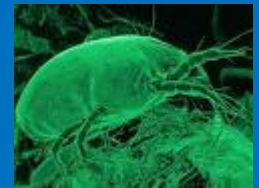


Allergy in Children

Dr Ian Humphrey

RCH & Melbourne Childrens Allergy Center Clayton



What is Allergy?

ALLERGY

Adverse reaction/hypersensitivity **immune mediated**

Large MW protein; haptens; carbohydrate (inulin, alpha gal,)
(food, pollen, insect, drug, animal, latex)

ATOPY

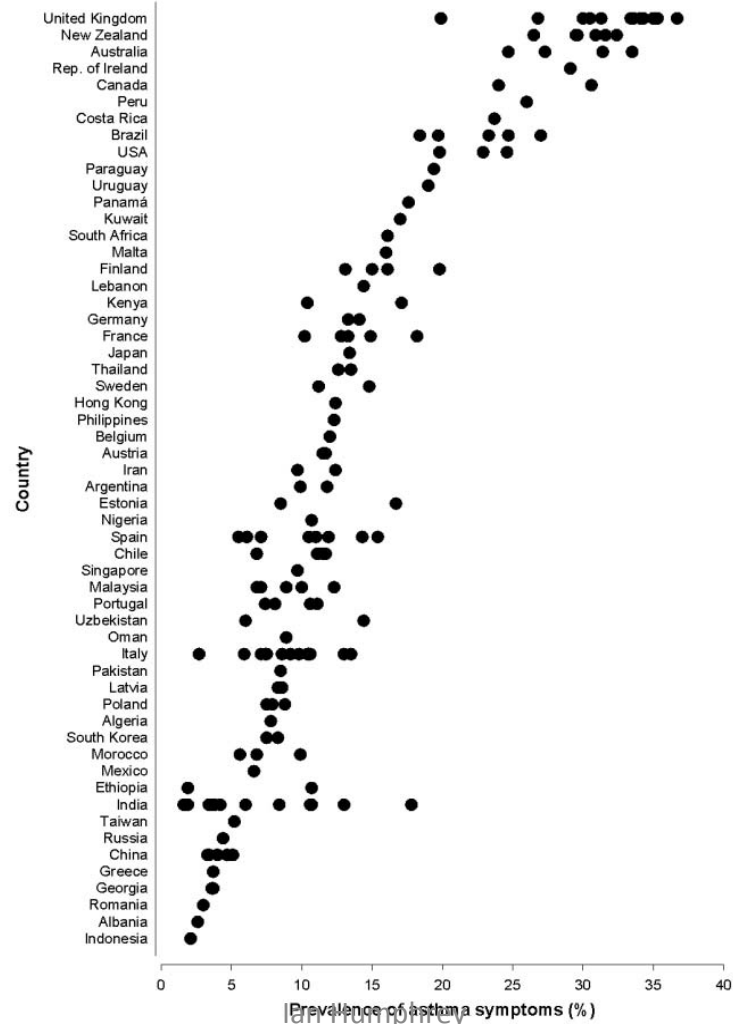
IgE , asthma, rhinoconjunctivitis, eczema, urticaria/angioedema, IgE allergies
Atopic (Allergic) March

INTOLERANCE

Adverse reaction **NOT immune mediated**

e.g. additives, FODMAP (lactose intolerance, fructose) fat malabsorption,
caffeine, tyramine, Gustatory rhinitis, auriculotemporal syndrome, **food poisoning, Scromboid (histamine)**, psychological.

ISAAC STUDY



Beasley R, et al. Lancet 1998; 351: 1225-32.

FOODS

- Egg
- Cow milk
(NOT lactose intolerance)
- Soy
- Wheat
- Nuts
- Fish
- Shellfish
- Any other food
 - Legumes
 - Fruit

INHALED ALLERGENS

- Indoor
 - Dust mite
 - Pets
 - Molds
 - Cockroach
 - (lizard)
 - (fish food)
- Outdoor
 - Grass
 - Trees
 - Weeds
 - Molds

Insect, Antibiotics, Drugs

FOOD ALLERGY IN CHILDREN

Food-induced allergic disorders in children

- IgE-mediated/acute onset Non-IgE-mediated/delayed onset
- Early Intermediate Delayed
- **Gastrointestinal tract**
 - Oral allergy syndrome,
 - gastrointestinal anaphylaxis
 - Proctitis, proctocolitis, enterocolitis, enteropathy, constipation, GORD
 - Eosinophilic gastroenteropathies
- **Respiratory tract**
 - Rhinitis, conjunctivitis, asthma, Chronic pulmonary disease (Heiner syndrome)
- **Skin**
 - Urticaria, angioedema, Atopic dermatitis
- **Anaphylaxis**
 - Food-dependent, exercise-induced anaphylaxis

FOOD ALLERGY IN CHILDREN

EARLY-minutes to hours .

urticaria, angioedema,

Anaphylaxis eczema

IgE mediated

INTERMEDIATE hours to days

Gastrointestinal

Not IgE mediated

LATE days to weeks

skin, gastro, respiratory

usually negative tests

Distressed infant

(“colic/silent reflux”)

Gastroesophageal reflux

Eosinophilic enteropathies

FPIES

Colitis/proctitis

Constipation

Failure to thrive

Iron deficiency

FOOD ALLERGY IN CHILDREN

DIAGNOSIS OF ALLERGIC DISEASE HISTORY

FOOD ALLERGY IN CHILDREN

DIAGNOSIS OF ALLERGIC DISEASE

HISTORY

EXAMINATION

FOOD ALLERGY IN CHILDREN

DIAGNOSIS OF ALLERGIC DISEASE

HISTORY

EXAMINATION

INVESTIGATION

SENSITISATION

IgE – skin prick test, RAST (Specific IgE)

Sensitisation v Allergy

Basophil histamine release

Epitopes/ Peanut Ara h2 / Hazelnut

T cell stimulation

IgG4 testing ??????????

