Rinitis refractaria a tratamiento: ¿Cuales son los siguientes pasos?

Nelson Rosário MD, PhD

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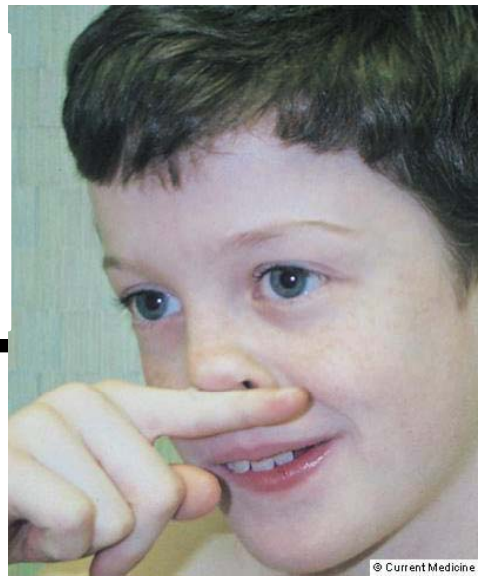
UNIVERSIDADE FEDERAL DO PARANÁ

Allergol Immunopathol (Madr). 2013;41(2):73–85

Allergologia et immunopathologia

www.elsevier.es/ai



ORIGINAL ARTICLE

The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three: A global synthesis

The largest: surveyed children (≈1,200,000), number of centres (233) and countries (98)

	Current asthma	Rhinoconjuntivitis	Eczema
6-7 years	11.7%	8.5%	7.9%
13-14 years	14.1%	14.6%	7.3%

Mallol J et al.

CLINICS 2011;66(9):1573-1577 DOI:10.1590/S1807-59322011000900012

CLINICAL SCIENCE

Is allergic rhinitis a trivial disease?

Dirceu Solé,[I] Inês Cristina Camelo-Nunes,[I] Gustavo F. Wandalsen,[I] Nelson A. Rosário,[II] Emanuel C. Sarinho,[III] Brazilian ISAAC Group

n=46,770 13 -14 y/o

A significant correlation was observed between the prevalence of current asthma and current rhinitis

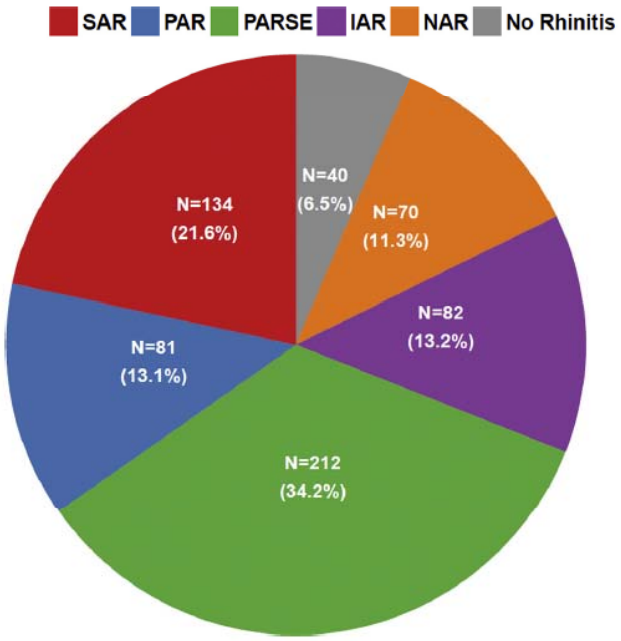
(rs = 0.82; 95%CI: 0.60–0.93, p<0.0001)

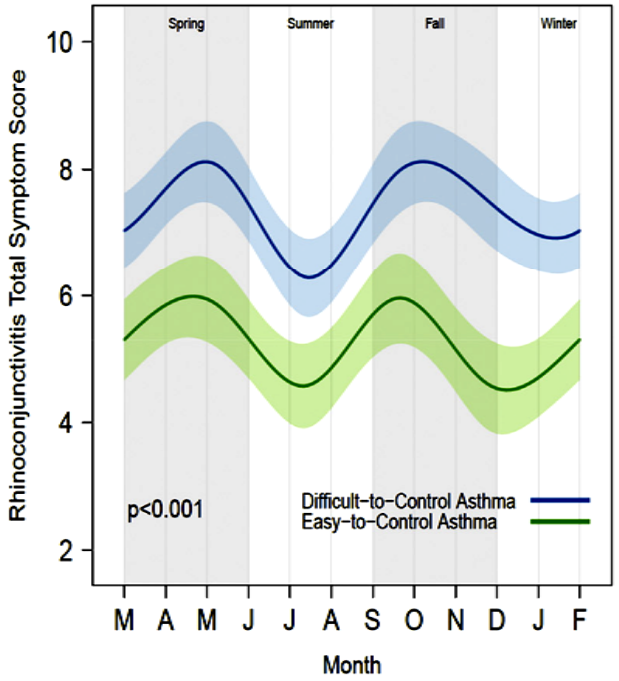
- Wheezing with exercise (OR 2.38- 3.25)
- Nocturnal cough in the last year (OR 2.99- 4.50)

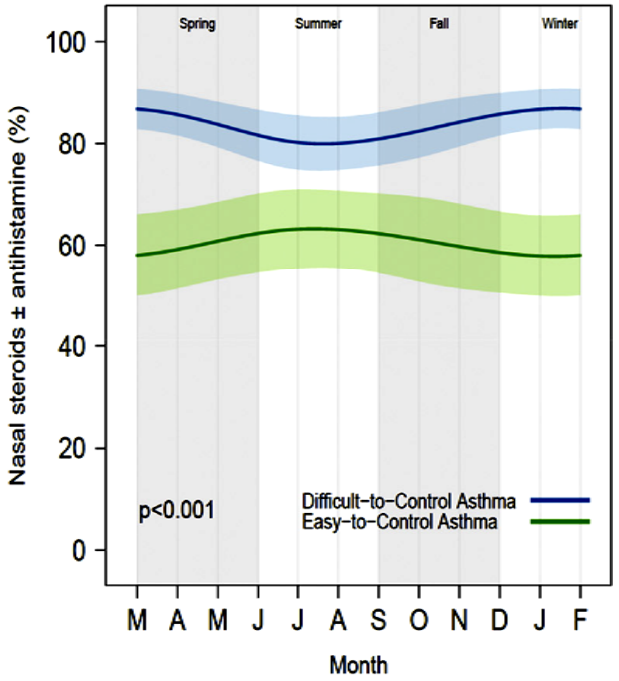
Rhinitis in children and adolescents with asthma: Ubiquitous, difficult to control, and associated with asthma outcomes

Alkis Togias, MD,[a] Peter J. Gergen, MD, MPH,[a] Jack W. Hu, MS,[b] Denise C. Babineau, PhD, MS,[b] Robert A. Wood, MD,[c]

To determine the prevalence of rhinitis and its phenotypes (SPT/IgEs) in urban children and adolescents with asthma (n=619)



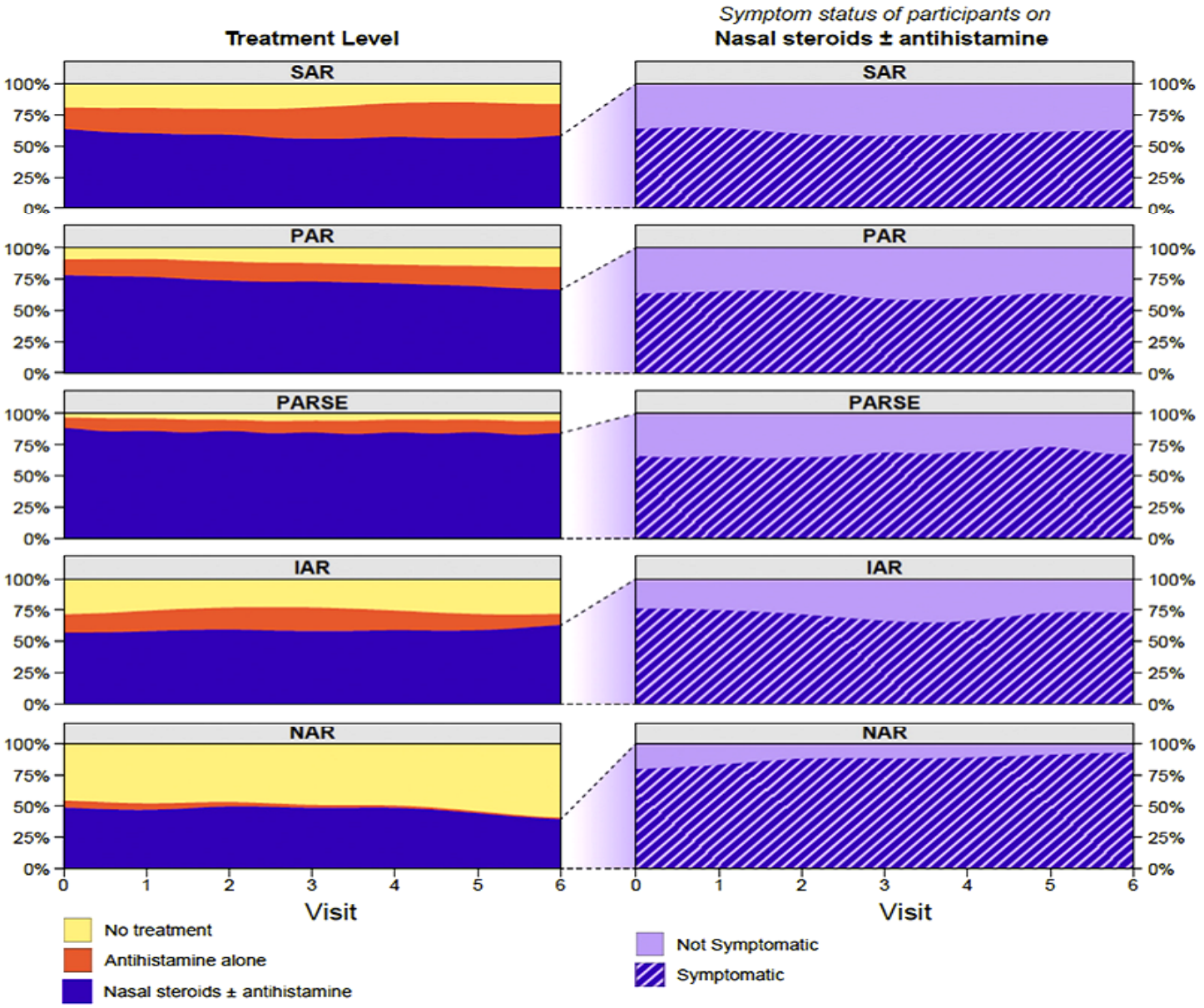




The activity of rhinitis in patients with difficult-to-control asthma was consistently greater

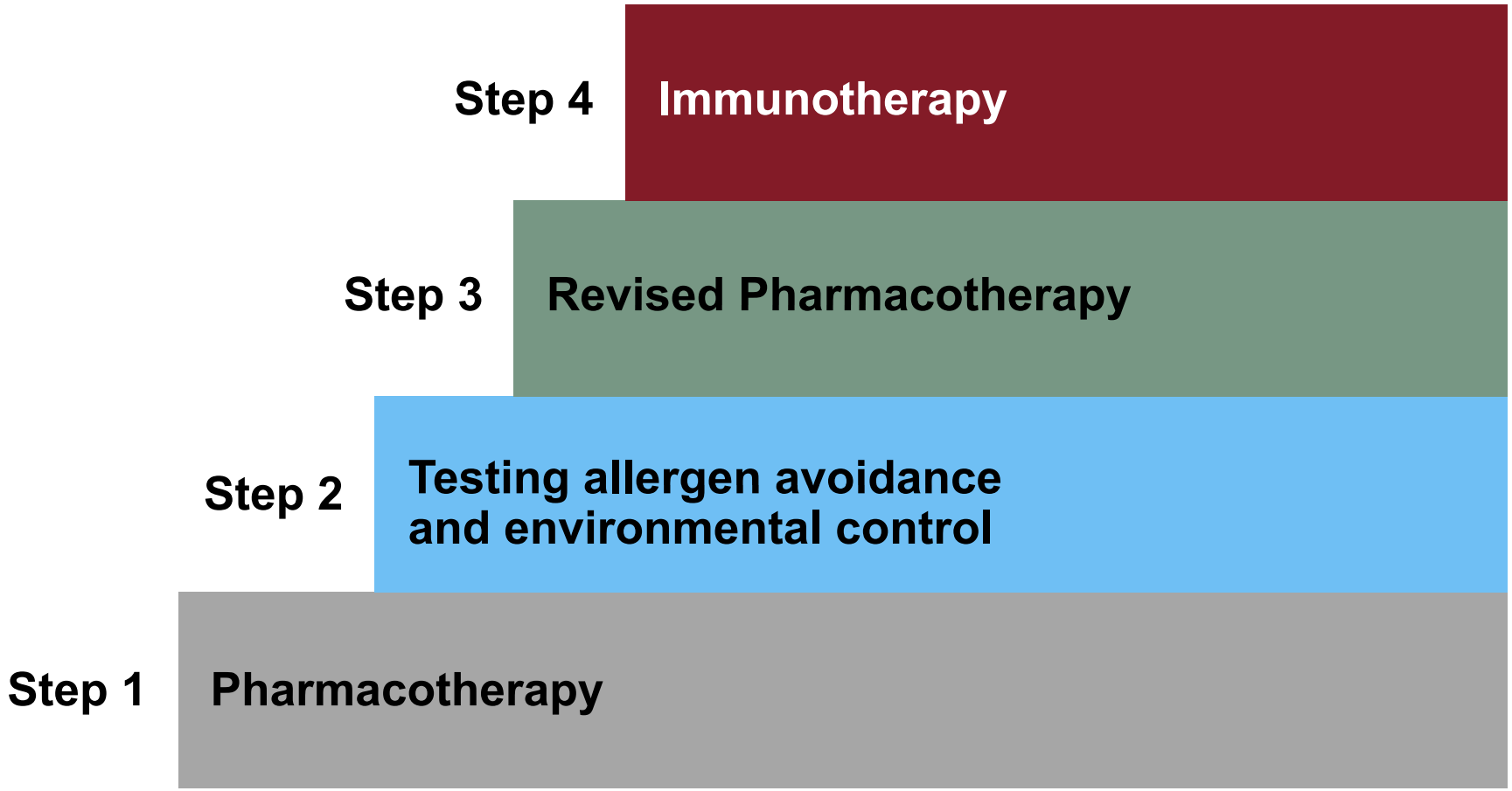
J Allergy Clin Immunol 2019;143:1003-11

Treatment level and control of symptoms



Togias A et al.J Allergy Clin Immunol 2019;143:1003-11

Tratamiento de Rinitis Alérgica en el Mundo Real



Opciones de Fármacos para Rinitis

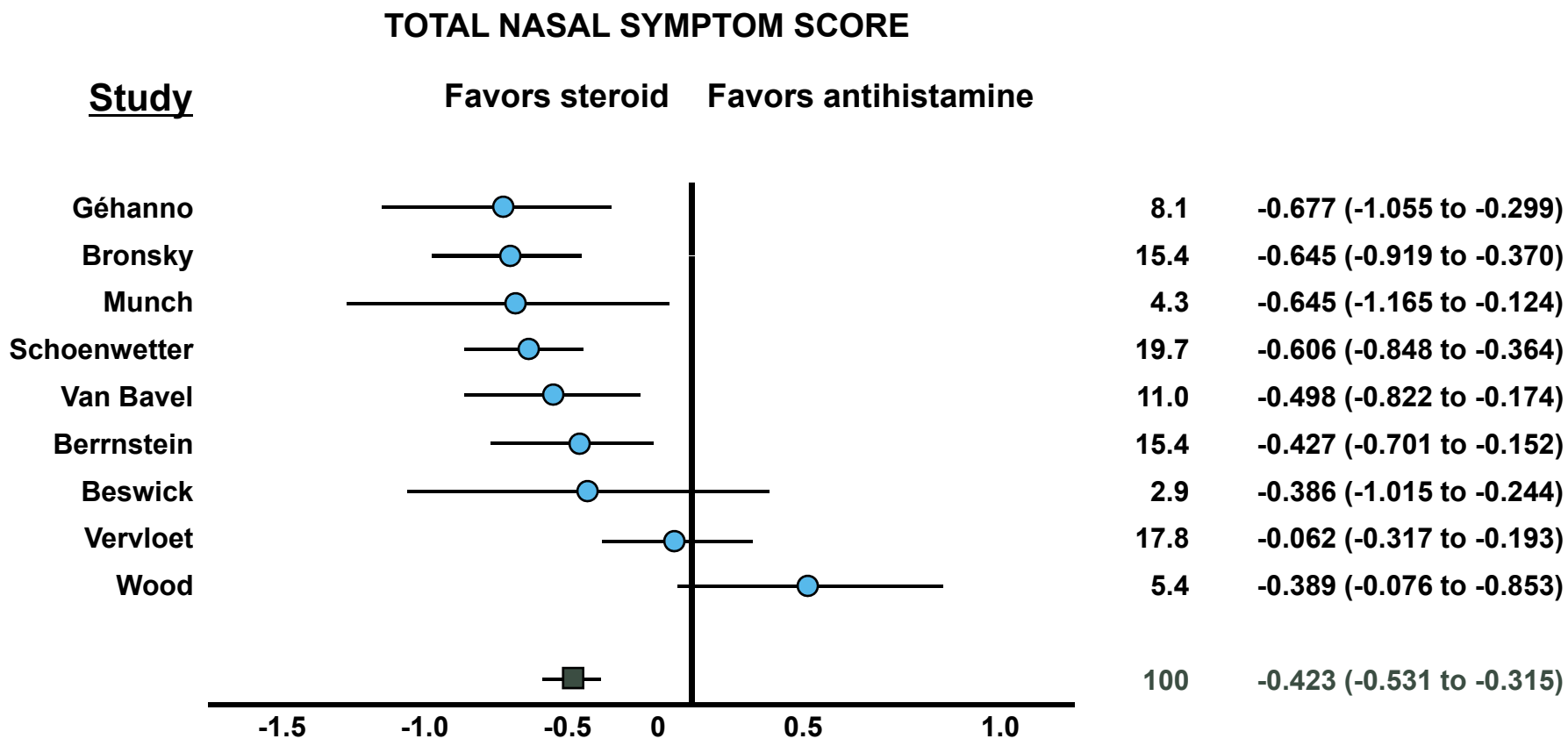
Agent	Sneezing	Itching	Congestion	Rhinorrhea	Ocular
Oral Antihistamine	++	++	+/-	++	++
Nasal Antihistamine	+	+	+/-	+	–
Intranasal Corticosteroid	++	++	++	++	+
Oral Decongestant	–	–	+	–	–
Intranasal Decongestant	–	–	++	–	–
Intranasal Mast Cell Stabilizer	+	+	+	+	–
Topical Anticholinergic	–	–	–	++	–

– provides no benefit + provides modest benefit

+/- provides minimal benefit ++ provides substantial benefit

Adapted with permission from The AAAAI Allergy Report.
http:// www.aaaai.org/ar/working_vol2/001.asp. .

Efficacy of nasal steroids versus antihistamines for nasal symptoms



Weiner JM, et al. *BMJ.* 1998;317:1624.

