Why is the control suboptimal in Allergic Rhinitis?

Joaquim Mullol, MD, PhD
Rhinology Unit & Smell Clinic
ENT Department, Hospital Clínic
Respiratory Immunoallergy, IDIBAPS
Barcelona, Catalonia
Epidemiology in the E.U
prevalence of AR - adults


### Prevalence of AR - ISAAC phase III

#### World regions

<table>
<thead>
<tr>
<th>Region</th>
<th>Gender</th>
<th>6-7 yr</th>
<th>13-14 yr</th>
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<td></td>
<td></td>
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<td>%</td>
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<td>2491</td>
<td>6.5</td>
</tr>
</tbody>
</table>

**N= 390,000**

**N= 800,000**

Mallol J, et al. *Allergol Immunopathol* 2013
ARIA-modified classification

**Intermittent**
- \( \leq 4 \) days per weeks
- OR \( \leq 4 \) continuous weeks

**Mild**
- NO items affected

**Moderate**
- 1 to 3 items affected
- Abnormal sleep
- Impairment of daily activities, sport, leisure
- Abnormal work and school
- Troublesome symptoms

**Persistent**
- > 4 days per week
- AND > 4 continuous weeks

**Severe**
- All 4 items affected

ARIA-modified classification

correlation of m-ARIA with VAS

Mild 0 - 4
Moderate >4 - 7
Severe >7 - 10
Allergic Rhinitis and Asthma comorbidity
Allergic Rhinitis and Asthma natural history in Europe

Uncontrolled rhinitis related factors

Disease-related factors (‘SCUAD’)
- Exogenous/endogenous/genetic factors
- Global airway disease

Diagnosis-related factors
- Incorrect diagnosis
- Concomitant local/systemic disease

Patient-related factors
- Inadequate intake of medication
- Poor adherence

Treatment-related factors
- Inadequate treatment
- Lack of symptom-oriented treatment

Uncontrolled upper airway disease

Hellings PW, Mullol J, et al. Allergy 2013
Allergic rhinitis adherence to INS in adults

Morisky Medical Adherence Score

<table>
<thead>
<tr>
<th>Education</th>
<th>MMAS-8</th>
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<tbody>
<tr>
<td>Primary school</td>
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<td>≤35</td>
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<table>
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<td>3.28</td>
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<th>Benefit from the drug</th>
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<tbody>
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<table>
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<th>Abroad days per month</th>
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<tr>
<td>≤5 days</td>
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<td>3.24</td>
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<tr>
<td>&gt;5 days</td>
<td>23</td>
<td>4.92</td>
<td></td>
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</table>

Emre O, et al, J Mullol. *Braz J Otorhinolaryngol* 2017  (Turkish AR patients)
Watery anterior rhinorrhea & sneezing

The patient may be allergic

YES

Nasal obstruction

Symptoms occurring at the same time every year

Bilateral eye symptoms: ± pruritus ± tearing ± redness

The patient is likely to be allergic

The patient is most likely allergic

Confirm diagnosis of allergic rhinitis by skin tests or serum-specific IgE

NO

Postnasal drip

Coloured discharge and/or facial pain

The patient is unlikely to be allergic

Suspect chronic rhinosinusitis

Confirm diagnosis of rhinosinusitis by ENT examination - CT scan

Smell loss in adult PER

NO loss of smell
- 25% (Mild)
- 75% (Moderate / Severe)

LOSS OF SMELL
- 15% (Mild)
- 85% (Moderate / Severe)

33% of AR

Guilemany JM et al, J Mullol. Laryngoscope  2009
Smell loss in paediatric AR (6-12yo)

prevalence

intensity - score

N = 1,260

Uncontrolled rhinitis related factors

Nasal mucosa

ALLERGIC rhinitis

INFECTIOUS rhinitis

MIXED rhinitis

NONALLERGIC rhinitis

Nasal anatomy

Turbinate
- Hypertrophy
- Bullosus medial concha

Septum
- Deviation
- Perforation

Valve
- External valve problem
- Internal valve problem

Nasopharynx
- Adenoid hypertrophy

Nasal symptom severity

Hellings PW, Mullol J, et al. Allergy 2017
Loss of smell in AR
clinical marker of severity & refractoriness

