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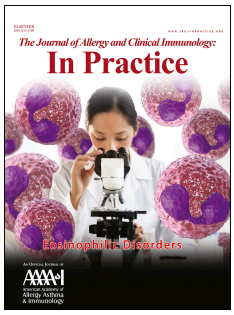

Emerging Therapies for Eosinophilic Gastrointestinal Diseases

Kathryn Peterson, MD, MS, Ekaterina Safroneeva, PhD, Alain Schoepfer, MD

PII: S2213-2198(21)00835-7

DOI: https://doi.org/10.1016/j.jaip.2021.07.031

Reference: JAIP 3760

To appear in: *The Journal of Allergy and Clinical Immunology: In Practice*

Received Date: 27 June 2021

Revised Date: 26 July 2021

Accepted Date: 26 July 2021

Please cite this article as: Peterson K, Safroneeva E, Schoepfer A, Emerging Therapies for Eosinophilic Gastrointestinal Diseases, *The Journal of Allergy and Clinical Immunology: In Practice* (2021), doi: https://doi.org/10.1016/j.jaip.2021.07.031.

Invited review for JACI in practice, vs 20210725_ES-AS-v4

Title: Emerging therapies for eosinophilic gastrointestinal diseases

Kathryn Peterson, MD, MSci[1], Ekaterina Safroneeva[2], PhD, Alain Schoepfer, MD[3]

Affiliations:

1 Division of Gastroenterology, University of Utah, Salt Lake City, United States of America

2 Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland

3 Division of Gastroenterology and Hepatology, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland

Medical writing: none

Disclosures:

KP has served as consultant for Allakos, AstraZeneca, Eli Lilly, Ellodi, Regeneron-Sanofi, Bristol Meyers Squibb, and Takeda. She serves on study board for Alladapt. She has independent research funding from Allakos and Chobani.

ES has received research funding from Dr Falk Pharma, GSK, Celgene/Receptos/BMS, Regeneron. She has received consulting fees from Celgene/Receptos/BMS, Dr Falk Pharma, Gossamer Bio, and Regeneron.

AS has received research funding from Adara/Ellodi, AstraZeneca, Dr Falk Pharma, GSK, Celgene/Receptos/BMS, Regeneron. He has received consulting fees from Abbvie, Adare/Ellodi, Amgen, AstraZeneca, Celgene/Receptos/BMS, Dr Falk Pharma, GSK, Gossamer Bio, Regeneron, and Sanofi-Genzyme.

Funding: Swiss National Science Foundation (grant number 32473B_185008 to ES, grant number 32003B_160115/1 to AS) and Swiss Eosinophilic Esophagitis Foundation (to AS).

Corresponding author:

Kathryn Peterson, MD, MSCI

30 North 1900 East SOM 4R118

Salt Lake City, Utah, 84132, United States

Tel: 801-587-3450

Email: Kathryn.Peterson@hsc.utah.edu

Abstract

Besides eosinophilic esophagitis (EoE), other eosinophilic gastrointestinal diseases (EGIDs), such as eosinophilic gastritis (EG), eosinophilic gastroenteritis (EGE), and eosinophilic colitis (EC), are increasingly diagnosed over the last decade. Whilst diagnosis and therapy of EoE have been standardized, the diagnosis and therapy of other EGIDs are areas of active research. Motivated by the increasing prevalence of these conditions, concerted efforts of different stakeholders have led to the evaluation of targeted biologic therapies for EGID management over the last couple of years, and several promising molecules are currently in the pipeline. This review article provides an overview of targeted biologic therapies for use in EGIDs.

Key words

Abbreviations: CCR3, C-C chemokine receptor type 3; EC, eosinophilic colitis; EoE, eosinophilic esophagitis; EG, eosinophilic gastritis; EGE, eosinophilic gastroenteritis; EGIDs, eosinophilic gastrointestinal diseases; IL, interleukin; MAdCAM-1, mucosal addressing cell adhesion molecule-1; Siglec-8, sialic acid–binding immunoglobulin-like lectin 8; TSLP, thymic stromal lymphopoietin; T2, type 2.