FOOD ALLERGY IN CHILDREN

DIAGNOSIS OF ALLERGIC DISEASE

HISTORY

EXAMINATION

INVESTIGATION

SENSITISATION

IgE – skin prick test, RAST (Specific IgE)

Sensitisation v Allergy

Basophil histamine release

Epitopes / Peanut Ara h2 / Hazelnut

T cell stimulation

FOOD ALLERGY IN CHILDREN

DIAGNOSIS OF ALLERGIC DISEASE

HISTORY

EXAMINATION

INVESTIGATION

SENSITISATION

CHALLENGE

Food, Drug, Vaccine, Pollen, Venom, Dander
(Open, Blinded, DBPCFC)

FOOD ALLERGY IN CHILDREN

MANAGEMENT

Avoidance

Plan of action

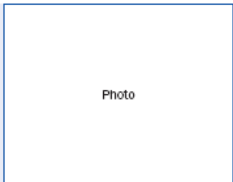
Review

FOOD ALLERGY IN CHILDREN

ACTION PLAN FOR Allergic Reactions

Name: _____

Date of birth: _____



Photo

Allergens to be avoided:

Family/carer name(s):

Work Ph: _____

Home Ph: _____

Mobile Ph: _____

Plan prepared by:

Dr _____

Signed _____

Date _____

MILD TO MODERATE ALLERGIC REACTION

- swelling of lips, face, eyes
- hives or welts
- tingling mouth, abdominal pain, vomiting

ACTION

- stay with person and call for help
- give medications (if prescribed)
- contact family/carer



Watch for any one of the following signs of Anaphylaxis

ANAPHYLAXIS (SEVERE ALLERGIC REACTION)

- difficult/noisy breathing
- swelling of tongue
- swelling/tightness in throat
- difficulty talking and/or hoarse voice
- wheeze or persistent cough
- loss of consciousness and/or collapse
- pale and floppy (young children)

ACTION

- 1 Call Ambulance If there are any signs of anaphylaxis - telephone 000 (Aus) or 111 (NZ)
- 2 Lay person flat and elevate legs. If breathing is difficult, allow to sit but do not stand
- 3 Contact family/carer

Additional information

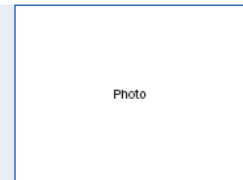


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www.allergy.org.au

ACTION PLAN FOR Anaphylaxis

Name: _____

Date of birth: _____



Photo

Allergens to be avoided:

Family/carer name(s):

Work Ph: _____

Home Ph: _____

Mobile Ph: _____

Plan prepared by:

Dr _____

Signed _____

Date _____

How to give EpiPen® or EpiPen® Jr



1. Form fist around EpiPen® and PULL OFF grey cap.



2. Place black end against outer mid-thigh (with or without clothing).



3. Push down HARD until a click is heard or felt and hold in place for 10 seconds.



4. Remove EpiPen® and be careful not to touch the needle. Massage the injection site for 10 seconds.

MILD TO MODERATE ALLERGIC REACTION

- swelling of lips, face, eyes
- hives or welts
- tingling mouth, abdominal pain, vomiting

ACTION

- stay with person and call for help
- give medications (if prescribed)
- locate EpiPen® or EpiPen® Jr
- contact family/carer



Watch for any one of the following signs of Anaphylaxis

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- swelling of tongue
- swelling/tightness in throat
- difficulty talking and/or hoarse voice
- wheeze or persistent cough
- loss of consciousness and/or collapse
- pale and floppy (young children)

ACTION

- 1 Give EpiPen® or EpiPen® Jr
- 2 Call ambulance* - telephone 000 (Aus) or 111 (NZ)
- 3 Lay person flat and elevate legs. If breathing is difficult, allow to sit but do not stand
- 4 Contact family/carer
- 5 Further EpiPen® doses may be given if no response after 5 minutes

If in doubt, give EpiPen® or EpiPen® Jr

EpiPen® Jr is generally prescribed for children aged 1-5 years.
*Medical observation in hospital for at least 4 hours is recommended after anaphylaxis.

Additional information



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FOOD ALLERGY IN CHILDREN

PREVENTION

Avoidance

Early introduction solids

Breast feeding & introduce solids

Which formula?

ASCIA guidelines

www.allergy.org

FOOD ALLERGY IN CHILDREN

- Breastfeeding during the period that foods are first introduced may help prevent the development of allergy to those foods
- Breastfeeding recommended for up to 6/12
- Hydrolysed formulas may reduce risk of allergic disease in high risk infants
- Infants unlikely to develop a new allergy to any milk already tolerated, if given regularly
- Exclusion of allergenic foods from the maternal diet not shown to prevent allergies

FOOD ALLERGY IN CHILDREN

- little evidence delaying introduction of solid foods > 6 months reduces risk of allergy.
- suggestions - delaying introduction of foods may actually increase allergy- not proven.
- insufficient evidence -support delay or avoidance of potentially allergenic foods for the prevention of food allergy or eczema.
- “Windows of opportunity/susceptibility

FOOD ALLERGY IN CHILDREN

TREATMENT

- Allergen immunotherapy
 - Temporary desensitisation
 - Or
 - True immune tolerance
- Chinese herbal
- IgE reduction (Omalizumab)
- Other

ANAPHYLAXIS

- 1. Acute onset of an illness** (minutes to several hours)
involvement of the skin, mucosal tissue, or both generalized hives, pruritis or flushing, swollen lips-tongue-uvula)

AND AT LEAST ONE OF THE FOLLOWING:

- a. Respiratory compromise**

dyspnoea, wheeze bronchospasm, stridor, reduced peak expiratory flow (PEF), hypoxemia

- b. Reduced blood pressure (BP)**

hypotonia (collapse), syncope, incontinence]

ANAPHYLAXIS

2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):

- **Involvement of the skin-mucosal tissue**
- **Respiratory compromise** (e.g. dyspnoea, wheeze bronchospasm, stridor, reduced PEF, hypoxemia)
- **Reduced BP or associated symptoms** (e.g. hypotonia (collapse), syncope, incontinence)
- **Persistent gastrointestinal symptoms** (e.g. crampy abdominal pain, vomiting)

ANAPHYLAXIS

3) Reduced BP after exposure to known allergen for that patient (minutes to several hours):

(a) Infants and children:

- low systolic BP (age specific)
- or
- greater than 30% decrease in systolic BP
(low systolic blood pressure for children is defined as:
less than 70mmHg from 1 month to 1 year;
Less than $[70\text{mmHg} \times (\text{age}^2)]$ from 1 to 10 years,
and less than 90mmHg from 11 to 17 years)

(b) Adults:

- systolic BP of less than 90mm Hg
- or
- greater than 30% decrease from that person's baseline

ANAPHYLAXIS

Reasons for potential overdiagnosis of anaphylaxis (Especially retrospectively)

- Subjective symptoms only
- Nonspecific signs
- Diagnostic error
- Hyperventilation
- Anxiety
- Panic attack (difficulty breathing)
- Vasovagal episode (faint)
- Munchausen syndrome / proxy (in a child)
- Scombroidosis
- Anisakiasis

ANAPHYLAXIS

Reasons for potential underdiagnosis of anaphylaxis

- First episode
- Trigger not apparent, hidden, or not previously recognized
- Idiopathic anaphylaxis

Failure to recognize (by patient or caregiver) because of:

- Cognitive, visual or auditory impairment
- Neurologic, psychiatric, or psychologic problems*
- Use of medications, including sedating H1-antihistamines or recreational drugs, or use of ethanol

