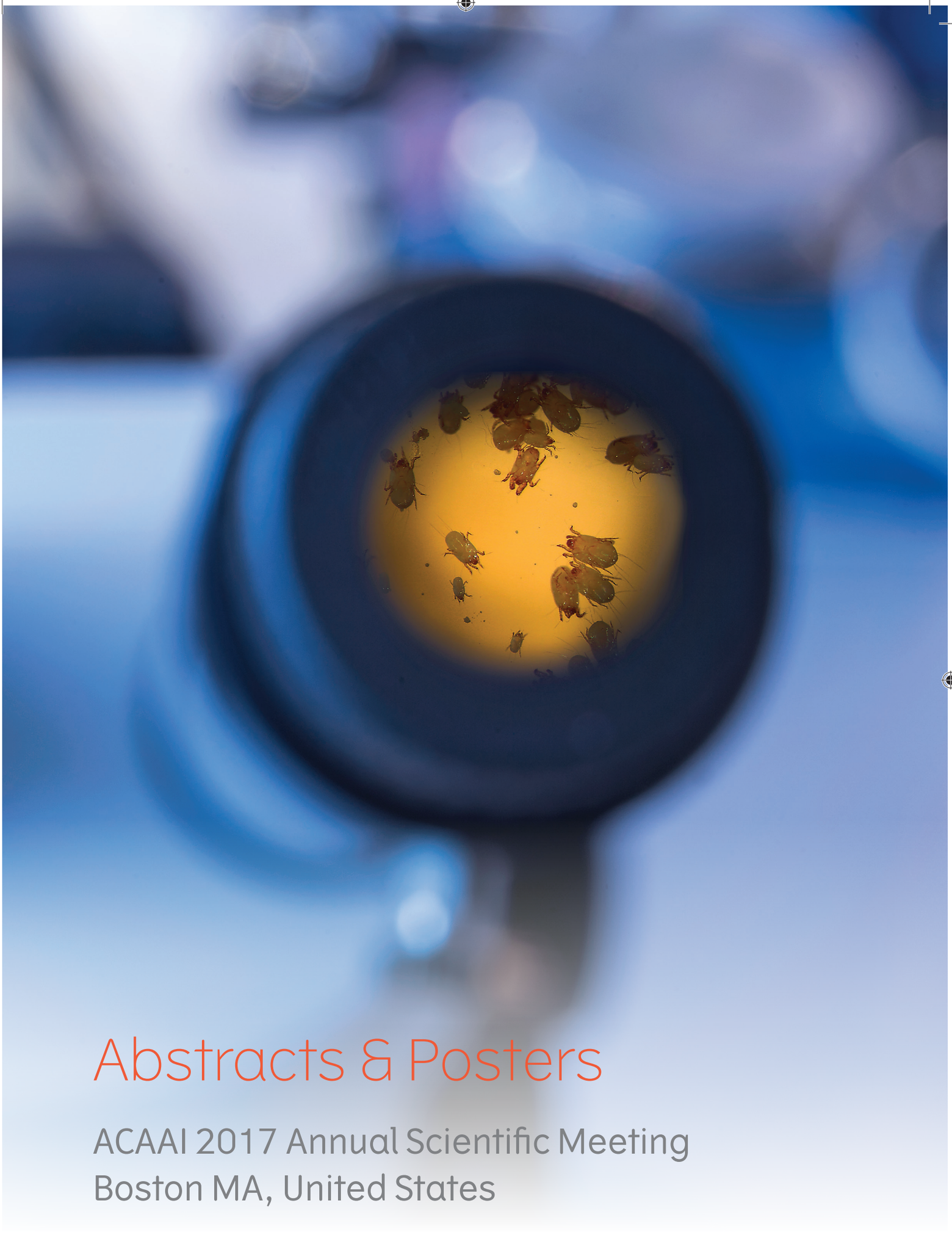

Abstracts & Posters

ACAAI 2017 Annual Scientific Meeting
Boston MA, United States

ALK

Dear ACAAI delegate

ALK welcomes you to the ACAAI 2017 Annual Scientific Meeting in Boston, MA.

As the world leader in allergy immunotherapy (AIT), we are proud to present 3 abstracts concerning the recently introduced SQ HDM SLIT-tablet with demonstrated efficacy in patients suffering from house dust mite induced allergic rhinitis.

One of the abstracts is focused on the clinical relevance of the SQ HDM SLIT-tablet in moderate-to-severe house dust mite allergic rhinitis. Another abstract looks more closely at the efficacy of treating nasal congestion symptoms, whereas the third abstract addresses the often debated aspect of efficacy in mono- versus poly-sensitized patients.