Introduction

Eosinophilic gastrointestinal diseases (EGIDs) include eosinophilic esophagitis (EoE), eosinophilic gastritis (EG), eosinophilic gastroenteritis (EGE), eosinophilic enteritis (EE) involving either duodenum (eosinophilic duodenitis), jejunum (eosinophilic jejunitis), or ileum (eosinophilic ileitis), and eosinophilic colitis (EC).[1,2] Due to relative ease of obtaining duodenal biopsies when compared to those from other parts of small intestine, patients with EGE are most likely to have confirmed gastric and duodenal involvement. A consensus exercise among international experts to unify the terminology of EGIDs and establish histologic cutoff values for tissue eosinophilia is currently ongoing.[3] These inflammatory gastrointestinal conditions are not classic inflammatory bowel diseases, but manifest by excessive infiltration of eosinophils throughout all layers of the gastrointestinal tract accompanied by that of other inflammatory cells, such as lymphocytes, mast cells, macrophages.[4] EGIDs are characterized by type 2 (T2) inflammatory infiltrate and are often associated with symptoms related to location and extent of involvement.[5,6]

EoE often presents with dysphagia, food aversion, nausea, or abdominal/chest pain.[3] Children may present with vague symptoms, such as food aversion and failure to thrive. EGE often presents with nausea, abdominal pain, or bloating.[6] EE may also present with nausea, abdominal pain, or bloating, and may also cause loose stools, symptoms similar to irritable bowel syndrome, anemia, or protein loss.[7] EC may present with loose stool or blood in stool associated with abdominal cramping/pain. Patients with EGIDs have increased risk of multiple site involvement.[5,7] For example, the risk of having EGE is increased in those with EoE. Symptom presentation of EE and EC may depend on the involved wall layers. Mucosal layer disease typically manifests with diarrhea, muscle layer disease presents with cramps and potentially strictures, whereas serosal disease typically manifests with eosinophilic ascites.[4-7] EoE is the most commonly identified EGID with established consensus on histopathologic

criteria for diagnosis.[8] Prevalence of EoE is estimated at 1/2000 inhabitants in industrialized countries, whereas EG, EGE, and EC are much less prevalent. Based on an insurance claims database, standardized estimated prevalence of EG, EGE, and EC were 6.3/100,000, 8.4/100,000, and 3.3/100,000, respectively.[9]

It appears that the immune dysregulation in EG, EGE, and EE mimics that seen in other eosinophil-related disorders. Studies on EoE serve a pivotal role in examining the immune responses for other EGIDs.[10,11] We can only assume that events similar to those that occur in EoE lead to subsequent onset of EG, EGE, and EE. It is likely that an initial insult in the form of food antigens, pollution, antibiotics, or infection results in the release of mucosal alarmins, such as interleukin (IL)-33, thymic stromal lymphopoietin (TSLP), and IL-25, in response to epithelial stress. These alarmins subsequently enhance the T2 responses by stimulating the release of cytokines, such as IL-4, IL-13, and IL-5, by innate lymphoid cells, dendritic cells, and additional immune cells with the subsequent recruitment of mast cells and eosinophils into tissues. Epithelial barrier disruption and tissue remodeling appear to be a hallmark of all EGIDs.

Experimental modeling of EoE in mice has demonstrated that adaptive immunity and T2 cytokines (especially IL-5 and IL-13) play a key role in the disease process.[12] Similar molecular mechanisms have been identified in asthma and eczema, two clinical entities strongly associated with EoE.[12] GWAS studies have identified genes, such as those encoding TSLP and its receptor, involved in susceptibility to atopic disease, such as EoE.[13] A recent study by Shoda *et al.* demonstrated that elevated plasma/serum eotaxin-3, thymus- and activation-regulated chemokine, IL-5, and TSLP levels were observed in EG patients compared to control subjects.[14] The plasma eotaxin-3 levels correlated with levels of gastric eotaxin-3 in the EG patients. Similar immune mechanisms have been identified in EGE, and it is likely at least some of these immune processes extend into EC as well.