Failure to diagnose (by health care professional) because

- Absence of skin symptoms and signs
- Patient not undressed or fully examined
- Vulnerable person: infant, elderly
- Patient who cannot describe subjective symptoms :
 - Aphonic or dysphonic
 - Dyspneic
 - Unconscious
- **Atypical**

ANAPHYLAXIS

- **Risk factors for fatal food-induced anaphylaxis**
 - Coexistent asthma (90–100% of fatalities),
 - age more than 10 years at the time of the fatal anaphylaxis episode (54– 65% of fatalities),
 - absence of or delayed access to an adrenaline auto-injector (80–87% of fatalities),
 - Peanut or tree nut allergy (38–81% of fatalities).
- Liew et al. reported risk factors for drug-induced anaphylaxis deaths as
 - elderly age group (75% of fatalities were aged 55–85 years),
 - the presence of cardiovascular (33% of fatalities) or respiratory (17% of fatalities) comorbidity.
 - No specific risk factors for fatality due to insect sting anaphylaxis were identified other than male predominance (95% males) [15].
- Simon and Mulla [25] reported risk factors associated with 89 fatal episodes of anaphylaxis identified over a 10-year period.
 - Older individuals,
 - in an emergency department
 - Months March, April, July, and August [25].

ANAPHYLAXIS

- **Prompt administration of adrenaline**

ADRENALINE AUTOINJECTORS Available in Australia are:

EpiPen, EpiPen Jr, Anapen, Anapen Jr

- 150 mcg (Junior) for children between 10 to 20 kg
- 300 mcg for children and adults over 20 kg (Not 30 kg)
- Not usually recommended for children less than 10kg

** These are based on expert opinion which is at variance with the approved product information

ANAPHYLAXIS

- . **IMPORTANT:** An adrenaline autoinjector should only be prescribed within the context of a comprehensive **ANAPHYLAXIS MANAGEMENT PLAN**

ANAPHYLAXIS MANAGEMENT PLAN

An EpiPen should only be prescribed within the context of a comprehensive anaphylaxis management plan that includes the following

REFERRAL TO AN ALLERGY SPECIALIST

ANAPHYLAXIS

Review by an allergy specialist should occur to;

- Ascertain if the correct trigger(s) have been identified
- Determine whether the allergy persists
- Provide re-education on EpiPen use
- Renew action plan
- Ensure the EpiPen has not expired.

ANAPHYLAXIS

- **1. ADRENALINE AUTOINJECTOR RECOMMENDED**
- History of anaphylaxis* (if patient is considered to be at continuing risk)

ANAPHYLAXIS

2. ADRENALINE AUTOINJECTOR **MAY** BE RECOMMENDED

History of a generalised* allergic reaction with one or more of the following factors:

Asthma - concurrent or past history

Age

- Adolescents and young adults have a greater risk of fatal food anaphylaxis. The majority of recorded fatal reactions to foods (~90%) occur in children over the age of 5 years.
- Adults have a greater risk of fatal stinging insect anaphylaxis than children.

Specific allergic triggers

Nut allergy (to peanuts or other nuts) - Most deaths from food anaphylaxis occur from nuts. Generalised allergic reactions can be triggered by exposure to trace or small amounts of nuts, which can be difficult to avoid. Subsequent allergic reactions to nuts may be unpredictable.
Stinging insect allergy (Bees, wasps, Jumper ants) in adults

Co-morbid conditions - Ischaemic heart disease

Limited access to emergency medical care - In remote locations early administration of adrenaline may not be possible unless an EpiPen is available.

These factors should be considered when deciding whether an EpiPen is prescribed, as they are known risk factors for more severe or fatal reactions.

ANAPHYLAXIS

3. ADRENALINE AUTOINJECTOR **NOT NORMALLY** RECOMMENDED

Asthma - in patients with asthma without anaphylaxis or generalised allergic reactions

Elevated specific IgE only (positive RAST and/or skin test) without a history of clinical reactions -
Positive test results alone do not necessarily mean there is allergic disease. These patients may be referred to an allergy specialist for assessment of their risk of allergy and anaphylaxis. This may include further investigations such as challenge testing.

Family (rather than personal) history of anaphylaxis or allergy
Whilst the risk for allergic disease is inherited, anaphylaxis is not inherited.

Local reactions to insect stings in adults and children

Generalised skin rash (only) to bee or wasp stings in children
Prospective follow-up studies of subsequent bee stings in children presenting with local reactions or generalised skin rash (only) show that these children are at a very low risk of experiencing anaphylaxis with subsequent stings.

Resolved food allergy

ANAPHYLAXIS

IDENTIFICATION OF THE ANAPHYLACTIC TRIGGER(S)

history, clinical examination, appropriate use and interpretation of allergy testing.

EDUCATION ON THE AVOIDANCE OF TRIGGER(S)

This is particularly important with food anaphylaxis.

PROVISION OF AN ANAPHYLAXIS ACTION PLAN

This should document the following;

Name of child/adult

Allergic triggers

Carer contact details

Symptoms and signs indicating when to use the EpiPen

Instructions on how to use the EpiPen.

Anaphylaxis action plans for EpiPen use can also be located at www.allergy.org.au

ANAPHYLAXIS

- Schools?
- Siblings
- Travel
- ASCIA e Training

ANAPHYLAXIS

- Prompt administration of adrenaline
- EpiPen or Anapen
- 150 mcg (Junior) to 20 kg
- 300 mcg above 20 kg (Not 30 kg)
- Antihistamines ?
- Corticosteroids ?
- Glucagon ?
- Fluid replacement ?

ANAPHYLAXIS

- Tryptase/mast cell disease
- PAF PAF acetylhydrolase
- Nitric oxide
 - Arginine vasopressin
 - Methylene blue

ALLERGEN IMMUNOTHERAPY

Specific immunotherapy, also called allergen immunotherapy,

Inducing allergen-specific T regulatory cells that reduce the late-phase response to the allergen

During a period of years, specific immunotherapy also reduces the specific IgE-antibody response, but that is not thought to be the basis of clinical efficacy. In parallel, specific immunotherapy typically induces an allergen-specific IgG response. The IgG response is probably driven by interleukin-10 generated as part of the regulatory T-cell response.

SCIT 100 years.

Pollens, mites, bee & wasp venom

SLIT

Indications

Efficacy

Safety

Contraindications

ALLERGEN IMMUNOTHERAPY



ALLERGEN IMMUNOTHERAPY

SCIT 100 years.

- Pollens, mites, bee & wasp venom
- Efficacy is usually partial, and patients continue to need to use some drugs for the relief of symptoms.
- Adverse reactions are well recognized.
- Most are minor but death from anaphylaxis, occur each year. (1 death / 2.5 million injections)
- Logistical - injections have to be given in a doctor's office by someone familiar with injection immunotherapy and with managing anaphylaxis.
- Patients have to stay in the doctor's office for at least 30 minutes after each injection. Many potential patients are unable to find the time for injections.

