

**Con** – The severe asthma patient with eosinophilic phenotype should always be treated with anti-IL-5 therapies

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# **Disclosures:**

**AstraZeneca – consultant**

**Merck – consultant**

**Global Life Science - consultant**

# Learning objectives

Upon completion of this learning activity, participants should be able to:

- To recognize the **appropriate** patient to treat with type 2 (eosinophilic) biologics

# How is the eosinophilic phenotype diagnosed?

- **Blood**
- **Sputum**
- **BAL**
- **Biopsy**

# **Refractory Asthma: Importance of bronchoscopy to identify phenotypes and direct therapy**

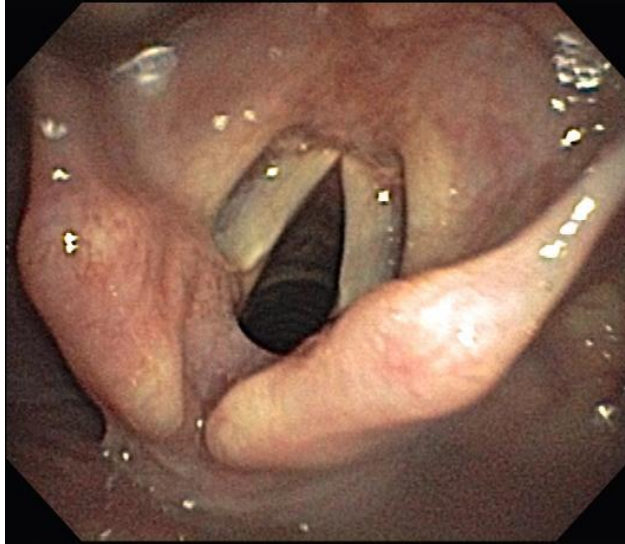
- **$\geq 18$  y/o, n = 58**
- **12% improvement post BD or  
PC20  $\leq$  6 mg/ml**
- **Met ATS criteria for refractory asthma**
- **Exclusion**
  - **Smoking history  $>$  5 pack years**
  - **Evidence of VCD by history or flow-volume loops  
compatible with VCD**

# Refractory Asthma: Bronchoscopy/phenotypes and direct therapy

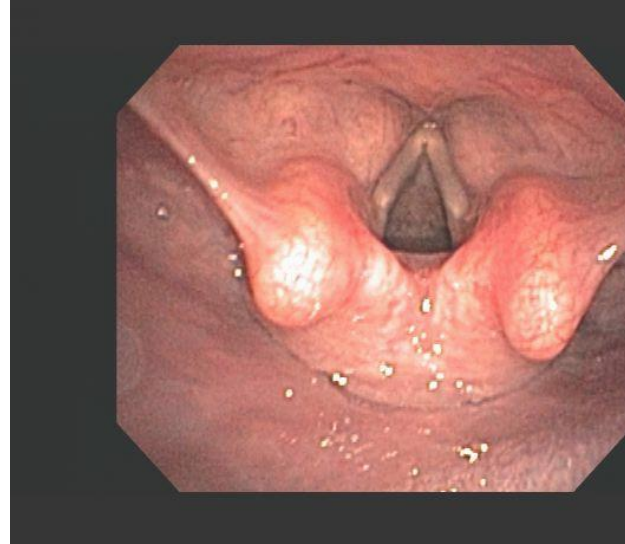
<b>Sample size</b>	<b>58</b>	<b>FEV<sub>1</sub>%</b>	<b>60.7 ± 18.3</b>
<b>M/F</b>	<b>22/36</b>	<b>FEV<sub>1</sub>/FVC</b>	<b>65.7 ± 13.9</b>
<b>Age</b>	<b>55 ± 13</b>	<b>PC20</b>	<b>1.6 ± 1.3</b>
<b>BMI (kg/m<sup>2</sup>)</b>	<b>31 ± 7</b>	<b>Sinus CT +</b>	<b>n = 41</b>
<b>IgE</b>	<b>282 ± 573</b>	<b>ACT</b>	<b>11.5 ± 4.1</b>
<b>Smoking Hx</b>	<b>n = 1</b>		

