Oral Immunotherapy and Anti-IgE Antibody-Adjunctive Treatment for Food Allergy:
Omalizumab facilitates oral desensitization in high-risk peanut allergy patients

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Oral food immunotherapy/desensitization

- OIT for food allergy has been studied for many years.
  - Based on allergen immunotherapy for hay fever—allergy shots.
  - Oral food desensitization works.
  - However, allergic reactions, including anaphylaxis, are very common, and 10-25% of patients have severe reactions, and are refractory to desensitization.
    - Children with higher food-specific IgE are more likely to fail desensitization (Meglio et al 2013. Pediat Aller Immunol.)
Can anti-IgE Antibody be used for food allergy?

Anti-IgE Antibody (omalizumab)

- Anti-IgE binds IgE and prevents mast cell degranulation.
- Reduces expression of FcεRI on mast cells and basophils.
- Circulating anti-IgE complexes act as antigen sink.
- Possible effects on DCs and monocytes, which express FcεRI.
Can omalizumab be used in food allergy?

- Anti-IgE increased the threshold dose of peanut eliciting a clinical reaction.
  - TNX-901 (450 mg x 4 doses) increased the tolerated dose from 178 to 2,800 mg peanut flour (Leung et al. 2003. NEJM).
  - Omalizumab increased the tolerated dose of peanut from a median of 15 to 500 mg flour (Sampson et al. 2011. JACI) or 80 to 6,500 mg (Savage et al. 2012. JACI).

- Anti-IgE pretreatment decreases acute reactions during rush immunotherapy for ragweed allergy (Casale et al. 2006. JACI).
Can omalizumab make oral immunotherapy faster and more effective?

- Subjects (Boston & Stanford) with significant milk allergy:
  - 11 children, 7-18 years of age.
  - Median Milk-specific IgE was 50 kU/L.

- Treatment protocol:
  - Receive omalizumab for 16 weeks.
  - During the last 7 wks of omalizumab, patients received milk, starting at a very low dose, which increased 20,000-fold.
  - Omalizumab was then stopped, but the patients continued on daily oral milk.
  - At 25 wks, oral food challenge, >8 oz of milk.
Overall Results, milk study

- One-day desensitization to 1 oz of milk.
  - 7 out of 11 patients passed.
  - One patient dropped out after first day of desensitization.

- After 7 additional weeks, tolerated a daily dose of 2 oz.
  - 9 out of 10 patients passed.

- At 6 months, oral challenge, total of 11 oz milk).
  - 9 out of 10 patients passed.
  - The 10th patient was taking 4 ounces of milk or milk products daily.

After the Milk Study, what’s next?

- Follow the milk-desensitized patients for at least 2 more years.
  - Make sure they remain tolerant of milk.
  - Determine if tolerance improves with time.
  - Examine the immune system for changes.
  - Will they still need daily milk to maintain tolerance?
- Can we use this approach for other foods?
Will Xolair Facilitate Desensitization of Peanut Allergic Patients?

• **Recruitment:**
  - Patients 7-25 years of age: 13 patients, median age, 10 y.
  - History of severe peanut allergy.
  - Median peanut specific IgE, 229 kU\textsubscript{A}/L (highest of any study).
  - All patients reacted on challenge with a median dose of 50 mg peanut flour (about \(\frac{1}{4}\) peanut).

• **Treatment:**
  - Xolair for a total of 20 weeks.
  - Desensitization over 8 weeks, starting at 0.1 mg of peanut, and increasing 40,000-fold to 4,000 mg (about 10 peanuts).
  - The Xolair was then stopped, but the children continued on daily oral peanuts.
  - 12 weeks later, oral food challenge.
• **Treatment:**
  - Xolair every 2-4 weeks.
  - Desensitization, over 8 weeks, starting at 0.1 mg of peanut, and increasing 40,000-fold to 4,000 mg (about 11 peanuts).
  - After stopping Xolair, continue daily peanuts.
  - 12 weeks later, oral food challenge.

ClinicalTrials.gov identifier: NCT01290913
Comparison to Previous Studies

• Our patients had the highest median peanut specific IgE.
• One day desensitization to 500 mg.
  – In our study, 13 of 13 patients were successful.
  – S. Jones: 10 of 39 tolerated 200 mg.
  – Hofmann: 6 of 28 subjects tolerated 200 mg.
• With omalizumab treatment, patients required a median time of 8 wks to reach maintenance.
• Without omalizumab, median time to reach maintenance: 20-30 wks.
Summary

• Among children with significant milk allergy, treatment with Xolair facilitated rapid oral desensitization.

• Among children with high-risk peanut allergy, treatment with Xolair facilitated rapid oral desensitization.

• The majority of peanut allergic patients were successfully desensitized with Xolair pretreatment and are now taking 10 or more peanuts per day!

• Patients still need to be followed, as reactions can still occasionally occur with oral doses.
Limitations

- Small samples size.
- Absence of a placebo group.
What’s next?

- Follow the patients over an additional 3-5 years.
- Validate results with larger studies.
- PRROTECT study.
  - Four site study
    - Boston Children’s Hospital (Schneider)
    - Children’s Hospital of Philadelphia (Spergel)
    - Lurie Children’s Hospital Chicago (Pongracic)
    - Stanford University (Nadeau)
  - 36 patients.
  - Funded by FARE and Genentech.
Acknowledgments

- Lynda Schneider, MD
- Rima Rachid, MD
- Jennifer LeBovidge, PhD
- Drs. Mudita Mittal, Michael Young, Frank Twarog, M. Pistiner
- Sara Little, Sara Spielman, Irene Borras, Tim Harrington
- Drs. Oettgen, Bonilla and McDonald
- Denis Biderot, PhD, Azza Abdel-Gadir, PhD
- Statisticians: Emily Blood, Leslie Kalish, Dionne Graham
- Kari Nadeau, MD, PhD, Stanford University
- Dave and Denise Bunning Food Allergy Project
- Jasmine and Paul Mashikian Fund
- Food Allergy Research and Education
- Translational Research Program, Boston Children’s Hospital
- Thrasher Research Foundation
- Genentech
- All of our patients, who participated in these studies, and who risked developing severe allergic reactions so that we could complete these studies.