GI Adverse Events During OIT

Richard L. Wasserman, MD, PhD
Dallas Food Allergy Center

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Leaders in Allergy & Asthma Care

Gastrointestinal Problems During OIT

- Oral itch
- Immediate, during dosing, vomiting with or without gagging
- Immediate, usually within 5-10 minutes of dosing, dyspepsia/abdominal pain with or without vomiting
- Abdominal pain within an hour of dosing
- Exercise induced abdominal pain or vomiting
- Delayed, >2 hours after dosing, vomiting with or without abdominal pain
- Diarrhea with or without abdominal pain

Immediate GI Problems

- Oral itch
  - Usually mild, may persist into maintenance
  - Wash the dose down with water or juice
  - Anti-histamine pretreatment
- Gagging
  - Aversion to taste or texture
- Immediate, during dosing, vomiting (a single episode) with or without gagging

Immediate Pain and Vomiting

- Immediate, usually within 5-10 minutes of dosing, dyspepsia/abdominal pain with or without vomiting
- IgE mediated reaction to the dose increase
- Return to the last tolerated dose
- Consider slower escalation

Abdominal Pain Within One Hour

- Local IgE mediated reaction within the small bowel
- IgE mediated reaction to the dose increase
- Return to the last tolerated dose
- Consider slower escalation

Exercise Induced Abdominal Pain

- Activity related abdominal pain within several hours of dosing
- A form of Food-dependent exercise-induced anaphylaxis (FDEIA)
- Isolated abdominal pain is uncommon
- Usually occurs within two hours of dosing but may be more delayed
- Adhere to post-dosing exercise limitation
- Consider slowing escalation

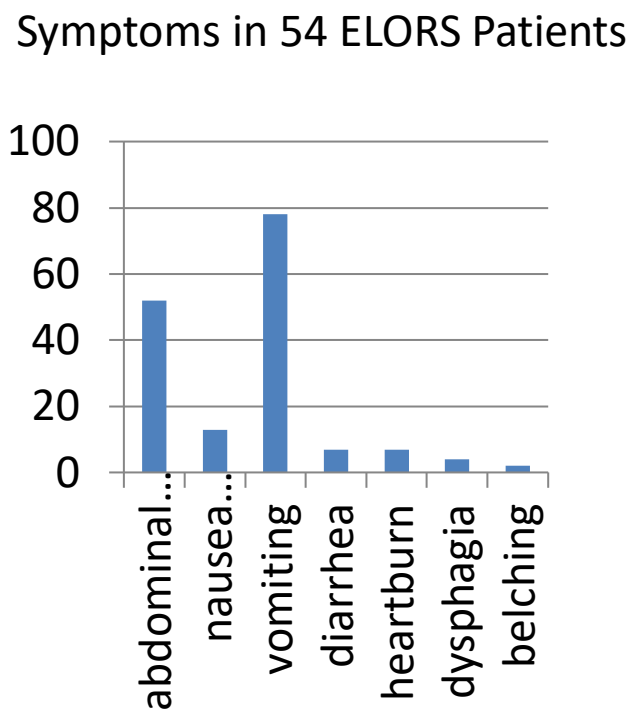
Eosinophilic Esophagitis-**L**ike **O**IT-**R**elated **S**yndrome – ELORS

- Vomiting or significant abdominal pain occurring more than two hours after dosing on more than one day

- Most demonstrate an increase in absolute eosinophil count over baseline

Eosinophilic Esophagitis Like, OIT-Related Syndrome (ELORS)

- Vomiting more than four hours after dosing is the predominant symptom
- 10.8% of treated patients
  - Peanut 13.7%
  - Milk 12.7%
  - Egg 0%
  - Cashew 6.3%
  - Multi-food 8.1%
- 32/54 patients treated
  - Dose reduction alone
  - Some treated with a PPI
  - 53% reached maintenance
- High pre-treatment IgE is the major risk factor