Mariño-Sánchez F, et al, Mullol J. JACI in Practice 2018

- Treatment refractoriness: 2.7 (1.3-5.6) *
- Severe Rhinitis (m-ARIA): 3.3 (1.6-6.9) **
- Obstructive Turbinate Enlargement: 2.5 (1.2-5.2) ***
- Obstructive Septal Deformity: 0.9 (0.4-1.9)
- Obstructive Adenoidal Hyperplasia: 5.3 (0.6-44)
- Asthma: 1.1 (0.5-2.2)
- Conjunctivitis: 1.7 (0.8-3.4)
- Well-controlled AR: 0.5 (0.3-0.7) **

Odds Ratio (logarithmic scale)

Normosmia  Smell Loss

Mariño-Sánchez F, et al, Mullol J. JACI in Practice 2018
AR severity & control
impact of treatment
Allergic Rhinitis landscape

Most patients have ‘moderate/severe’ AR

Many patients have mixed forms of AR

Many patients are becoming polysensitized

European Survey
- 67.2% = moderate or severe
- 42.5% = persistent disease

Evolution of treatment-resistant phenotypes
- Severe Chronic Upper Airway Disease (SCUAD)

SCUAD
- approx. 30% of AR patients

Canonica et al. Allergy 2007
Settipane et al. Allergy Asthma Proc 2001
Mösges et al. Allergy 2007
Bousquet et al. J Allergy Clin Immunol 2009
Allergic Rhinitis – Finland landscape

the patient’s voice allergy survey

In Sweden, the cost of rhinitis is 2.7 billion € / yr in terms of lost productivity

Hellgren et al. *Allergy* 2010
Allergic Rhinitis landscape

need of multiple medications to achieve control

- up to 90% of AR patients take ≥2 medication to treat AR
- 60% of all AR patients are “very interested” in finding a new medication
- 25% “constantly” trying different medications

Patients (%)

- up to 90% of AR patients take ≥2 medication to treat AR
- 60% of all AR patients are “very interested” in finding a new medication
- 25% “constantly” trying different medications

Canonica et al. Allergy 2007
Bousquet et al. Int Arch Allergy Immunol 2012
Schatz et al. Allergy 2007
Demoly et al. Allergy 2002
Bousquet et al. Allergy 2008
Allergic Rhinitis – France landscape

need for more effective medications

- 990 AR patients recruited by 161 GPs in France
- 72.5% were currently taking allergic rhinitis medication

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>rhinorrhea</td>
<td>89%</td>
</tr>
<tr>
<td>sneezing</td>
<td>82%</td>
</tr>
<tr>
<td>nasal congestion</td>
<td>82%</td>
</tr>
<tr>
<td>nasal itching</td>
<td>68%</td>
</tr>
<tr>
<td>ocular symptoms</td>
<td>68%</td>
</tr>
</tbody>
</table>

The majority of treated AR patients remain symptomatic

Global discomfort caused by AR during the previous week (VAS)

Uncontrolled

Bousquet et al. Int Arch Allergy Immunol 2013
Allergic Rhinitis – UK landscape

use of multiple medications to control ...

moderate/severe AR patients on ≥ 2 medications (N=1,000 p)

The need for MORE and FASTER effective treatment was the primary reason for co-medicating

Allergic Rhinitis – UK landscape... remain symptomatic on treatment

- 96.2% of AR patients were on treatment
- 70.5% were using multiple treatments (mainly INCS and oral antihistamines)

Allergic rhinitis was poorly controlled with current mono- and multiple-therapies

Allergic Rhinitis - Spain landscape
use of ≥2 medications for control

duration of symptoms

severity of disease

N= 1,008 physicians

Allergic Rhinititis - Spain landscape poorly controlled despite optimal treatment

Distribution of Severe subgroup from Baseline to 4 weeks

- Controlled: 55.8%
- Uncontrolled: 44.2%

Allergic Rhinitis - Spain landscape costs according to AR severity – FERIN

Colás C et al. Allergy 2017
methods to assess control of AR
Allergic rhinitis
perceived shortcomings of disease

- **AR SEVERITY** (untreated)
  level / degree of symptoms, impact on Quality of Life

- **AR CONTROL** (impact of treatment)
  assessment or not of treatment objectives
  combining: severity, QoL, nasal function, exacerbations