# Different Degrees of Upper Airway Pathology

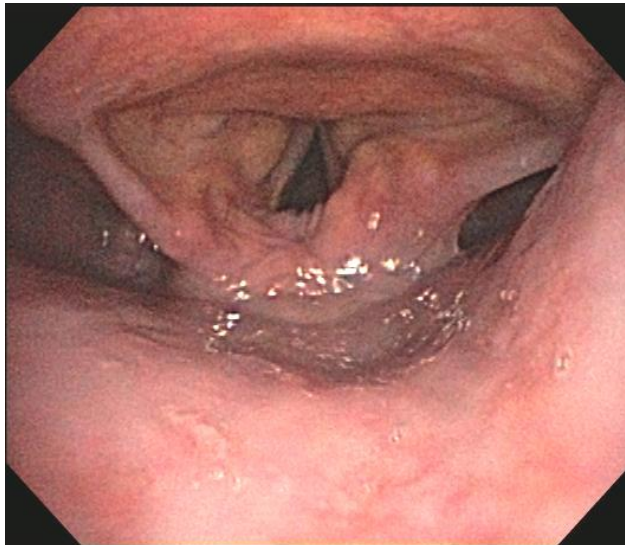
**Normal**  
**SGI = 2**



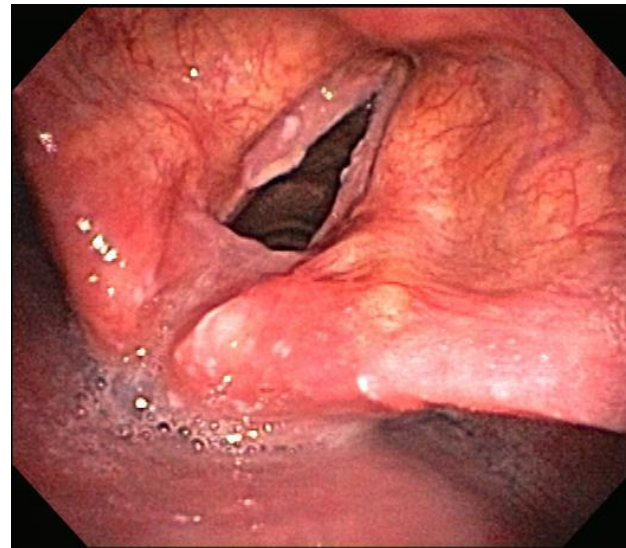
**Mild**  
**SGI = 6**



**Moderate**  
**SGI = 16**



**Severe**  
**SGI = 22**

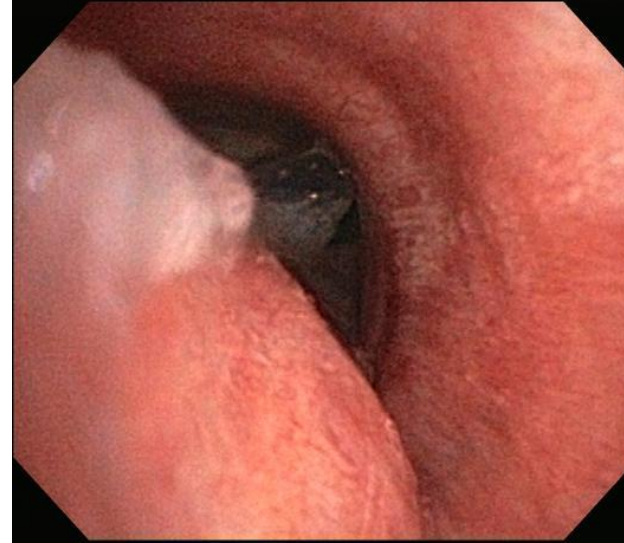


# Lower airway: Secretions

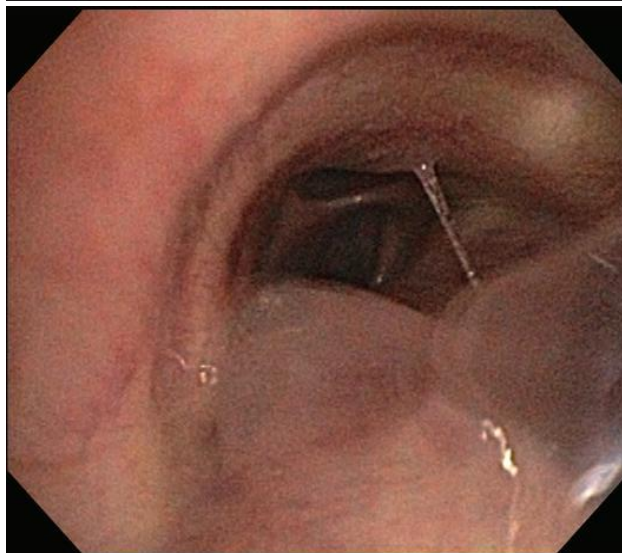