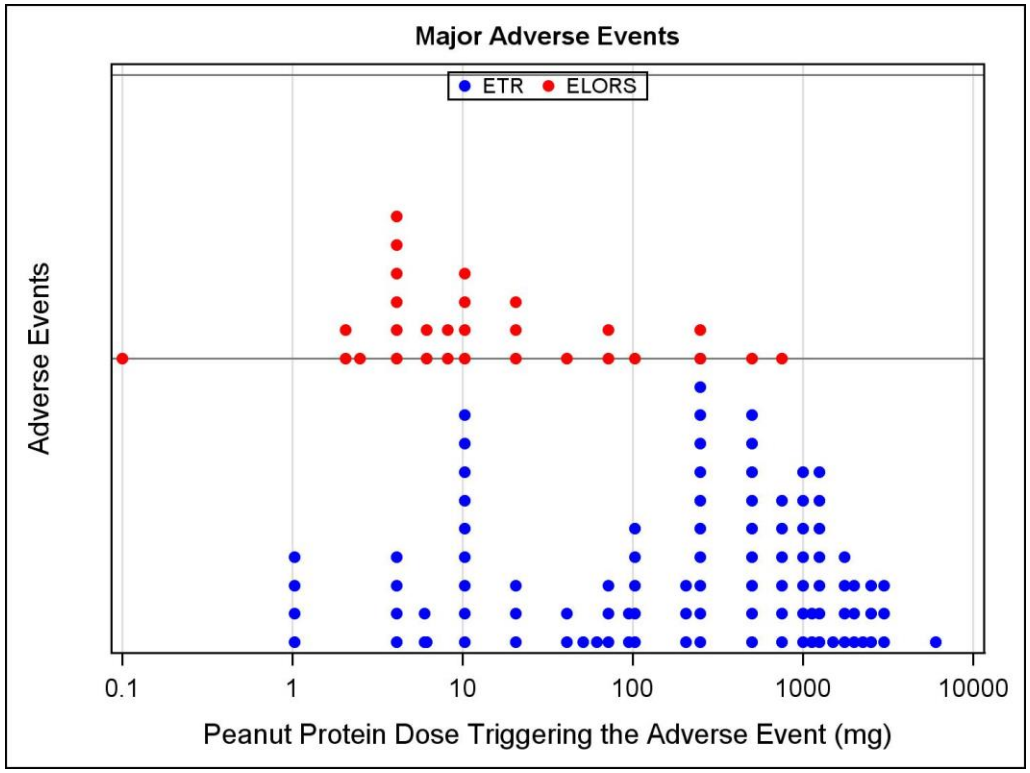
ELORS Incidence By Food

Food	Total	ELORS	ELORS (%)
Egg	81	9	11
Milk	121	15	12
Peanut	446	60	13
Tree nut (single)	56	3	5

ELORS Decreases Success

Food	Treated	Reached Maintenance (%)	Reached Maintenance With ELORS (%)
Egg	81	81	22
Milk	121	76	20
Peanut	446	85	53
Tree nut (single)	56	89	67

Major Adverse Events During Peanut OIT Dose Escalation – First 270 Patients



Eosinophilic Esophagitis-Like, OIT-Related Syndrome (ELORS)

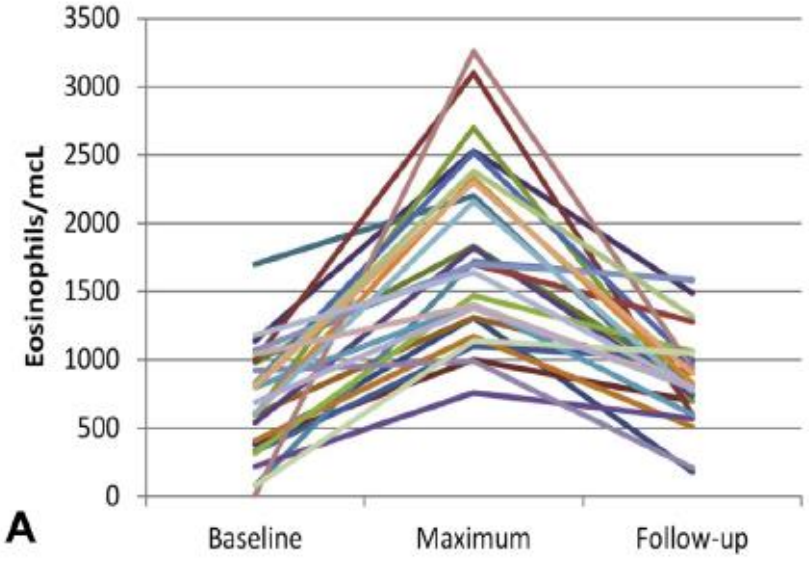
- Risk factors
  - Young age
  - High food specific IgE
  - High baseline absolute eosinophil count
- Treatment
  - Dose reduction
  - Proton pump inhibitor
  - Oral glucocorticoid
- Delays but doesn't preclude successful OIT in all patients
- Outcome - 32/54 (59%) of patients reached maintenance