- **RESPONSIVENESS TO TREATMENT**
  assessment of treatment objectives

Demoly P, et al. *Clin Transl Allergy* 2013
Allergic rhinitis
questionnaires to assess control

- **CARAT** (Control of AR and Asthma Test)
  
  AR and asthma / 10 items / 4-point scale
  
  Fonseca JA, et al. *Clin Transl Allergy* 2012

- **RCAT** (Rhinitis Control Assessment Test)
  
  allergic rhinitis / 6 items / 5-point scale
  

- **ARCT** (AR Control Test)
  
  allergic rhinitis / 6 items / 5-point scale
  
Allergic rhinitis
control by Visual Analogue Scale (VAS)

In general, how bothersome are today your symptoms of allergic rhinitis?

not at all bothersome

2.3

poorly controlled

5.0

uncontrolled

well controlled

intolerable bothersome

0

10

Allergic rhinitis control by Visual Analogue Scale (VAS)

Impact of treatment on the control of AR
Seasonal Allergic Rhinitis
MP-AzeFlu better than first-line treatment

MP-AzeFlu provided significantly greater nasal symptom relief than FP or AZE alone (day 14)

Superiority of MP-AzeFlu present from day 1 and sustained

Meltzer EO, Mullol J, et al. In Arch Allergy Immunol 2013
Allergic rhinitis
INS + anti-H₁ intranasal formulations

- **MP-AzeFlu (FP+AZE intranasal formulation)**
  Meltzer EO, et al. *Int Arch Allergy Immunol* 2013

- **Fluticasone propionate + olopatadine**
  LaForce CF, et al. *Allergy Asthma Proc* 2010

- **Fluticasone furoate + levocabastine**

- **Mometasone furoate + olopatadine**
  US 20040097474 A1
Allergic rhinitis

MP-AzeFlu improves VAS control

severity phenotype

allergen season phenotype

Allergic rhinitis
MP-AzeFlu improves VAS control (day 3)

seasonal AR
perennial AR

AR control according to treatment evolution of a single Allergy Diary App user

Bachert C, Bousquet J, Hellings P. *Clin Transl Allergy* 2018
Persistent allergic rhinitis
MP-AzeFlu on severity & smell loss

reduces severity (VAS) improves smell (TDI score)

Treatment recommendations to control AR
treatment algorithm based on AR control

Assessment of control in treated symptomatic patient

- **VAS < 5/10**
  - **1st Line** (Anti H1 O/IN or INCS Or LTRA or INCS+AZE)
  - **Intermittent rhinitis**
    - No allergen exposure
    - Step-down treatment or STOP
  - **Persistent rhinitis**
    - No allergen exposure
    - Maintain or step up treatment
  - Re-assess VAS daily up to 48-72 hr
  - **VAS < 5/10**
    - If symptomatic: continue treatment
    - If no symptoms: consider step down treatment
  - **VAS ≥ 5/10**

- **VAS ≥ 5/10**
  - **Step-up treatment** INCS or INCS+AZE
  - Re-assess VAS daily up to D7
  - **VAS < 5/10**
    - Step up and Re-assess VAS daily
  - **VAS ≥ 5/10**
    - Consider referral to specialist and AIT

treatment algorithm based on AR control

Assessment of control in untreated symptomatic patient

- **VAS < 5/10**
  - Initiate treatment ANY 1st line
    - 1st Line (Anti H1 oral/IN or INCS or LTRA or INCS+AZE*)
  - Re-assess VAS daily up to 48-72 hr
  - If symptomatic: continue treatment
    - If no symptoms: consider step down treatment or STOP

- **VAS ≥ 5/10**
  - Initiate treatment
    - Intermittent rhinitis: ANY
    - Persistent rhinitis: INCS or INCS+AZE
  - Re-assess VAS daily up to 7-14 days
  - Step up and Re-assess VAS daily up to 7-14 days

  - **VAS < 5/10**
    - Consider referral to specialist and AIT
  - **VAS ≥ 5/10**
    - Consider referral to specialist and AIT

*: consider INCS+AZE if previous treatment ineffective (historical)
Precision Medicine

treatment algorithm based on AR control

Hellings PW, et al. Allergy 2017
Precision Medicine

multidisciplinary AR treatment algorithm

Hellings PW, et al. Allergy 2017