Inner-City Asthma and Anti-IgE

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Disclosure Slide

• Employment
  – University of Wisconsin

• Financial Interests
  – Advisory Boards: Merck
  – Consultant: Amgen, Novartis, GlaxoSmithKline, MedImmune, Genentech

• Data Monitoring Boards and Study Oversight Committees
  – Boston Scientific
  – Genentech
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• Research Interests
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• Gifts
  – Nothing to Disclose

• Other Interests
  – Nothing to Disclose
Why Focus on Inner City Asthma in Children and Adolescents?

- Asthma is both more common and more severe in U.S. inner cities
- High allergen loads
  - Cockroach
  - Mouse
  - House dust mite
- Given the likely importance of allergen – IgE interactions to disease, particularly in the inner city, it was hypothesized that asthma control would improve by modulating IgE-dependent contributions to asthma
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
Asthma control of participants at enrollment (n=419)

- Days of asthma symptoms the previous 2 weeks: 4.9±4.2
- Childhood ACT® score in the last month (4–11 years): 18.9±4.1
- ACT® score (12 years and over): 18.8±4.2
- FEV₁ (% predicted value): 92.1±17.1
- FEV₁/FVC: 77.1±9.9
- ≥1 Hospitalization/past year: 25%
- ≥1 Unscheduled visit/past year: 78%
- Male subjects: 58%
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) (n=208)
What were the effects of omalizumab on the daily dose of inhaled corticosteroids (budesonide equivalents [µg/day])?
What were the effects of omalizumab on exacerbations?

Difference of $-16.5\%$ with an exacerbation ($p<0.001$)

Control $\text{(n=211)}$
Omalizumab $\text{(n=208)}$
Asthma exacerbations also have seasonal patterns
The September Epidemic of Asthma Exacerbations

• Canadian asthma hospitalization admission data
• Timing and magnitude of peaks in asthma hospitalization
  – 5-15 y/o children: 17.7 days after Labor Day
  – Preschoolers 1.7 days later
  – Adults 6.3 days later
• Peak season for:
  – HRV
  – Some allergens (Alternaria, ragweed)
Asthma Hospitalization Rates Ages 5-15 Yrs

What are the effects of omalizumab on the percentage of participants experiencing exacerbations over the year?
The importance of IgE and allergic sensitization in virus-provoked asthma exacerbations
What role does IgE play in asthma exacerbations?

- Evaluated the contribution of rhinovirus infections and atopic status to wheezing episodes in children (7 to 12 years old) in Costa Rica
- 287 Children
  - 96 with acute wheezing
  - 65 stable asthma
  - 126 non-asthmatic control subjects
Probability of current wheezing based on increasing titers of IgE antibodies to *D pteronyssinus* in children with negative test results for rhinovirus by using real-time PCR (A) compared with children with positive test results for rhinovirus (B).

Does IgE affect interferon induction to rhinovirus and its replication?

Total Serum IgE Levels

What contribution does IgE make to a respiratory virus provoked asthma exacerbation?

- Elevated IgE
  - Exacerbation

- Reduced IgE
  - No Exacerbation

Inflammation  Virus Regulation  Inflammation  Virus Regulation
Who are the candidates for the most favorable response to omalizumab?
Cockroach Sensitization & Exposure’s Effect on Omalizumab Efficacy

- Exacerbations
- Symptoms Days
- Inhaled corticosteroids

Cockroach Sensitive and Exposed?
What factors contribute to whether a respiratory infection provokes asthma and how might IgE fit into this process?

Seed (Virus)
RV-subclasses (Class A and C)

Soil (Host)
Allergic Inflammation
Innate immune response

Airway
Inflammation
Hyperresponsiveness

Asthma
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