$X^2 = 26.82$; *df* = 8; *P* < 0.001

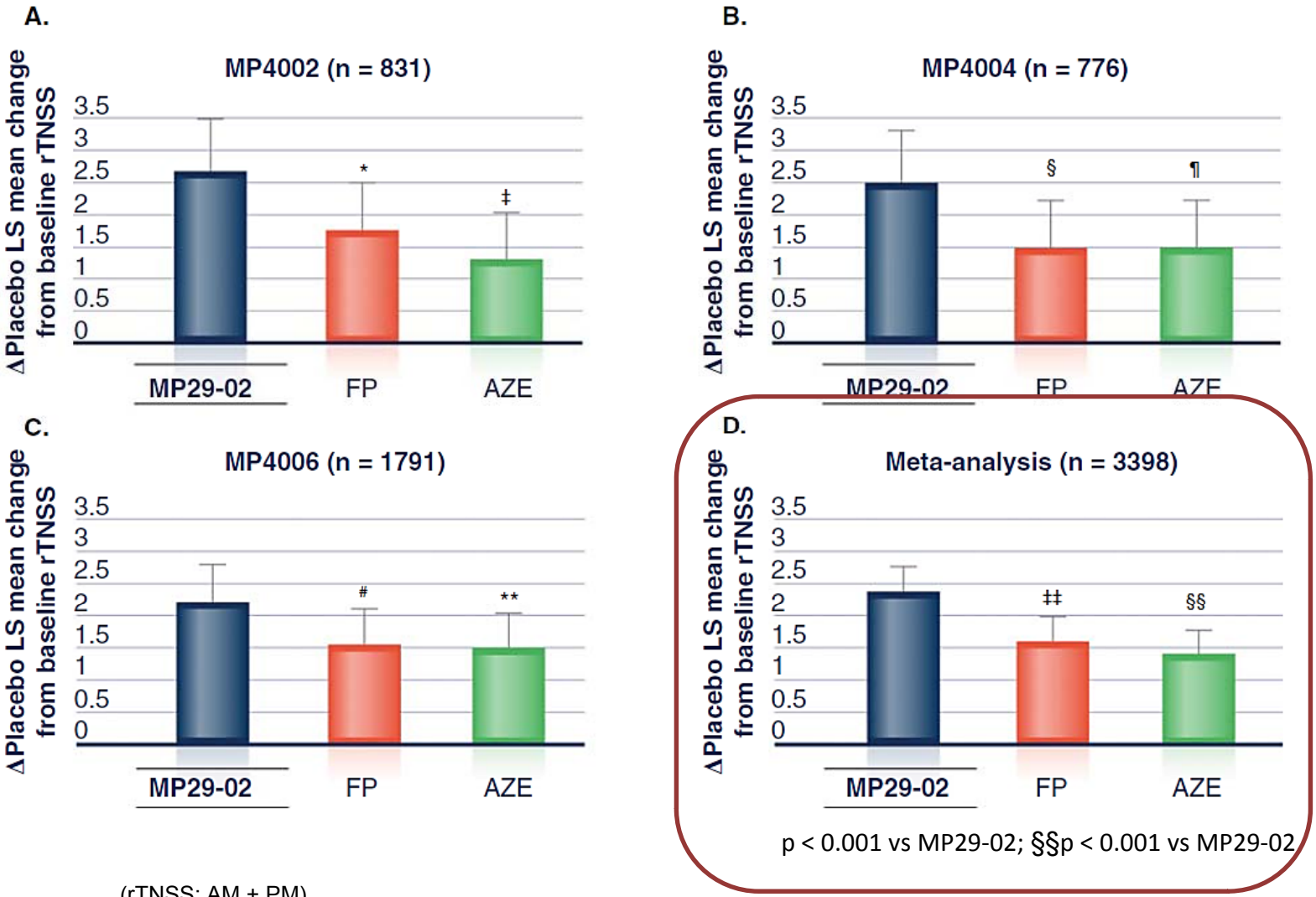
A novel intranasal therapy of azelastine with fluticasone for the treatment of allergic rhinitis

Warner Carr, MD,[a] Jonathan Bernstein, MD,[b] Phil Lieberman, MD,[c] Eli Meltzer, MD,[d] Claus Bachert, MD, PhD,[e] David Price, MD,[f] Ullrich Munzel, PD Dr rer nat,[g] and Jean Bousquet, MD, PhD[h] *Mission Viejo and San Diego, Calif, Cincinnati, Ohio, Memphis, Tenn, Ghent, Belgium, Aberdeen, United Kingdom, Bad Homburg, Germany, and Montpellier, France*

- N=3398, ≥12 años edad, RA sazonal, mod/grave
- 3 estudios multicêntricos, randômicos, controlados placebo y activo, grupos paralelos
- 14 dias de tratamiento en diferentes temporadas
- Variável primária de eficácia:
  rTNSS suma de mañana y noche,
  Variación entre basal y período de tratamiento.

J Allergy Clin Immunol 2012;129:1282-9

Effect of MP29-02 on overall rTNSSs in patients with moderate-to-severe SAR

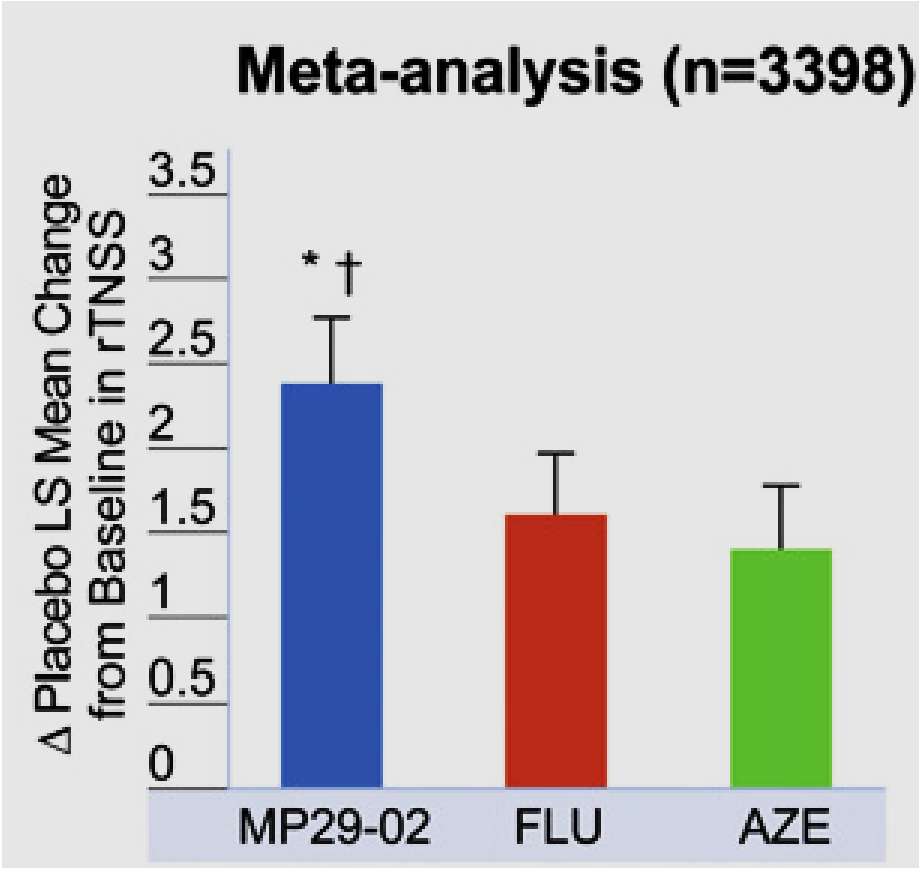


(rTNSS; AM + PM)

Carr W et al. J Allergy Clin Immunol 2012;129:1282-9

Azelastine and Fluticasone propionate

Overall rTNSSs (morning plus evening) in patients with moderate-to-severe SAR



Carr W et al J Allergy Clin Immunol 2012;129:1282-9.

DYMISTA (azelastine hydrochloride and fluticasone propionate) nasal spray, for intranasal use
Initial U.S. Approval: 2012

RECENT MAJOR CHANGES

- Indications and Usage, Allergic Rhinitis (1) 2/2015

INDICATIONS AND USAGE

DYMISTA contains an H_1-receptor antagonist and a corticosteroid, and is indicated for the relief of symptoms of seasonal allergic rhinitis in patients 6 years of age and older who require treatment with both azelastine hydrochloride and fluticasone propionate for symptomatic relief. (1.1)

Azelastine and Fluticasone propionate

The combination A/F in the management of AR :

(i) provides twice the relief afforded by INS;

(ii) is 2–3 times more effective than INS in reducing nasal congestion and ocular itch, the most bothersome symptoms associated with AR;

iii) provides rapid symptom control in real life.

Meltzer E. et al., Int Arch Allergy Immunol, 2013 (161): 369-77.

Azelastine and Fluticasone propionate

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610 moderate-to-severe SAR patients (≥ 12 years old) RCT DBPC , 14-day, parallel group

Meltzer E. et al., Int Arch Allergy Immunol, 2013 (161): 369-77.

Safety of a novel intranasal formulation of azelastine hydrochloride and fluticasone propionate in children: A randomized clinical trial

William Berger, M.D.,[1] Ellen Sher, M.D.,[2] Sandra Gawchik, D.O.,[3] and Stanley Fineman, M

Randomized, 3-month, parallel-group open-label AZE/FP (n =304) or fluticasone propionate (FP) (n=101) Age groups: 4 to 6 years, 6 to 9 ys, and 9 to 12 ys.

The incidence of treatment-related adverse events (TRAEs) was low, AZE/FP (16%) FP only (12%) of mild intensity and resolved spontaneously.

Epistaxis was the most frequent TRAE in both groups (9%)

Allergy Asthma Proc 2018;39:110-6

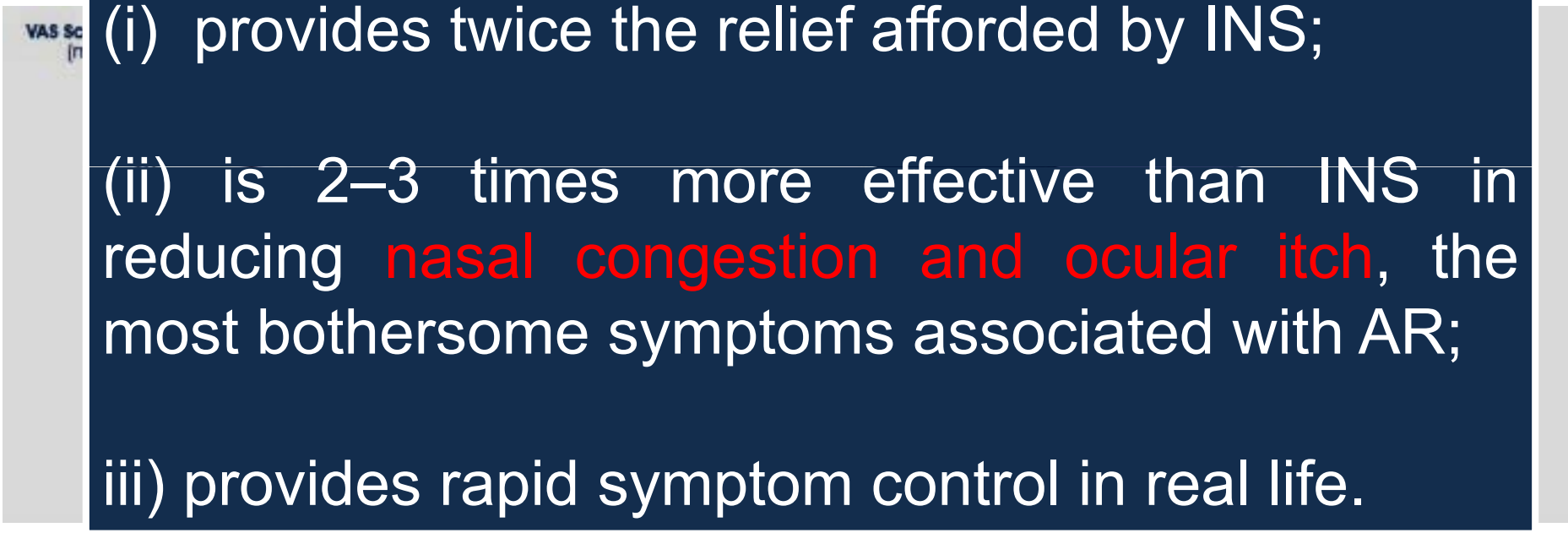
(A) Patient recorded VAS score following treatment with Dymista®

Dymista® in the management of AR :

(i) provides twice the relief afforded by INS;

(ii) is 2–3 times more effective than INS in reducing nasal congestion and ocular itch, the most bothersome symptoms associated with AR;

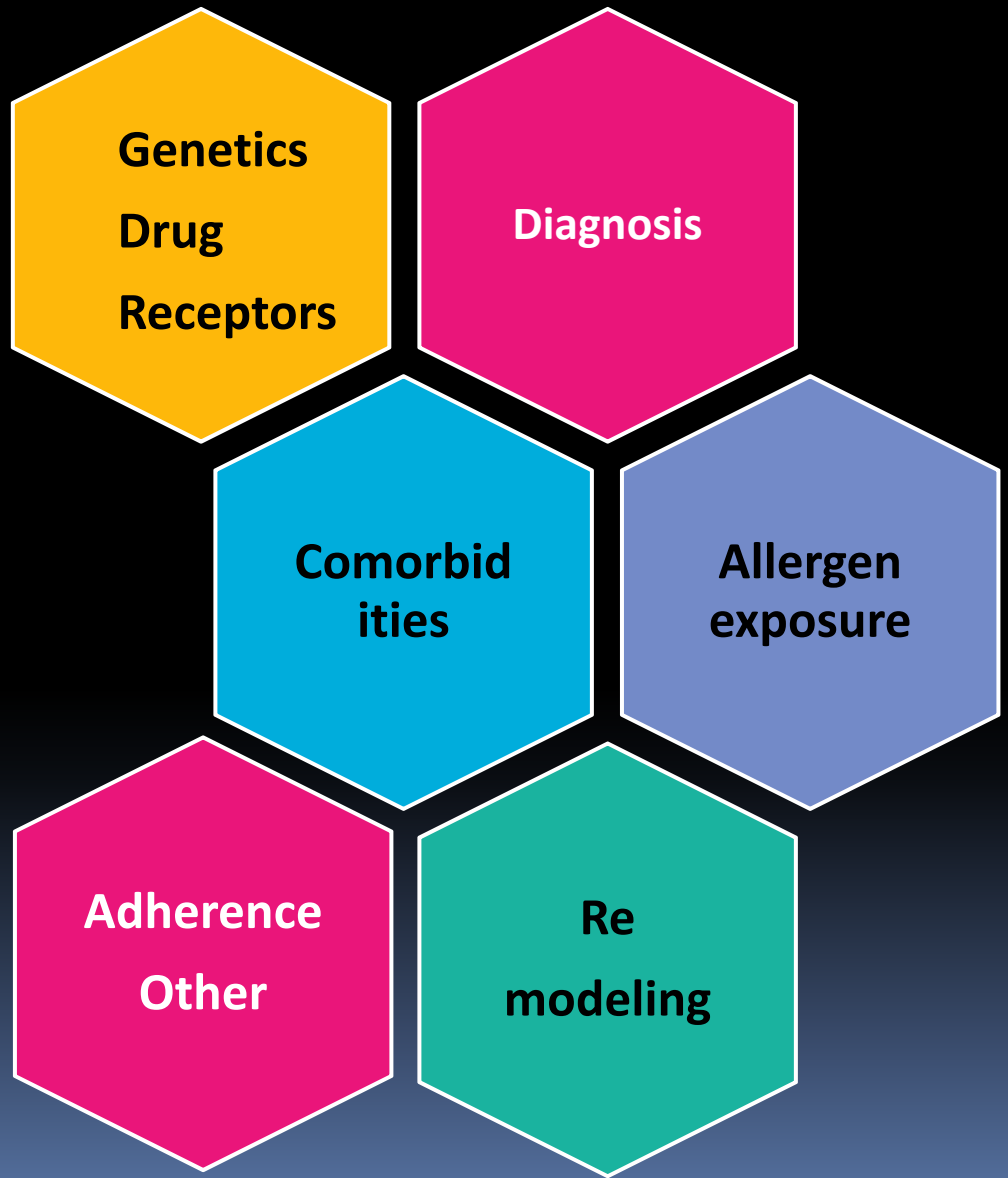
iii) provides rapid symptom control in real life.

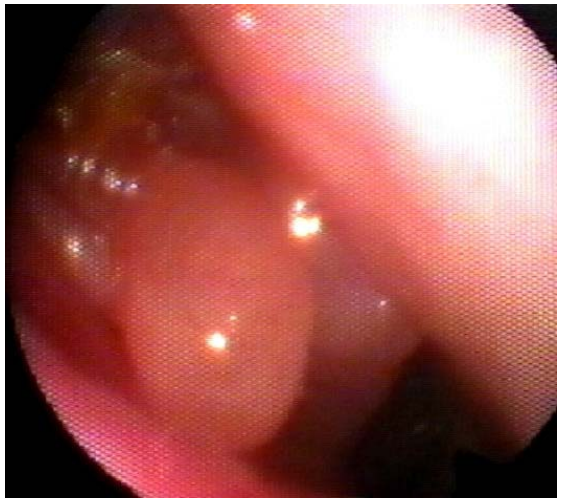


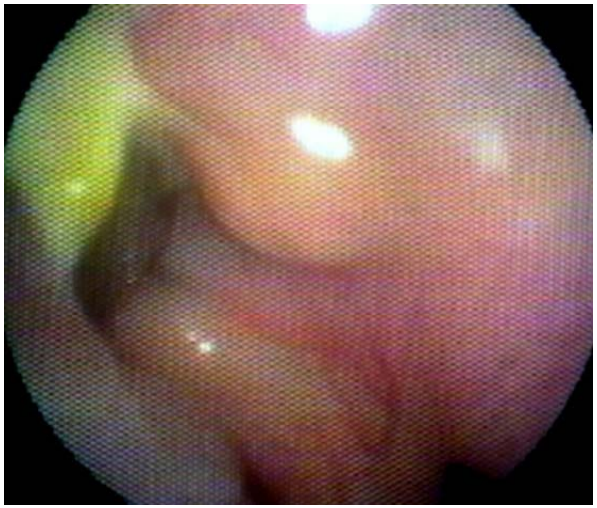
(B) Response following 3 days' treatment .

Meltzer E. et al., Int Arch Allergy Immunol, 2013 (161): 369-77.