ALLERGEN IMMUNOTHERAPY

- For either form of specific immunotherapy, the patient's symptoms must be shown to be due to one or a few dominant allergens.
- These allergens are then selected for immunotherapy with the expectation that the patient will not have substantial residual disease caused by other allergies.
- If the patient's symptoms are due to multiple or poorly defined allergens, then he or she will probably do better with pharmacotherapy, which should deal with symptoms regardless of which allergen is responsible.
- There are some differences of perspective in this regard between allergists in the United States, who tend to view all sensitizations as being relevant, and European allergists, who tend to focus on allergens with the highest degree of sensitization.

ALLERGEN IMMUNOTHERAPY

- **SUBLINGUAL IMMUNOTHERAPY**
- (Sublingual, swallow)
- local irritation in the mouth and under the tongue; 47% and 52%.
- Local pruritus affects about 50% of all patients, but it is usually transient and does not progress to anaphylaxis. (50% chance that this side effect will disappear within 8 days after treatment)
- Other local side effects reported occasionally include ear pruritus, palatal edema, and throat irritation. If troublesome, these side effects may be managed by empirical premedication with antihistamines.
- No systemic allergic reactions were reported in the clinical trials of commercial airborne-allergen extracts.
- 3 case reports of anaphylaxis after sublingual immunotherapy. None of these reactions occurred with the commercially available grass-pollen tablet. Two reports describe anaphylaxis after administration of individualized mixtures of allergens the third case was reported in a trial of sublingual immunotherapy for an allergy to latex.

ALLERGEN IMMUNOTHERAPY

SLIT precautions

- Side effects
- Vaccination
- Febrile illness
- Mouth wounds
- Asthma attack or worsening.

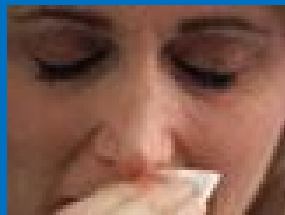
Clinical study VO53.06

A study designed from the outset to evaluate the long-term efficacy and safety of pre- and co-seasonal daily administration of a sublingual 5-grass pollen extract tablet in adult patients suffering from grass-pollen-induced allergic rhinoconjunctivitis

Evaluation criteria (1/2)

- Primary efficacy endpoint:
- the Average Adjusted Symptom Score (AAAdSS*, the rhinoconjunctivitis total symptom score adjusted for rescue medication use) over the grass pollen period.

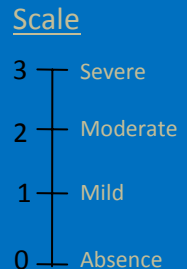
The 6 individual rhinoconjunctivitis symptom scores:



- sneezing
- rhinorrhoea
- nasal pruritus
- nasal congestion



- watery eyes
- ocular pruritus



Authorized rescue medications:

- Antihistamines (eye drops and/or oral)
- Corticosteroids (nasal)
- Corticosteroids (oral)

Evaluation criteria (2/2)

- Secondary efficacy endpoints:
 - Average Combined score (ACS)
 - Rescue medication score (RMS)
 - antihistamines (oral and/or eye drops) = 1 point*
 - nasal corticosteroids = 2 points*
 - oral corticosteroids = 3 points*
 - Individual symptoms scores
 - Quality of life
 - Immunological markers (IgG₄)
 - Skin Prick Test
 - Safety

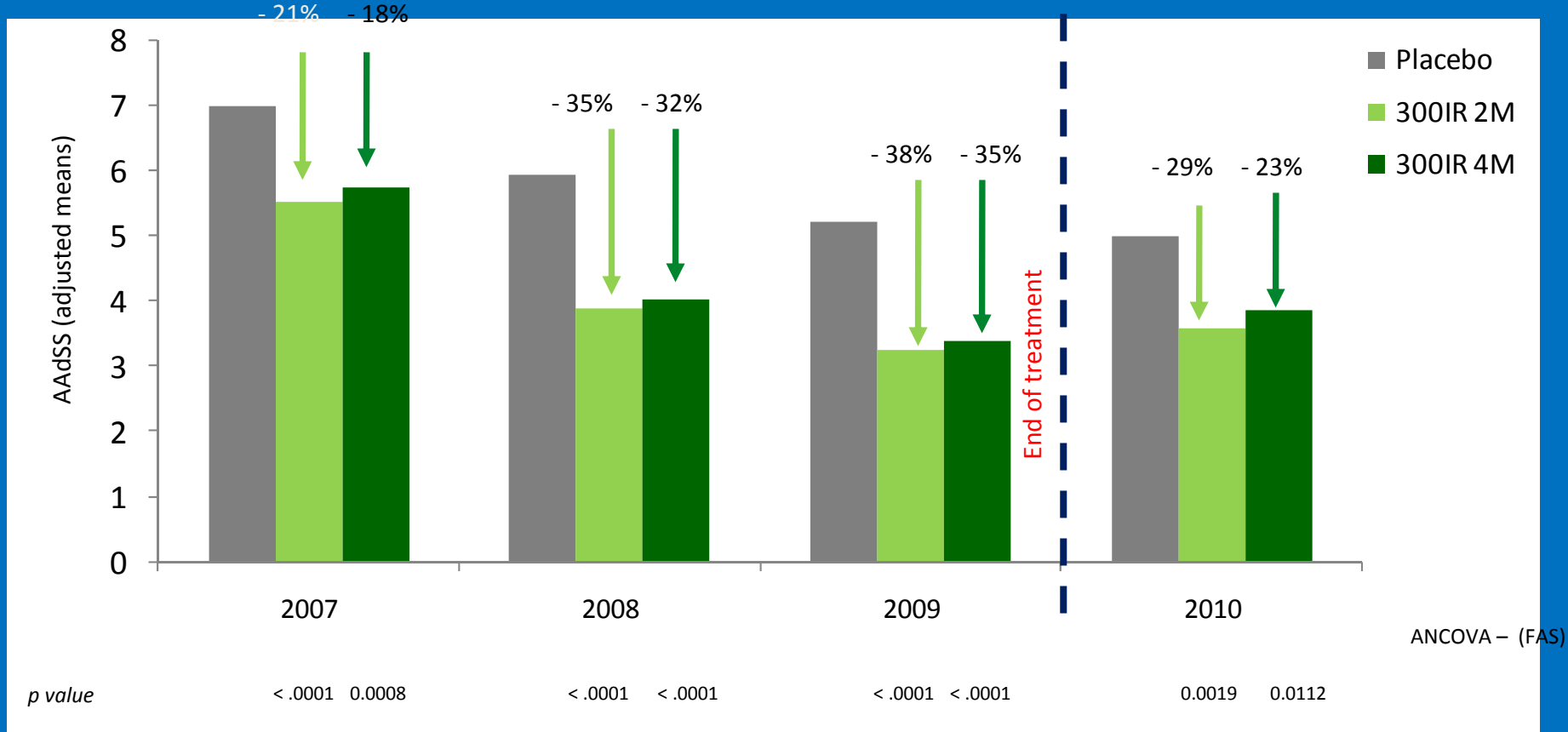
Results

Primary efficacy endpoint (AAdSS)