**0 = No  
Secretions**



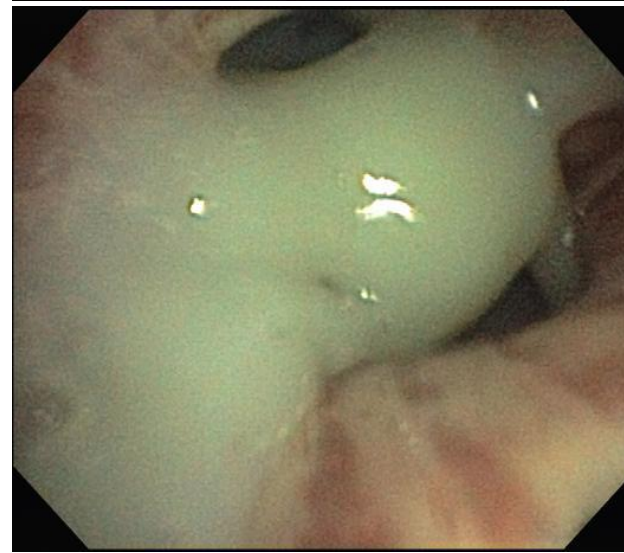
**1 = Mild**



**2 = Moderate**



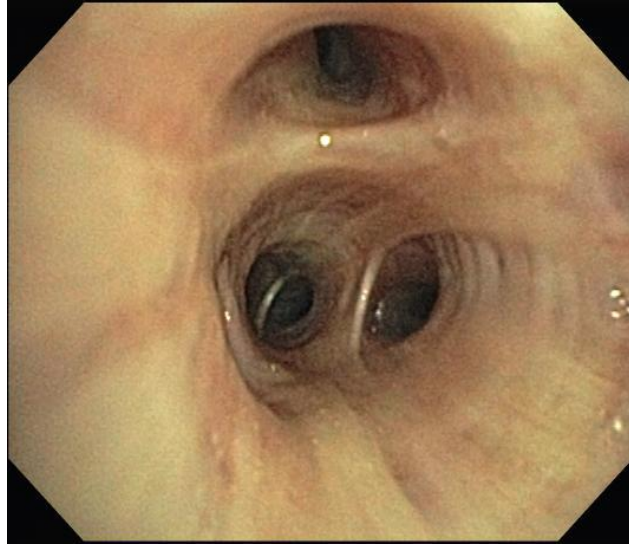
**3 = Severe**



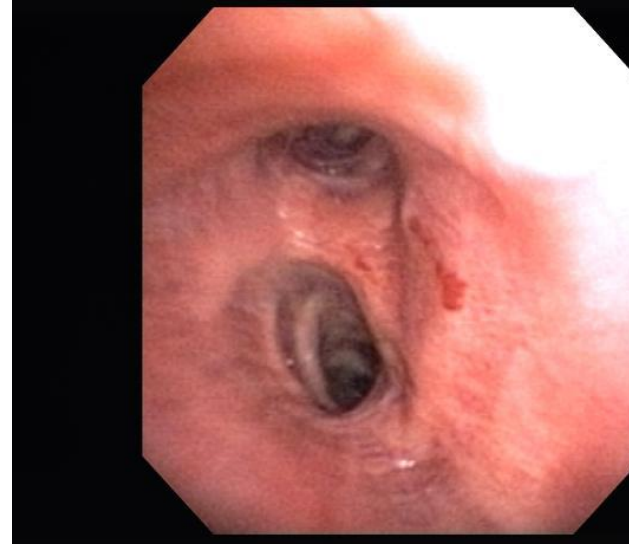


# Lower airway: Friability

**0 = No  
Friability**



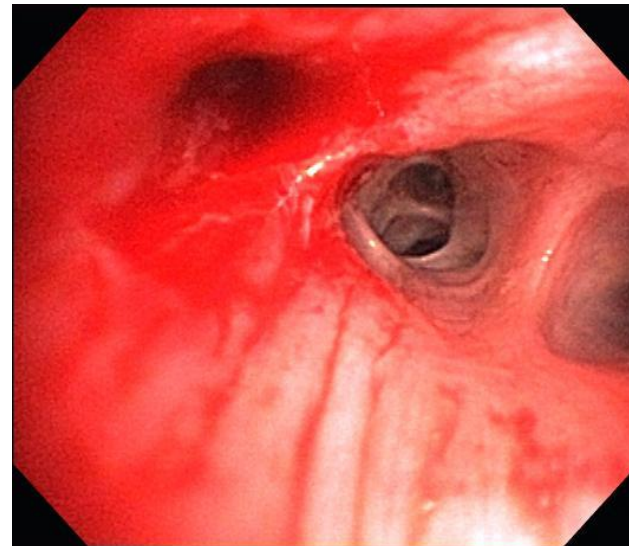