No therapy for management of EGIDs is currently approved by the US Food and Drug Administration. In EoE, approximately 2/3 and 1/3 of patients failed to reach histologic remission following treatment with proton-pump inhibitors and topical corticosteroids, respectively, compared to >85% of patients treated with placebo.[15] Therefore, due to lack of efficacy at least 20-30% of EoE patients require therapeutic approaches other than topical corticosteroids and proton-pump inhibitors.[16] Proton-pump inhibitors and topical corticosteroids have no established efficacy in non-EoE EGIDs.

This article reviews data on use of biologic therapies in patients with EGIDs. As EoE is best studied of all EGIDs, most data on use of biologic therapies are available for EoE. The different therapeutic options used in EoE, EG, and eosinophilic duodenitis are summarized in **Table 1**.

Biologic therapies targeting interleukin 5

IL-5 functions by enhancing the maturation and release of eosinophils from the bone marrow into the circulating blood, trafficking of eosinophils into tissues, and promoting eosinophil survival. IL-5 is also crucial for the recruitment of physiological resident intestinal eosinophils.[17] IL-5 was a prime target for initial trials in EoE, as tissue obtained from murine EoE models and human esophageal tissue from EoE patients demonstrated upregulation of IL-5.[18] IL-5 knock out mice were protected from developing EoE despite antigen stimulation. The efficacy of anti-IL-5 antibodies, mepolizumab and reslizumab, have been previously evaluated in EoE.

Mepolizumab is a fully humanized monoclonal IgG1 antibody specific for human IL-5. Mepolizumab blocks the binding of human IL-5 to the α-chain of the IL-5 receptor (IL-5Rα) complex, which is mainly expressed on the eosinophil cell surface. Efficacy of mepolizumab was evaluated in a small proof-of-concept trial of four adult patients with EoE.[19] In this series,

subjects received three monthly doses (10 mg/kg, maximum 750 mg) of mepolizumab intravenously, and the esophageal histology and general health-related quality of life were compared between baseline and 12 weeks following first infusion. Following treatment, patients had improved clinical activity and quality of life, and decreases in esophageal eosinophilia were observed. In a subsequent randomized placebo-controlled study of 11 adult patients, 5 patients received up to 4500 mg of mepolizumab up to four times over 9 weeks, whilst 6 patients received placebo.[20] No patient achieved histologic remission of <5 eosinophils/high-power field, the primary end point of the study. However, 66% and 65% reduction of esophageal eosinophilia was noted at week 4 and 13, respectively. The patient-reported symptom improvement was not significant. Interestingly, authors observed no reduction in the resident duodenal eosinophils or mast cells, although these cells were diminished in esophagus. In a study of 59 children with EoE, subjects were randomized to monthly doses of 0.55 mg/kg, 2.5 mg/kg, or 10 mg/kg of mepolizumab for a total of 3 infusions without a placebo arm.[21] At 12 weeks following first infusion, 5/57 patients achieved histologic remission of <5 peak eosinophils/high-power field, the primary endpoint of the study. Peak esophageal eosinophils/high-power field were <20 in 31.6% of children. Given that patients with low baseline symptom score were recruited, the ability of the study to detect change in symptom score following treatment was limited.

Reslizumab was studied in a randomized, placebo-controlled trial of 226 adolescents and children ≤18 years of age); the study failed to demonstrate significant clinical improvement following treatment with 1, 2, or 3 mg/kg of reslizumab relative to placebo despite reducing esophageal eosinophilia by 59-67%.[22] At one of the trial's centers, twelve subjects participating in the original randomized controlled trial (RCT) and open label extension (OLE) were kept on reslizumab for nine years.[23] These patients received a median of 40 doses of reslizmab (range 2-116) in total between the RCT/OLE and the extension from compassionate

use. Symptoms improved on treatment in this small cohort along with a reduction in esophageal eosinophil count to 3 cells/ high-power field even with expanding diet.