Seasons 1 to 4

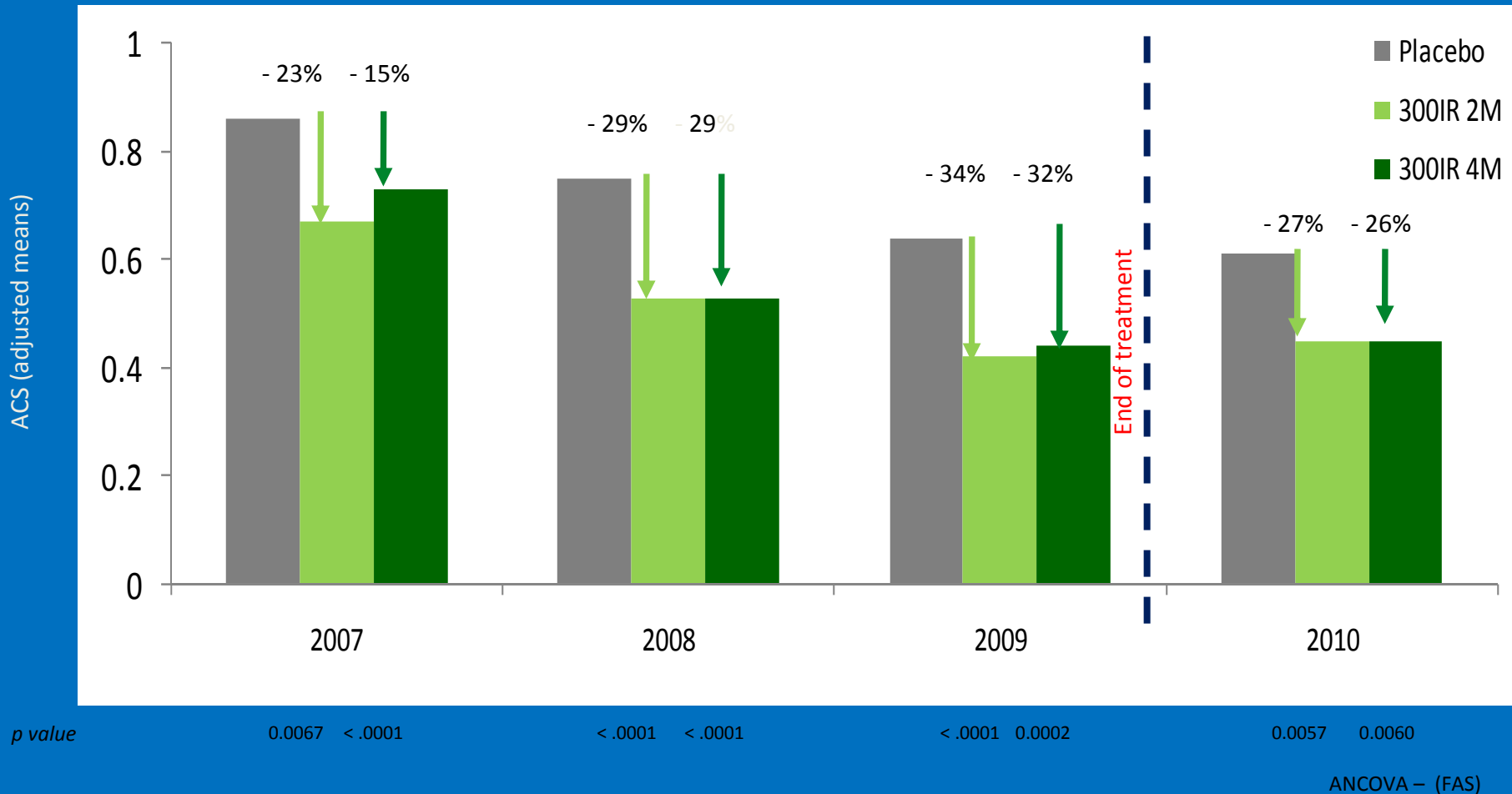
Primary efficacy endpoint: AAdSS

Pollen season - years 1 to 4



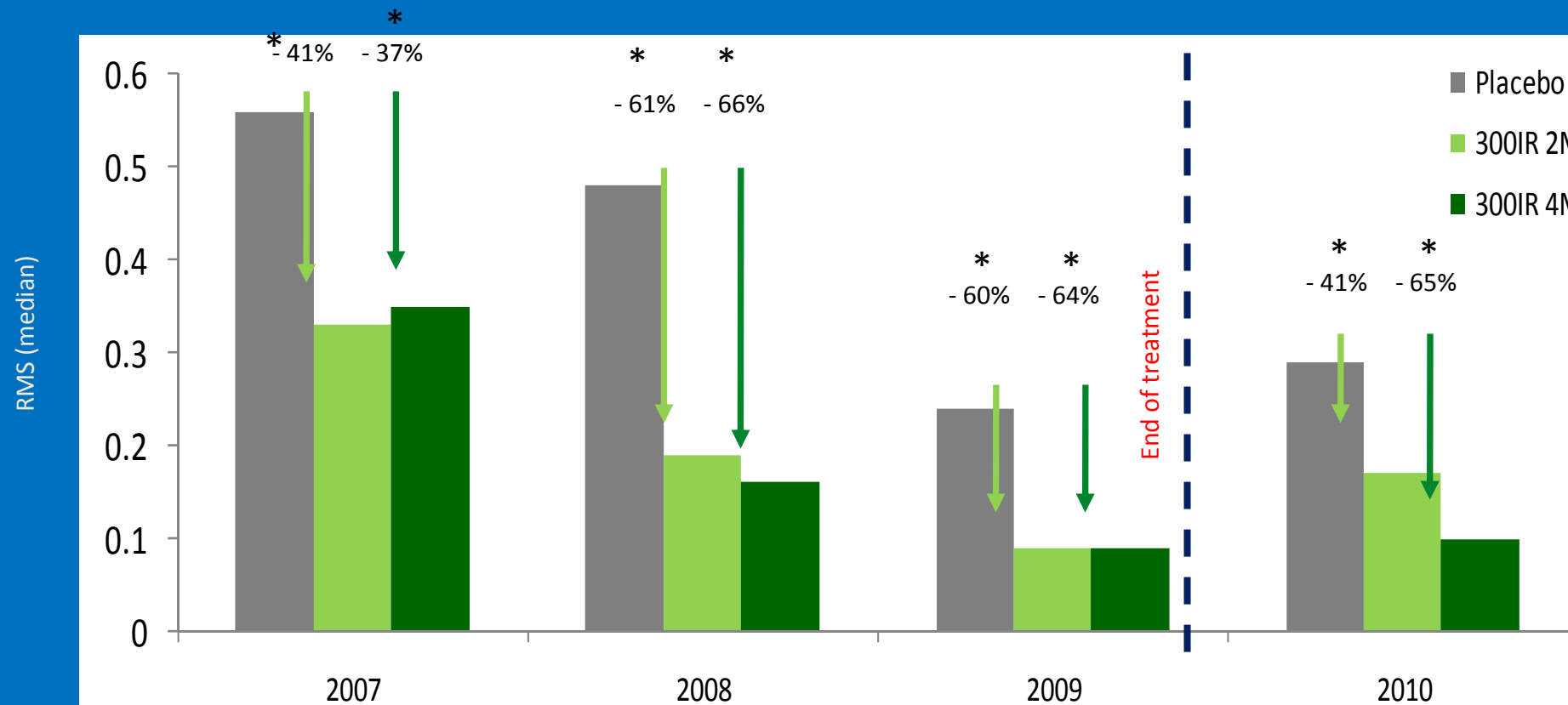
- From the first season on, significant difference between active and placebo
- Continued efficacy following cessation of the treatment

