How Can We Measure Adherence and Outcomes with Allergen Immunotherapy?

A Guide for the Practicing Allergist

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Session 3303:
Update on the Efficacy and Safety of Subcutaneous (SCIT) vs. Sublingual (SLIT) Allergen Immunotherapy for the Practicing Allergist
Presented at the 2013 Annual Meeting of the American Academy of Allergy, Asthma, and Immunotherapy
February 23, 2013
San Antonio, TX

Research jointly funded by the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology
Special Thanks

- Linda Cox
- Donald Aaronson
- David Brown
- Thomas Casale
- David Lang
- Richard Lockey
- James Sublett
- AAAAI and ACAAI for Joint Research Funding
- Colleagues at BioMedEcon: Amy Bronstone, Shirley Wang
- Coauthors: David Brown, Paul Fass, Ira Finegold, Gary Gross, David Lang, Eli Meltzer, Bryan Leatherman
- Members of the Academy, College and Joint Council
Topics: Real World Findings

- Overview of
  - Retrospective claims analysis
  - Matched cohort analysis
- AIT as both
  - Safe and effective
  - Profound treatment failure
- In pharmaceutical clinical trials, investigators know that treatments can fail because
  - The intervention lacks clinical benefit
  - The intervention is unsafe, and/or
  - Patients do not adhere to the carefully designed protocol
    - Safeguards may include
      - Careful patient selection
      - Run-in periods
      - Frequent clinic visits
- As new modes of administration and treatments become available, we must have a benchmark of current treatment against which to measure effects of new treatments
  - SLIT (payers will focus on adherence)
  - Novel immune-modifying interventions
  - Accelerated regimens

AIT is both
- Compellingly safe and effective
- A profound treatment failure

Whether due to efficacy or adherence
- Treatment failure = Treatment failure
- Treatment failure is catastrophic
Topics: Real World Findings

- WASTE OF $ TO INTERVENE YET
  - Let’s do our homework and identify the WHYs before the WHATs
  - My appeal for collaboration
    - Linda Cox and I would like to collaborate with you to survey patients and physicians
    - Relationships between adherence and
      - Patient factors
        - Adult v child
        - Demographics
        - Family considerations
          - Illness burden of family
          - Ability to take time off from work for AIT
      - Disease-related factors
        - Allergy severity
        - Comorbid allergy-related and non-allergy-related conditions
      - Physician characteristics
        - Collaborative v directive
        - Training, specialty
      - Systems characteristics
        - Insurance reimbursement
        - Time in waiting room, referral systems, parking, hours in waiting room

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Description of Retrospective Claims Analysis

Patient Receives Physician-based Outpatient Care

Physician seeks reimbursement

Physician submits claim to insurer. Data include:
- Patient ID
- Date of service
- CPT /HCPCS (procedures)
- ICD-9 (primary and up to 20 2º diagnoses)

Claims are received by insurer, electronically filed and adjudicated

Facilities, Physicians seek reimbursement

Physician submits claim to insurer. Data include:
- Patient ID
- Date of admission, discharge
- Venues of care
- CPT /HCPCS (procedures, labs)
- ICD-9 (primary and up to 20 2º dx)

Patient Receives Inpatient, ED or Nursing Care

Patient Fills Prescription

Pharmacy seeks reimbursement

Pharmacy submits claim to insurer
- Patient ID
- NDC (drug name, dose, strength, form, route of administration)
- Date of fill *
- Quantity *
- Number of days supply*
* Data for adherence calculations (gaps, possession ratios, discontinuations, etc.)

With the appropriate incantations and wave of the wand, some researchers may obtain HIPAA-compliant electronic data from key sources (e.g., State Medicaid, Private Plans, Medicare, Employer Groups)
Benefits and Drawbacks

**Benefits of Retrospective Claims Analyses**
- Can longitudinally track individual patients (HIPAA-compliant) to assess and inform
  - Clinical course of illness
  - Relationship between patterns & outcomes of care
  - Best practices
- In contrast to results from prospective, randomized, controlled, trials, findings from retrospective claims analyses
  - Represent “real world” findings
  - Are not influenced by
    - Stringent and carefully designed patient selection
    - Rigorous scheduled follow-up
    - Require less $ and faster time to complete analysis of existing, historical data
    - Sample sizes are typically in the tens of thousands