**1 = Mild**



**2 = Moderate**



**3 = Severe**

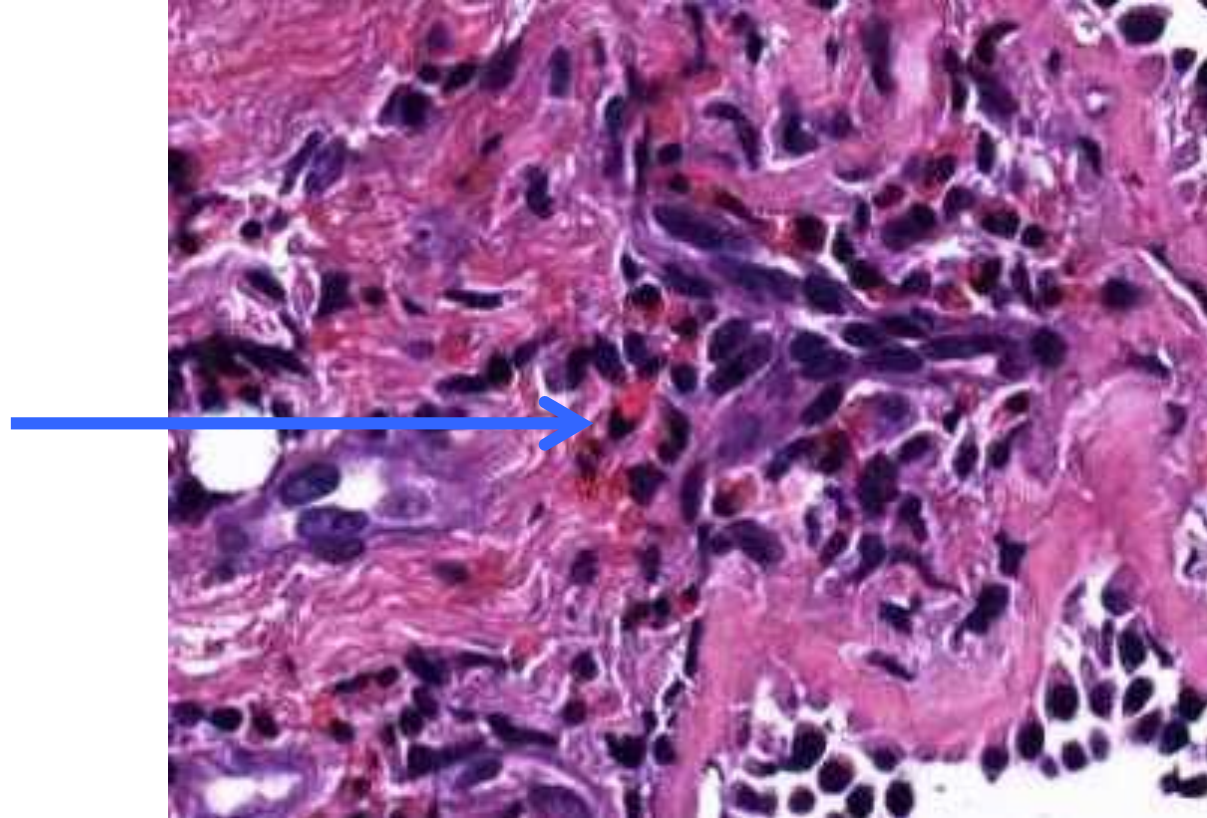


# Five phenotypes defined

- **Tissue eosinophilia**
- **Subacute bacterial infection (SBI)**
- **GER**
- **Combination**
- **Nonspecific**
- **No statistical differences between each group based on IgE, blood eosinophils, or skin testing**

