Supplemental

Supplemental Table 1: Clinical Trials of Biologic Agents in Eosinophilic Esophagitis and Gastroenteritis

Target	Agent	Study Design	Patients	Age (years)	Duration	Primary Endpoint	Results	Secondary Endpoints
IgE	Omalizumab[66]	Randomized, double-blind, placebo-controlled trial	Eosinophilic esophagitis (n=30)	3 children, 27 adults	16 weeks	Esophageal pathology (peak esophageal eos/hpf)	No significant reduction in esophageal eosinophils compared to placebo	No improvement in dysphagia score (non-validated PRO)
	Omalizumab[108]	Open label	Eosinophilic esophagitis (n=24)	14-71	12 weeks	Esophageal pathology (% reduction in peak esophageal eos/hpf) and symptoms	33% achieved pathologic endpoint with omalizumab	47% of patients with symptom improvement
IL-5	Benralizumab[91]	Open label	Hypereosinophilic syndrome with gastrointestinal involvement (n=7)	18-65	12 weeks	Gastrointestinal pathology (peak eos/hpf)	Significant improvement in pathology	
	Mepolizumab[86]	Open label	Eosinophilic esophagitis (n=4)	18-57	12 weeks	Esophageal pathology (mean and maximum eos/hpf)	Significant improvement in pathology	Significant improvement in peripheral eosinophilia
	Mepolizumab[87]	Randomized, double-blind,	Eosinophilic esophagitis	adults	4-13 weeks	Esophageal pathology	No significant improvement	Significant reduction in

		placebo-controlled trial	(n=11)			(peak eos/hpf <5)	(no patients in either arm achieved primary endpoint)	mean eos/hpf
	Mepolizumab[88]	Randomized, double-blind, parallel group	Eosinophilic esophagitis (n=59)	2-17	12 weeks	Esophageal pathology (% of patients with peak eos/hpf <5)	8.8% achieved pathologic endpoint with mepolizumab	Significant reduction in peak and mean eos/hpf; No significant symptom improvement (non-validated PRO)
	Reslizumab[89]	Randomized, double-blind, placebo-controlled trial	Eosinophilic esophagitis (n=226)	5-18	16 weeks	Co-primary: Esophageal pathology (% change in peak eos/hpf); Physician's global assessment of symptoms	Significant improvement in pathology with reslizumab (59-67%) compared to placebo (24%); No significant improvement in symptoms over placebo	No significant change in Children's Health Questionnaire over placebo
TNF-alpha	Infliximab[109]	Open label	Eosinophilic esophagitis (n=3)	34-41	4 weeks	Esophageal pathology (eos/hpf)	No significant decrease in counts	Symptom improvement in 2/3 patients
IL-13	QAX576[104]	Randomized, double-blind, placebo-controlled trial	Eosinophilic esophagitis (n=25)	18-50	12 weeks	Esophageal pathology (% of patients with 75% reduction	QAX576 40% compared to placebo 13% (NSS)	Significant improvement in mean eosinophil count with

						in peak eos/hpf)		QAX576; No difference in Mayo Dysphagia Questionnaire
	RPC4046[20]	Randomized, double-blind, placebo-controlled trial	Eosinophilic esophagitis (n=99)	18-65	16 weeks	Esophageal pathology (Change from baseline in mean eos/hpf)	RPC4046 180 mg -94.76 ($p<0.0001$); RPC4046 360 mg -99.90 ($p<0.0001$); Placebo -4.42	Significant improvement in endoscopic features (EREFS); Trend for improvement in symptoms of dysphagia
IL-4Ralpha	Dupilumab[21]	Randomized, double-blind, placebo-controlled trial	Eosinophilic esophagitis (n=47)	18-65	12 weeks	Dysphagia (Straumann Dysphagia Index, non-validated PRO)	Significant improvement in symptoms compared to placebo	Significant improvement in % change in peak esophageal eos/hpf (dupilumab -92.9%; placebo +14.2%; $p<0.0001$) and endoscopic features (EREFS)