**Drawbacks**
- Generally limited to “billable” services
  - Example:
    CPT 95004 (skin prick test) may be recorded for a particular patient on a specific day, but results may not be recorded in the claims database because they do not influence reimbursement for that activity
- Patterns and outcomes of care are easily discerned, but rationale underlying findings are not
  - Example
    We found that less than 20% of patients (adults and children) who initiated AIT completed at least 3 years of treatment. However, from the claims data at hand, we cannot determine with assuredness the primary factors that underlie “premature” discontinuation.
Retrospective Claims Analysis

AIT IS HIGHLY EFFECTIVE
Pre-Post Study in CHILDREN

- 7-year (1997-2004) retrospective claims analysis of Florida Medicaid-enrolled children (age <18 years) newly diagnosed with AR (with or without asthma) and naïve to AIT
- We compared mean health care use and costs of SAME CHILDREN: 6 months pre-AIT initiation versus 6 months post-AIT discontinuation

Pre-Post Study in CHILDREN

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- We compared mean health care use and costs of SAME CHILDREN: 6 months pre-AIT initiation versus 6 months post-AIT discontinuation

<table>
<thead>
<tr>
<th># Inpt Stays</th>
<th># Outpt Visits</th>
<th># Rx Fills</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.8 *</td>
<td>-7.8 **</td>
<td>-3.2 **</td>
</tr>
</tbody>
</table>

Mean Change in Health Care Use 6 Months Pre- versus 6 Months Post-AIT Initiation

Mean Change in Health Care Costs 6 Months Pre- versus 6 Months Post-AIT Initiation

- Inpt $: -$2,316 **
- Outpt $: -$233 **
- Rx $: -$54 **
- TOTAL $: -$401 **

* P=0.05
** P<0.001

Matched Cohort Study in Children

- 10-year (1997-2007) retrospective, matched cohort, claims analysis of Florida Medicaid-enrolled children (age <18 years) newly diagnosed with AR (with or without asthma) and naïve to AIT
- Compared 18-month health care use and costs: AIT versus matched noAIT groups*

*Matched AIT to no AIT patients on age at 1st AR dx; sex; race/ethnicity diagnosis of asthma, conjunctivitis, atopic dermatitis

Matched Cohort Study in Children

- 10-year (1997-2007) retrospective, matched cohort, claims analysis of Florida Medicaid-enrolled children (age <18 years) newly diagnosed with AR (with or without asthma) and naïve to AIT
- Compared 18-month health care use and costs: AIT versus matched noAIT groups

Differences in Per-Patient Median Health Care Costs Between AIT-Treated Patients and Matched Controls During 18 Month Period

- Median, per-patient Outpt, Rx, and Total Cost differences were significant (P<0.001) at all assessment periods (3, 6, 12 and 18 months)
- Not significant at any assessment period (3, 6, 12 or 18 months)

Do AIT Benefits Conferred to Children Extend to Adults?

- 12-year (1997-2009) retrospective, matched cohort, claims analysis of Florida Medicaid-enrolled adults and children newly diagnosed with AR (with or without asthma) and naïve to AIT
- Compared 18-month health care use and costs: AIT versus matched noAIT groups

<table>
<thead>
<tr>
<th>Inpt $</th>
<th>Outpt $</th>
<th>Rx $</th>
<th>Total $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Children</td>
<td>Adults</td>
<td>Children</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adults</td>
<td></td>
</tr>
<tr>
<td>$(3,921)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$(5,590)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*AIT-related cost savings calculated as the mean cost for matched control group minus the mean cost for the AIT-treated group. Positive numbers indicate that AIT resulted in cost savings.

Patients were matched on age at AR diagnosis; gender; race/ethnicity; and the presence of asthma, conjunctivitis, or dermatitis.

The Failure of AIT in the U.S.

- Received by few potentially appropriate patients (~3%)\(^1,2\)
- High rates of premature discontinuation\(^2,3\)
- Wide variation in initiation and persistence by demographic, illness, and insurance characteristics\(^2,3\)

