Assessing the compliance & persistence of allergen immunotherapy in allergic rhinitis using a retrospective pharmacy database from The Netherlands

Menno Kiel, MD MSc (kiel@bmg.eur.nl)  
Roy Gerth van Wijk, MD PhD  
Esther Röder, MD  
Maiwenn Al, PhD  
Wim Hop, PhD  
Maureen Rutten-Van Mölken, PhD

I. Introduction

ALLERGIC RHINITIS & ALLERGEN IMMUNOTHERAPY

Allergic rhinitis

- More commonly known as ‘hayfever’, but also including hypersensitivity to house dust mites
- Not restricted to nasal complaints, but also potential other symptoms: eyes, lungs (‘allergic asthma’), chronic fatigue & concentration problems, sleeping disturbance
- Approx. 20% of Europeans affected, more in urban areas
- Significant expense, both prescription and OTC drugs which suppress symptoms.
- Also: preventive “vaccination” using allergen immunotherapy; well established and part of Dutch basic benefits package

Allergen immunotherapy

- Basic idea: desensitize immune system for 3 yrs by administering extract(s) of the offending allergen(s)
- Routes of administration:
  1. sublingual (SLIT): daily drops or tablets under tongue in domestic setting
  2. subcutaneous (SCIT): monthly injections arm(s)/leg(s) in clinical setting
- Safe, but side effects do occur (especially in SCIT). Effectiveness heavily dependent on compliance & persistence
- Total costs of allergen immunotherapy in Netherlands (2010): €45M/yr.

PHARMO® database

- The PHARMO® Record Linkage System (RLS) contains pharmacy drug dispensing records collected from over 200 pharmacies throughout NL, 2 million subjects
- Data extraction based on WHO-ATC code for allergen immunotherapy, yielding pharmacy visiting dates and drug/prescriber/cost info of:
  - 8996 adult patients taking
    - SCIT and/or SLIT against grass/tree pollen, mites
    - from 1994 through 2009
- PHARMO records linked to SCP database for background info on sex, age, SES, geographic location etc.
Database analysis

- A SAS® macro was obtained, constructed by Catalan & LeLorier for the analysis of long-term persistence in statin use (Catalan & LeLorier, ViH Nov 2000)
- Macro adapted for use of analysis in allergen immunotherapy:
  - persistence (duration of treatment, target: 3yrs)
  - compliance (if missed pharmacy visits)

### III. Results

**ANALYSIS OF COMPLIANCE & PERSISTENCE**

#### Analysis of compliance & costs

- Of 1126 fully persistent patients (both groups), 38.4% were noncompliant, being on average 1.2 times late at the pharmacy.
- Total and per patient direct pharmaceutical costs rise as treatment progresses (undiscounted)

<table>
<thead>
<tr>
<th>Year of treatment</th>
<th>Cumulative total costs (€)</th>
<th>Interval mean costs (€)</th>
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<tbody>
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<td>778</td>
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<tr>
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<td>1,597</td>
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<tr>
<td>3</td>
<td>10,589,368</td>
<td>2,915</td>
</tr>
</tbody>
</table>

#### Analysis of persistence

- Further analyses based on within-group Cox-regression due to PHA violation. Significant predictors of premature discontinuation:
  - Prescriber effect: allergologist vs. GP: HR_{SCIT} 1.4; HR_{SLIT} 1.5
  - Consistent and ± equal Age-effect: HR < 1/yr
  - Geo-effect (North/East/South vs. Western NL): HR_{SCIT} 1.1-1.2; HR_{SLIT} 0.8-0.9
- KM curve of survival (p<0.001):
  - SCIT: 1.7y (21% 3+ yrs)
  - SLIT: 0.9y (6% 3+ yrs)

#### NONCOMPLIANCE & (COSTS OF) NONPERSISTENCE

IV. Discussion

**Analysis of persistence**

- SCIT
- SLIT

**Analysis of compliance & costs**

- Of 1126 fully persistent patients (both groups), 38.4% were noncompliant, being on average 1.2 times late at the pharmacy.
- Total and per patient direct pharmaceutical costs rise as treatment progresses (undiscounted)
Noncompliance (costs of) nonpersistence

- Compliance seems decent, but only measured in persistent patients. In line with literature on the subject.
- Only about 6% of SLIT users and 21% of SCIT users achieve a minimum total treatment duration of 3 yrs, though hazard rate of RoA (SCIT vs. SLIT) itself hard to predict due to violation of PHA.
- Though easy to use, daily SLIT treatment seems hard, monthly SCIT treatment preferred, and, in these long and intensive treatments, GP care is preferred over specialist outpatient care.
- Costs of nonpersistence are impressive, but are not completely forgone: some long-term effects on symptoms may certainly be expected, but discounting is problematic.