Which Patients for Anti-IgE?

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Disclosure Slide

• **Employment**
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  Nothing to Disclose
Introduction

• In asthma, omalizumab treatment has been shown to
  – Reduce symptoms
  – Reduce the need for ongoing controller medications
  – Prevent exacerbations

• Omalizumab is effective in children and adults
  – Primary indication is moderate-to-severe asthma

• Patient selection for omalizumab remains a partially answered question
Goals

- Review omalizumab’s use in clinical trials
  - Severe asthma
  - Children living in US inner cities
- Review features of omalizumab
  - Prevention of exacerbations
  - Patient selection
- Conclusions
What are the current indications for omalizumab in asthma?

- EPR-3 Steps 5 and 6
- Allergic Asthma
- IgE and weight levels compatible with dosing schedules (150 to 375 mg/d every 2 to 4 weeks)
What has been learned from clinical trials with omalizumab?

- To evaluate the efficacy and safety of omalizumab in patients with inadequately controlled severe asthma on high dose inhaled corticosteroids and LABA
Study Design

Randomize (N=850)

Screen symptoms while on stable high-dose ICS + LABA

Omalizumab + high-dose ICS/LABA ± additional controllers

Placebo + high-dose ICS/LABA ± additional controllers

End of Treatment

RCT of omalizumab added to stable, high-dose ICS/LABA + other controllers for 48 weeks.
Key Inclusion Criteria

- 12 to 75 years
- High-dose ICS + LABA (at least fluticasone/salmeterol 500/50 μg bid or equivalent) ± other controllers
- FEV\textsubscript{1} \geq 40\% and <80\% predicted at screening
- Persistent symptoms
  - Need for rescue medication \geq 2 d/wk and \geq 1 nighttime awakening per week
- At least 1 asthma exacerbation 12 months prior to screening requiring systemic corticosteroids while receiving high-dose ICS + LABA

FEV\textsubscript{1} = forced expiratory volume in one second.
## Baseline Asthma Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=421)</th>
<th>Omalizumab (n=427)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of asthma, y, mean (SD)</strong></td>
<td>24.7 (15.8)</td>
<td>22.8 (15.4)</td>
</tr>
<tr>
<td><strong>FEV\textsubscript{1} % predicted, mean (SD)</strong></td>
<td>64.4 (13.9)</td>
<td>65.4 (15.2)</td>
</tr>
<tr>
<td><strong>FEV\textsubscript{1}/FVC, mean (SD)</strong></td>
<td>0.72 (0.1)</td>
<td>0.72 (0.2)</td>
</tr>
<tr>
<td><strong>Baseline AQLQ (S) (1-7 scale), mean (SD)</strong></td>
<td>3.9 (1.1)</td>
<td>4.0 (1.1)</td>
</tr>
<tr>
<td><strong>Baseline rescue medication use per day, mean (SD)</strong></td>
<td>4.1 (3.2)</td>
<td>4.0 (2.9)</td>
</tr>
<tr>
<td><strong>Baseline symptom scores (0-9 scale), mean (SD)</strong></td>
<td>3.9 (1.8)</td>
<td>3.9 (1.8)</td>
</tr>
<tr>
<td><em><em>Number of exacerbations in the past year,</em> mean (SD)</em>*</td>
<td>1.9 (1.5)</td>
<td>2.0 (2.2)</td>
</tr>
<tr>
<td><strong>Hospitalized for asthma in previous year, n (%)</strong></td>
<td>41 (10)</td>
<td>53 (12)</td>
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</table>

*Includes asthma exacerbation requiring treatment with systemic steroid in the year prior to screening and during the run-in period.
Primary Endpoint: Rate of Asthma Exacerbations Over 48 Weeks

**0.88**  
Placebo

**0.66**  
Omalizumab

\[ \Delta -25\% \]

\[ P=0.0058^* \]

\[ n=421 \]

\[ n=427 \]

*Poisson regression including terms for treatment, concomitant asthma medication strata, dosing regimen, and number of exacerbations in the prior year.*
Conclusions

• Omalizumab was effective in severe asthma as indicated by a reduction in exacerbations