THE FAILURE OF AIT: Poor Adherence in terms of treatment initiation

Medicaid Adults (≥18 yrs) 7/97-6/08 N=3,008,865

- No AR N=2,917,762
- AR N=91,103

1997-2008

- Never Received AIT N=85,997
- Ever Received AIT N=5,106

ADULTS

- 3%
- 5.6%

Medicaid Children (<18 yrs) 7/97-6/08 N=3,604,711

- No AR N=3,310,933
- AR N=293,778

- Never Received AIT N=283,760
- Ever Received AIT N=10,018

CHILDREN

- 8%
- 3.4%

Definitions of Terms
- AR
- ICD-9 477.X
- AIT
- CPT 95115, 95117,95120, 95125, 95144, 95165, 95180, 95199
- Comorbid allergy-related illness
  - Asthma
    - 493.X
  - Atopic dermatitis
    - ICD-9 691.8
  - Conjunctivitis
    - ICD-9 372.X
- Comorbid illness severity (Charlson Comorbidity Index)\(^1\)
  - None to mild
  - Moderate
  - Severe
- Premature AIT discontinuation
  - AIT <3 years
- Newly diagnosed AR
  - Index AR preceded by a full year in which no AR diagnoses occurred
- De novo AIT
  - New AR diagnosis and 1\(^{st}\) AIT claim followed (rather than preceded) newly diagnosed AR
- Buildup phase
  - 1\(^{st}\) 6 months of AIT
- Maintenance phase
  - AIT following build-up phase

THE FAILURE OF AIT: Poor Adherence in terms of treatment initiation (1\textsuperscript{st} 5 administrations)

<table>
<thead>
<tr>
<th>Number of IT Injections</th>
<th>Likelihood of Discontinuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9%</td>
</tr>
<tr>
<td>2</td>
<td>12%</td>
</tr>
<tr>
<td>3</td>
<td>13%</td>
</tr>
<tr>
<td>4</td>
<td>14%</td>
</tr>
<tr>
<td>5</td>
<td>15%</td>
</tr>
</tbody>
</table>

After the 1\textsuperscript{st} Injection, the likelihood of D/C IT is 9%

After the 2\textsuperscript{nd} Injection, the likelihood of D/C IT is 12%

After the 3\textsuperscript{rd} Injection, the likelihood of D/C IT is 13%

After the 4\textsuperscript{th} Injection, the likelihood of D/C IT is 14%

After the 5\textsuperscript{th} Injection, the likelihood of D/C IT is 15%
THE FAILURE OF AIT: Poor Adherence in terms of treatment duration

### AIT Duration

#### Adults (N=1,265)

<table>
<thead>
<tr>
<th>Duration</th>
<th>N</th>
<th>%</th>
<th>Cum %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only 1</td>
<td>230</td>
<td>18.2%</td>
<td>18.2%</td>
</tr>
<tr>
<td>&lt;6 months</td>
<td>379</td>
<td>30.0%</td>
<td>48.2%</td>
</tr>
<tr>
<td>6 to &lt;12 months</td>
<td>127</td>
<td>10.0%</td>
<td>58.2%</td>
</tr>
<tr>
<td>1 to &lt;2 years</td>
<td>170</td>
<td>13.4%</td>
<td>71.6%</td>
</tr>
<tr>
<td>2 to &lt;3 years</td>
<td>121</td>
<td>9.6%</td>
<td>81.2%</td>
</tr>
<tr>
<td>3 to &lt;4 years</td>
<td>67</td>
<td>5.3%</td>
<td>86.5%</td>
</tr>
<tr>
<td>≥4 years</td>
<td>171</td>
<td>13.5%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Mean (SD) 552 days (761)
Median 217 days

#### Children (N=2,886)

<table>
<thead>
<tr>
<th>Duration</th>
<th>N</th>
<th>%</th>
<th>Cum %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only once</td>
<td>334</td>
<td>11.6%</td>
<td>11.6%</td>
</tr>
<tr>
<td>&lt;6 mos</td>
<td>854</td>
<td>29.6%</td>
<td>41.2%</td>
</tr>
<tr>
<td>6-12 mos</td>
<td>392</td>
<td>13.6%</td>
<td>54.8%</td>
</tr>
<tr>
<td>1-2 yrs</td>
<td>462</td>
<td>16.0%</td>
<td>70.8%</td>
</tr>
<tr>
<td>2-3 yrs</td>
<td>338</td>
<td>11.7%</td>
<td>82.5%</td>
</tr>
<tr>
<td>3-4 yrs</td>
<td>183</td>
<td>6.3%</td>
<td>88.8%</td>
</tr>
<tr>
<td>≥4 yrs</td>
<td>323</td>
<td>11.2%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Mean (SD) 554 days (653)
Median 296 days

Only 17.5% of children completed a 3-year course of AIT
Only 18.8% of adults completed a 3-year course of AIT
Please contact

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