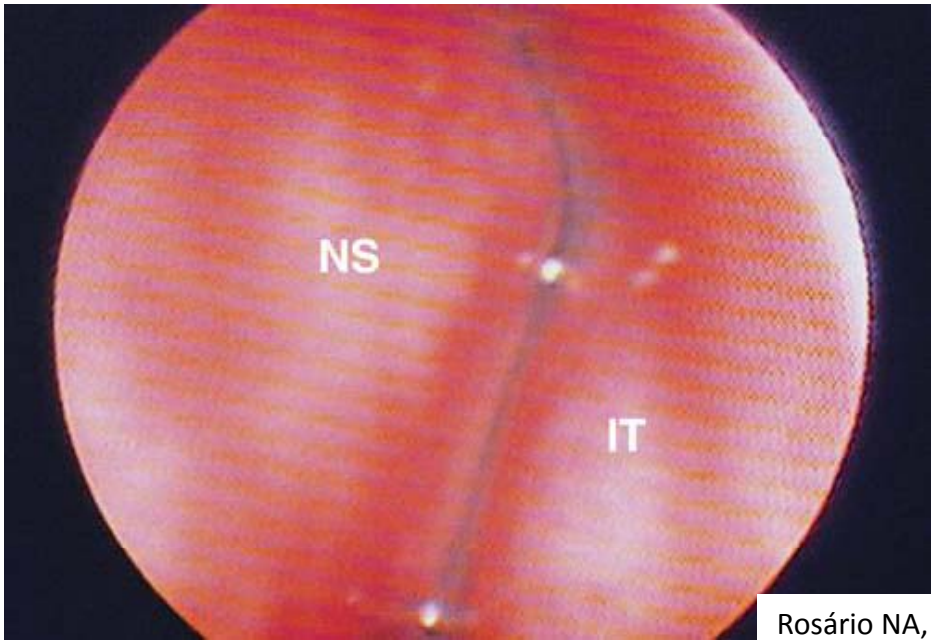
Rinitis que no responde





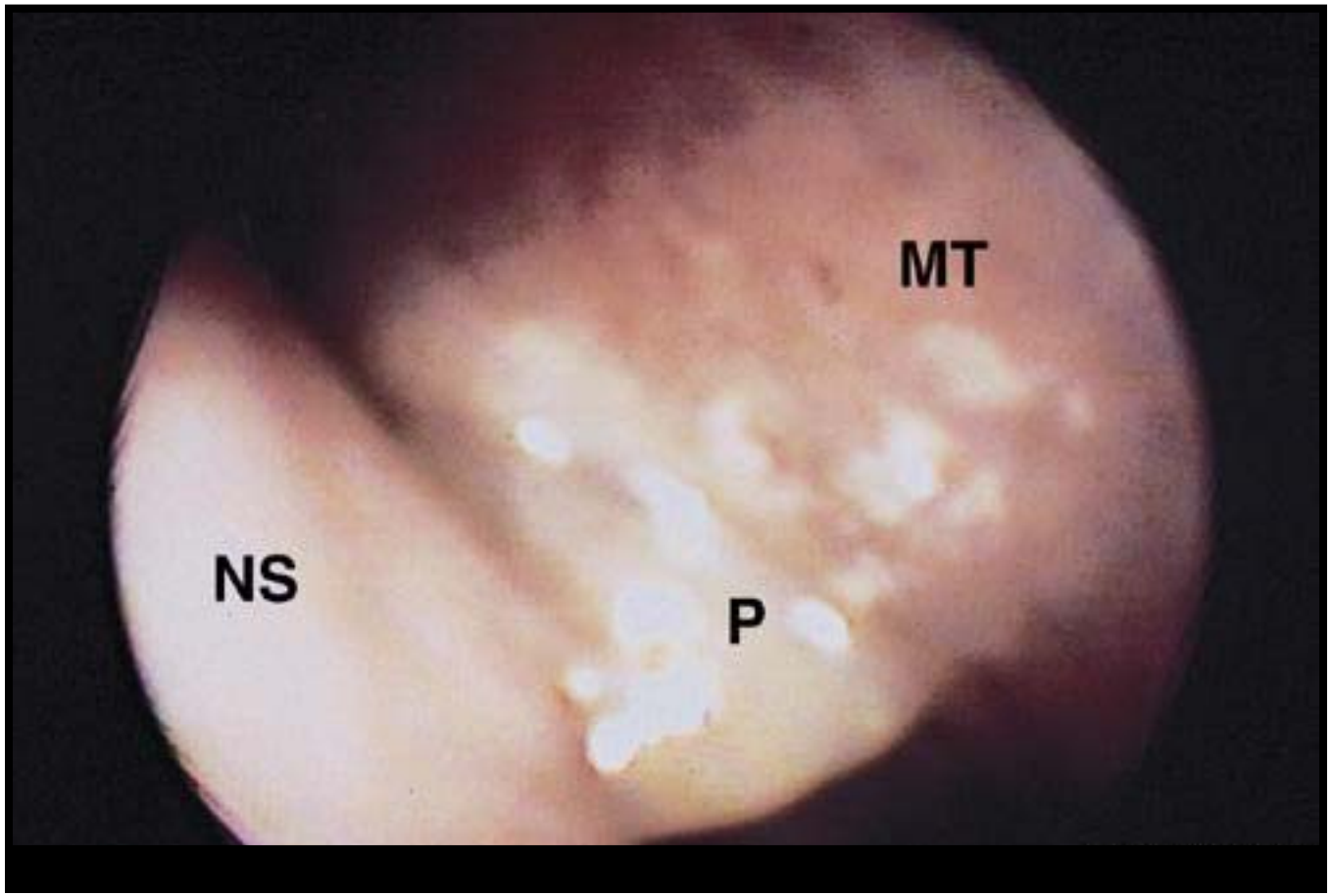


Poliposis Nasal

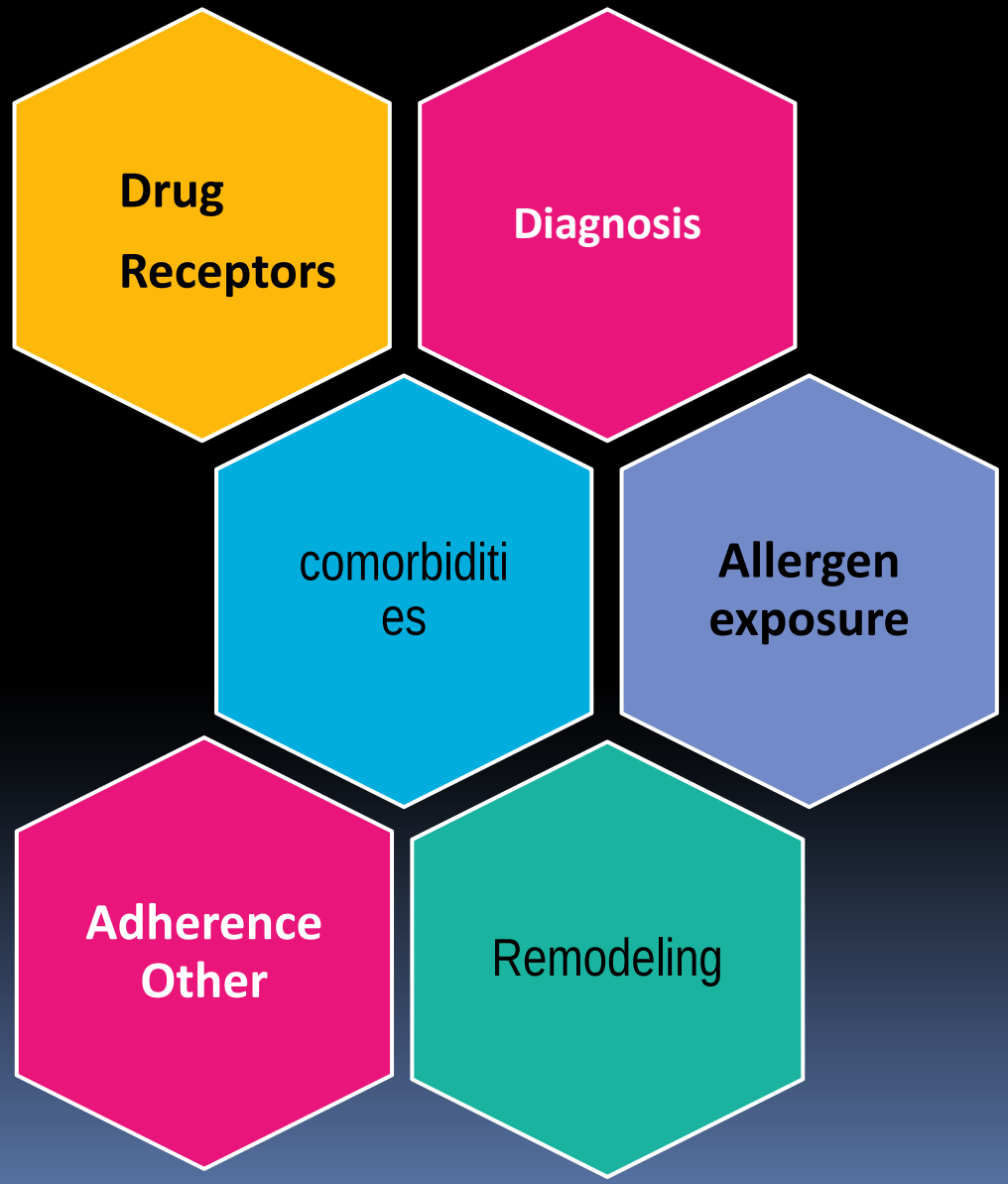


Rosário NA, Riedi CA. Allergol Immunopathol (Madr) 2013; 41: 137–9.

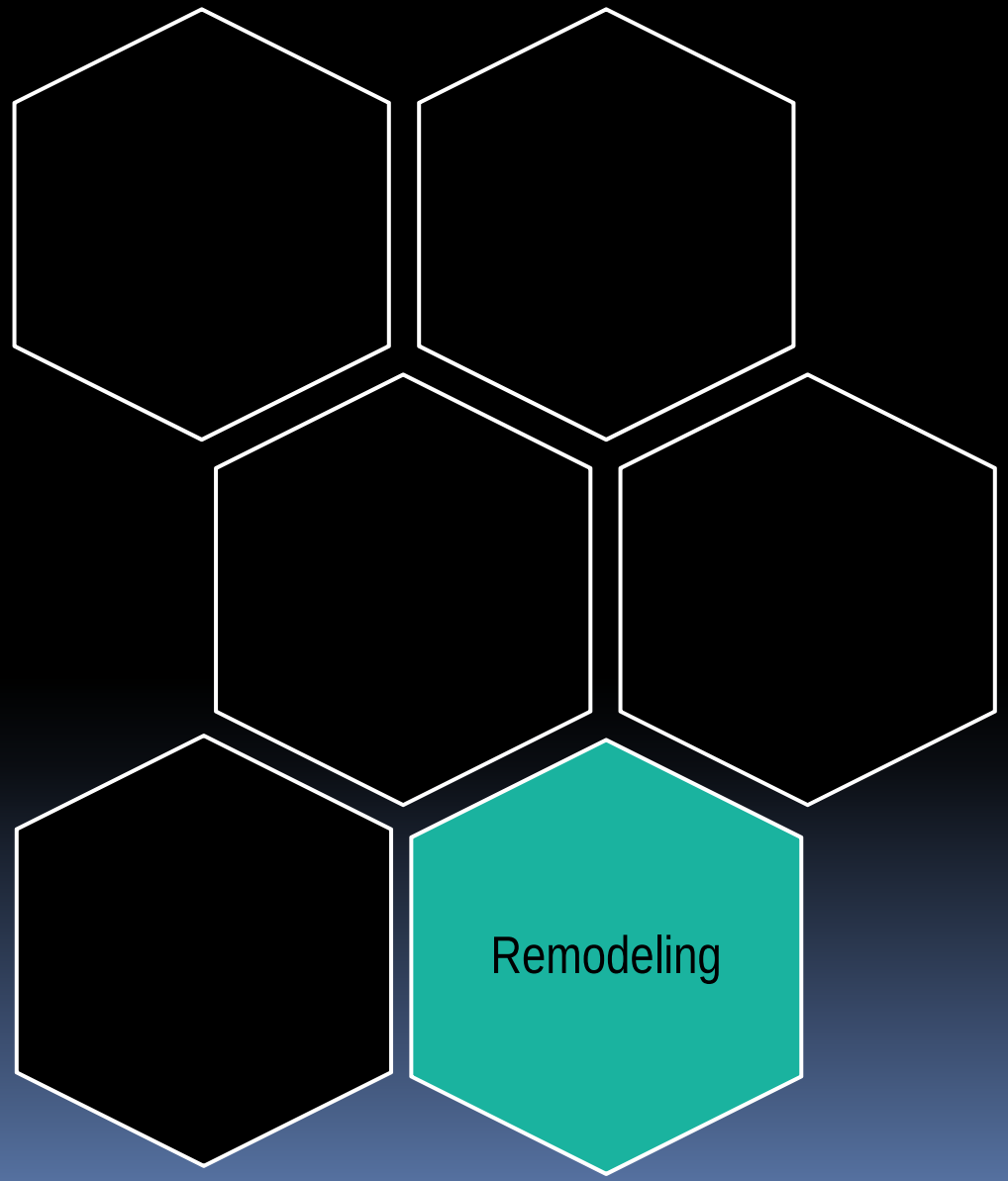
Pólipo nasal entre o septo e corneto médio



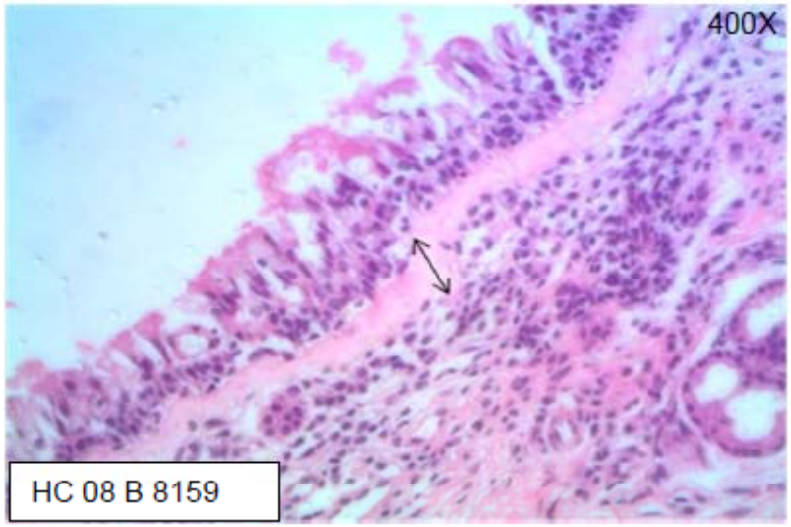
Rinitis que no responde



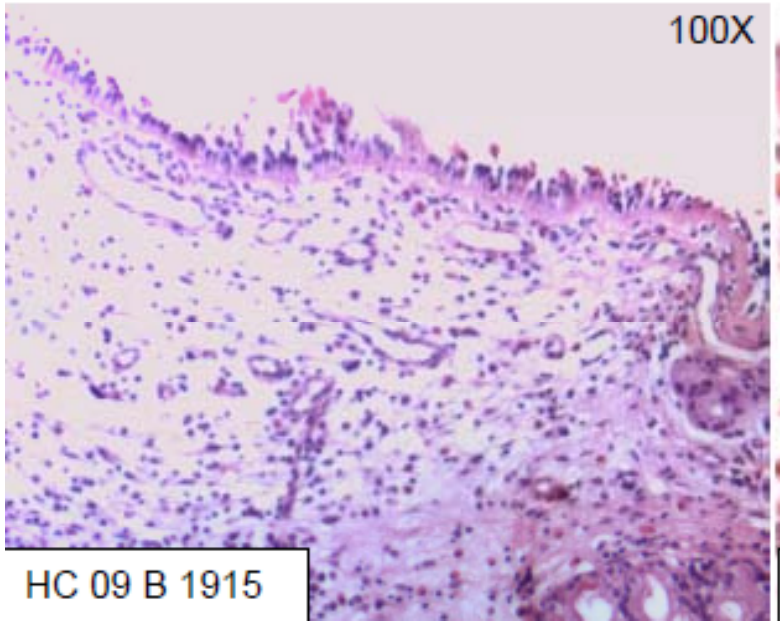
Rinitis que no responde

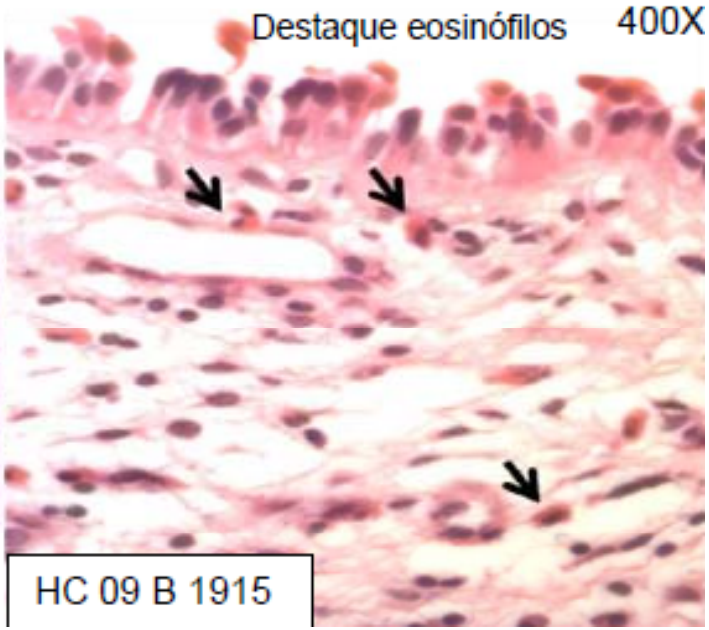


Ausência de cílios e espessamento da MB >20µm)



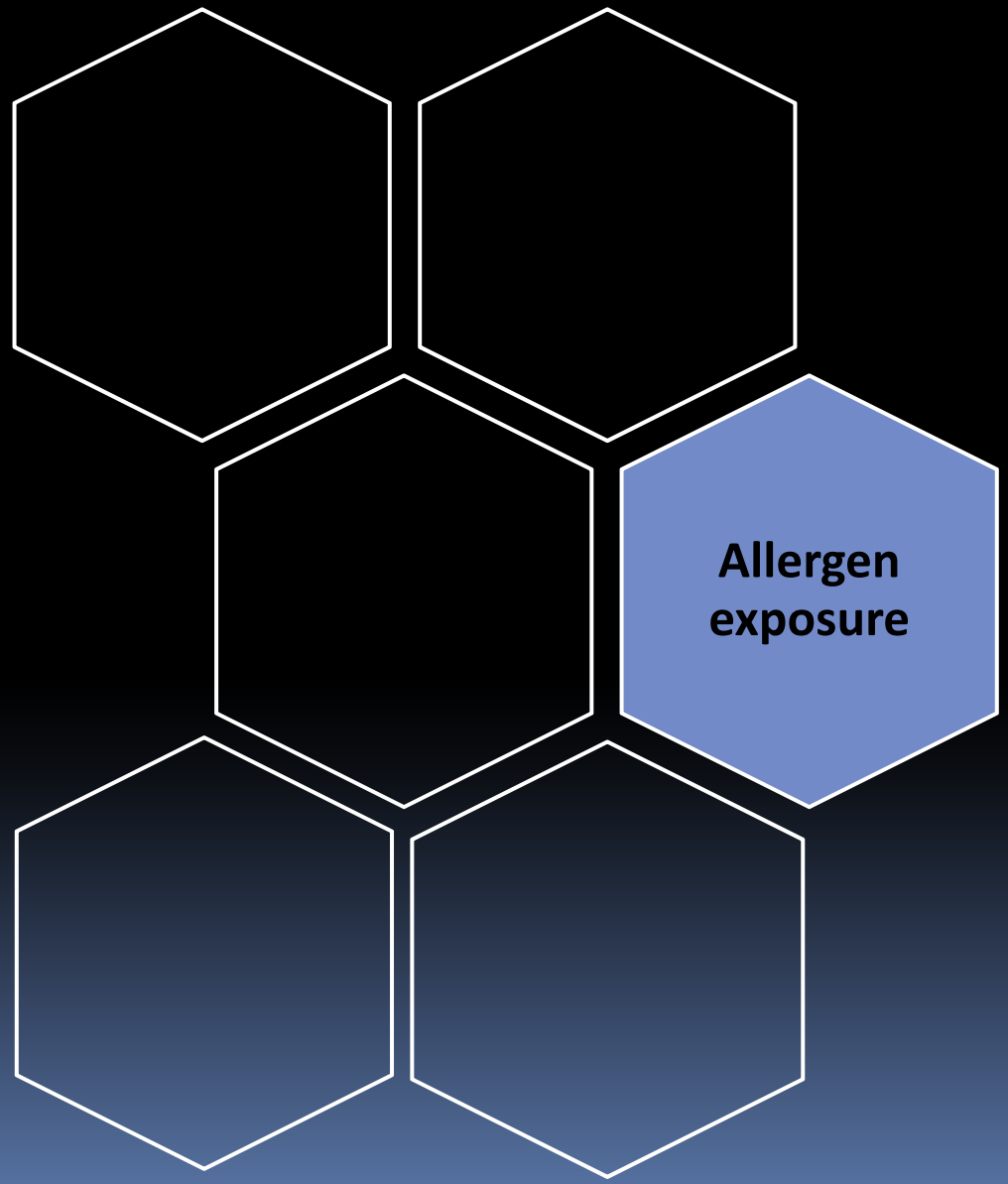
Erosão da camada superior de células e camada de células basais intacta
Infiltrado eosinofílico