# Tissue eosinophilia: >10 eos/hpf

**Eosinophils**

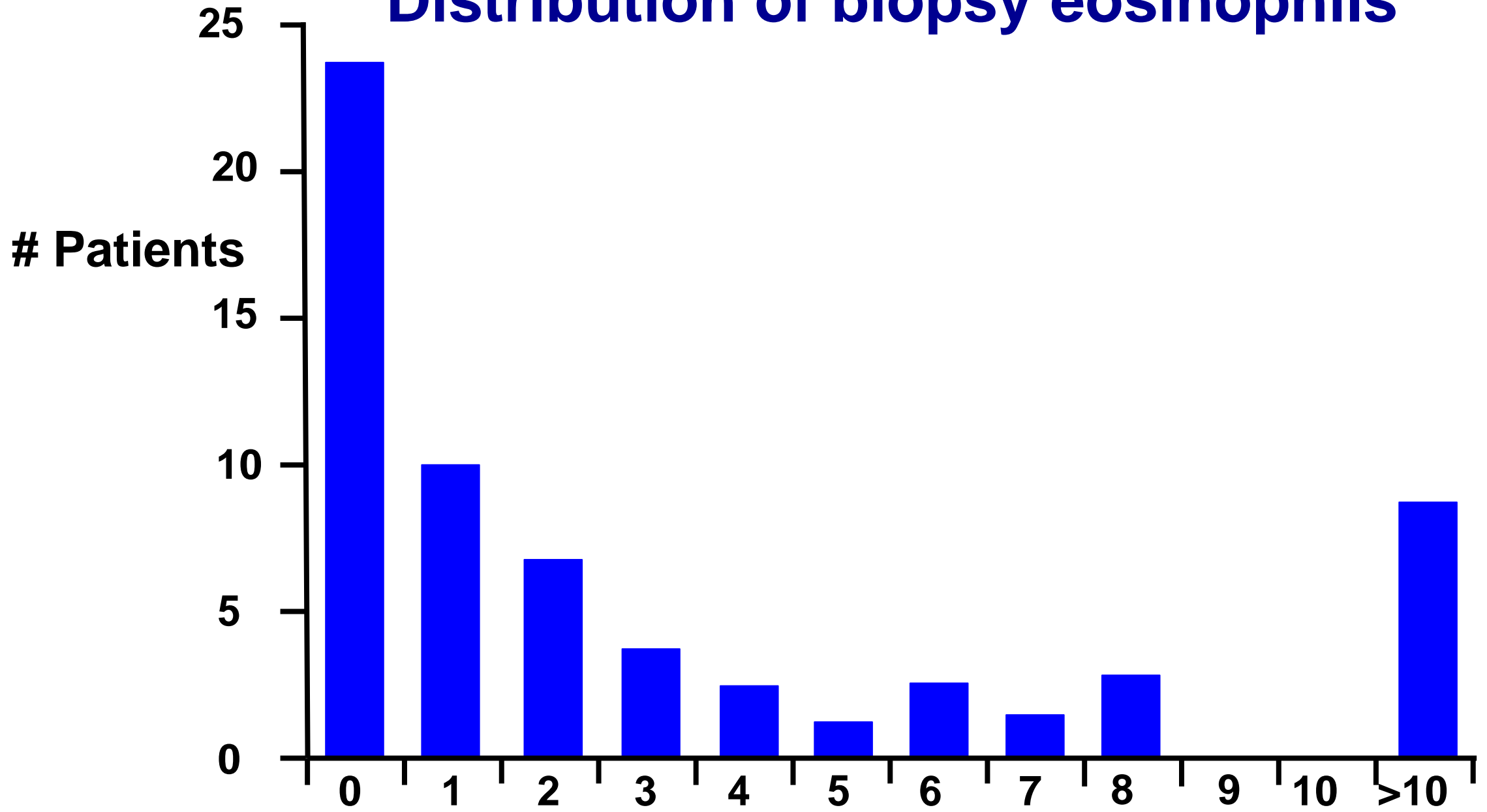


**Sole criterion n=4**

**Combination phenotype n=4**

**SBI n= 2 (not Tx)**

# Distribution of biopsy eosinophils



# Tissue vs. BAL eosinophils n = 58

- **$r = 0.44$ ,  $p = 0.001$**
- **However**
  - **n = 13, eos on bx and 0 in BAL**
  - **n = 7 on BAL and 0 on Bx**
  - **n = 12 with 0 on either**

# History

**51 y/o F with a 6 year history of adult onset asthma. High dose ICS/LABA, oral steroid bursts 5 time a year, one hospitalization.**