In conclusion, the majority of the trials with mepolizumab and reslizumab have failed to demonstrate significant symptom improvement. Some have argued that the lack of validated patient-reported outcome measures and timing of symptom assessment in these mepolizumab and reslizumab trials possibly contributed to their ultimate failure in showing clinical improvement. Therefore, these medications may have at least partial efficacy in treatment of eosinophilic disease and may need to be evaluated using novel validated patient-reported outcome tools.[24]

An additional IL-5-mediated drug target is IL-5Rα.[25] Benralizumab is a monoclonal antibody that targets IL-5Rα found on eosinophils leading to apoptosis of these cells (antibody dependent cell mediated cytotoxicity). It has demonstrated efficacy in eosinophilic asthma and is currently approved by the United States Food and Drug Administration (US FDA) for this condition.[26] Benralizumab is currently undergoing trials in EoE as well as EG.

Biologics targeting interleukin-4 and interleukin-13

IL-13 is a pivotal cytokine implicated in T2-mediated disease, such as asthma and atopic dermatitis, that have similar immune mechanisms to EoE and potentially non-EoE EGIDs. Esophageal epithelial cells, when stimulated by IL-13, develop an epithelial signature similar to that seen in EoE patients.[27] IL- 13 may also contribute to barrier dysfunction of the epithelium especially in the esophagus via its effects on Calpain 14.[28] Three monoclonal antibodies with direct or indirect effects on IL-13-induced pathways have been studied in EoE: RPC4046, QAX576, and dupilumab. Both RPC4046 and QAX576 work by directly targeting IL-13. Dupilumab functions by binding to the IL-4 receptor α, which functions as a conduit for both IL-

13- and IL-4-mediated immunity. Dupilumab is currently approved by US FDA for treatment of T2-mediated diseases, such as asthma, eczema and chronic rhinosinusitis with nasal polyposis. Dupilumab currently holds orphan drug status for EoE. Although these three antibodies have never been evaluated for the treatment of non-EoE EGIDs, the Consortium for Eosinophilic Gastrointestinal Disease Researchers is working to set up a proof-of-concept study of dupilumab in patients with EG.

QAX576 is a monoclonal antibody directed against IL-13. QAX576 was originally studied in a 12 week, randomized, blinded Phase 2 trial in adults with EoE.[29] In this trial, 23 adult patients were randomized to 6 mg/kg of QAX576 or placebo every 4 weeks for three months. By the end of 12 weeks, the treatment with QAX576 resulted in a significant decrease in esophageal eosinophilia (the mean esophageal eosinophil count decreased by 60% with QAX576 versus an increase of 23% with placebo [P = .004]), and the decrease was sustained up to 6 months. However, the study missed its primary endpoint overall (responder rate for > 75% reduction of the peak esophageal eosinophilia). There was a trend towards improvement in dysphagia in the QAX576-treated subjects. It does not appear that the development of this monoclonal antibody will be pursued.

RPC4046 is a biologic designed to block IL-13 from binding to its receptors.[30] In a randomized, controlled trial, 99 adults with EoE were randomized into three different arms: 10 mg/kg loading dose followed by 360 mg subcutaneously weekly, 5 mg/kg loading dose followed by 180 mg subcutaneously weekly, or placebo for 16 weeks.[31] A statistically significant reduction in symptoms and esophageal eosinophil counts were observed in the RPC4046-treated patients compared to placebo. In approximately 50% of patients in the drug-treated arms, reduction of peak esophageal eosinophilia to <15 cells/high-power field was observed. The histologic outcome of <6 eosinophils/high-power field recommended by US FDA was achieved in 20-25% of drug-treated patients. Similar to the anti-IL-5 therapies, symptomatic

improvement appeared to lag behind improvement in esophageal peak eosinophil counts. However, at 52 weeks in the open label extension study with 360 mg, significant symptomatic and clinical improvement was maintained on the 360 mg dose.[32]

Dupilumab is a fully human IgG4 monoclonal antibody directed against the alpha subunit of IL-4 receptor (IL-4Rα). By binding to IL-4Rα, dupilumab affects downstream IL-13 signaling. Dupilumab effectiveness in adults with EoE was evaluated in a randomized, double-blind, placebo-controlled Phase II trial, the results of which were recently published.[33] In this trial, 47 patients with EoE received either dupilumab (600 mg loading dose followed by 300 mg weekly) or placebo for 12 weeks. In patients treated with dupilumab, the mean peak esophageal eosinophils/high-power field decreased by 86.8% at week 12. Over 65% of dupilumab-treated patients reached an outcome of less than 6 eosinophils/ high-power field. At week 10, a significant improvement in dysphagia was reported in dupilumab-treated patients compared to those treated with placebo. Esophageal distensibility was increased as measured by esophageal EndoFLIP. A Phase 3 randomized clinical trial has recently completed enrollment, and the results are pending.