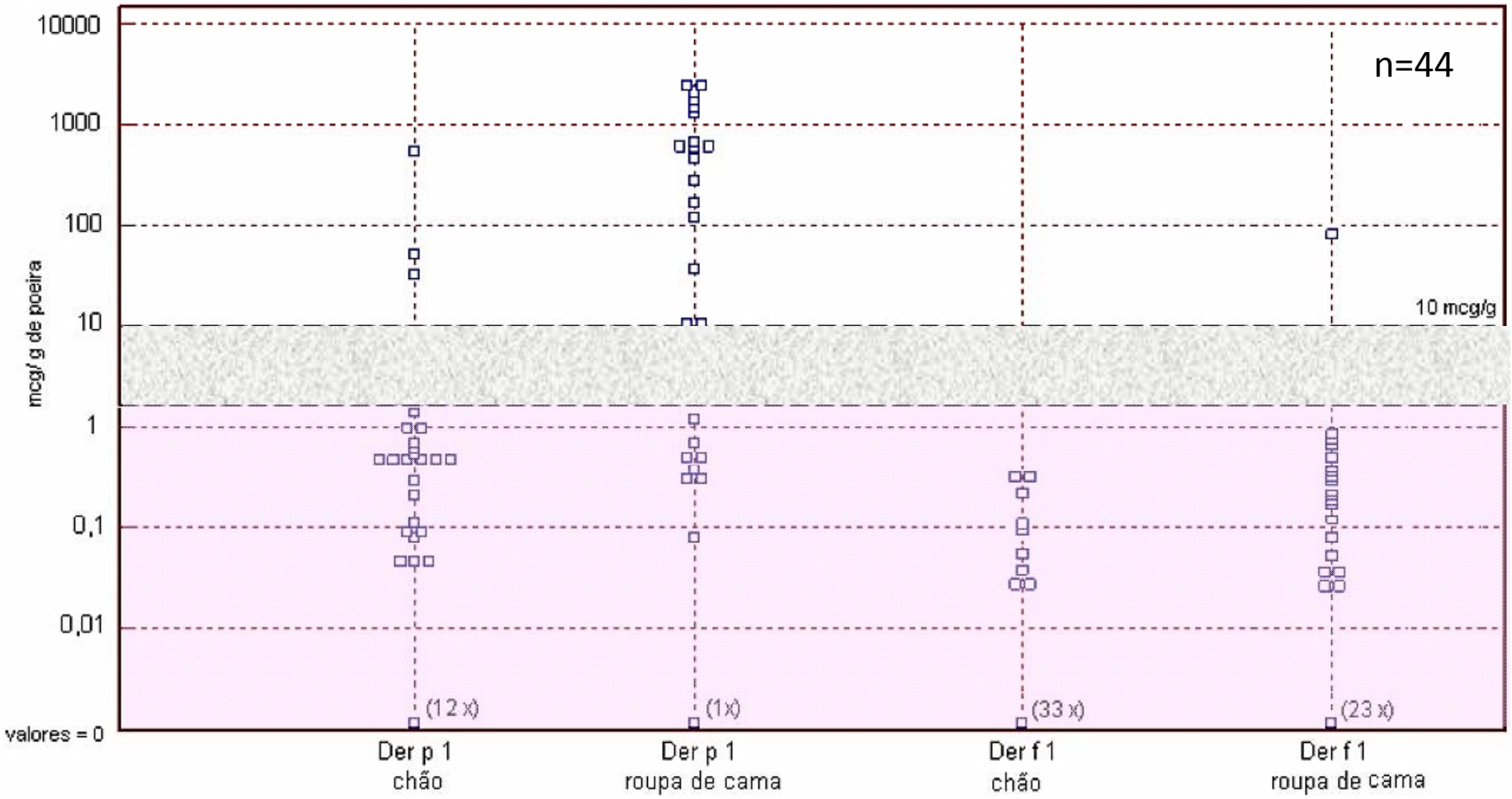


Kovalhuk LC... Rosario NA. Braz J Otorhinolaryngol. 2019

Rinitis que no responde



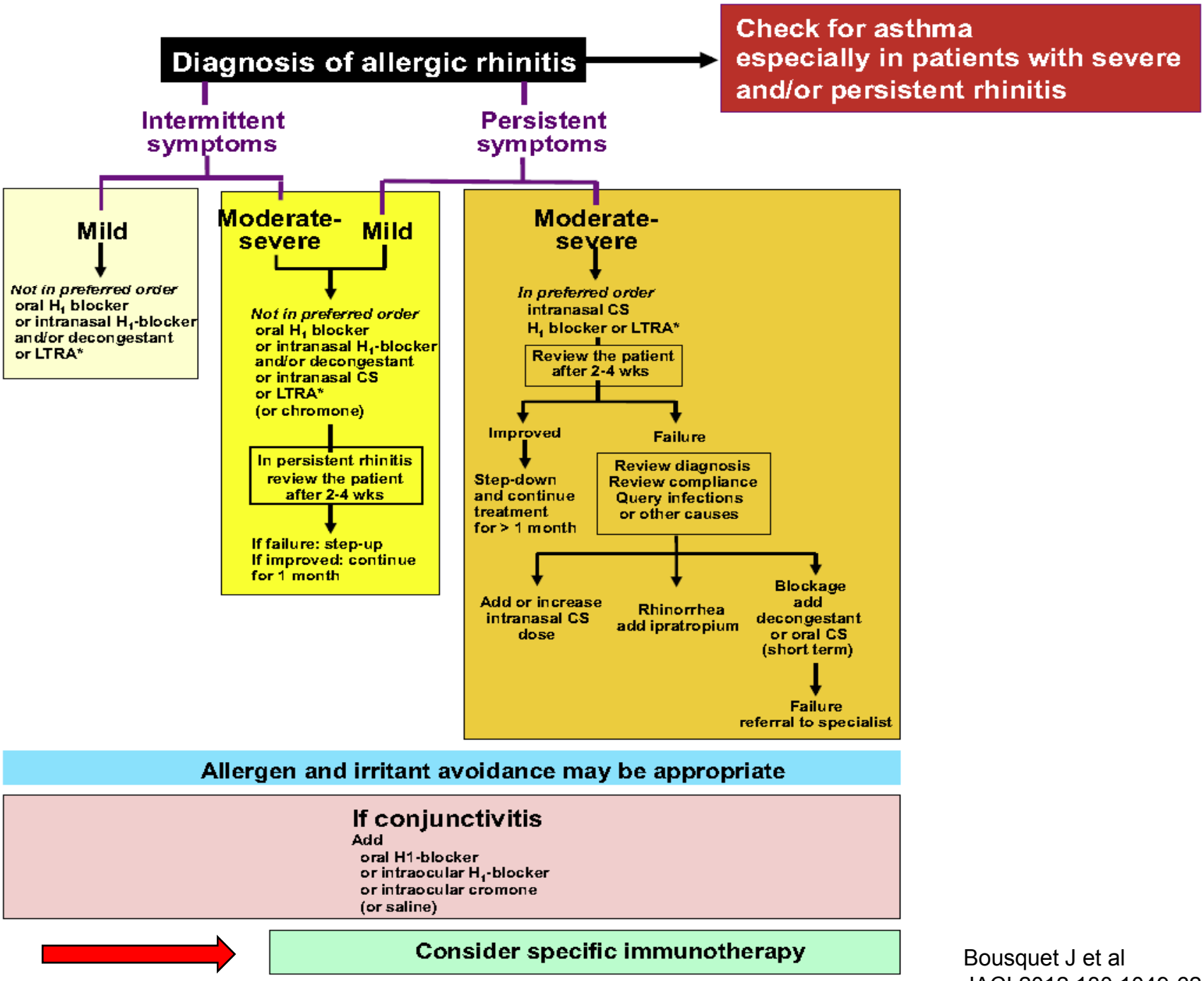
Mite allergens in floor dust and bed samples



82 % > 2 mcg / g

7 % > 2 mcg / g

Souza CT, Rosario NA *Rev. bras. alerg. imunopatol. 2012;35:47-52*



Bousquet J et al
JACI 2012;130:1049-62

Inmunoterapia es eficaz en asma, rinitis alérgica, dermatitis atópica y la alergia al veneno de hymenoptera.

El diagnóstico depende de la historia, examen físico y demostración de reacción mediada por IgE (preferentemente de pruebas cutaneas).

Rutas de Administración de Alérgenos Inmunoterapia

Subcutánea

Local (nasal,brônquica)

Oral

Sublingual

Intralinfática

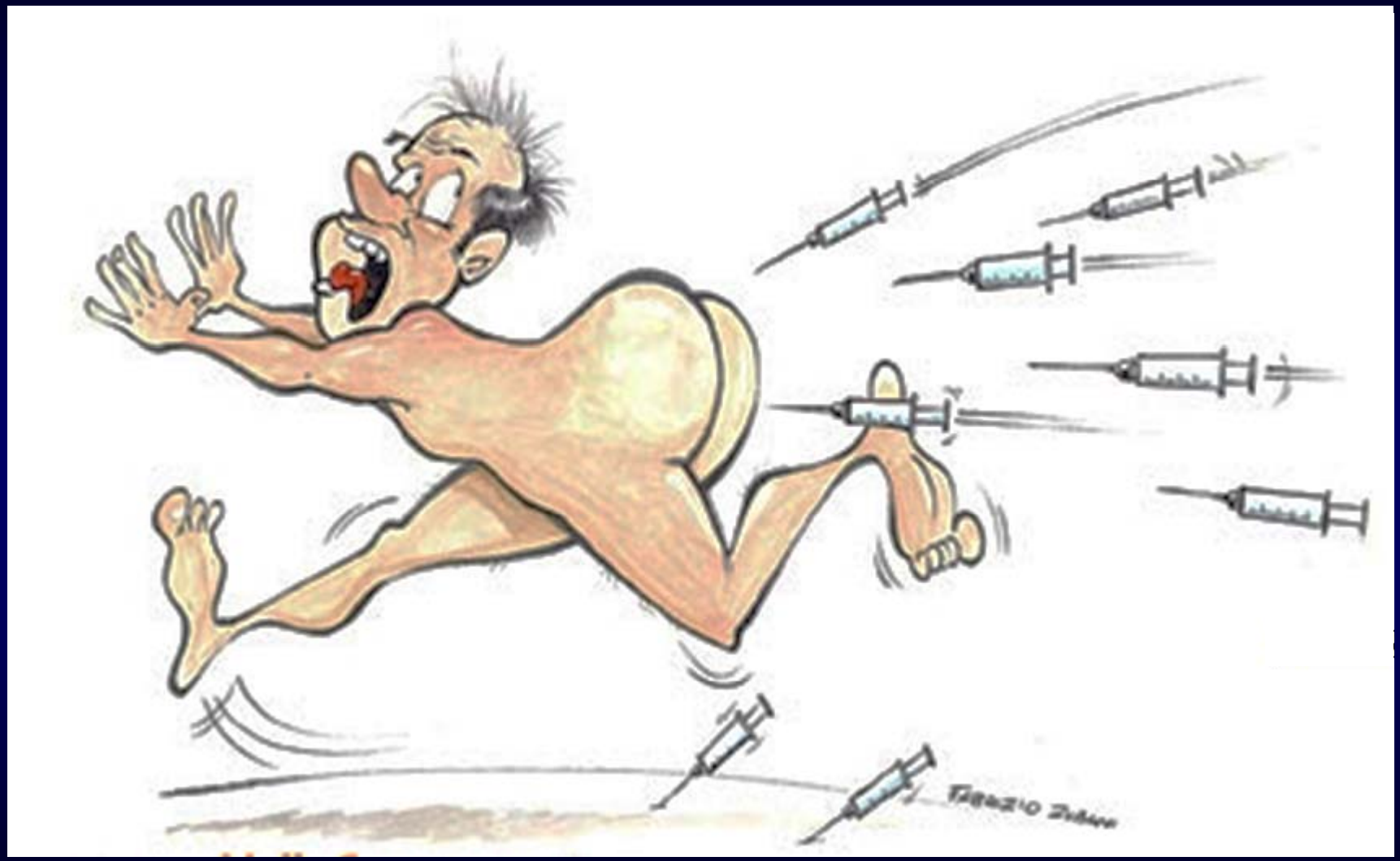
Epicutânea

Intradérmica (baja dosis)

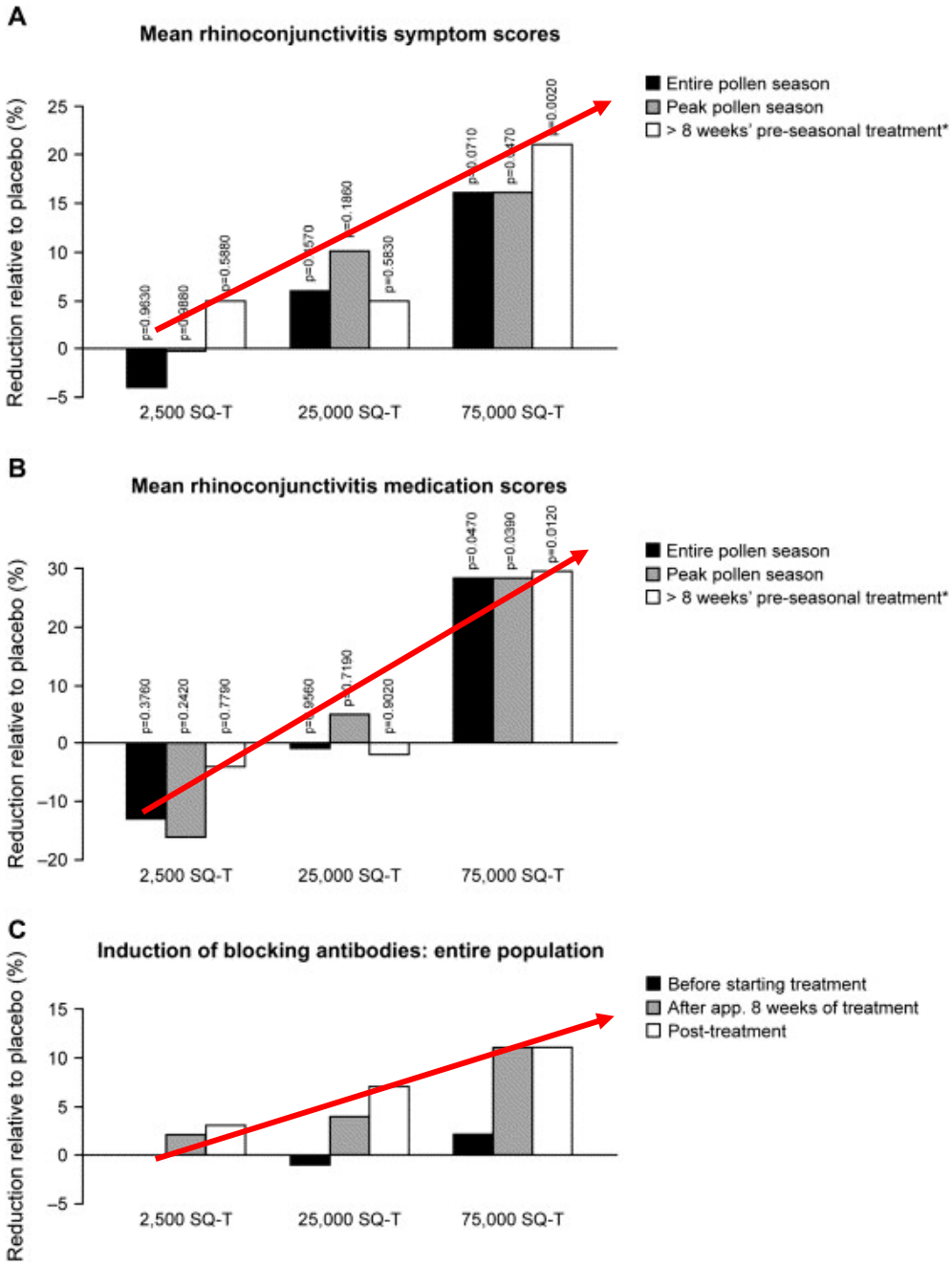
Transcutánea

SCIT x SLIT ¿Qué es mejor?

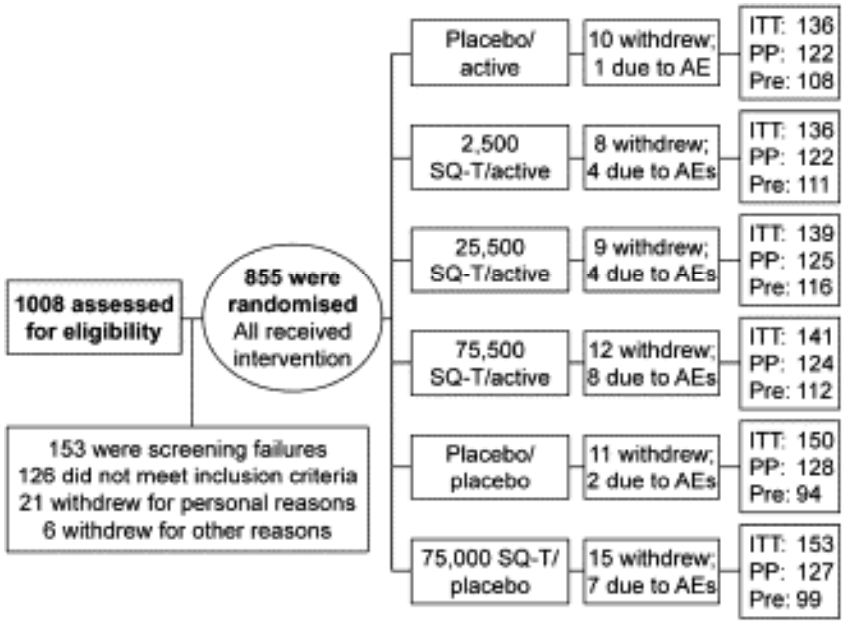
Burks W. et al. J Allergy Clin Immunol , 2013;131: 1288 - 96

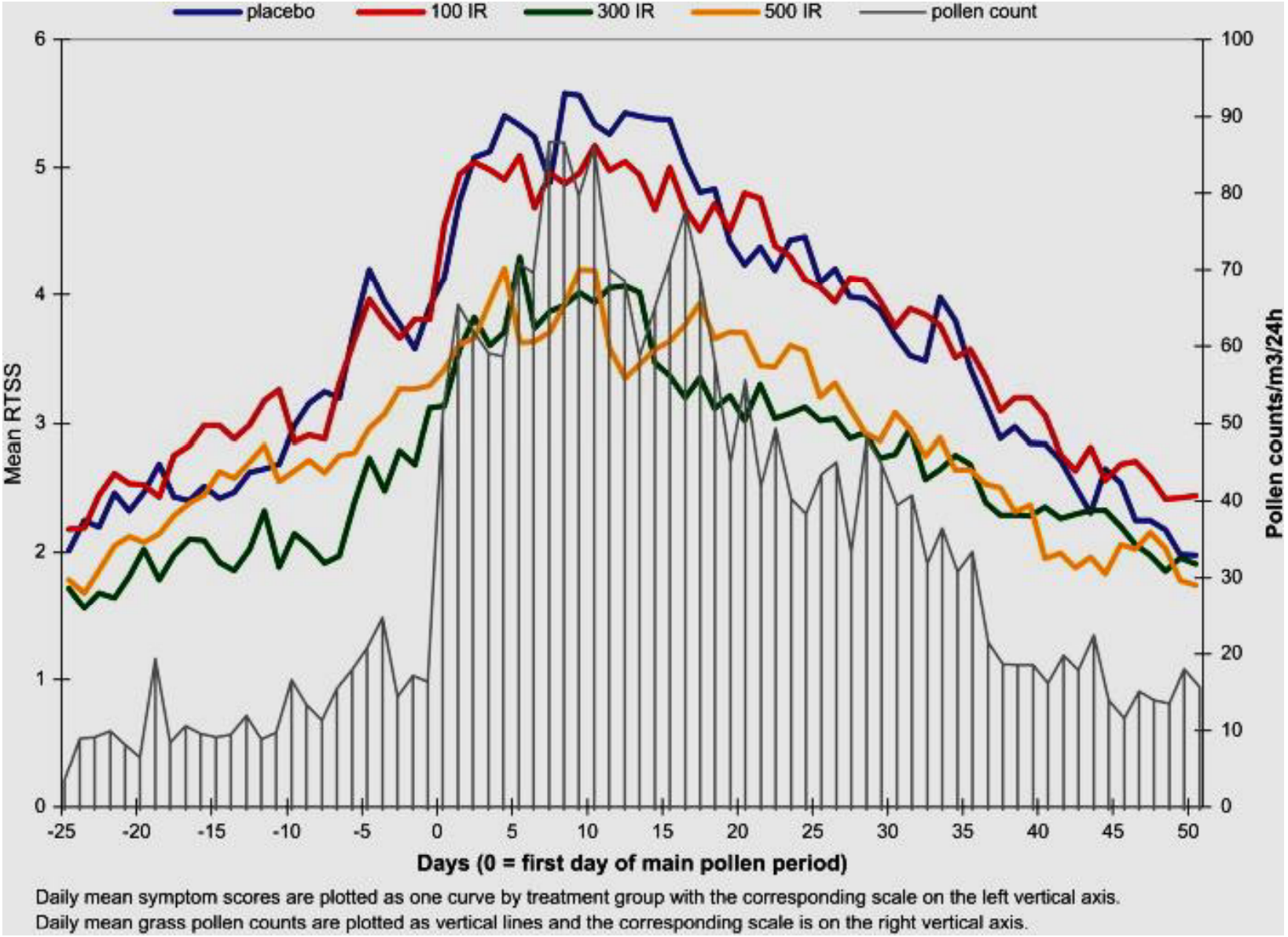


Nelson Rosário



Durham SR, JACI 2006





300 IR/mL correspond to approximately 25 mcg/mL of the group 5 major allergens.

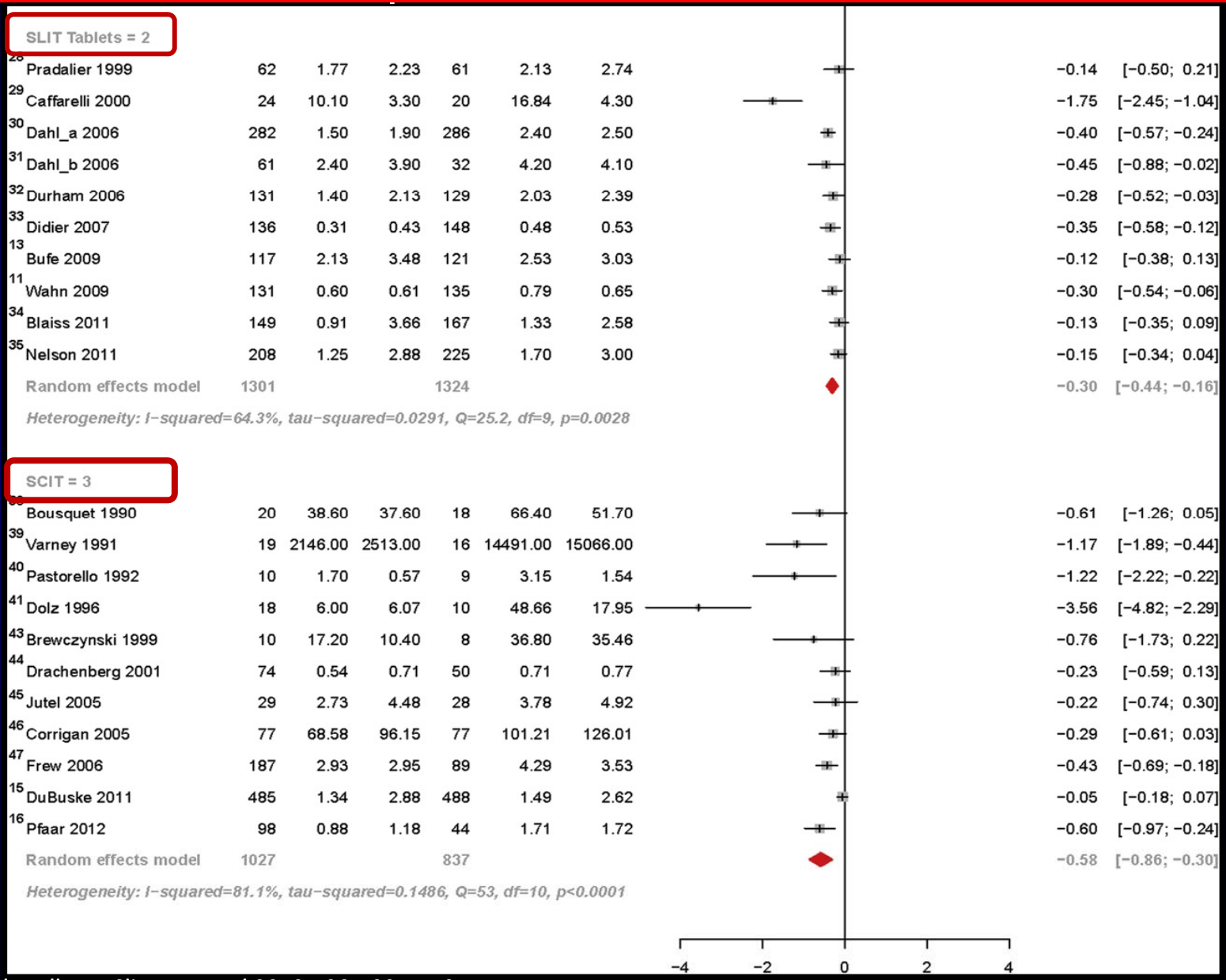
Didier et al J Allergy Clin Immunol 2007;120:1338

SCIT is more effective than SLIT in reducing symptoms of rhinoconjunctivitis to grass

- meta-analysis of 36 RCTs
- indirect comparison of SCIT with SLIT
- difference in symptom and medication scores with active therapy compared with placebo in patients with SAR.

