CLINICALLY MEANINGFUL ENDPOINTS IN EoE

North American Society of Pediatric Gastroenterology, Hepatology and Nutrition
Washington D.C.
October 10, 2015
Glenn T. Furuta
University of Colorado School of Medicine
Digestive Health Institute
Gastrointestinal Eosinophilic Diseases Program
Children’s Hospital Colorado
Aurora, CO

Eosinophilic Esophagitis Symptom Activity Index (EEsAI)

- Alain Schoepfer
- Alex Straumann
- Katia Safronueva
- Institute of Social and Preventive Medicine
  University of Bern
  Bern, Switzerland

Goals

1. Understand Challenges To Develop Meaningful Endpoints
2. Recognize Current Endpoints For EoE Clinical Trials And The Rationale For their use
If you cannot measure it, you cannot change it
Robert Sandler
Workshop summary

Workshop report from the National Institutes of Health Taskforce on the Research Needs of Eosinophil-Associated Diseases (TREAD)

Susan E. Bachner, MD,* Wendi Busch, MD,† William W. Bower, MD,* Joseph Satterfield, MD,* Glisson T. Farak, MD,* Gerald J. Gilot, MD,* Amy H. Allen, MD,* James J. Lee, PhD,* Anthony M. Lebowitz, MD,* Workshop Chairperson, PhD,* Normann Moghadam, PhD,‡ Jeremy S. Cohen, MD,‡ Lawrence B. ElRAFT, MD,‡ Miroslawa Szczeklik, MD,‡ Michael R. Stein, MD,§ and Anthony G. Henderson, MD,§ reviewing Editors: Arif, DeSio, York, Wu, London, Weigl, and Lyon, Basel.

Table II

<table>
<thead>
<tr>
<th>Disease entity</th>
<th>Issues to be addressed</th>
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1. Identify best method for diagnosis,

2. Define optimal therapy and rationale for disease management.
3. Understand the role of inflammation in eosinophil diseases.
4. Evaluate the role of cell signaling in eosinophil diseases.
5. Understand the mechanism of cell signaling in eosinophil diseases.
6. Understand the role of cell signaling in eosinophil diseases.
7. Understand the role of cell signaling in eosinophil diseases.
8. Understand the role of cell signaling in eosinophil diseases.
9. Understand the role of cell signaling in eosinophil diseases.

Editorial

Working with the US Food and Drug Administration: Progress and timelines in understanding and treating patients with eosinophilic esophagitis

Michael D. Rothberg, MD, PhD,* Thomas A. Thorpe, MD,† Mark A. McGovern, MD,‡ Marsha L. Rose, MD,§ and Paul L. Stoloff, MD,* "Alessio Stolfo, MD,§ and Vivian A. W. Weigl, MD,§ and Anthony G. Henderson, MD,§ reviewing Editors: Arif, DeSio, York, Wu, London, Weigl, and Lyon, Basel.

### TABLE I. Progress in EoE

<table>
<thead>
<tr>
<th>Topic</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
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<tbody>
<tr>
<td>Molecular understanding</td>
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<tr>
<td>Genetics</td>
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<tr>
<td>Preclinical modeling</td>
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<td>Controlled clinical trials</td>
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<tr>
<td>Assessment tools</td>
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<td>Histology</td>
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<td>Endoscopic assessment</td>
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<td>Clinical outcome tools</td>
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<td>Molecular markers</td>
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<tr>
<td>FDA-approved drugs</td>
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<tr>
<td>FDA-approved dietary treatment</td>
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</tbody>
</table>
Feel
Form
Function

EoE-PRO or biologic markers or both?

Migraine
Lower back pain
EoE-dysphagia

Asthma
EoE
Crohn's disease
Ulcerative colitis

Arterial hypertension
Hyperlipidemia
EoE-eosinophil

Schoepfer A, Safroneeva E. Dig Dis 2014

How to measure disease activity in eosinophilic esophagitis

A. Schoepfer,1 E. Safroneeva,2 A. Strasser3

1Division of Gastroenterology and Hepatology, Centre Hospitalier Universitaire Vaudois (University Hospital Lausanne), Lausanne. 2Division of Social and Preventive Medicine, University of Bern, Bern, and 3Praxis Bümmlerhof, Sıvrio End. Clínic, Olten, Switzerland
Symptoms in Children

- Developed using physitian input
- Evaluated in an RCT in 31 pediatric patients aged 2-18 years
- Weight-based scoring algorithm
- Validated in children

Pediatric reflux symptom index (PIHSI) (1.3)
- Developed using physician input
- Evaluated in 31 pediatric patients 2-18 years of age
- Validated in children

Pediatric reflux symptom index (PRASI) (2.0)
- Developed using physician input
- Evaluated in 31 pediatric patients 2-18 years of age
- Validated in children

Pediatric reflux symptom index (PRASI) (1.5)
- Developed using physician input
- Evaluated in 31 pediatric patients 2-18 years of age
- Validated in children

Frequency

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Never (less than once a week)</th>
<th>Almost never (1 or more times a week)</th>
<th>Sometimes (1 time a day)</th>
<th>Often (2 or more times a day)</th>
<th>Almost always (over 6 times a day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How often do you have chest pain, ache, or hurt?</td>
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<tr>
<td>2. How bad is the chest pain, ache, or hurt?</td>
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</table>

Severity

<table>
<thead>
<tr>
<th>Severity</th>
<th>Not bad at all</th>
<th>A little bad</th>
<th>Kind of bad</th>
<th>Bad</th>
<th>Very bad</th>
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The adult eosinophilic oesophagitis quality of life questionnaire: a new measure of health-related quality of life

- Valid and reliable
- 37 items
- 5 factors
  - eating
  - social
  - emotional
  - social anxiety
  - choking anxiety
EoE QoL

1. I find EoE to be a stressful disease.
2. I have to be cautious about eating because I have EoE.

PedsQL Eosinophilic Esophagitis Module: Feasibility, Reliability, and Validity

Worry
- I worry about having EoE
- I worry about getting sick in front of other people
- I worry about what other people think about me because of EoE
- I worry about going to the doctor
- I worry about getting an endoscopy (scope, EGD)
- I worry about getting allergy testing
Endoscopic grading

Mild: White lesions occupying < 10% of the esophageal surface area

Severe: White lesions involving > 10% of surface area of esophagus

Hirano I et al GUT 2013
EoE Histology

Peak eosinophil number
Basal layer hyperplasia, eosinophilic abscesses, eosinophil degranulation

EoE-PRO or biologic markers or both?

PRO
Migraine
Lower back pain
EoE-dysphagia

Biologic feature
Asthma
EoE
Crohn's disease
Ulcerative colitis
Arterial hypertension
Hyperlipidemia
EoE-eosinophil

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