Average Combined Score (ACS): Worst Pollen Period - years 1 to 4



- The Average Combined Score results are consistent with the Average Adjusted Symptom Score throughout the 4 years at worst pollen period.

Rescue Medication score Pollen season - year 1 to 4

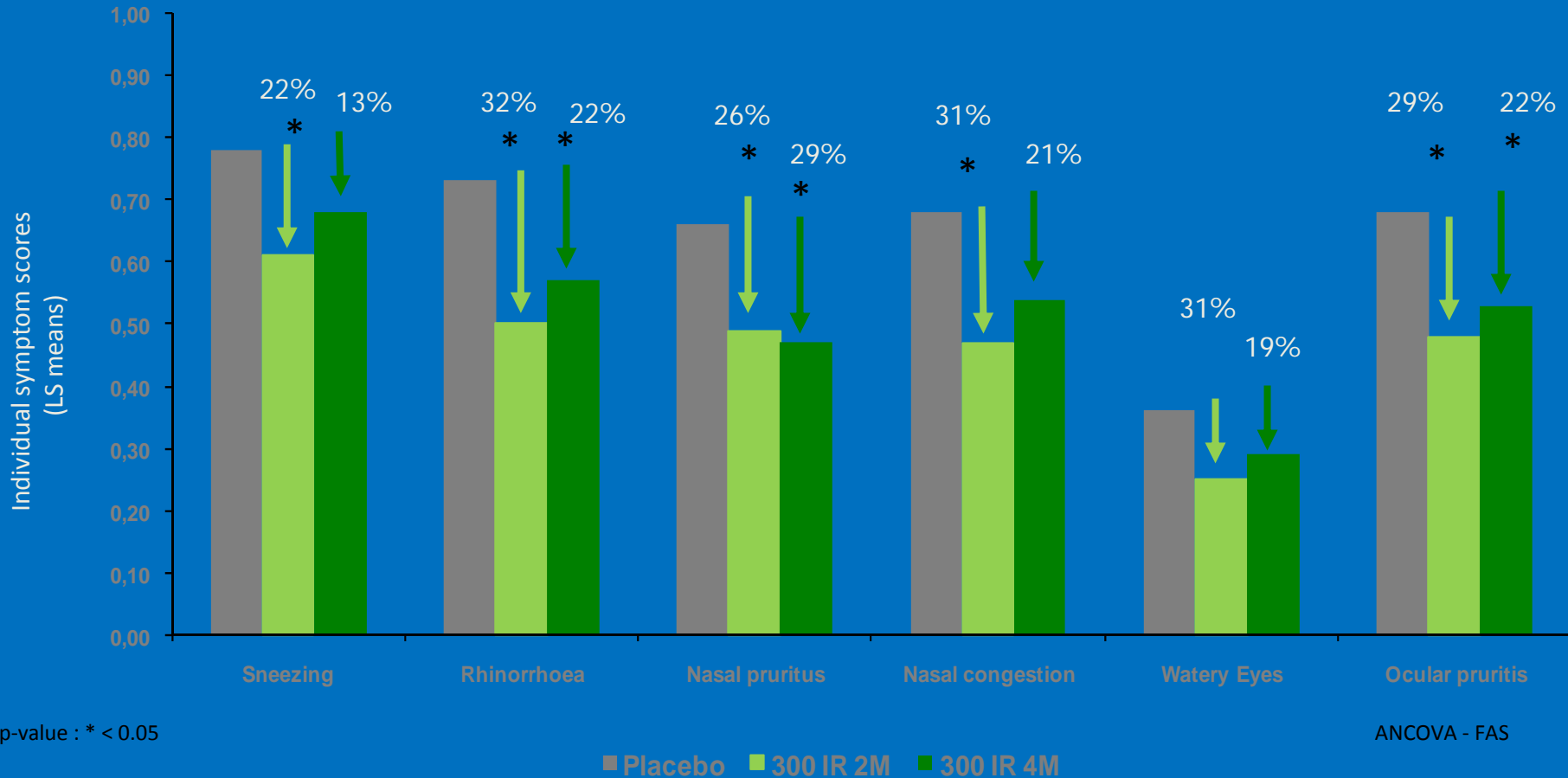


p-value: * < 0.05

ANCOVA – (FAS)

- In both active arms, rescue medication use remained significantly reduced one year following treatment cessation