Di Bona et al. J Allergy Clin Immunol 2012;130:1097-1107.

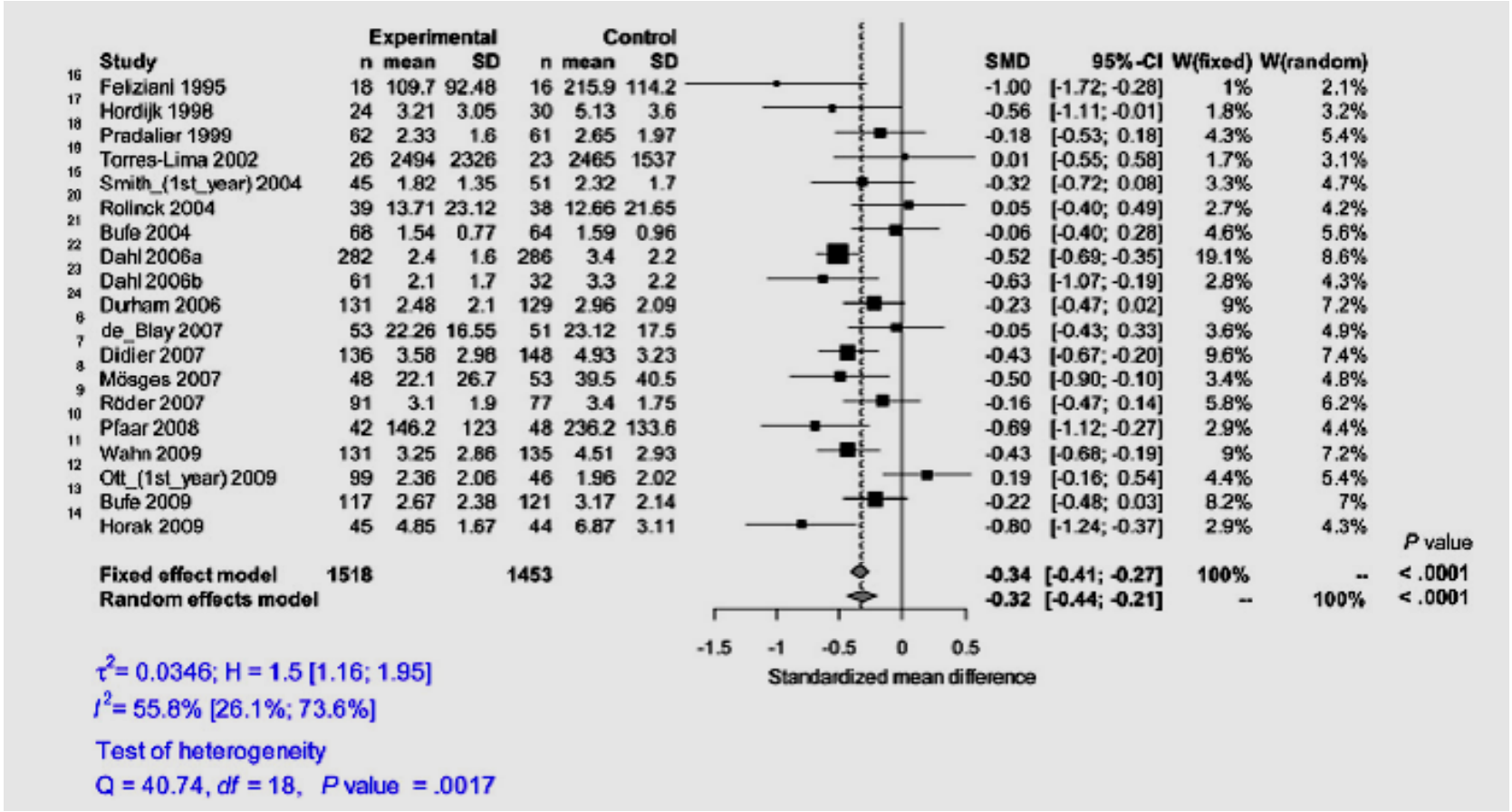
Meta-analysis of 36 RCTs of allergen specific immunotherapy vs placebo for seasonal AR



Di Bona et al. J Allergy Clin Immunol 2012;130:1097-1107.

Efficacy of sublingual immunotherapy with grass allergens for seasonal allergic rhinitis: A systematic review and meta-analysis

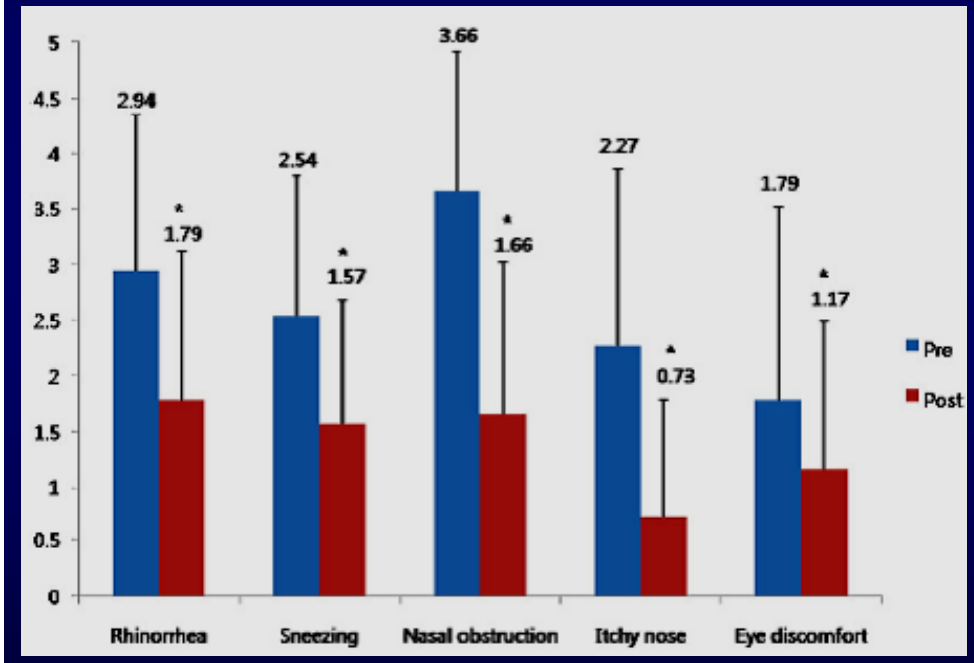
Danilo Di Bona, MD, PhD,[a,e] Antonella Plaia, PhD,[b] Valeria Scafidi, PhD,[a,c] Maria Stefania Leto-Barone, MD,[d] and Gabriele Di Lorenzo, MD[d] *Palermo, Italy*

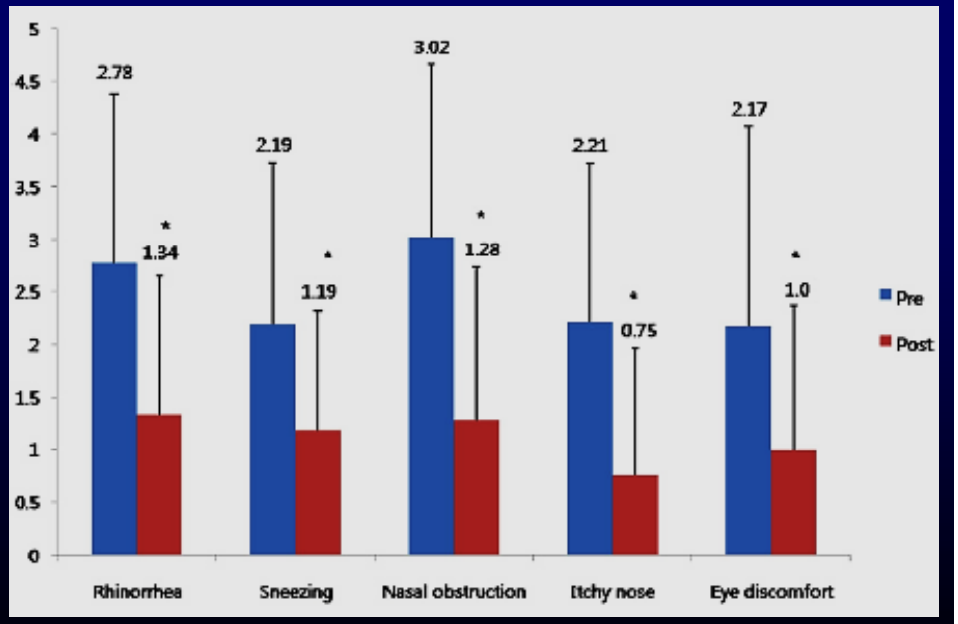


JACI 2010;126:558

Efficacy of sublingual immunotherapy with house dust mite extract in polyallergen sensitized patients with allergic rhinitis

Ji-Eun Lee, MD*; Yoon-Seok Choi, MD*; Min-Su Kim, MD*; Doo Hee Han, MD*;
Chae-Seo Rhee, MD*†; Chul Hee Lee, MD*†; and Dong-Young Kim, MD*†





Effectiveness of Subcutaneous Versus Sublingual Immunotherapy for the Treatment of Allergic Rhinoconjunctivitis and Asthma: A Systematic Review

Yohalakshmi Chelladurai, MBBS, MPH[a], Catalina Suarez-Cuervo, MD[a], Nkiruka Erekosima, MD, MPH[a], Julia M. Kim, MD, MPH[b], Murugappan Ramanathan, MD[c], Jodi B. Segal, MD, MPH[b], and Sandra Y. Lin, MD[c]
Baltimore, Md

J Allergy Clin Immunol: In Practice 2013;1:361-9

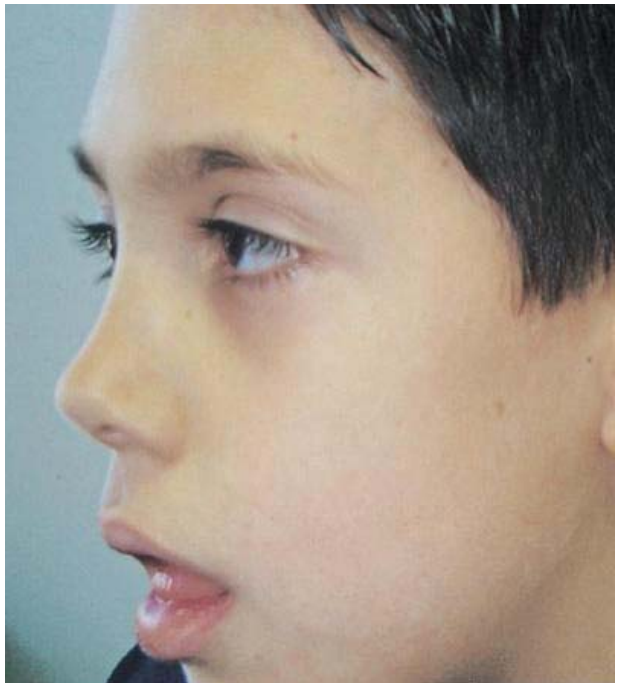
What is already known about this topic? Both subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) are effective in treatment of allergic rhinoconjunctivitis and asthma.

What does this article add to our knowledge? SCIT is better than SLIT in reducing symptoms of asthma (low-grade evidence) and rhinoconjunctivitis (moderate-grade evidence).

How does this study impact current management guidelines? Both SCIT and SLIT should remain treatment options until high-quality evidence allows for more definitive comparisons of the 2 therapies.

Allergic asthma and rhinoconjunctivitis were reported in 4 and 6 clinical trials, respectively. 555 subjects, published between 1989 and 2011.

Low strength of evidence: additional research is likely to change the conclusions.
Moderate strength: additional research is unlikely to change the conclusions although it might
High strength of evidence: additional research is unlikely to change the conclusions.



Surgery?

Biologics?

Original Article

Omalizumab for the Treatment of Inadequately Controlled Allergic Rhinitis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

Sophia Tsabouri, MD, PhD[a], Xanthippi Tseretopoulou, MD[b], Konstantinos Priftis, MD, PhD[c], and Evangelia E. Ntzani, MD, PhD[b] *Ioannina and Athens, Greece*

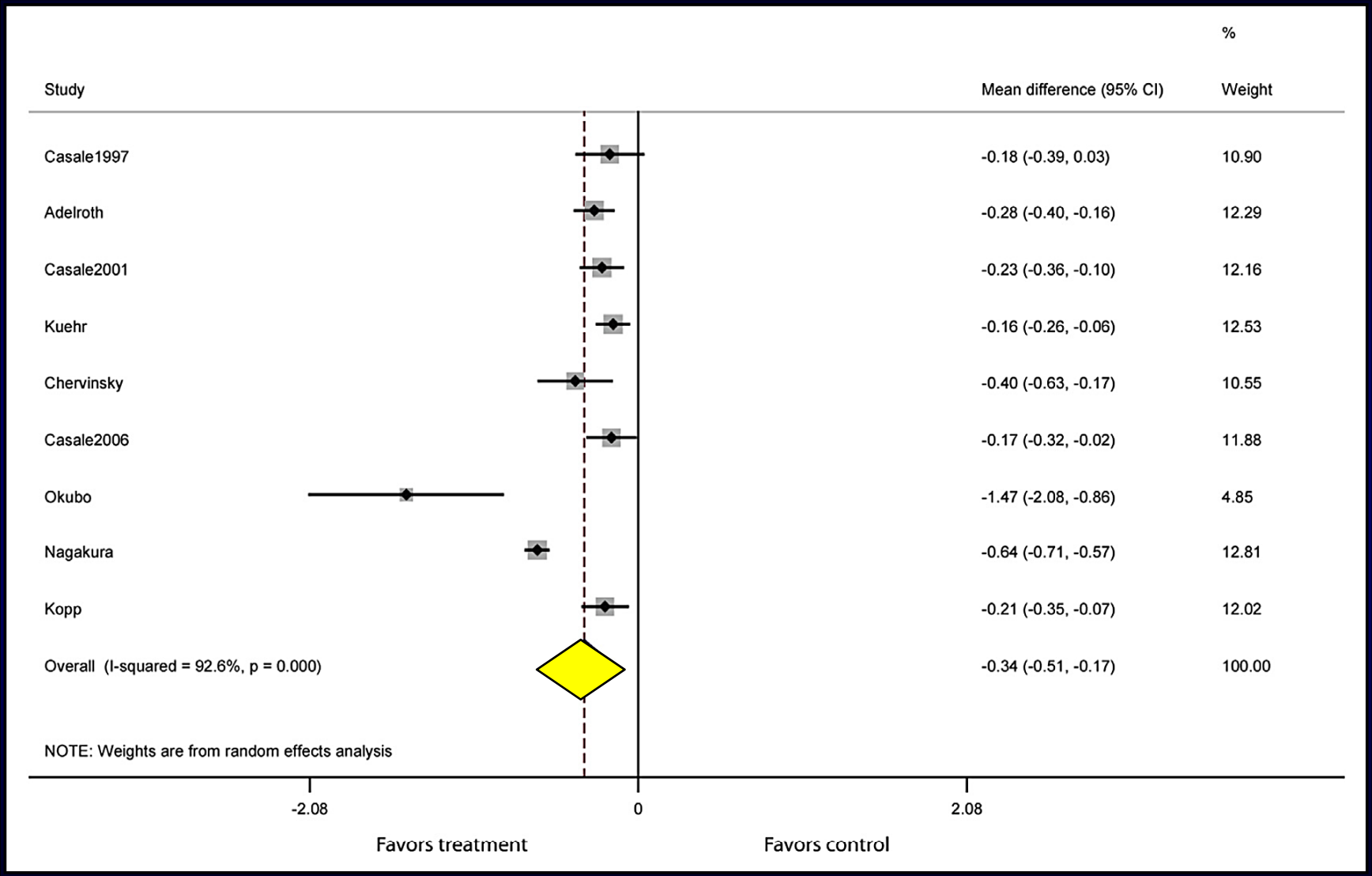
What is already known about this topic? Several clinical trials have evaluated omalizumab in inadequately controlled allergic rhinitis by using various clinical outcomes and comorbidities. Despite a relative effect direction consistency, a systematic appraisal of the evidence that focuses on the assessed outcomes and their clinical importance is lacking.

What does this article add to our knowledge? Omalizumab is generally well-tolerated and associated with a statistically significant symptom relief, decreased rescue medication use, and improvement of quality of life in patients with inadequately controlled allergic rhinosinusitis.

How does this study impact current management guidelines? Combination therapy could be a meaningful improvement over current standard therapy for the complex cases of allergic rhinitis. Larger clinical trials and economic studies are needed to address issues of rare events occurrence and cost-effectiveness, respectively.

J Allergy Clin Immunol Pract 2014;2:332-40

Efficacy of omalizumab in reducing the DNSSS



daily nasal symptom severity score

J Allergy Clin Immunol Pract 2014;2:332-40

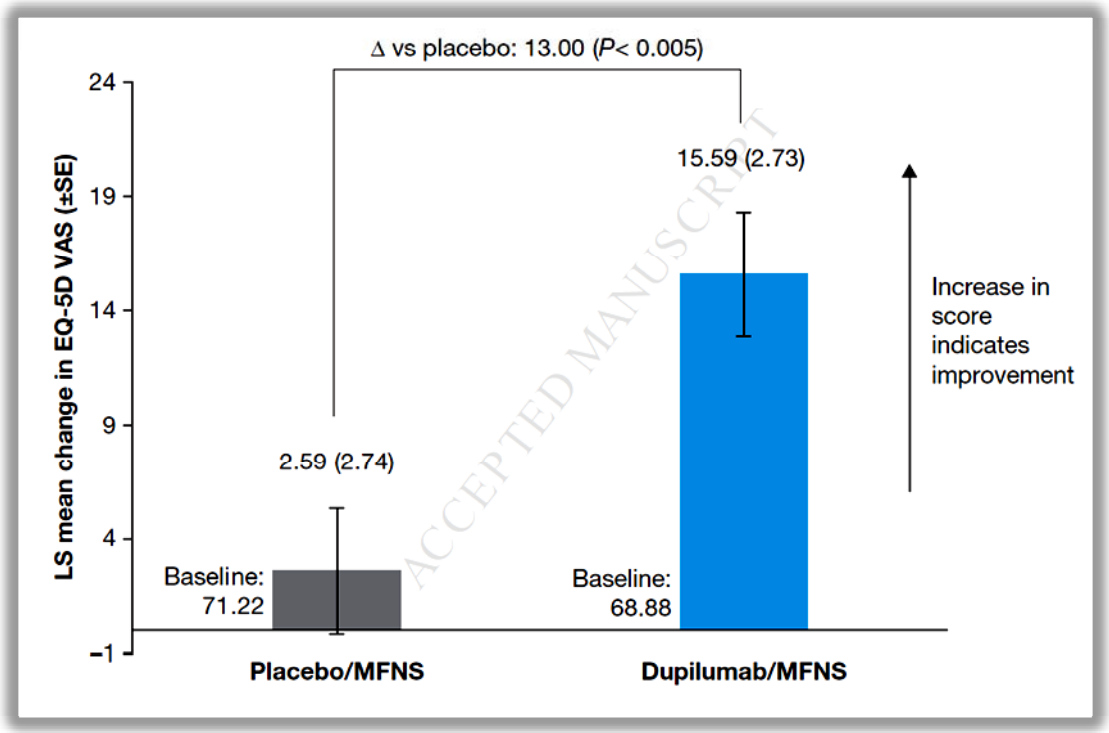
Characteristics of the studies

Study	Country	Year	Mean age (y)	Indication	Omalizumab dose	Control	Mean DNSSS (placebo)	Follow-up, wk	N all	Outcomes assessed
Casale et al[13]	USA	1997	34	SAR, ragweed (+)	0.150 mg/kg every 2 wk	Placebo	0.73	12	240	Average all daily SS, total days with symptoms, rescue medication, QoL (Juniper, SF-36), AE
Adelroth et al[14]	Sweden, Finland, Norway	2000	33	SAR, birch pollen (+)	300 mg (0,4w) or 300 mg (0,3,6w)	Placebo	0.7	8	251	7-symptom, 4-point scale, rescue medication, AE
Casale et al (OSARTG)[12]	USA	2001	34.5	SAR, ragweed (+)	50, 150, or 300 mg every 3 wk	Placebo	0.75	9	536	DNSSS, rescue medication, AE
Kuehr et al (ORSG)[16]*	Germany	2002	12†	SAR, birch pollen (+), grass pollen (+)	0.016 mg/kg per IU/mL of IgE every 4 wk	Placebo	0.24	24	221	DNSSS, rescue medication, AE
Chervinsky et al[17]‡	USA	2003	34	PAR, dust, dog or cat skin test (+)	0.016 mg/kg per IU/mL of IgE every 4 wk	Placebo	1	16	289	DNSSS, rescue medication, rQoL, global evaluation, AE
Vignola et al (SOLAR)[18]	Multi-center	2004	38.5	Concomitant asthma and PAR	0.016 mg/kg per IU/mL of IgE (IU/mL) per 4 wk	Placebo	NA	28	405	Wasserfallen rhinitis clinical symptom scores, rescue-medication use, rQoL evaluations, patient and investigator global evaluations of treatment effectiveness
Casale et al (ITNG)[19]*§	USA	2006	33.3	SAR, ragweed (+)	0.016 mg/kg per IU/mL of IgE (IU/mL) per 4 wk	Placebo	0.69	21	159	Daily allergy SS, AE
Okubo et al[15]	Japan	2006	32	SAR, cedar pollen (+)	150, 225, 300, or 375 mg every 2 to 4 w	Placebo	1.88	24	100	DNSMS, DNSSS, rescue medication, AE
Nagakura et al[20]	Japan	2007	35.3	SAR, cedar pollen (+)	150, 225, 300, or 375 mg every 2 to 4 w	Suplatast tosilate	1.46	12	308	DNSMS, DNSSS, rescue medication, AE
Kopp et al (DUAL)[21]*	Germany	2008	30†	Concomitant asthma and SAR, grass and/or rye (+)	Based on the patient's body weight and total serum IgE	Placebo	0.38	20	140	Mean daily symptom severity score, mean daily rescue medication, QoL
Kamin et al (ORSG)[22]*	Germany	2010	12	SAR, birch pollen (+), grass pollen (+)	Dependent on body weight and total serum IgE	Placebo	NA	36	221	AE

