (43%) Mayo Dysphagia Questionnaire	6/21 (28%) Mayo Dysphagia Questionnaire
Moawad, US, 2013 ⁸	Fluticasone propionate Metered-dose inhaler 880 mcg 8 weeks	Esomeprazole 40 mg 8 weeks	Adults 21/21	4/21 (19%) < 7 eos/HPF	7/21 (33%) < 7 eos/HPF	12 ± 16 Mayo Dysphagia Questionnaire	1.4 ± 4.5* Mayo Dysphagia Questionnaire
Butz, US, 2014 ⁹	Fluticasone propionate Metered-dose inhaler 1760 mcg 12 weeks	Placebo 12 weeks	Children and adults 28/14	15/28 (53%)* < 1 eos/HPF	0/14 (0%) < 1 eos/HPF	No differences	

Gupta, US, 2015 ¹⁰	Budesonide Viscous solution Low-dose 2-9 yr 0.35 mg 10-18 yr 0.5 mg Medium-dose 2-9 yr 1.4 mg 10-18 yr 2 mg High-dose 2-9 yr 2.8 mg 10-18 yr 4 mg 12 weeks	Placebo 12 weeks	Children	Low 12% Medium 42% High 76%* $\leq 1 \text{ eos/HPF}$	Placebo 0% $\leq 1 \text{ eos/HPF}$	Symptom resolution on Clinical Symptom Score Low 17% Medium 31% High 17%	Symptom resolution on Clinical Symptom Score Placebo 33%
Miehlke, Germany, 2016 ¹¹	Budesonide Effervescent tablets (ET) Viscous suspension (VS) 2 mg 4 mg 2 weeks	Placebo 2 weeks	Adults 19/19/19/19	ET 2 mg 100%* ET 4 mg 97%* VS 2 mg 94%* $< 15 \text{ eos/HPF}$	0% $< 15 \text{ eos/HPF}$	4.9 ± 1.4 4.2 ± 2.1 4.5 ± 1.8 Dysphagia Symptom Score	4.7 ± 1.9 Dysphagia Symptom Score

* Grey-marked areas denote statistical significance

Supplementary Table 6. Swallowed topical steroid initial dosing for eosinophilic esophagitis treatment²²⁷.

Drug	Target population	Induction dosing (usually divided doses)	Maintenance dosing (usually divided doses)
Fluticasone propionate ^{a,b}	Children ^d	880-1760 mcg/day	440-880 mcg/day
	Adults	1760 mcg/day	880–1760 mcg/day
Budesonide ^{b,c}	Children ^d	1-2 mg/day	1 mg/day
	Adults	2-4 mg/day	2 mg/day

^a If an inhaler is used, the patient should be instructed to puff the medication into their mouth during a breath hold.

^b Regardless of the form of administration (nebulized or swallowed), patients should fast at least 30–60 min after medication in order to minimize esophageal drug clearance.

^c Oral viscous budesonide preparation consists of mixing 1–2 mg budesonide with 5 mg of sucralose or similar.

^d Specific doses in children will be determined by age, height or weight.

Supplementary Table 7. Evidence for Statements 29 - 33 (Effectiveness of dietary treatment for induction of histological remission in both pediatric and adult EoE patients).

Studies	Quality assessment					Summary of findings				Comments
	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations ^a	Quality of evidence	Effectiveness rate	95% CI	Comparator	
Elemental diet for achieving histologic remission in EoE (importance of outcome: critical for decision making)										
Efficacy: Proportion of patients with <15 eos/hpf after therapy.										
1 SR (13 observational studies)	moderate ^b	moderate	none	None	None	⊕⊕⊕⊕ Moderate	90.8 %	84.7 - 95.5	NA	12 studies included pediatric patients; only 1 included adults
Allergy test-directed elimination diets for achieving histologic remission in EoE (importance of outcome: critical for decision making)										
Efficacy: Proportion of patients with <15 eos/hpf after therapy.										
1 SR (14 observational studies)	moderate ^b	high	none	moderate	Several testing approaches were considered ^c	⊕⊕⊕⊕ Moderate	45.5 %	35.4 - 55.7	NA	12 studies included pediatric patients; 2 included adults ^d
Six-food empiric elimination diets for achieving histologic remission in EoE (importance of outcome: critical for decision making)										
Efficacy: Proportion of patients with <15 eos/hpf after therapy.										
1 SR (7 observational studies)	moderate ^b	low	none	moderate	Some variation in foods excluded	⊕⊕⊕⊕ Moderate	72.1 %	65.8 - 78.1	NA	4 studies included pediatric patients; 3 included adults

^aIncluding publication bias.

^bMainly due to lack of blinding.

^cThe studies have tested regimens based on skin prick testing (SPT) alone, SPT plus atopy patch testing (APT), SPT plus serum IgE, and SPT plus APT plus prick-prick testing.

^dSignificant differences between children (47.9 %) and adults (32.2 %) were noted.

^eFoods excluded in a six-food elimination diet varied regarding to cereals (from excluding only wheat, gluten-containing cereals and also rice and corn) and legumes (only soy bean or every kind of legumes).