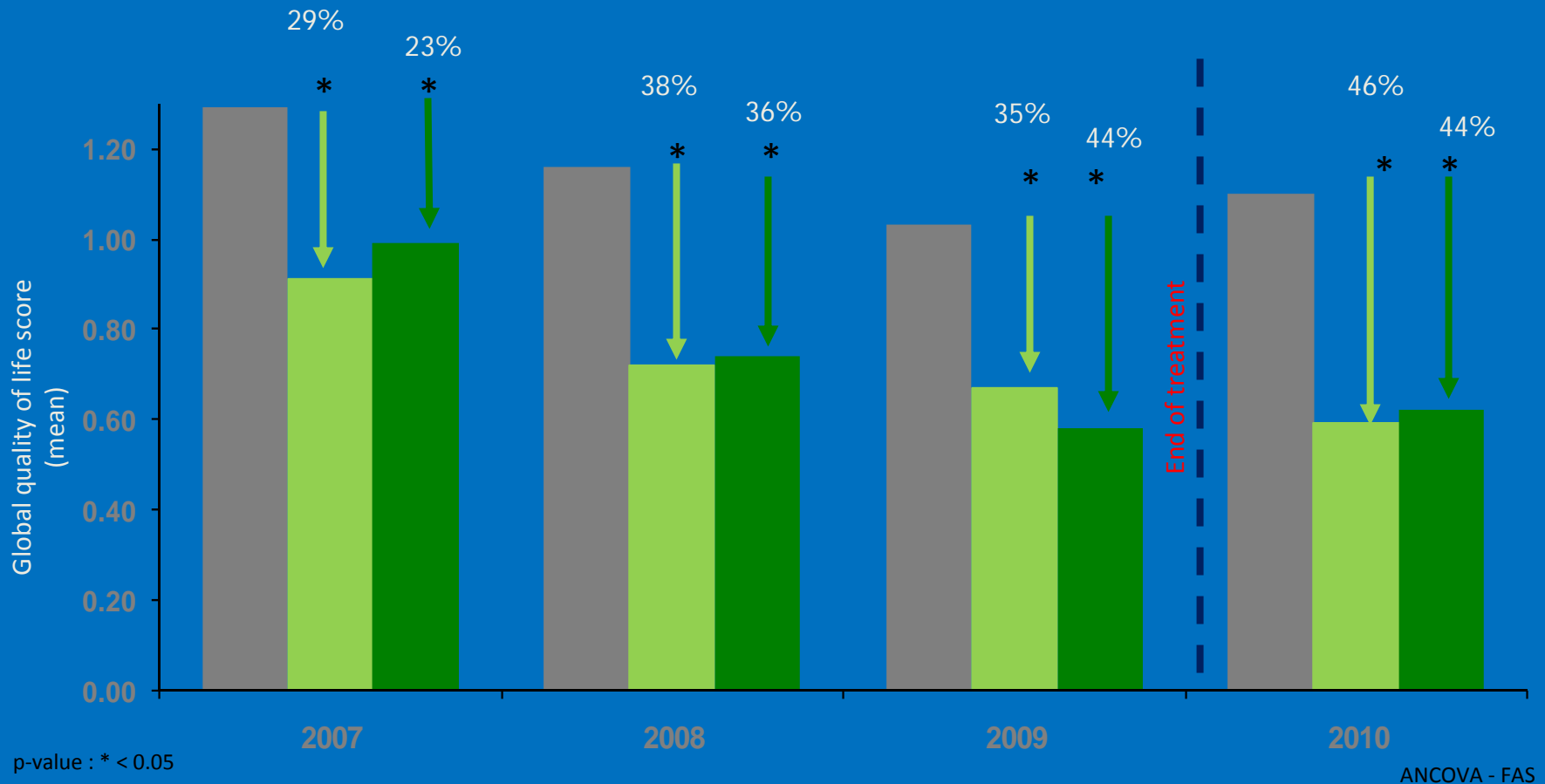
Individual symptom scores Pollen season – year 4



- 1 year after treatment cessation, a sustained effect was observed across individual symptoms.

Quality of life

Pollen season – years 1 to 4



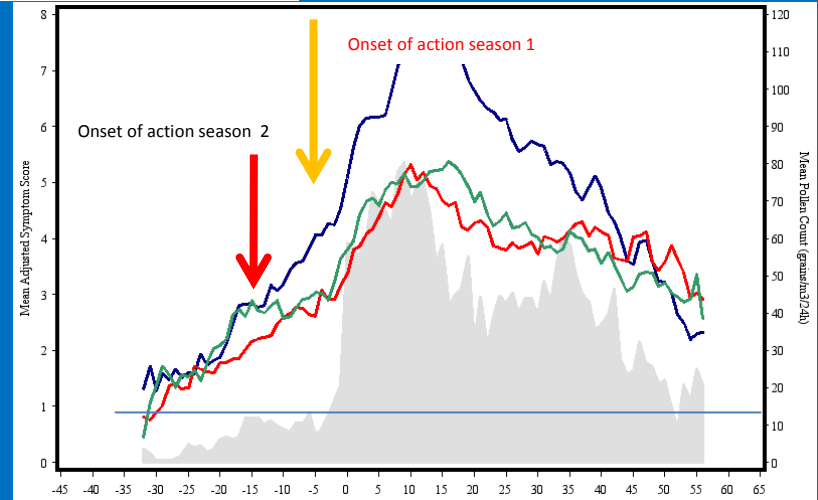
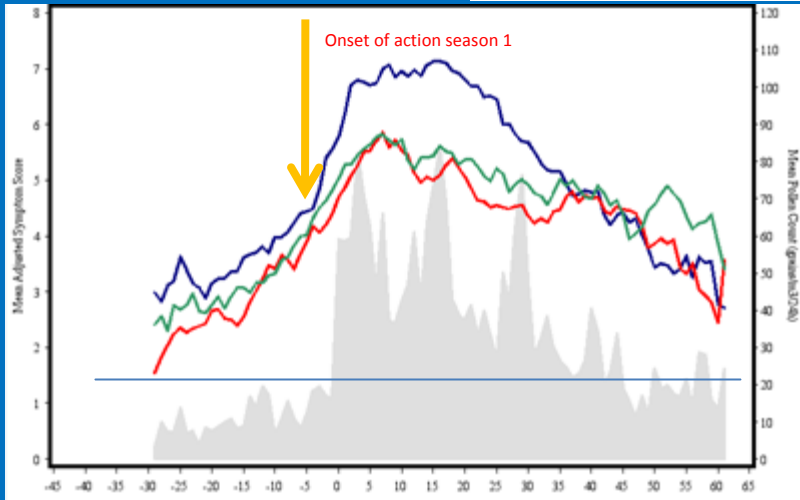
- The statistically significant improvement in quality of life was observed in each pollen season and persisted in the year following treatment cessation.