**Blood eosinophil total = 392. Started on anti-IL-5. No improvement in sx or FEV1, but **blood eos = 0.****

**Referred – bronch bx eos = 32 per hpf. Also, SBI. Switched to a receptor blocker anti-IL-5. Treated the SBI.**

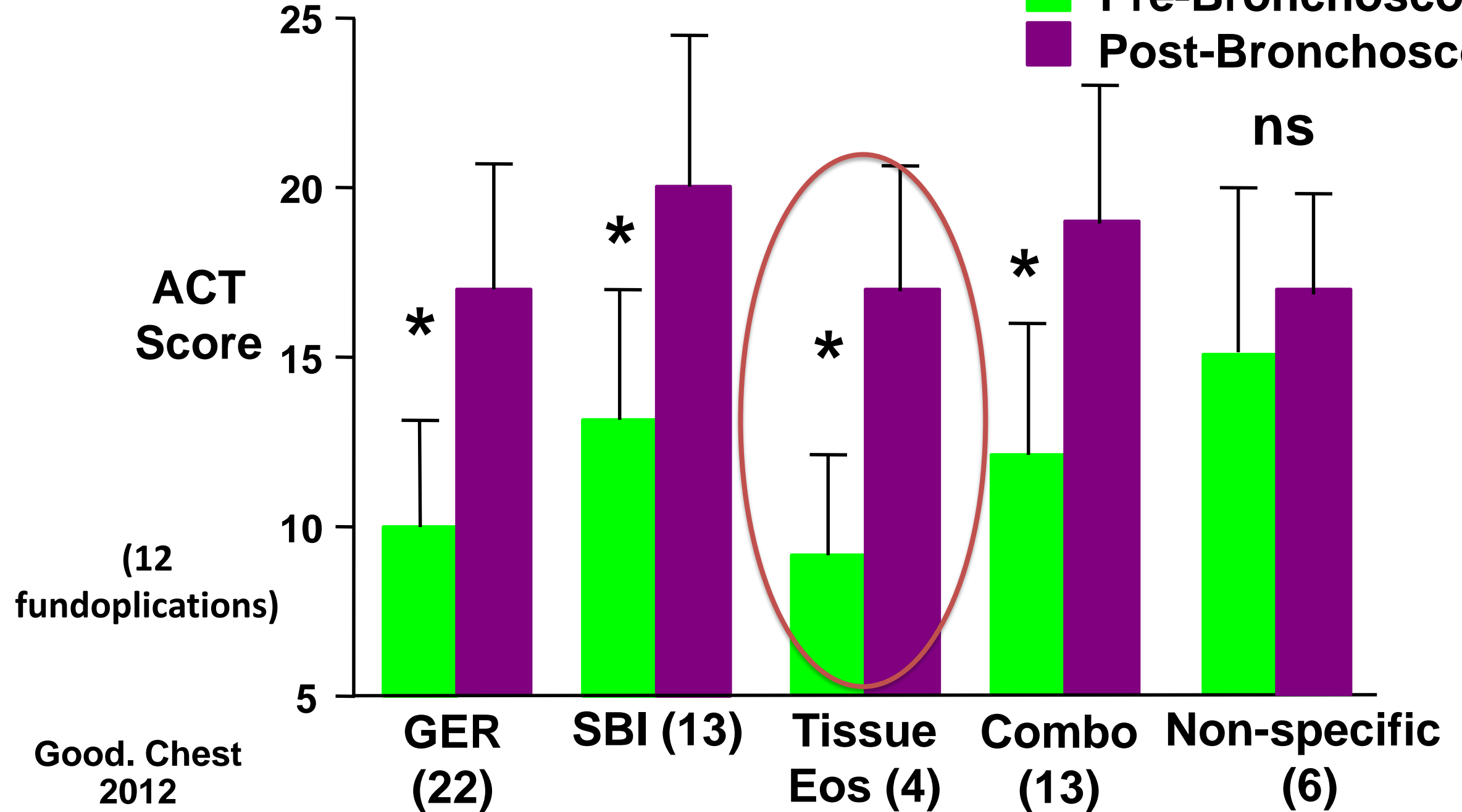
**Dramatic improvement.**

# Treatment

**Personalized and directed**

# Asthma