Anti-Siglec-8 antibody

Sialic acid–binding immunoglobulin-like lectin 8 (Siglec-8) is an inhibitory receptor expressed on eosinophils and mast cells. Anti-siglec-8 antibody was shown to reduce eosinophil counts in murine EGE. Lirentelimab is a humanized, anti–Siglec-8 monoclonal antibody that is capable of depleting tissue and blood eosinophils.[34] Lirentelimab has proven efficacy in T2 diseases, such as conjunctivitis (NCT03379311) and urticaria (NCT03436797).

Lirentelimab was the first biologic to be investigated for its efficacy in EG and/or eosinophilic duodenitis (ED). Specifically, 65 EG/ED patients participated in a randomized, placebo-

controlled trial of lirentelimab (2 dosing regimens).[35] Assessments of eosinophil counts in the gastric and duodenal tissues were performed before and following 12-week treatment; assessment of esophageal eosinophilia was carried out in those patients, who had a prior diagnosis of EoE. Mean decrease in gastric/duodenal eosinophils was 86% in lirentelimab-treated patients compared to 9% in placebo. Total symptom score decreased by 48% in the lirentelimab arm and only by 22% in the placebo arm. Sustained tissue eosinophil suppression was seen in patients participating in the open label extension part of the study. Twenty patients with concomitant esophageal eosinophilia were analyzed in this study. Of the 14 patients treated with lirentelimab, 13 patients demonstrated resolution of esophageal eosinophilia. Of the 9 patients treated with placebo, only one patient reached that outcome. Although reduction in symptoms following treatment with lirentelimab was observed, complete symptom response was not reported. Therefore, it appears that eradication of eosinophils from patients with EGID may not completely resolve the immune dysfunction and tissue dysregulation. Another pathomechanism might be that eosinophil-derived granule proteins, such as eosinophil-derived neurotoxin, have the potential to provoke long-lasting enteric neuropathy that can explain symptom persistence despite resolution of tissue eosinophilia. Lirentelimab is currently under investigation in Phase III trials for patients with EG, EoE, and eosinophilic duodenitis (clinicaltrials.gov NCT04322708, NCT04620811, NCT04322604, NCT04856891).

The Role of Selective Depletion of Eosinophils

As we continue to learn about EGIDs, it is likely that different disease phenotypes will emerge. By identifying molecular drivers of these conditions, we will be able to personalize biologic therapies to the right patient populations. One advantage of therapies like lirentelimab and benralizumab is that they primarily deplete eosinophils and may work well throughout the gastrointestinal tract. However, it is worth pointing out that these therapies also deplete mast

cells and basophils; depletion of these cells may further attenuate the inflammatory response.[36] Hence, the mechanism of action of lirentelimab and benralizumab in EGIDs should be further investigated. Whilst eosinophils are considered to be multifunctional leukocytes, they are also effector cells. It is not clear if depleting these cells is sufficient for management of all forms of EGIDs, as corticosteroids most frequently used for EoE management have inhibitory effects on multiple types of immune cells. It is likely that inhibition of common upstream pathways, such as IL-4/IL-13 pathway, might offer universal relief to EGID patients affected by more than one atopic condition.

Regardless of their mechanism, all biologic therapies, including eosinophil-depleting medications, currently under evaluation for use in EGIDs require long-term safety and efficacy/effectiveness data; data to date suggest that such therapies may be safe when used for several years. Although we typically associate eosinophils with T2 immunity, there are ample data to suggest that eosinophils may offer a regulatory or protective role in specific diseases, such as arthritis. This protective effect may be lost with continued use of these medications.