• No safety concerns

• No indications as to which were “best patients” for omalizumab
What other observations provide insight on omalizumab’s use in allergic asthma?
Because allergen sensitization and exposure are an important determinant of asthma severity and response to therapy, we hypothesized that the addition of omalizumab (anti-IgE) to guidelines-based treatment would improve disease control in allergic inner-city children with moderate-to-severe asthma and persistent symptoms.
Enrollment characteristics

- 6 to 20 years of age with a diagnosis of persistent asthma
- Allergy to a perennial allergen
- Inner-city resident
- At recruitment, participants had uncontrolled asthma
- Weight and total serum IgE levels were suitable for omalizumab dosing
Study design

- Enrollment (4 weeks)
  - Asthma control assessed
  - Using a guidelines-based algorithm, treatment was begun or adjusted to achieve asthma control
- Randomization and treatment (60 weeks)
  - Following an adjustment of asthma medications during enrollment, participants were randomized to receive omalizumab or placebo every 2–4 weeks for 60 weeks
<table>
<thead>
<tr>
<th>Asthma control of participants at enrollment (n=419)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Days of asthma symptoms the previous 2 weeks</td>
</tr>
<tr>
<td>• Childhood ACT® score in the last month (4–11 years)</td>
</tr>
<tr>
<td>• ACT® score (12 years and over)</td>
</tr>
<tr>
<td>• FEV₁ (% predicted value)</td>
</tr>
<tr>
<td>• FEV₁/FVC</td>
</tr>
<tr>
<td>• ≥1 Hospitalization/past year</td>
</tr>
<tr>
<td>• ≥1 Unscheduled visit/ past year</td>
</tr>
<tr>
<td>• Male subjects</td>
</tr>
</tbody>
</table>
What were the effects of omalizumab on the number of days with asthma symptoms in the last 2 weeks?

Difference of -0.48 day (p<0.001) (n=211)
What were the effects of omalizumab on exacerbations?

Difference of -16.5% with an exacerbation (p<0.001) (n=211) (n=208)
What were the effects of omalizumab on the daily dose of inhaled corticosteroids (budesonide equivalents [µg/day])?
Asthma is a “seasonal” disease

- Symptoms are less during the summer
- Symptoms, need for medications and frequency of exacerbations increase in the fall and spring
What was the effect of omalizumab on the seasonal pattern of asthma and its control?
What are the effects of omalizumab on days of asthma symptoms in the past 2 weeks over the year?
What are the effect of omalizumab on the daily dose of inhaled corticosteroids (budesonide equivalents [µg/day])?
What effect did omalizumab have on the September epidemic of asthma or seasonal asthma?
What are the effects of omalizumab on the percentage of participants experiencing exacerbations over the year?
The importance of allergic sensitization and exposure to “September epidemics”

Cockroach → Mast Cell → Exacerbation

Virus → Omalizumab
Are there predictors of response to omalizumab?

- IgE
- Allergen sensitization
- Allergen exposure
- Baseline lung function
- Sex
- Exacerbations
The Effect of Cockroach Sensitization and Exposure on Omalizumab Efficacy

- Exacerbations: No = 1.6, Yes = 3.6, P = 0.04
- Symptoms Days: No = -0.4, Yes = -1.1, P = 0.07
- Inhaled corticosteroids: No = -93, Yes = -268, P = 0.05
Baseline Predictors: summary

**SIGNIFICANT**
- Cockroach sens/exp [A,S,I]
- Derf IgE $\geq 0.35$ kU$_A$/L [S,I]
- Total IgE $\geq 100$ IU/ml [I]
- Weight: BMI $\geq 25$ [A]
- $\geq 1$ Unscheduled visit prior year [A,I]

(A = exacerbation; S = symptoms, I = Dose ICS)

**NONSIGNIFICANT**
- Age: 6-11 yrs vs 12-20 yrs
- Gender
- Atopy
- Cockroach IgE
- (FEV$_1$)
Patient characteristics associated with a favorable response to omalizumab

- Sensitization
- Exposure
- Total IgE
- ↑ BMI
- ↑ Healthcare utilization
Advantages to omalizumab for the treatment of asthma

- Not antigen-specific
- More effective in the face of active allergic disease – sensitization and exposure
- Onset of actions within 4 weeks
- Principal effect is on a major factor in asthma morbidity – exacerbations
- Safety indices are favorable