J Allergy Clin Immunol Pract 2014;2:332-40

Dupilumab improves outcomes in patients with chronic rhinosinusitis with nasal polyps and comorbid asthma

RCT, DBPC, 16-week treatment
Adult patients with bilateral NP and chronic symptoms of rhinosinusitis despite INCS treatment ≥2 months 300 mg weekly,as add-on to Mometasone for 16 wks



Bachert C et al. J Allergy Clin Immunol In Practice 2019

Dupilumab in Persistent Asthma with Elevated Eosinophil Levels

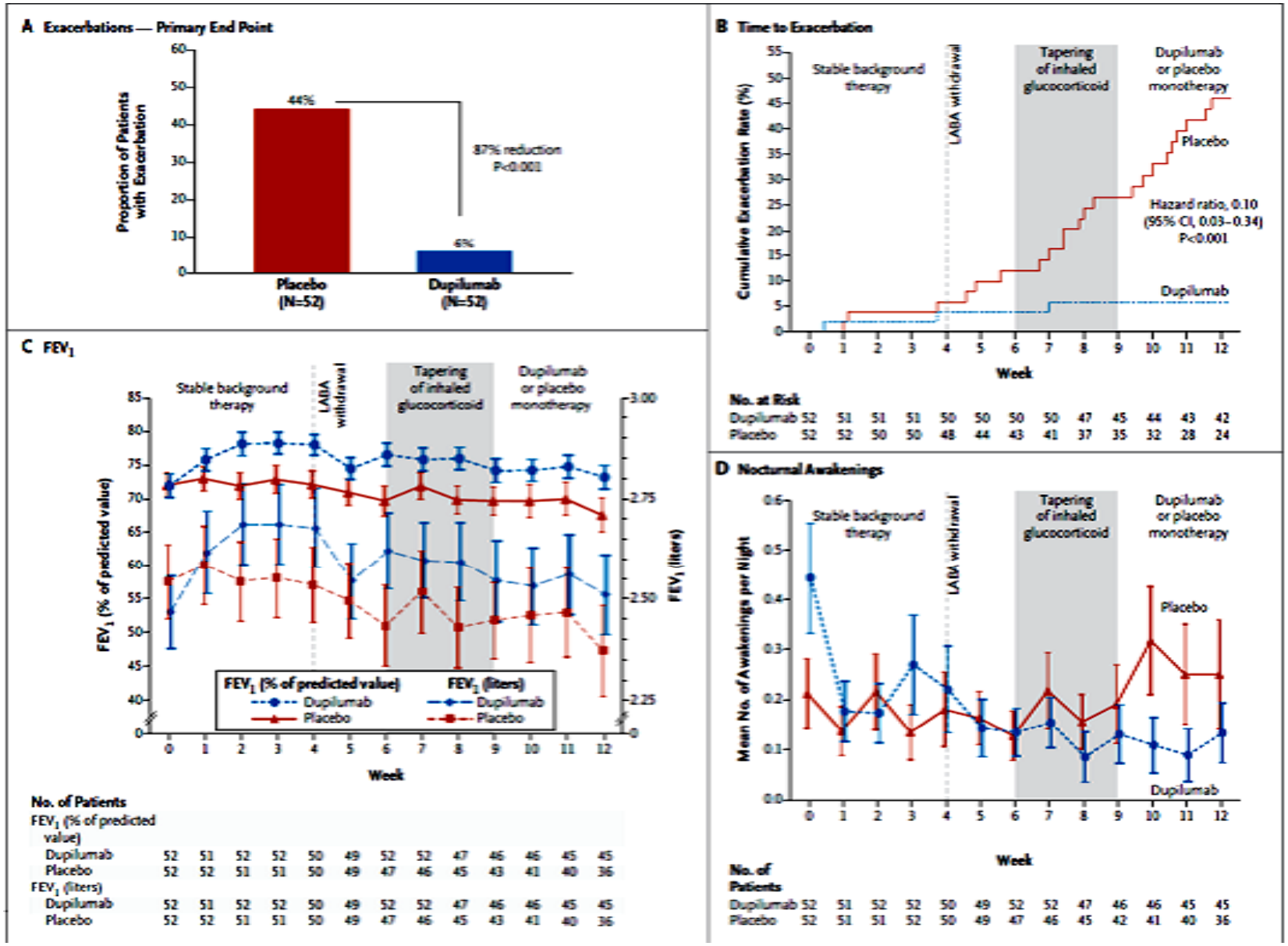
Fully human monoclonal antibody to the interleukin-4 receptor α subunit that inhibits both interleukin-4 and interleukin-13 signaling (Th2 cytokines).

Persistent, moderate-to-severe asthma on ICS+LABA
Elevated eosinophil levels.

Dupilumab → fewer asthma exacerbations when LABA+ICSs were withdrawn, with improved lung function and reduced levels of Th2-associated inflammatory markers.

Wenzel S et al. N Engl J Med 2013;368:2455-66.

Dupilumab in Persistent Asthma with Elevated Eosinophil Levels



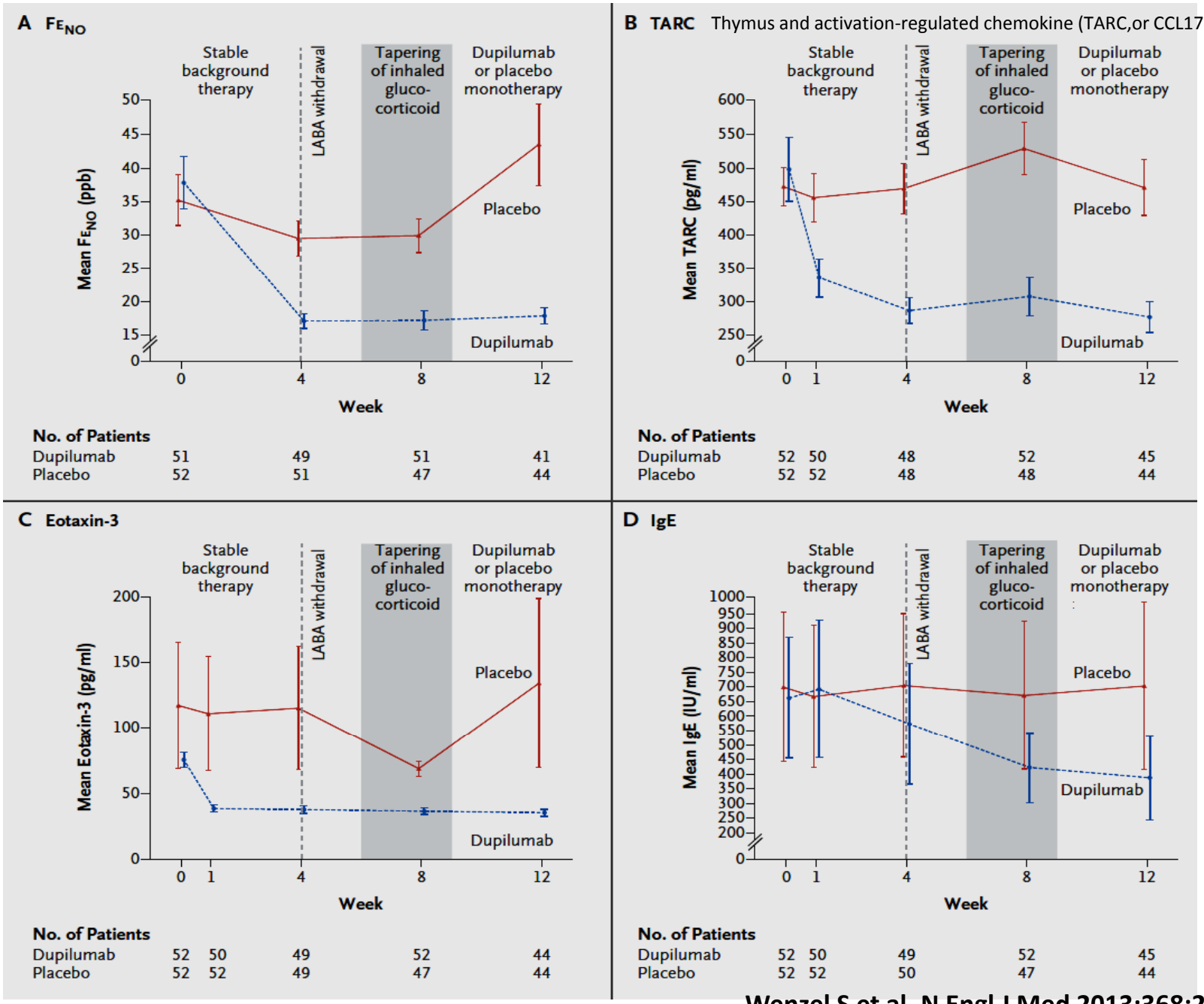
Wenzel S et al. N Engl J Med 2013;368:2455-66.

Th2 cytokines interleukin-4 and interleukin-13 have a role in asthma blocking both cytokines may be more effective than targeting either alone.

Levels of the biomarkers FeNO, serum IgE, eotaxin-3, and TARC decreased with dupilumab, confirming the biologic activity of the drug.

In patients with persistent, moderate-to-severe asthma and elevated eosinophil levels who used inhaled glucocorticoids and LABAs, dupilumab therapy, as compared with placebo, was associated with fewer asthma exacerbations when LABAs and inhaled glucocorticoids were withdrawn, with improved lung function and reduced levels of Th2-associated inflammatory markers.

Wenzel S et al. N Engl J Med 2013;368:2455-66.



Wenzel S et al. N Engl J Med 2013;368:2455-66.

7 studies found for: dupilumab

Modify this search | How to Use Search Results

List | By Topic | On a Map | Search Details

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Include only open studies | Exclude studies with unknown status

Rank	Status	Study
1	Recruiting	**Long-Term Safety Evaluation of Dupilumab in Patients With Asthma** **Condition:** Asthma **Interventions:** Drug: dupilumab SAR231893 (REGN668); Drug: fluticasone propionate and salmeterol; Drug: budesonide and formoterol; Drug: mometasone furoate and formoterol
2	Recruiting	**An Evaluation of Dupilumab in Patients With Moderate to Severe Uncontrolled Asthma** **Condition:** Asthma **Interventions:** Drug: dupilumab SAR231893 (REGN668); Drug: placebo
3	Recruiting	**Study to Determine the Safety and Effectiveness of Dupilumab (REGN668/SAR231893) for Treatment of Atopic Dermatitis (AD)** **Condition:** Atopic Dermatitis (AD) **Interventions:** Drug: dupilumab; Drug: placebo
4	Active, not recruiting	**An Evaluation of Dupilumab in Patients With Nasal Polyposis And Chronic Symptoms Of Sinusitis** **Condition:** Nasal Polyps **Interventions:** Drug: dupilumab SAR231893 (REGN668); Other: placebo; Drug: mometasone furoate nasal spray

Rinitis que no responde

Correct Diagnosis

Co-morbidities

Allergen (over)exposure

Genetics

Remodeling

Surgical condition

Immunotherapy

Biologics

Curitiba, Prefeitura de 1916

Muchas gracias !

nelson.rosario@ufpr.br

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Allergic Rhinitis and its Impact on Asthma (ARIA) Classification of AR

Intermittent
< 4 days per week
OR < 4 weeks

Persistent
≥ 4 days per week
AND ≥ 4 weeks

Mild

- Normal sleep
- No impairment of daily activities, sport, leisure
- Normal work and school
- No troublesome symptoms in untreated patients

Moderate-severe
(one or more items)

- Abnormal sleep
- Impairment of daily activities, sport, leisure
- Abnormal work and school
- Troublesome symptoms

ARIA classification is a new system based on duration and severity.

Bousquet J, et al. *J Allergy Clin Immunol*. 2001;108(5 Suppl):S147-S334.

Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 Revision

J Allergy Clin Immunol 2010;126:466-76

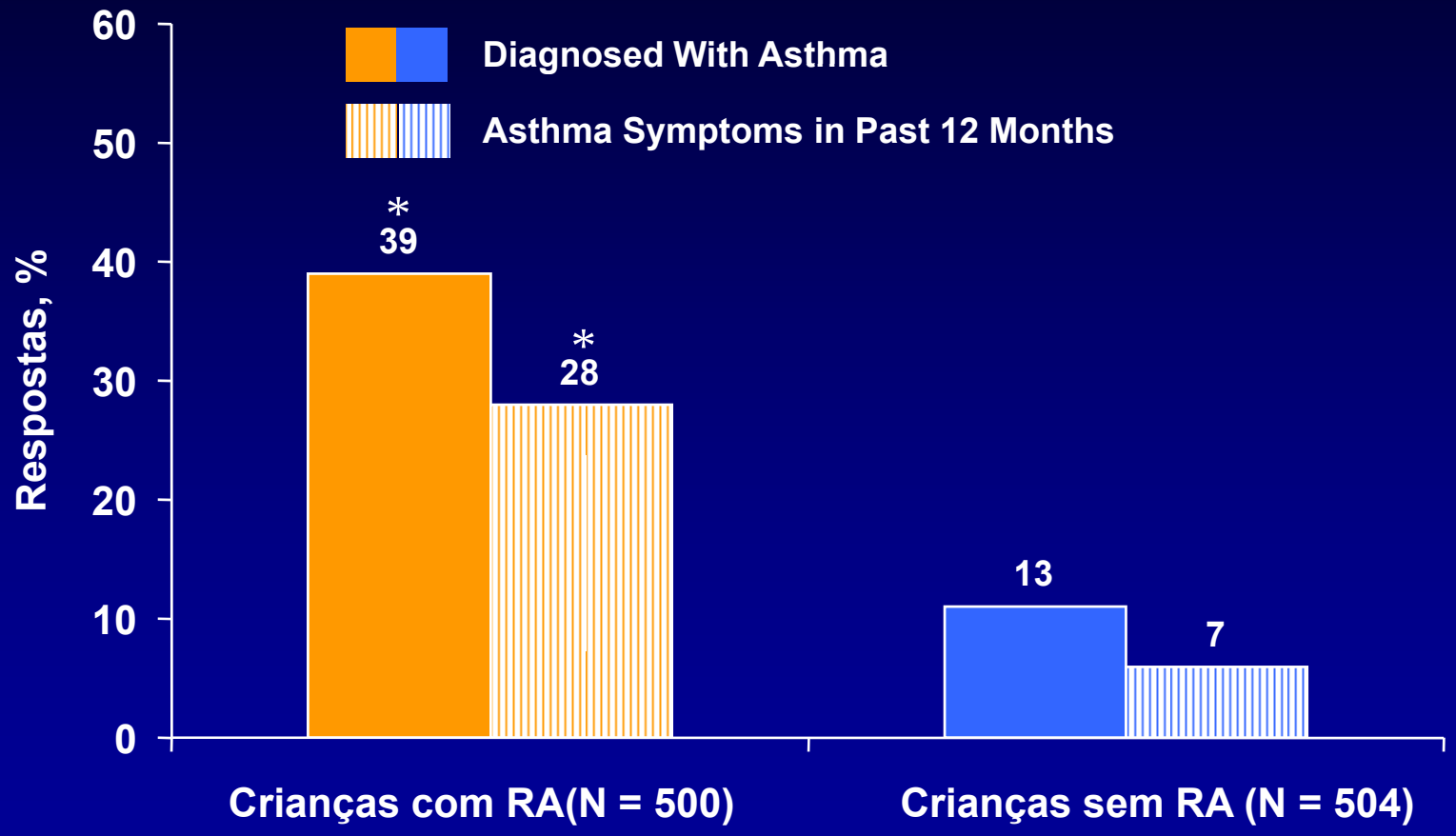
Jan L. Brożek, MD, PhD,[a] Jean Bousquet, MD, PhD,[b,c,d] Carlos E. Baena-Cagnani, MD,[e] Sergio Bonini, MD,[f,g]

Should oral H1-antihistamines be used for the treatment of AR?

- we recommend new-generation oral H1-antihistamines that do not cause sedation and do not interact with cytochrome P450 (strong recommendation /low-quality evidence).
- we suggest new-generation oral H1-antihistamines that cause some sedation and/or interact with cytochrome P450 (conditional recommendation / low-quality evidence).

GRADE: Grading of Recommendations Assessment, Development and Evaluat

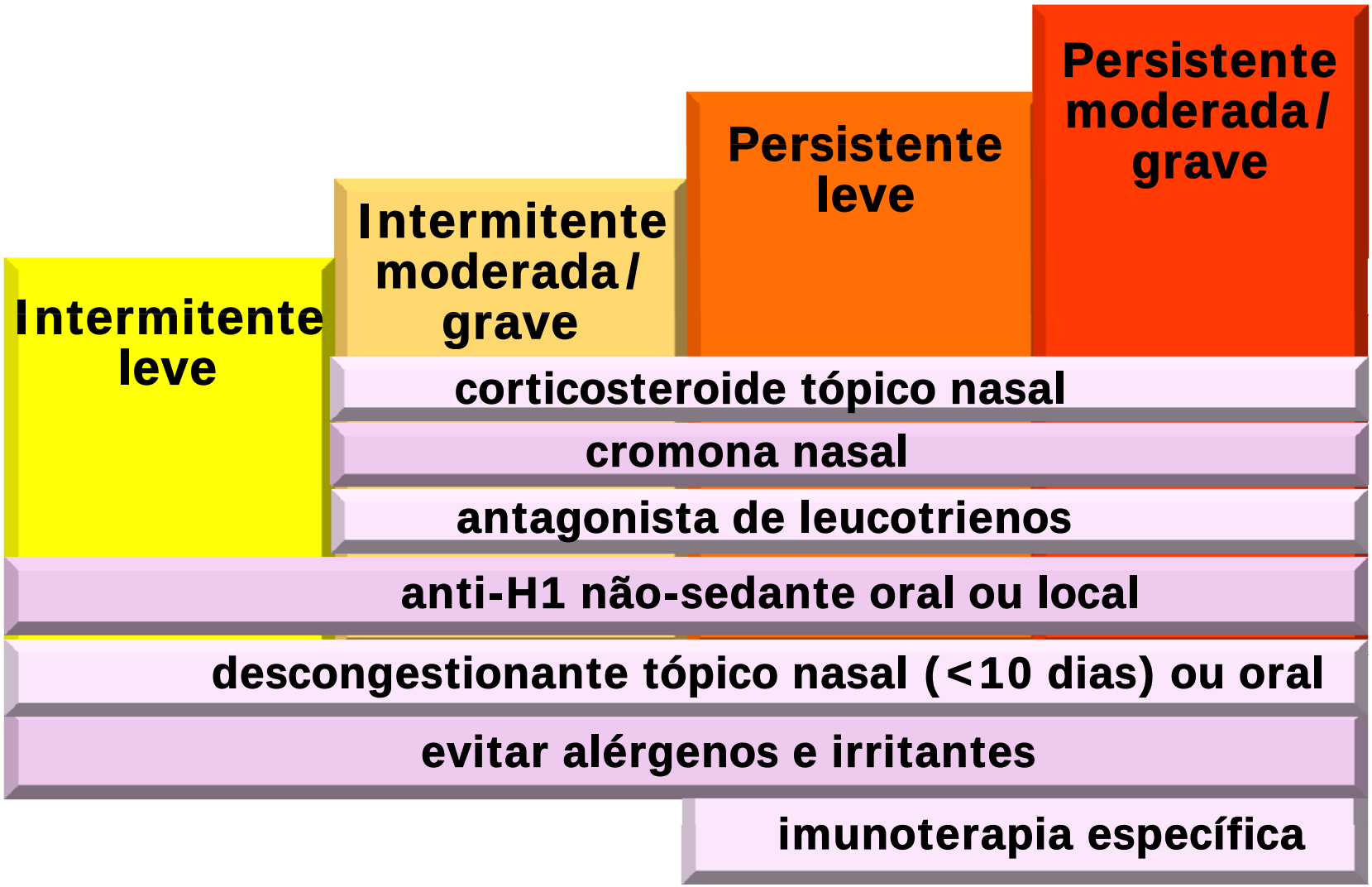
Prevalência de Asma em Pacientes Com e Sem RA