Control Test n = 58

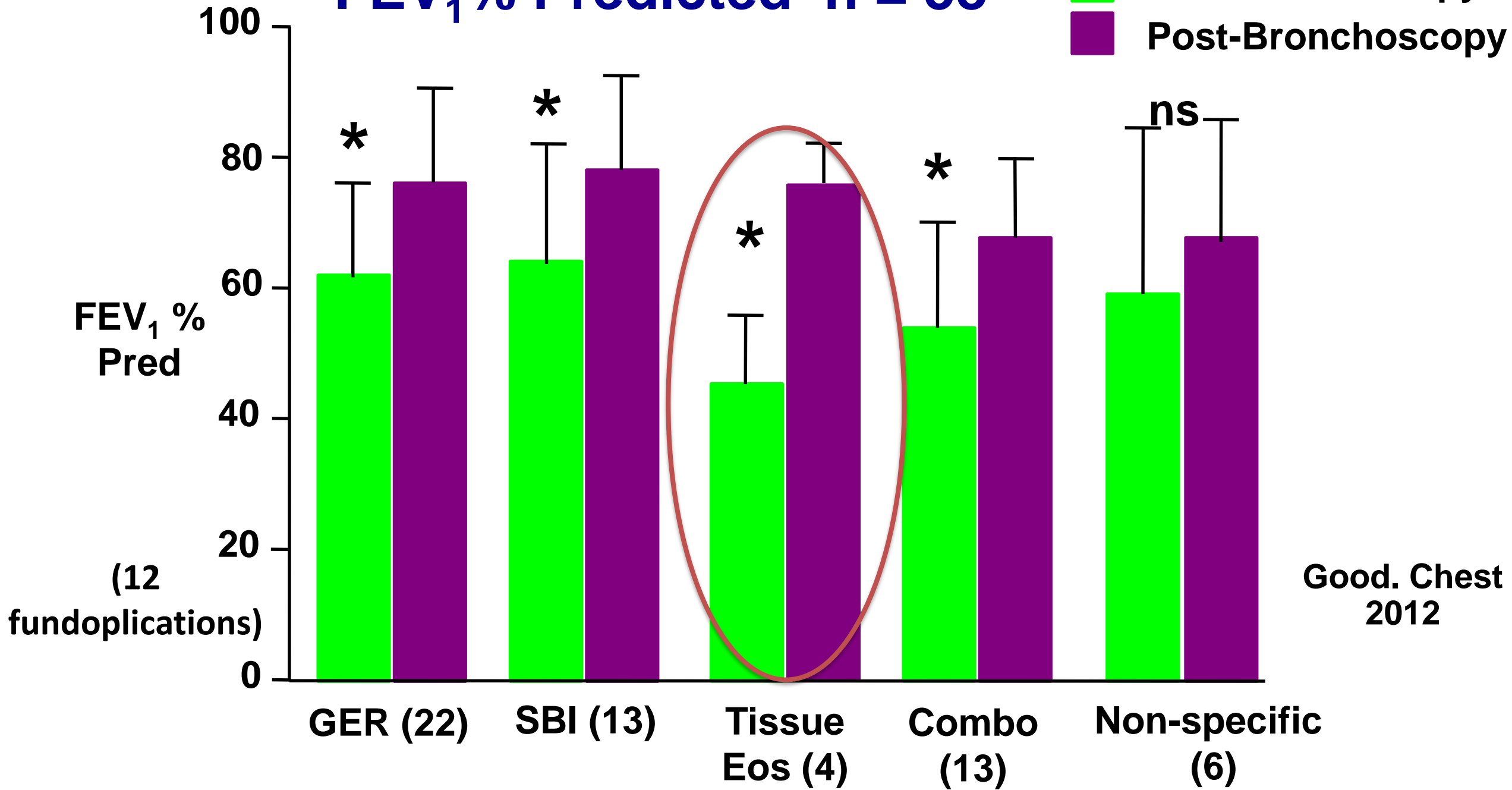
Pre-Bronchoscopy  
Post-Bronchoscopy





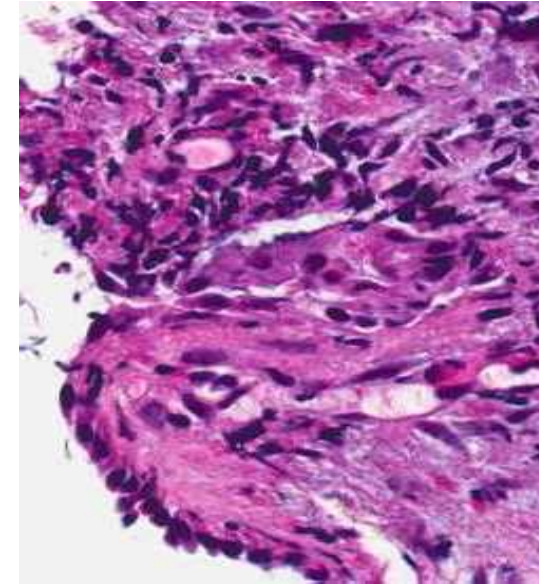
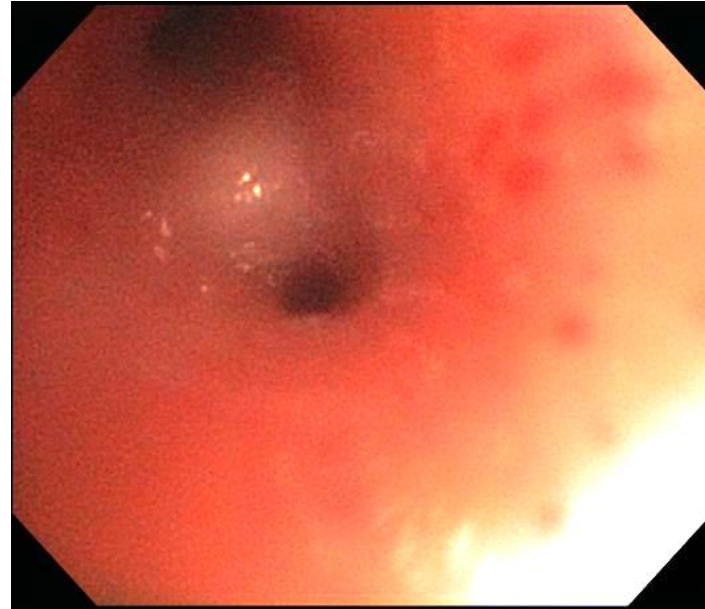
# FEV<sub>1</sub>% Predicted n = 58

Pre-Bronchoscopy  
Post-Bronchoscopy

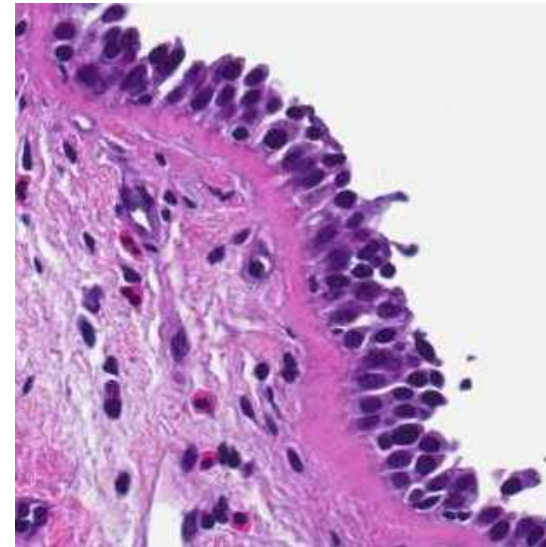
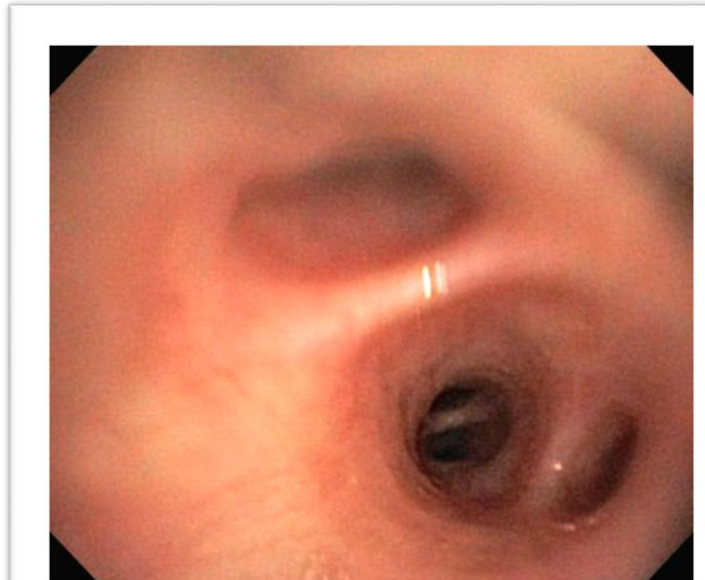


