Title: Identifying predictive biomarkers and treatment response profiles in patients with eosinophilic esophagitis: a longitudinal study

Funding: Mixed funding from University of Pavia and Policlinico San Matteo

PIs: Prof. Antonio Di Sabatino, Prof. Marco Vincenzo Lenti

Research field: Immunology, Allergology, Anatomic Pathology, Gastroenterology, Precision Medicine

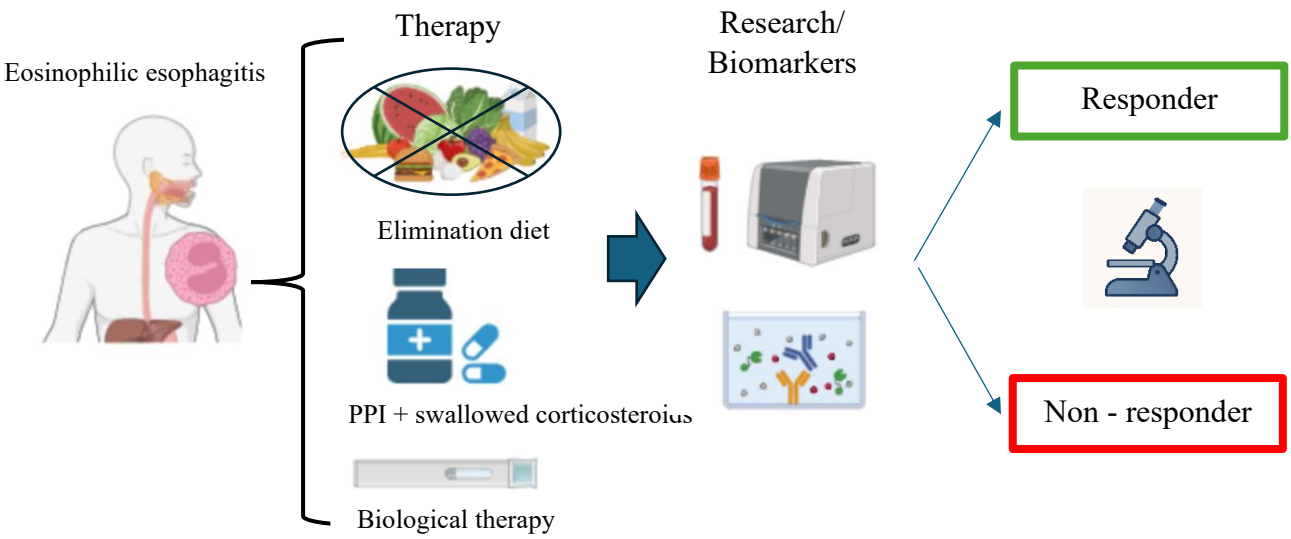
Abstract: Eosinophilic esophagitis (EoE) is a chronic immune-mediated inflammatory disorder of the esophagus, characterized by a significant eosinophil infiltration of the esophageal mucosa and symptoms such as dysphagia, difficulty swallowing, potentially leading to esophageal strictures. The diagnosis of EoE is based on the combination of clinical symptoms and histological analysis, with a diagnostic cut-off of at least 15 eosinophils per high-power field (HPF) in at least 6 esophageal biopsies from at least two segments. Despite the available therapeutic options, including elimination diets, proton pump inhibitors (PPIs), and swallowed corticosteroids, and a biological agent, targeting interleukin 4 (IL4) and interleukin 13 (IL3), the response to these treatments varies significantly among patients. Currently, no algorithms are available to guide the selection of the most appropriate therapy for individual patients. The response rate to first-line treatments is similar across different drugs, averaging around 60%, but it remains impossible to predict in advance which patients will respond to a given treatment.

This study, which includes both retrospective and prospective components, aims to identify clinical, biochemical, and histological biomarkers predictive of response to first-line therapy by analyzing parameters that reflect the underlying pathogenesis of EoE. Key pathogenic processes—such as type 2 inflammation, fibrosis, epithelial barrier dysfunction, and altered vascular permeability—will be considered. Additionally, an unsupervised analytical approach will be employed to uncover potential patient subgroups and novel predictive patterns.

Additionally, the study will focus on identifying patients who will experience side effects to these first-line therapies and those who early develop disease-related complications.

By utilizing clinical variables, allergology profiles of patients with EoE, histological analysis of esophageal samples and molecular biology analysis of samples, the study aims to define personalized predictive profiles that can improve the therapeutic management of EoE patients. The results may support the adoption of more targeted therapeutic approaches, improving treatment effectiveness and reducing treatment side effects.

Techniques: total and specific immunoglobulin E (IgE) and immunoglobulin G (IgG) with ricombinant allergens by ImmunoCAP® (Thermofischer, Sweden), skin prick test for aero- and food-allergens, histologic analysis, including hematoxylin and eosin, immunohistochemistry for plasmalemma vesicle-associated protein-1 (PV-1) and eosinophilic granular proteins, molecular biology techniques (quantitative PCR), enzyme-linked immunosorbent assay (ELISA).


Eosinophilic esophagitis
Therapy
Elimination diet
PPI + swallowed corticosteroids
Biological therapy
Research/
Biomarkers
Responder
Non - responder