Other potential therapies for EGIDs

There are a few case series of biologic therapies that are approved by US and European regulators for use in inflammatory bowel disease and that were utilized in patients with EG/EGE and corticosteroid-refractory EoE. Vedolizumab, a humanized monoclonal antibody, targets gastrointestinal-homing integrin α4β7 and prevents binding of α4β7 expressed by lymphocytes to mucosal addressing cell adhesion molecule-1 (MAdCAM-1) expressed exclusively on the endothelium of intestinal mucosal vessels. In so doing, vedolizumab inhibits T lymphocytes from trafficking into intestinal tissues in response to inflammation. Vedolizumab also binds to eosinophils, as these cells also express α4β7 integrin. Two case reports of Crohn's disease

patients with concomitant EoE, whose EoE improved under vedolizumab, provide initial proof-of-concept for possible utility of the vedolizumab for management of EoE.[37,38] Vedolizumab was also used in 5 EG/EGE patients, with two out of five patients documenting improvement in both symptoms and eosinophilia.[39] Tofacitinib, a Januskinase 1 and 3 inhibitor, was successfully used in one patient for treatment of corticosteroid-refractory EoE.[40]

Many of the potential targets first identified for drug development for other atopic conditions, such as eczema or asthma, might also be appropriate for drug development in the field of EGIDs and have shown promise in murine models of EGIDs.

Incomplete efficacy of current biologics may be related to targeting of downstream targets in the immune response rather than upstream ones. Thus, some potential therapies are targeting the alarmins on epithelium, such as IL-33, IL-25, and TSLP, to inhibit the initiation of the T2 response. Group 2 innate lymphoid cells are activated via IL-33 and TSLP and produce and activate T2 cytokines, which induce basophil and eosinophil and mast cell recruitment and differentiation in tissues. Studies of an anti-IL-33 antibody demonstrated its ability to inhibit the accumulation of lung eosinophilia in murine models of asthma. Blockade of all three alarmins shows further promise in murine models of asthma.[41] Alarmin TSLP, which plays important role in pathogenesis of both EoE and EG, is a pro-inflammatory cytokine produced along the surface of the gastrointestinal tract and regulates immune responses on epithelial surfaces. TSLP may be activated by T2 cytokines or triggered by allergens or RNA viruses.[42] The data on the use of tezepelumab, a monoclonal antibody directed against TSLP, in asthma patients have been encouraging; the drug reduces exacerbations and T2 biomarkers (IL-5 and IL-13) in the blood of asthmatics. It is likely that the medications targeting this molecule will one day be evaluated in EGIDs.

C-C chemokine receptor type 3 (CCR3) inhibitors are currently being investigated as potential therapies for EGIDs. Signaling through CCR3, the ligand for eotaxins, is responsible for

eosinophil recruitment into the tissues. In murine models, CCR3 antagonism inhibits the influx of eosinophils into the stomach and small intestine.[43] Currently there are no human trials of CCR3 inhibitors underway for patients with EGIDs.

IL-15 as well as IL-15Rα mRNA expression were increased in esophageal biopsies from active EoE patients compared to healthy individuals. IL-15 and IL-15Rα mRNA expression appears to be elevated in EoE patients refractory to corticosteroids. Anti-IL-15 treatment reduces esophageal eosinophilia in the experimental Aspergillus mouse model of EoE.[44] Currently neither clinical nor safety data on antagonism of IL-15 in human T2-mediated disease are available, but the results of proof-of-concept study in adults with EoE are eagerly awaited.

Eosinophilic Colitis

Due to its extremely rare nature, studies on immune mechanisms in EC are currently lacking. Whilst it is relatively straight forward to hypothesize that eosinophil depleting therapies might be useful in patients with EC, more studies are needed to urgently needed understand the immune mechanisms behind this enigmatic disease.