Treatment effect earlier in subsequent pollen seasons

AdSS – Pollen season - years 1 to 4 - FAS

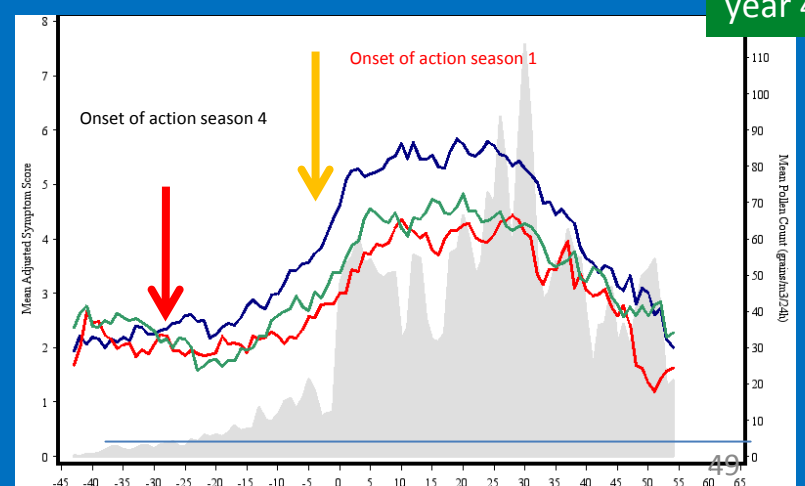
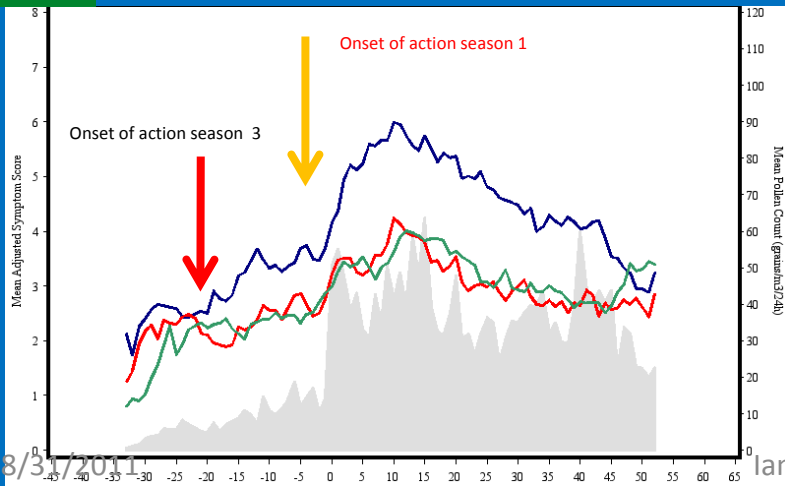
year 1

year 2

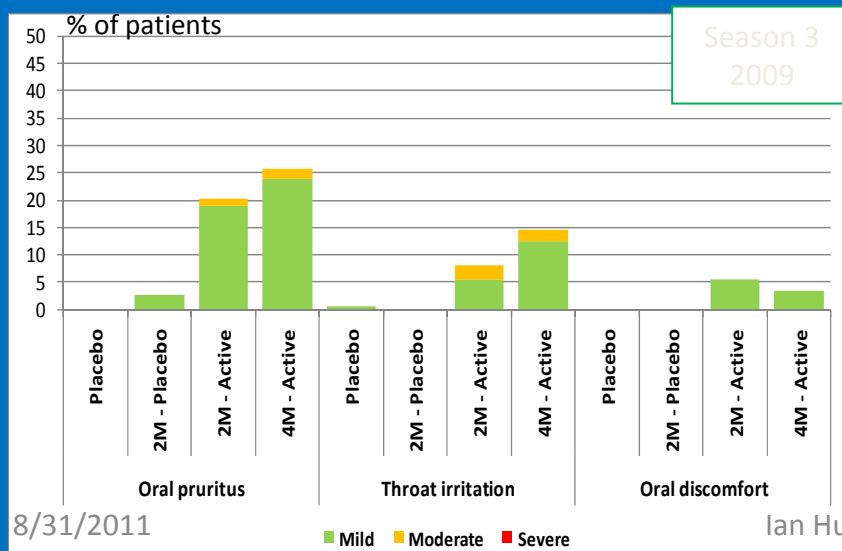
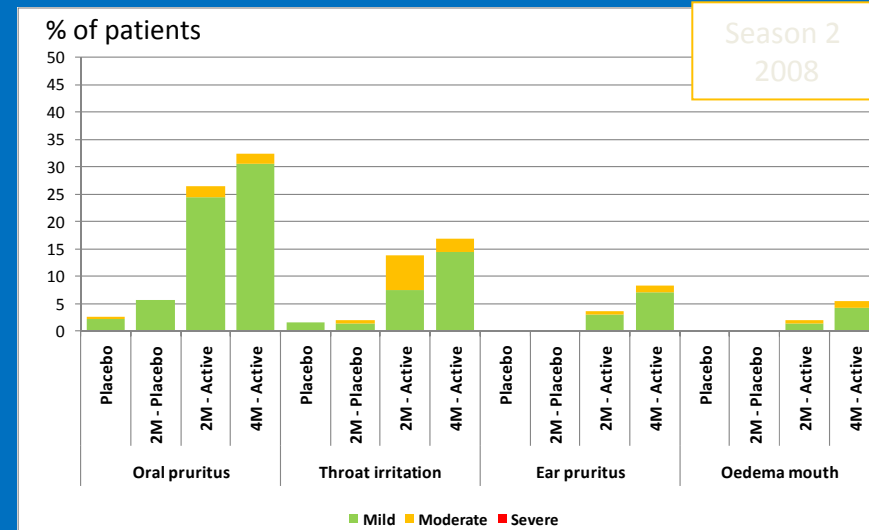
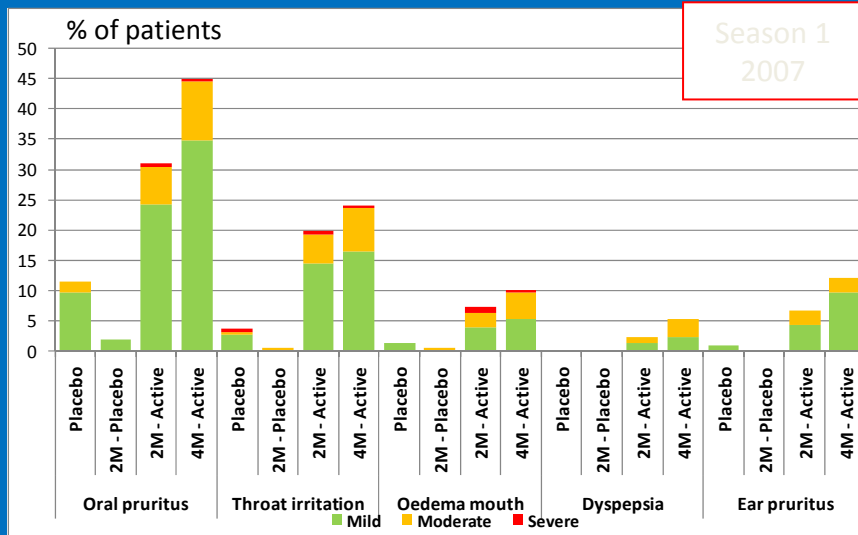


year 3

year 4



Treatment Emergent Adverse Events ($\geq 5\%$ in any treatment group)



Compared with treatment at season 1, treatment at seasons 2 and 3 showed a progressive:

- ✓ Decrease in the incidence of AE
- ✓ Decrease in the intensity of AE

Conclusions

- Sustained efficacy of the 5 grass SLIT tablet administered pre- and co-seasonally from the first pollen season
- Efficacy increased during the second and third pollen seasons
- Long-term efficacy (in the year following treatment cessation) of an intermittent regimen
- The improvement in quality of life seen throughout the treatment period persisted after treatment cessation
- The 5 grass SLIT tablet was generally well tolerated

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