Supplementary Table 8. Summary of the results of prospective studies on empiric six- (SFED), four- (FFED), or two- (TFED) food group elimination diets FFED, showing the number and the most common food triggers identified through individual food reintroduction

First author, year of publication, country	Diet Population	Histologi c remission	Number of culprit foods identified through individual reintroduction of either six, four or two food groups			Most common food triggers identified through individual food reintroduction
			1	2	>2	
Kagalwalla, 2011, USA ⁵	SFED Children	74%	72%	8%	8%	Milk 74% Wheat 26% Eggs 17%
Gonsalves, 2012, USA ²	SFED Adults	70%	85%	15%		Wheat 60% Milk 50%
Lucendo, 2013, Spain ³	SFED Adults	72%	36%	31%	33%	Milk 62% Wheat 29% Egg 26% Legumes 24%
Molina-Infante, 2014, Spain ⁶	FFED Adults Multicenter	54%	45%	45%	-	Milk 50% Egg 36% Wheat 31% Legumes 18%

Kagalwalla, 2015, US ⁷	FFED Children Multicenter	71%	74%	21%	5%	Milk 68% Egg 26% Wheat 21%
Philpott, 2016, Australia ¹	SFED Adults	-	56%	17%	13%	Milk 43% Wheat 43% Eggs 34%
Molina-Infante, 2016, Spain	TFED Adults Multicenter	40%	85%	15%	-	Milk 60% Wheat 25% Milk and wheat 15%

Supplementary Table 9: Unmet aspects on EoE arisen during guidelines development to be address in the future.

<p>GENERAL</p> <ul style="list-style-type: none"> - Increased disease awareness - Multidisciplinary management of EoE, involving gastroenterologists, pediatricians, allergists, pathologists, dietitians and ENT specialists. - Structured childhood and transition programs
<p>CONCEPT AND EPIDEMIOLOGY</p> <ul style="list-style-type: none"> - Etiology and pathophysiology in responders to PPI therapy (GERD, food allergens or both) - Interactions between GERD and EoE - Identification of environmental risk factors influencing EoE for preventive purposes - Why antigens contained in staple foods for centuries are causing now EoE? - Are there distinct causative food triggers in areas different from Europe, North America and Australia? - Updated epidemiologic trends in children and out of Europe and North America
<p>DIAGNOSIS AND DISEASE ACTIVITY ASSESSMENT</p> <ul style="list-style-type: none"> - Definition of standardized criteria for disease remission and improvement. - Early identification of clinical phenotypes (inflammatory, fibrostenotic, both) - Non- or minimally-invasive diagnostic tools for disease monitoring - Optimization of scores evaluating disease activity through symptoms, endoscopic findings, and quality of life. - The role of the EndoFLIP™ device to identify patients requiring esophageal dilation during follow-up due to impaired esophageal distensibility - Safety of repeat propofol sedation for endoscopy in children - Standardization of eosinophil count method (size of HPF, number of HPF to be examined, mean vs. peak count) - Multicenter external validation of EoEHSS score to standardize histologic assessment of esophageal biopsies. - To improve our diagnostic accuracy in patients with suspected EoE and < 15 eos/HPF or asymptomatic subjects with ≥15 eos/HPF
<p>NATURAL HISTORY</p> <ul style="list-style-type: none"> - Natural history of patients with suspected EoE and < 15 eos/HPF or asymptomatic with ≥ 15 eos/HPF - Prediction of patients with a progressive phenotype order to guide long-term strategies - Whether maintenance medical (including PPIs) and dietary therapy can reverse the progressive course of EoE
<p>TREATMENT</p> <ul style="list-style-type: none"> - Ideal treatment endpoints (symptoms, esophageal inflammation and/or remodeling, EoE gene expression) - Adequate duration of all short-term therapeutic intervention (2, 4, 8, 12 weeks). Are we missing slow responders? - The significance of partial response with any therapeutic intervention (e.g., a 50% reduction in eosinophil count) - The role of combination therapy (PPI plus either corticosteroids or diet). Are we missing partial responders? - Which patients will and will not require maintenance therapy - Frequency of endoscopy in follow-up - Treatment of patients refractory to PPIs, topical steroids and elimination diet

PPI therapy

- Drug and doses required for initial therapy
- Influence of CYP2C19 genotype in initial response to PPI therapy
- The role of other acid suppressive drugs (e.g., vonoprazan)
- Safety issues with maintenance therapy
- More studies in children are required

Swallowed topical corticosteroids

- Drug, doses, duration, and delivery system for initial and maintenance therapy
- Safety issues with maintenance therapy, especially in children

Elimination diet

- Novel food allergy testing is required to detect triggering foods in EoE
- Whether step-up dietary therapy, first eliminating the one or two more common food triggers in EoE, can optimize our clinical practice and engage patients with diets.
- Long-term efficacy of dietary therapy in adherent patients
- Cross reactivity of food allergens (e.g, cow's milk with other animal milks, wheat with other cereals)
- Nutritional adequacy, and psychological and economic impact of maintenance dietary therapy, especially in children
- Effect of long term food avoidance on QoL of patients with EoE.