Summary

Although distal EGIDs are less common than EoE, it appears that similar immune mechanisms are at play. Therefore, therapies that are efficacious/effective in EoE may also work well in controlling distal disease. Although it remains to be seen whether "one shoe fits all" therapy approach for all EGIDs will pan out, the results of the Lirentelimab study laid the groundwork for future research in this area. Targeting the eosinophils or mast cells/basophils is a promising approach for management of EGIDs, especially the non-EoE EGIDs, immune physiology of

which is difficult to characterize due to the paucity of patients presenting with these diseases and the under-recognition of these conditions. Therapies directed primarily toward eradication of eosinophilia may work well throughout the gastrointestinal tract, as they are not selective for a specific immune pathway, only the target cell itself. Inhibition of common upstream pathways linked to T2-mediated diseases (*i.e.* alarmins, IL-4/IL-13 pathways) may offer universal relief to EGID patients, who often suffer from multiple atopic conditions. Although long term safety and efficacy data on most biologic therapies reviewed in this paper are currently lacking, it is likely that in the future EGID patients will have multiple options to choose from for optimal management of their conditions. The future research on the utility of biologic therapy in EGIDs may not only aid researchers and clinicians to find appropriate medications for patients refractory to their existing therapies, like swallowed topical corticosteroids in EoE, but will help to identify phenotypes of eosinophil-associated diseases, and will pave the way for much anticipated precision medicine approaches.

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Drug	Mechanism of action	Evaluated in the following eosinophilic GI diseases	Number of studies, total number of patients included (including placebo), references (REF)	Main results
Mepolizumab	Fully humanized IgG1 mAb blocking IL-5	EoE	5 / 128 REF 19,20,21	Reduction of tissue eosinophilia Minor symptomatic improvement (not primary endpoint)
Reslizumab	Humanized IgG4 mAb blocking IL-5	EoE	1 / 227 REF 22,23,24	Reduction of tissue eosinophilia
Benralizumab	Humanized mAb blocking IL-5Ralpha	HES	1 / 5 patients with HES with gastrointestinal involvement REF 26	9/10 benralizumab-treated patients reached endpoint of at least 50% reduction in absolute eosinophil counts
QAX576	Humanized mAb against IL-13	EoE	1 / 25 REF 29	Trial did not meet primary endpoint of >75% reduction of esophageal peak eosinophil counts. QAX576-treated patients had significant reduction of tissue eosinophilia compared to placebo (-60% vs. +23%). No significant effect on clinical activity (not primary endpoint) Clinical program abandoned
RPC4046	Humanized mAb against IL-13	EoE	1 / 99 REF 31,32	Significant reduction of tissue eosinophilia and endoscopic activity. Strong trend towards reduction of dysphagia.
Dupilumab	Humanized mAb	EoE	1 / 47	Significant improvement of esophageal eosinophilia,

	against IL-4Ralpha (blocks IL-4 and IL-13)		REF 33	endoscopic activity, and symptoms
Lirentelimab	Humanized mAb against Siglec-8	EoG, EoD (or both)	1 / 65 REF 35,36	Significant change of tissue eosinophilia (-86% under lirentelimab vs. 9% under placebo) and symptoms (-44% reduction in symptom score under lirentilumab vs. -22% under placebo)
Vedolizumab	Humanized mAb against α4β7	EoE	2 case reports of Crohn's disease patients with concomitant EoE REF 37, 38 Case series of 5 patients with EG/EGE REF 39	Histologic and clinical improvement of EoE under vedolizumab 2 out of 5 responded clinically and histologically
Tofacitinib	Januskinase inhibitor (JAK1 and JAK3)	EoE	1 case report REF 40	Histologic and clinical improvement of EoE under tofacitinib
Tezepelumab	Humanized mAb against TSLP	No data available	REF 41,42	Tezepelumab reduces number of asthma exacerbations
Anti-CCR3	Humanized mAb against CCR3	No human data available	REF 43	Anti-CCR3 antibody inhibites eosinophil infiltration in Angiostrongylus contonensis-infected IRC mice
Anti-IL15	Humanized mAb against IL15	No human data available	REF 44	Anti-IL15 reduces eosinophil infiltration in an aspergillus fumigatus mouse model of EoE

Table 1: biologic therapies and small molecules for eosinophilic gastrointestinal diseases. Abbreviations: IL, interleukin; mAb, monoclonal antibody; EoE, eosinophilic esophagitis; EoG, eosinophilic gastritis; EoD, eosinophilic duodenitis; EGE, eosinophilic gastroenteritis; EoC, eosinophilic colitis; HES, hypereosinophilic syndrome; TSLP, thymic stromal lymphopoietin

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