- Crianças com RA têm ≥ 3 vezes mais chance de ter diagnóstico ou sintomas de asma que as sem RA ($p<0.001$)

Tratamento da rinite alérgica (ARIA)

Allergic Rhinitis and its Impact on Asthma

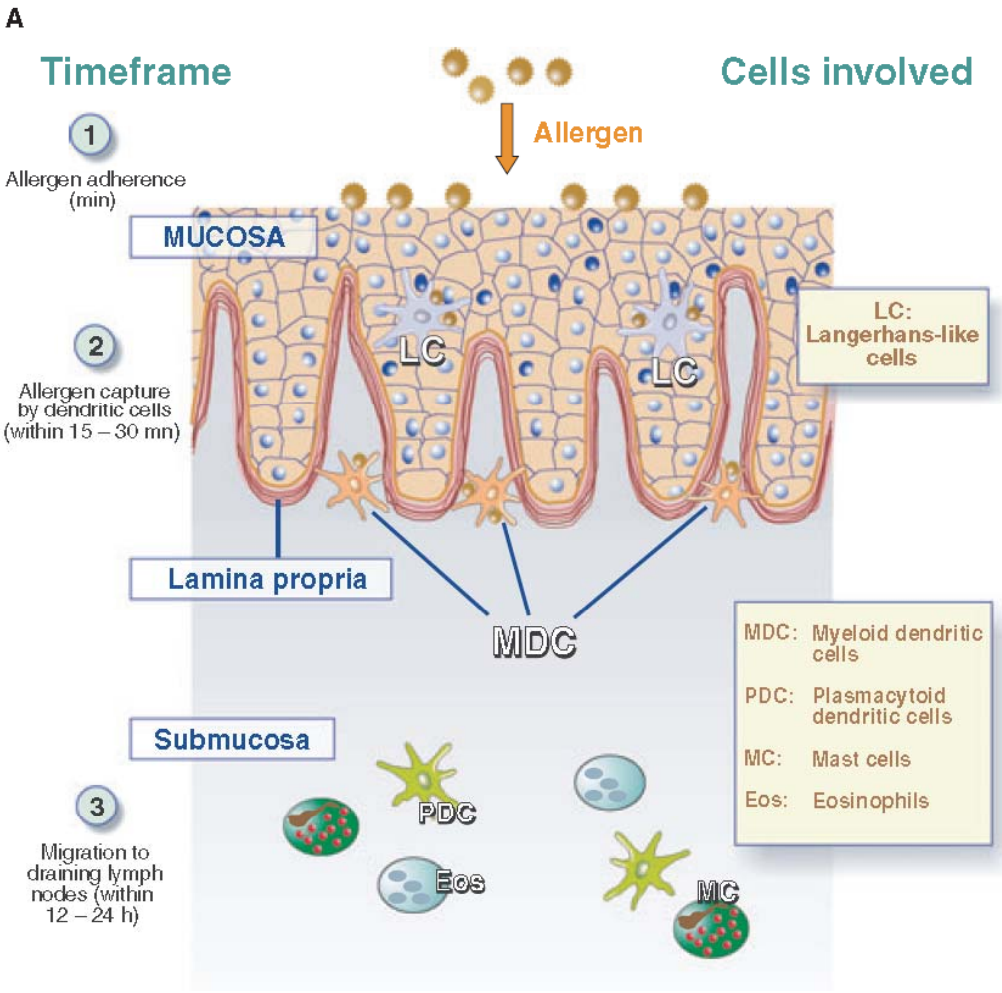


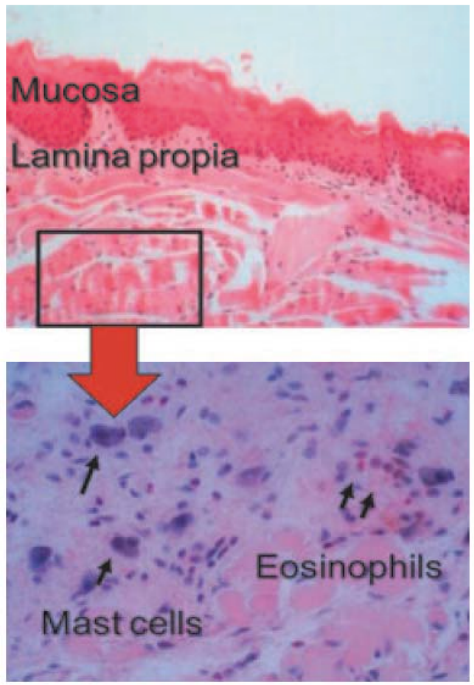
Bousquet et al - Allergy 2008;63(Sup86):8-160

REVIEW ARTICLE Allergy 2012; 67: 302–311.

Sublingual allergen immunotherapy: mode of action and its relationship with the safety profile

M. A. Calderón[1], F. E. R. Simons[2], H.-J. Malling[3], R. F. Lockey[4], P. Moingeon[5] & P. Demoly[6]





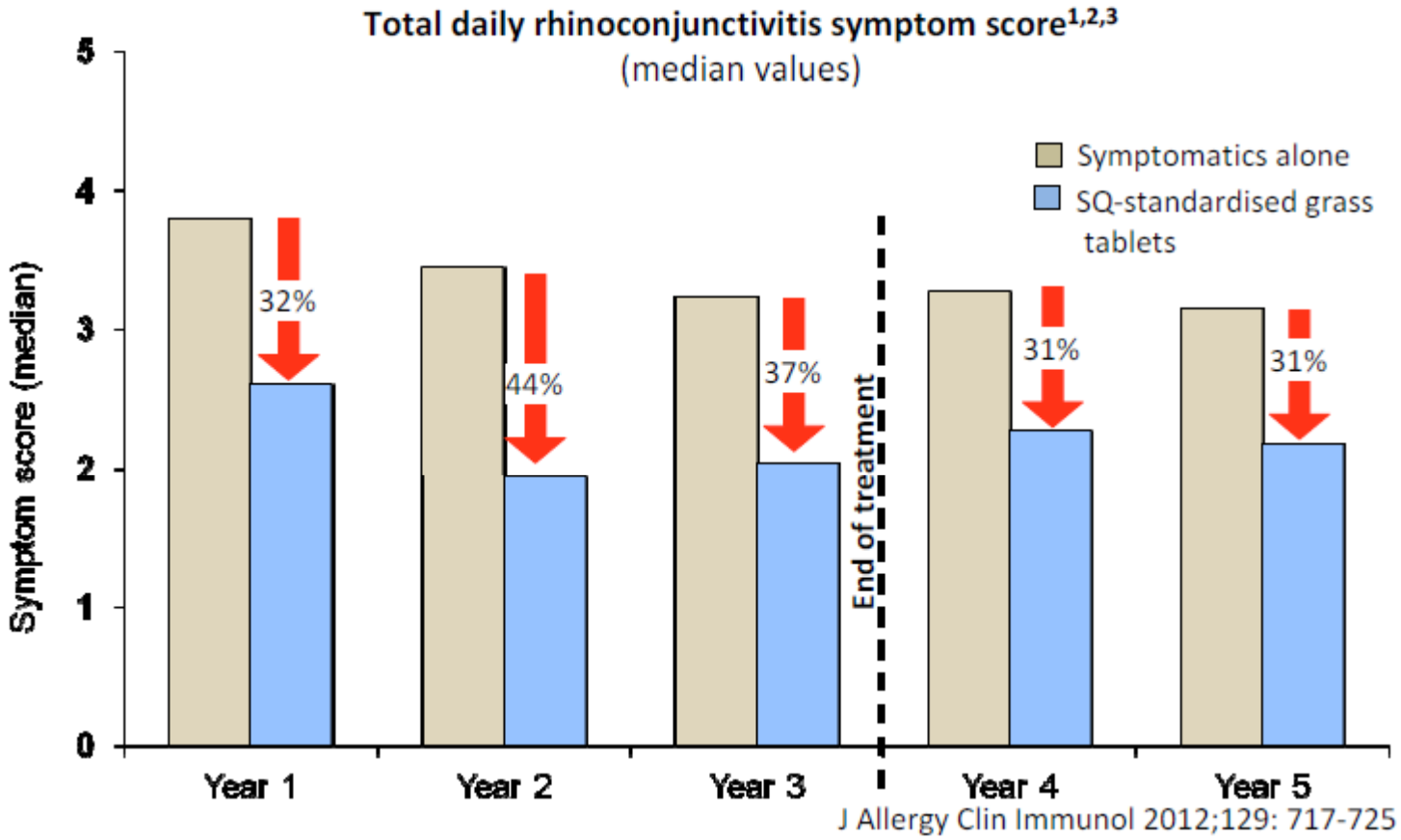
Allergy 2012; 67: 302–311.

Clinical efficacy of SLIT and SCIT in comparative studies

Authors	Year	Study design	Patients (*n*)	Patient age range	Allergen extract	Treatment duration	SLIT allergen dose (-fold the SCIT dose)	Conclusion in terms of efficacy
Bernardis et al. (9)	1996	Open, controlled, no placebo	23	5–26	*Alternaria tenuis*	2 years	×3.6	SLIT > SCIT
Quirino et al. (10)	1996	RCT, double-dummy, no placebo	20	13–39	Five grasses	1 year	×2.4	SLIT = SCIT
Mungan et al. (11)	1999	RCT, single-blind, placebo	36	18–46	Der p, Der f	1 year	×80	SLIT = SCIT
Khinchi et al. (12)	2004	RCT double-dummy, placebo	58	20–58	Birch	2 years	×210	SLIT = SCIT
Herrscher (13)	2006	Patient survey	328	3–71	Multi-allergen extracts	Typically 9–18 months	×5–10	SLIT = SCIT
Mauro et al. (14)	2007	RCT, no placebo	47	18–59	Alder, birch, and hazel	*Not stated*	×92	SLIT = SCIT

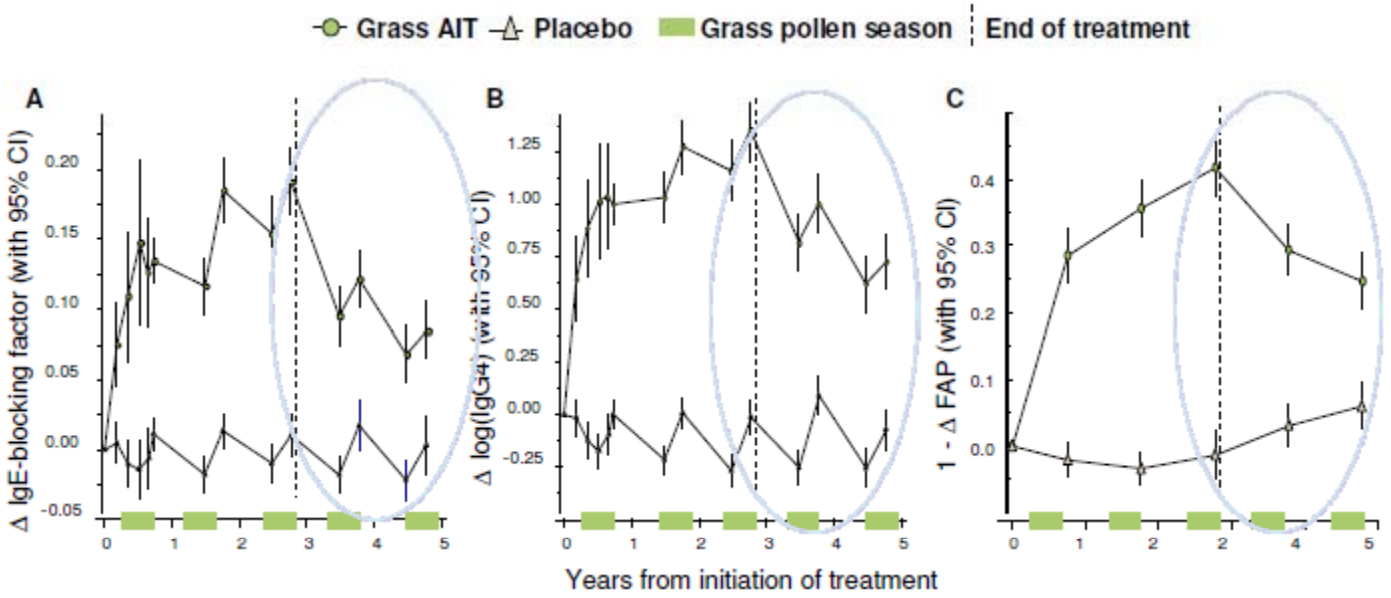
Allergy 2012; 67: 302–311.

Grass allergen tablet sublingual immunotherapy: Efficacy sustained 2 yrs after 3 years treatment



J Allergy Clin Immunol 2012;129: 717-725

Persistent Immunological changes



J Allergy Clin Immunol 2012;129:717-725


The Skin Prick Test:
European Standards

Holgate *World Allergy Organization Journal* 2014, **7**:17
http://www.waojournal.org/content/7/1/17

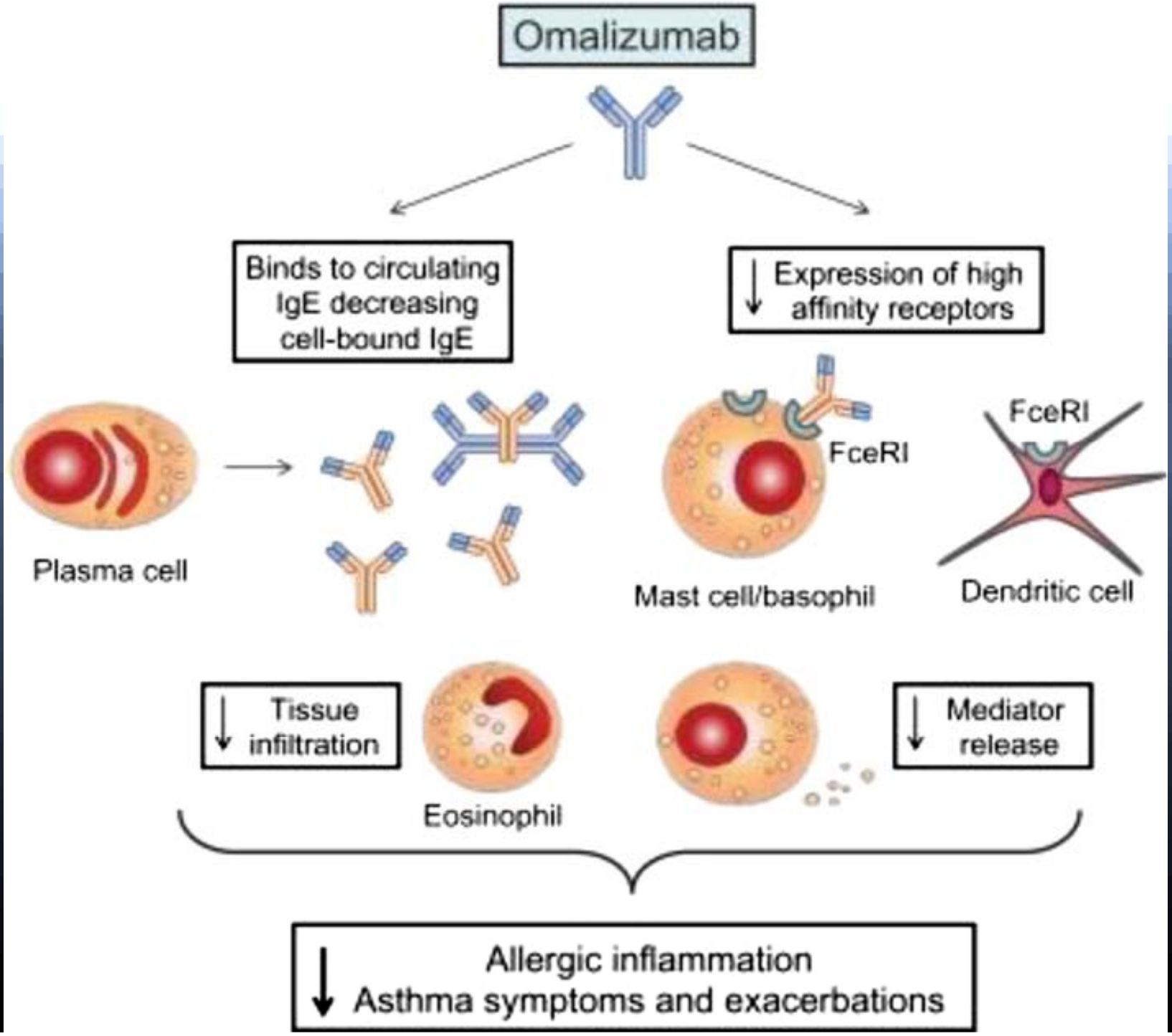
WAO journal
WORLD ALLERGY ORGANIZATION

REVIEW **Open Access**

New strategies with anti-IgE in allergic diseases

Stephen T Holgate

Disease	Responsiveness to omalizumab	Reference
Non-allergic asthma	Some reported benefits, but controversial	- Menzella F, Piro R, Facciolongo N, Castagnetti C, Simonazzi A, Zucchi L. Long-term benefits of omalizumab in a patient with severe non-allergic asthma. Allergy Asthma Clin Immunol. 2011; 7: 9. - Domingo C, Pomares X, Angril N, Rudi N, Amengual MJ, Mirapeix RM. Effectiveness of omalizumab in non-allergic severe asthma. J Biol Regul Homeost Agents. 2013; 27: 45–53.
Churg-Strauss (C-S) Syndrome	Anecdotal evidence of efficacy, but also reports of uncovering latent C-S disease	- Giavina-Bianchi P, Giavina-Bianchi M, Agondi R, Kalil J.Administration of anti-IgE to a Churg-Strauss syndrome patient. Int Arch Allergy Immunol. 2007; 144: 155–8. - Wechsler ME, Wong DA, Miller MK, Lawrence-Miyasaki L. Churg-strauss syndrome in patients treated with omalizumab. Chest. 2009; 136: 507–18.
Allergic rhinitis	Well documented benefit, but questionable cost-effectiveness	- Vashisht P, Casale T. Omalizumab for treatment of allergic rhinitis. Expert Opin Biol Ther. 2013; 13: 933–45.
Atopic dermatitis (AD, eczema)	Efficacious in severe refractory AD	- Kim DH, Park KY, Kim BJ, Kim MN, Mun SK. Anti-immunoglobulin E in the treatment of refractory atopic dermatitis. Clin Exp Dermatol. 2013; 38: 496–500.


Omalizumab
Binds to circulating IgE decreasing cell-bound IgE
↓ Expression of high affinity receptors
Plasma cell
FceRI
FceRI
Mast cell/basophil
Dendritic cell
↓ Tissue infiltration
Eosinophil
↓ Mediator release
↓ Allergic inflammation
↓ Asthma symptoms and exacerbations

The placebo effect in allergen-specific immunotherapy trials

Table 2 Changes from baseline as well as changes in the per cent of the AUC of SMS in the placebo group during the studies

Extract	SMS at baseline (mean)	SMS mean change from baseline 1st yr	SMS mean change from baseline 2nd yr	Placebo effect SMS %*	
				1st year	2nd year
SCIT HDM 1	181.7	−44.2	−53.9	**−24.3**	**−29.7**
SCIT HDM 2	251.7	−83.7	−102.0	**−33.2**	**−40.5**
SCIT grasses	599.3	−98.8	−148.3	**−16.5**	**−24.7**
SLIT grasses	484.0	−6.2	+3.6	**−1.3**	**+0.7**
SCIT Birch 1	396.9	−205.5	−97.4	**−51.8**	**−24.5**
SCIT Birch 2	286.8	−16.8	−52.4	**−5.9**	**−18.3**

Legend: *calculated as change/baseline (in%).