# Tissue eosinophilia phenotype: Response to omalizumab Rx

RLL Pre Rx

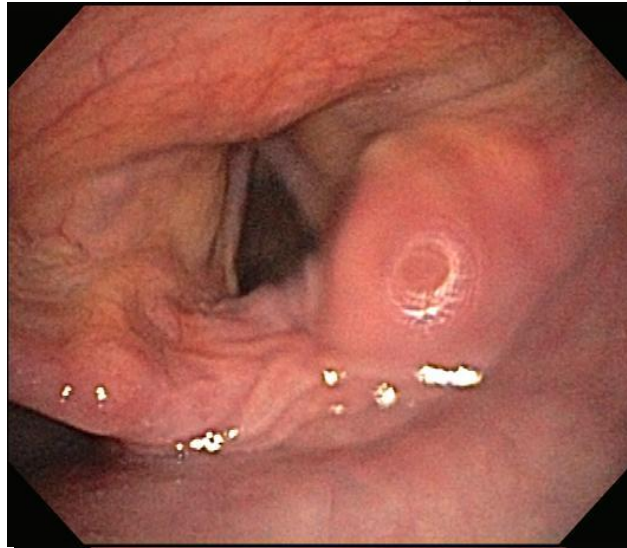


RLL post Rx

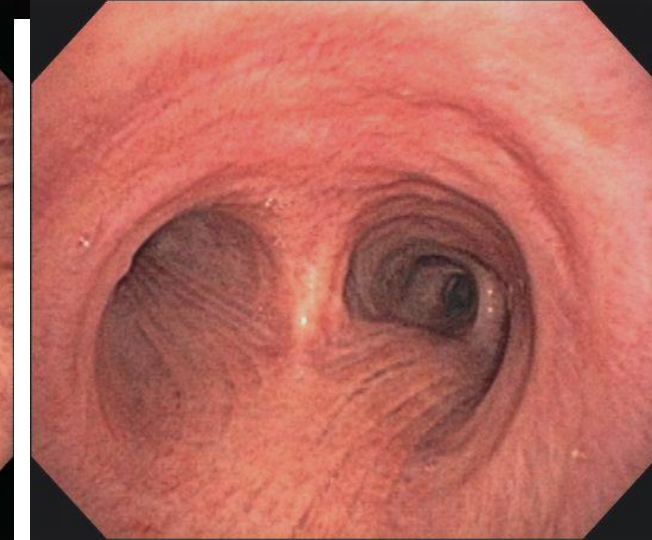
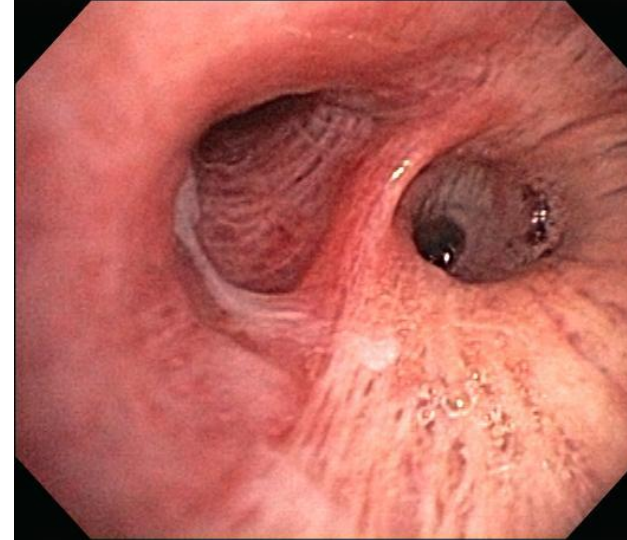


# 12 months of aggressive anti-reflux therapy improves SGI

**Pre Rx**



**Post Rx**



**Con - Cost of anti-IL-5 therapy**

**Approximately \$35,000 per year**

# Severe/Refractory Asthma

- Need to document the **exact** phenotype(s) and method of analysis so as to treat with personalized, directed therapy
- This will improve
  - Asthma control
  - Lung function
- Further investigation is needed
  - Next Gen Seq for microbes, Type 2 and non-type 2 asthma (can be in combination)
    - Non-invasive methods if possible
  - The exact tissue eosinophil number that is important for treatment