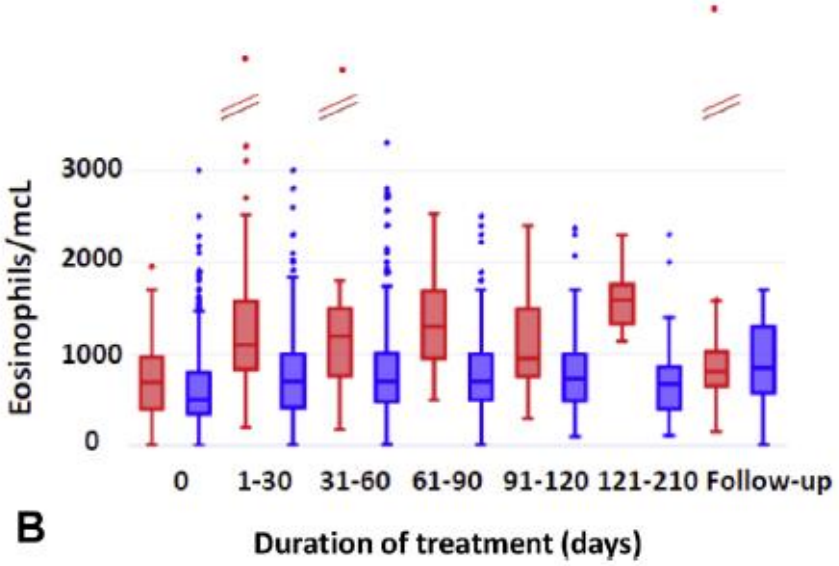
Oral Immunotherapy-Induced Gastrointestinal Symptoms and Eosinophilic Responses (OITIGER)

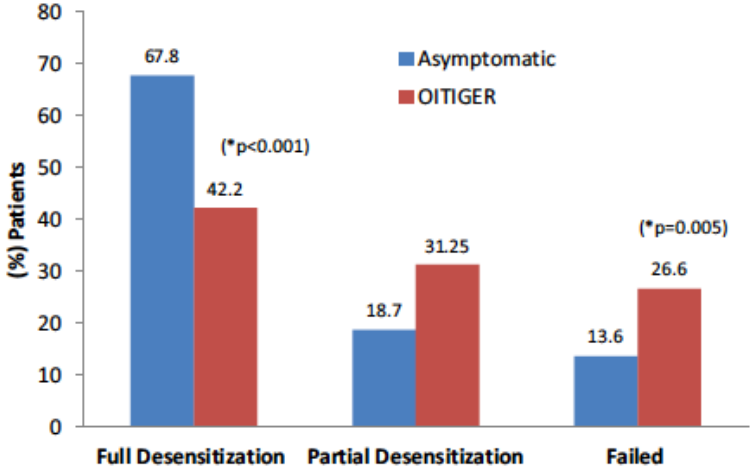
- Abdominal pain or vomiting unrelated to dosing on three separate days
- 8.2% of 794 patients – 55/614 milk – 9/130 peanut – 1/41 egg – 0/9 sesame
- Treated by reducing the dose a median of 50%
  - 69% treated by dose reduction
  - 28% temporarily suspended treatment
- Monitor absolute eosinophil count

Goldberg MR, et at. 2020. JACI:IP 8:125-131

OITIGER Outcomes







Can OITIGER Data Inform OIT Practice in North America?

- OIT protocol involves multiple dose escalations over several days every four weeks
- Risk Factors
  - Higher starting dose
  - More rapid escalation
- Difficult to extrapolate to protocols using weekly or biweekly single dose escalations

Diarrhea

- Diarrhea with or without lower abdominal pain is rare in OIT
- May be IgE mediated or eosinophilic
- Consider dose reduction strategy for management

Summary

- Gastrointestinal adverse events occur commonly during OIT
- Gastrointestinal adverse events are the most common cause of delay or discontinuation of OIT
- Gastrointestinal adverse events are much more frequent during escalation than maintenance
- Most patients can be managed with dose reduction, slower escalation, and increased dosing interval