472 adults treated with placebo in RCT

Narkus et al. Clinical and Translational Allergy 2013, 3:42

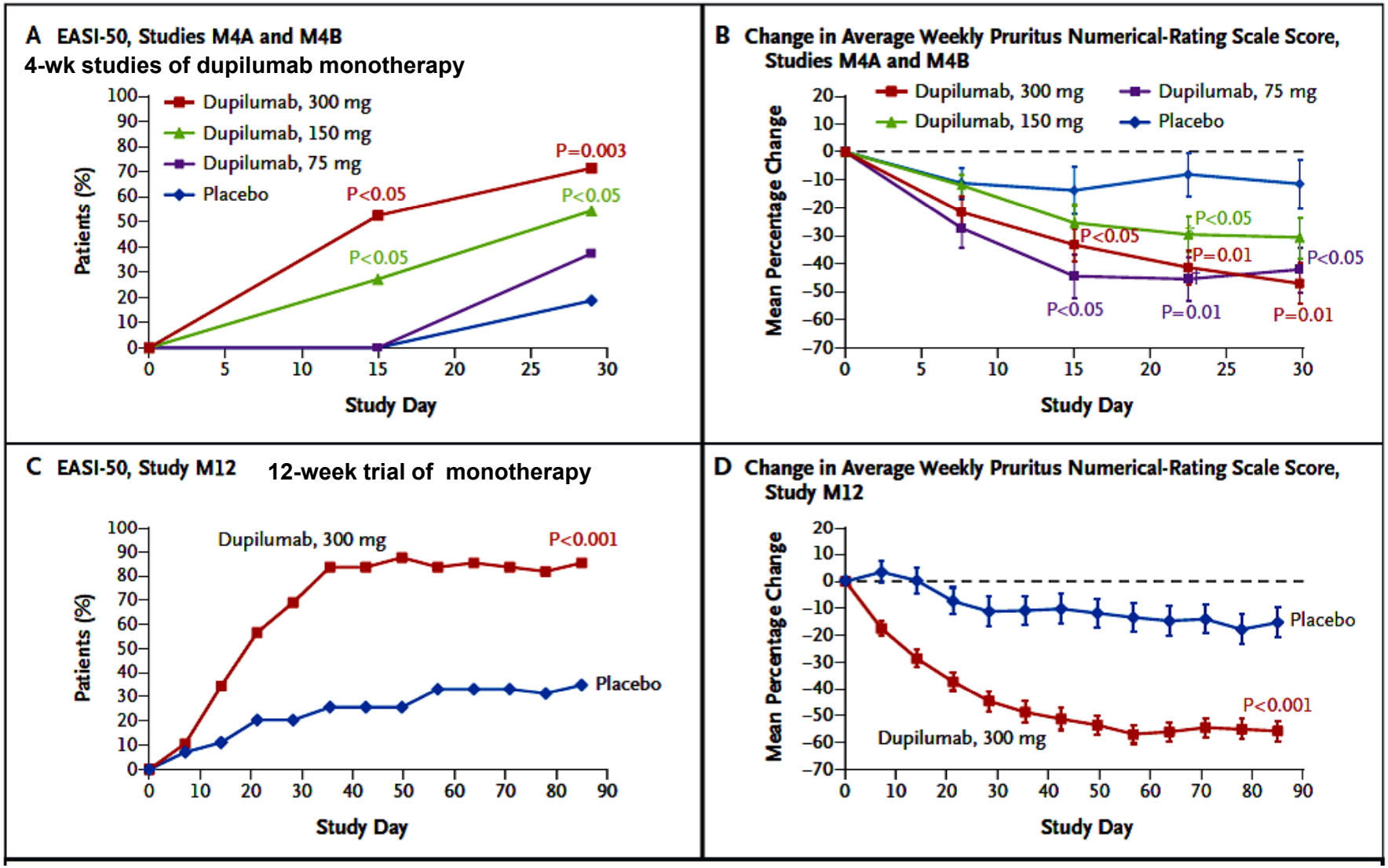
ORIGINAL ARTICLE

Dupilumab Treatment in Adults with Moderate-to-Severe Atopic Dermatitis

Lisa A. Beck, M.D., Diamant Thaçi, M.D., Jennifer D. Hamilton, Ph.D.,

Fully human monoclonal antibody to the interleukin-4 receptor α subunit that inhibits both interleukin-4 and interleukin-13 signaling.

N Engl J Med 2014;371:130-9.



50% improvement Eczema Area and Severity Index score .

Beck LA et al. N Engl J Med 2014;371:130-9.

Table 3. Adverse Events.*

Variable	4-Wk Monotherapy		12-Wk Monotherapy		4-Wk Combination Therapy	
	Placebo (N=16)	Dupilumab (N=51)	Placebo (N=54)	Dupilumab (N=55)	Placebo and Topical Glucocorticoids (N=10)	Dupilumab and Topical Glucocorticoids (N=21)
Any adverse event — no. of patients (%)	14 (88)	44 (86)	43 (80)	42 (76)	7 (70)	12 (57)
Mean no. of adverse events per patient	2.50	2.14	2.94	2.96	1.40	1.95
Serious adverse event — no. of patients (%)	1 (6)	1 (2)	7 (13)	1 (2)	1 (10)	0
Study discontinuation due to adverse event — no. of patients (%)	1 (6)	0	3 (6)	1 (2)	1 (10)	0
Skin infection — no. of patients (%)	2 (12)	2 (4)	13 (24)	3 (5)	1 (10)	1 (5)

* The adverse events included here, which are listed according to the preferred terms in the *Medical Dictionary for Regulatory Activities* (version 13.1 for study M4A, version 14.0 for Study M4B, and version 14.1 for Studies M12 and C4), were those that occurred in at least 5% of the patients in any study group.

Beck LA et al. N Engl J Med 2014;371:130-9.

Review

Allergy Asthma Immunol Res. 2012 March;4(2):62-67.
http://dx.doi.org/10.4168/aair.2012.4.2.62
pISSN 2092-7355 • eISSN 2092-7363

AAIR
Allergy, Asthma & Immunology Research

Asthma and Rhinitis in South America: How Different They are From Other Parts of the World

Herberto José Chong Neto,[1] Nelson Augusto Rosário,[1]* Dirceu Solé,[2]; Latin American ISAAC Group

Prevalence of current rhinoconjunctivitis in children and adolescents

Country/Center	6-7-yr ISAAC I (%)	13-14-yr ISAAC I (%)	6-7-yr ISAAC IIII (%)	13-14-yr ISAAC III (%)
Brazil				
Aracaju[28-30,32]	-	-	9.3	12.3
Belo Horizonte[28-30,32]	-	-	-	11.4
Brasília[14,28-30,32]	-	-	-	12.3
Caruaru[28-30,32]	-	-	-	12.3
Curitiba[16,18,28-32]	-	14.1	-	17
Feira de Santana[28-30]	-	-		13.9
Itabira[28-31]	-	-	-	-
Itajaí[28-30]			9.4	10.6
Maceió[28-30]	-	-	10.8	13.6
Manaus[28-30]	-	-	10.5	12.5
Nova Iguaçu[28-30]	-	-	11.6	12.1
Passo Fundo[21,28-30,32]	-	-	-	15.8
Porto Alegre[2,18,28-32]	10.6	17.6	-	14.2
Recife[2,18,28-32]	10.3	11.3	-	14.2
Rural Santa Maria[28-30,32]	-	-	-	7.8
Salvador[2,18,28-32]	-	25	16.7	21.1
Santa Maria[28-30,32]	-	-	-	10
Santo André[28-30,32]	-	-	13.2	13.8
São Paulo[2,18,25,28-32]	12.5	12.6	12	15.6
São Paulo West[28-30]	-	-	13.3	8.8
Uberlândia	-	-	-	-
Vitória da Conquista[28-30]	-	-		19.8
Chile				
Calama[2,28-30]	-	-	-	22.9
Central Santiago[2,18,28-30]	11.2	15.7	-	-
Chiloe[2,28-30]	-	-	-	19.1
Punta Arenas[2,9,28-30]	8.8	8.4	11.2	14.1
South Santiago[2,9,28-30]	11.2	15.7	13.7	26.3
Valdivia[2,9,28-30]	8	9.8	11.9	26.3

Chong, Rosario, Solé Allergy Asthma Immunol Res. 2012;4:62-7.

Allergic rhinitis (AR) symptoms and non-AR symptoms in infants in the 1st yr of life.

(n=1003)

	AR Symptoms n=484	Non-AR Sx's n=519	p value
Age at onset (mean±SD)	6±3.3 mos		
Male	246 (50.8)	267 (51.5)	.84
<3 Wheezing episodes	133 (27.5)	155 (29.8)	.44
≥3 Wheezing episodes	112 (23.1)	85 (16.4)	.001
AR Physician Diagnosis	157 (32.4)	46 (8.9)	.0001
AH	109 (22.5)	116 (22.4)	.99
INS	96 (19.8)	67 (12.9)	.001
AH/INS		40 (7.7)	.001

Chong Neto et al 2013

Diagnóstico

Diagnóstico clínico

- História clínica
- Antecedentes pessoais e familiares de atopia
- Exame físico
- Testes cutâneos/IgE específicas

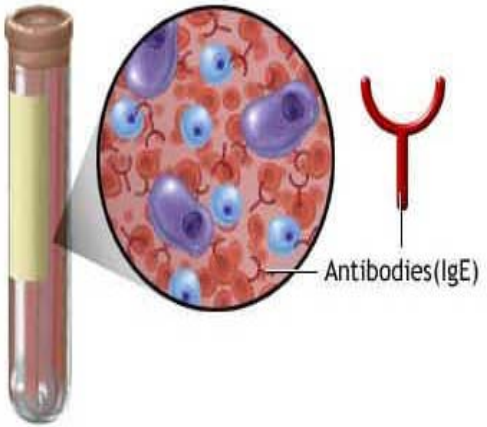
Hiperemia conjuntival

Mucosa pálida/violácea

Rinite Alérgica

Exames subsidiários

- Hemograma completo
- IgE sérica total
- Testes cutâneos de hipersensibilidade imediata
- IgE sérica específica
- Provocação nasal
- Citologia nasal
- Testes de permeabilidade nasal
  - Rinomanometria
  - Rinometria acústica
- Teste de olfação



IV Consenso Brasileiro sobre Rinites. Braz J Otorhinolaryngol 2017

Testes Cutâneos Alérgicos

- Percutâneo - Prick

- Intradérmico

Nelson Rosário

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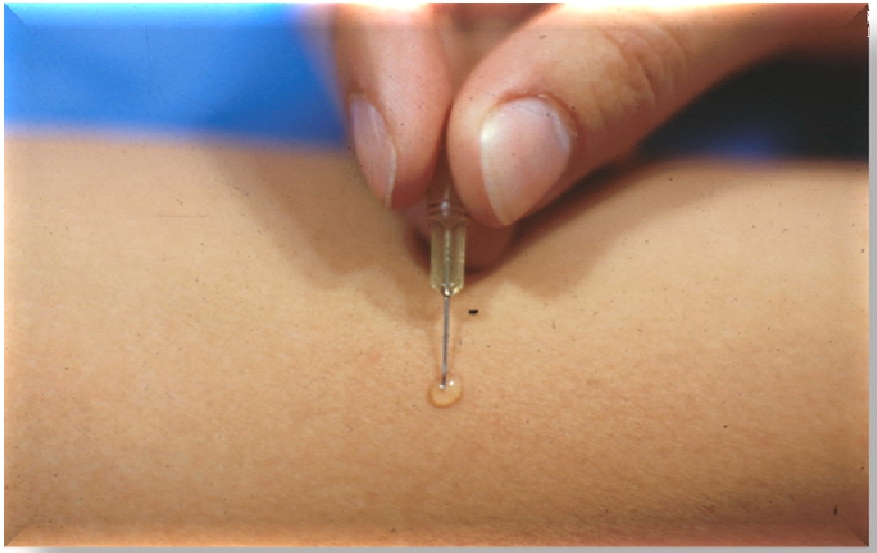

Prick/puntura. **Alérgeno é introduzido por puntura na superfície da pele.**

Intradérmico. **Alérgeno diluído é injetado na derme.**

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\+ wheal < 2 mm, with erithema

++ wheal 2-5 mm

+++ wheal > 5 mm

++++ pseudopods

Titulação dos testes cutâneos

Diagnóstico confirmado?

Qual o sintoma mais importante,

para o paciente?

para o seu tratamento?

Frequência e Intensidade dos sintomas

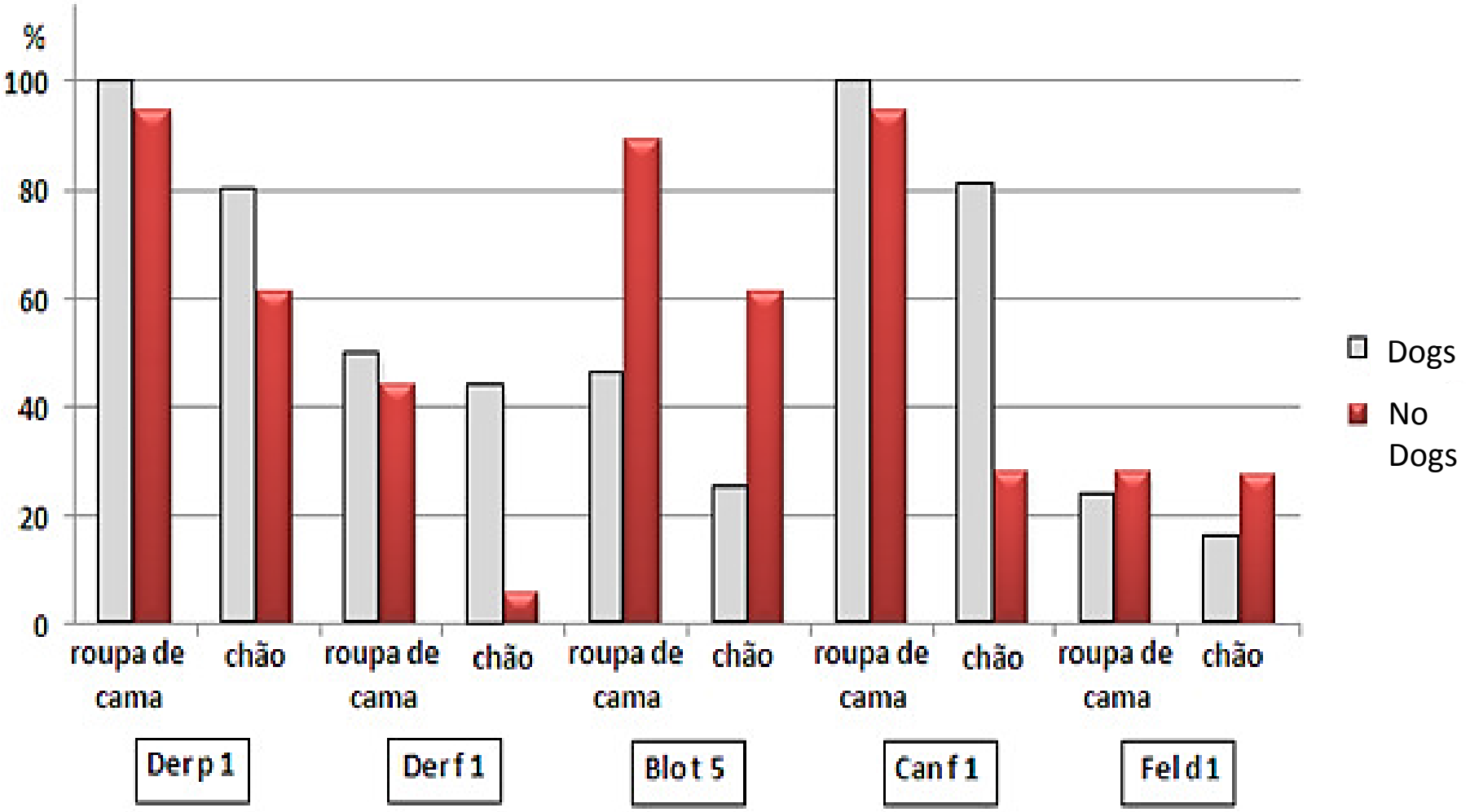
Allergen distribution (mcg/g) in dust and bed samples in houses with and without a dog

ALÉRGENOS	Com cão # (n=26)	Sem cão # (n=18)	p ∞
Der p 1 Roupa Cama	171 (0,3 - 2493)	3,36 (0 -10,8)	**0,001**
Chão	0,6 (0 - 546)	0,07 (0 - 3,9)	**0,009**
Der f 1 Roupa Cama	0,025 (0 - 86)	0 (0 - 0,82)	0,23
Chão	0 (0 -2)	0 (0 - 0,04)	**0,01**
Blo t 5 Roupa cama	0 (0 - 1,4)	0,055 (0 - 0,17)	0,69
Chão	0 (0 -5,6)	0,04 (0 - 0,15)	0,25
Can f 1 Roupa Cama	0,51 (0,03 - 3,66)	0,05 (0 - 4,4)	**0,01**
Chão	0,2 (0 -4,69)	0 (0 -1,64)	**0,0004**
Fel d 1 Roupa Cama	0 (0 - 2,1)	0 (0 - 0,18)	0,78
Chão	0 (0 - 5,6)	0	0,25

∞ Mann-Whitney; # Mediana (min – max)

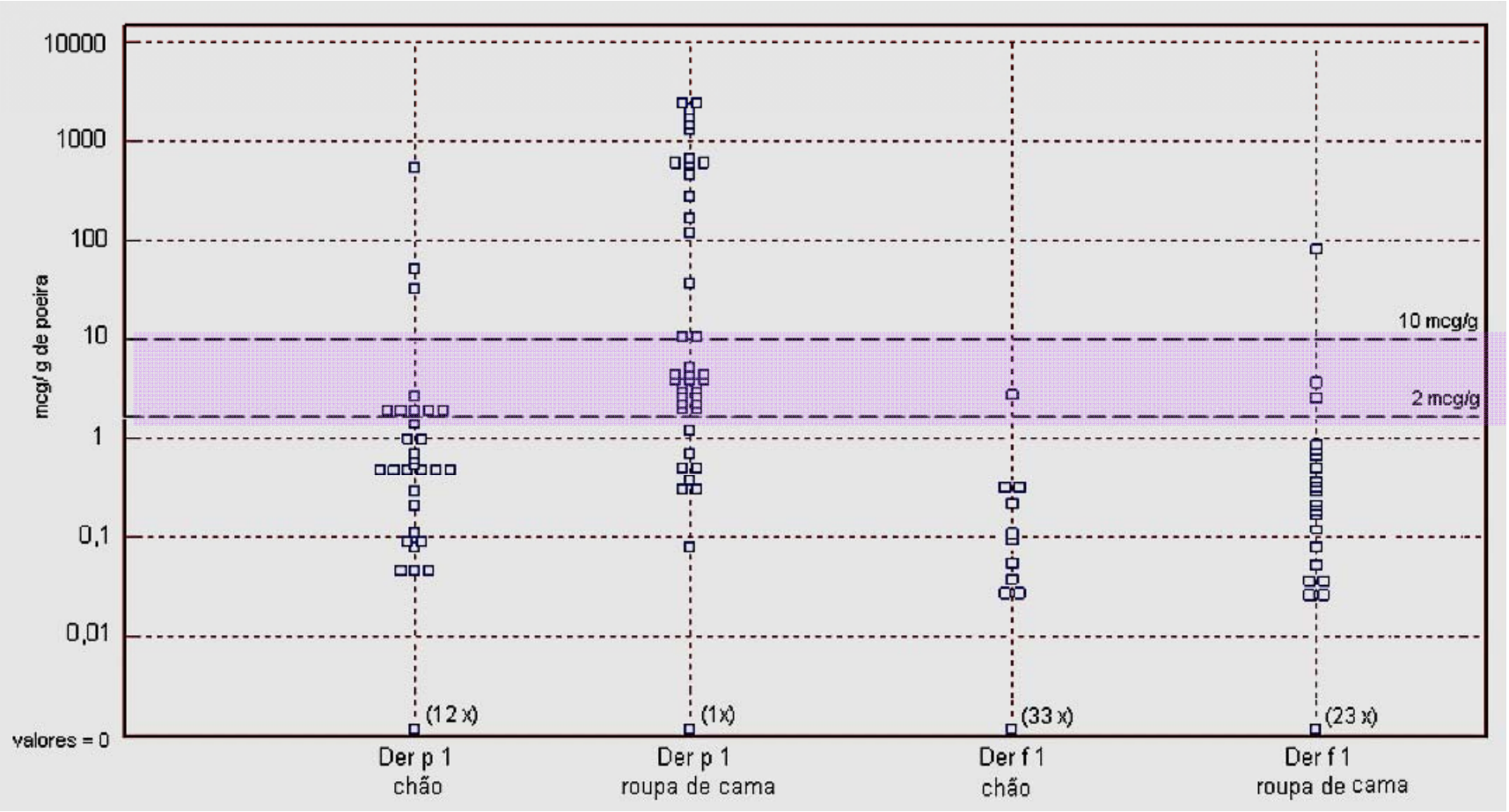
Souza C & Rosario N. *Rev. bras. alerg. imunopatol. 2012;35:47-52*

Frequency of allergens in samples from bed linen and floor of homes with dogs



Souza C & Rosario N. *Rev. bras. alerg. imunopatol. 2012;35:47-52*

Mite allergens in floor dust and bed samples



Souza C & Rosario N. *Rev. bras. alerg. imunopatol. 2012;35:47-52*

Diagnóstico correto → tratamento individual
segurança e satisfação do paciente

DYMISTA (azelastine hydrochloride and fluticasone propionate) nasal spray, for intranasal use
Initial U.S. Approval: 2012

RECENT MAJOR CHANGES

- Indications and Usage, Allergic Rhinitis (1) 2/2015

INDICATIONS AND USAGE

DYMISTA contains an H_1-receptor antagonist and a corticosteroid, and is indicated for the relief of symptoms of seasonal allergic rhinitis in patients 6 years of age and older who require treatment with both azelastine hydrochloride and fluticasone propionate for symptomatic relief. (1.1)