ALK is committed to sustain, develop and disseminate allergy immunotherapy and anaphylaxis management worldwide.

Enjoy the congress and please join us at our stand in the exhibition area to learn more about our concepts and ongoing research activities at ALK.

Hendrik Nolte, MD, PhD
Senior Vice President
Research & Development

Clinical relevance of the SQ HDM SLIT-tablet in moderate-to-severe house dust mite allergic rhinitis

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Introduction

The SQ house dust mite (HDM) SLIT-tablet (ALK, Denmark) is efficacious in adults and adolescents with HDM allergic rhinitis. Here clinical relevance data from a North American, randomized, DBPC trial (clinicaltrials.gov: NCT01700192) is presented.

Methods

1482 subjects aged ≥12 years with moderate-to-severe HDM allergic rhinitis were randomised to 12 SQ-HDM or placebo for up to 1 year. Post-hoc the numbers of rhinitis exacerbation days and mild days were calculated: a rhinitis exacerbation day was a day with an allergic rhinitis symptom score of 6, or 5 with one individual symptom scored 3 (i.e. symptom that caused interference with daily life); a mild day was a day with no individual symptom scored higher than 1 (i.e. symptom caused minimal awareness) and no antihistamine use.

Results

The estimated probability for a rhinitis exacerbation was 23.4% for placebo and 12.7% with 12 SQ-HDM (OR=0.48; 95% CI [0.34; 0.68]; p<0.001) over the 8 weeks efficacy assessment period. The estimated probability for a mild rhinitis day was 35.0% for placebo and 48.3% with 12 SQ-HDM (OR=1.73; 95% CI [1.21; 2.49]; p=0.003). Assuming similar conditions, efficacy over 1 year may be estimated to 85 days versus 46 days with rhinitis exacerbation and 128 days versus 176 days with mild days in the placebo group compared with 12 SQ-HDM.

Conclusion

Treatment with 12 SQ-HDM reduced the patient's probability for having rhinitis exacerbation days and increased the probability for having mild days. These findings illustrate the clinical relevance of the SQ HDM SLIT-tablet in adolescents and adults with moderate-to-severe HDM allergic rhinitis.

Clinical relevance of the SQ HDM SLIT-tablet in moderate-to-severe house dust mite allergic rhinitis

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Introduction

The SQ house dust mite (HDM) SLIT-tablet (ALK, Denmark) has been shown to be efficacious in adults and adolescents with HDM allergic rhinitis (1,2). The primary outcome of a North American randomised, double-blind, placebo-controlled trial (clinicaltrials.gov: NCT01700192) with the SQ HDM SLIT-tablet showed a 17.2% reduction in Total Combined Rhinitis Score (2). Here, in order to further explore the clinical relevance of these results, post-hoc analysis of the number of rhinitis exacerbation days and mild days is presented (see box for definition).

Methods

1482 patients aged ≥12 years with moderate-to-severe HDM allergic rhinitis were randomized (1:1) to 12 SQ-HDM or placebo treatment once daily for up to 1 year. Patients had a clinical history of house dust mite (HDM)-induced allergic rhinitis/rhinoconjunctivitis of 1 year duration or more, with or without asthma, and HDM allergy status was confirmed by positive SPT and IgE tests. Randomization was stratified by asthma status (yes/no) and age (<18/≥18 years). Patients were required to record rhinitis, conjunctivitis, and asthma symptom scores in an e-diary in the morning during the Baseline and again during the last 12 weeks of the trial. Rescue medications were provided to patients to be taken as directed by the Investigators. Efficacy was measured during the last 8 weeks of the treatment period (Figure 1).

Results

The estimated probability for a rhinitis exacerbation was 23.4% for placebo and 12.7% with 12 SQ-HDM (OR=0.48; 95% CI [0.34; 0.68]; p<0.001) over the 8 weeks efficacy assessment period (Figure 2). The estimated probability for a mild rhinitis day was 35.0% for placebo and 48.3% with 12 SQ-HDM (OR=1.73; 95% CI [1.21; 2.49]; p=0.003). The same pattern of decreased probability of AR exacerbation days and increased probability of mild AR days was also seen in the pivotal European trial (3). Since HDM allergy is a perennial disease, it is of interest to understand the year round impact of these data. Assuming similar conditions as during the 8-week assessment period, efficacy over 1 year may be estimated to 85 days versus 46 days with rhinitis exacerbation and 128 days versus 176 days with mild days in the placebo group compared with 12 SQ-HDM.

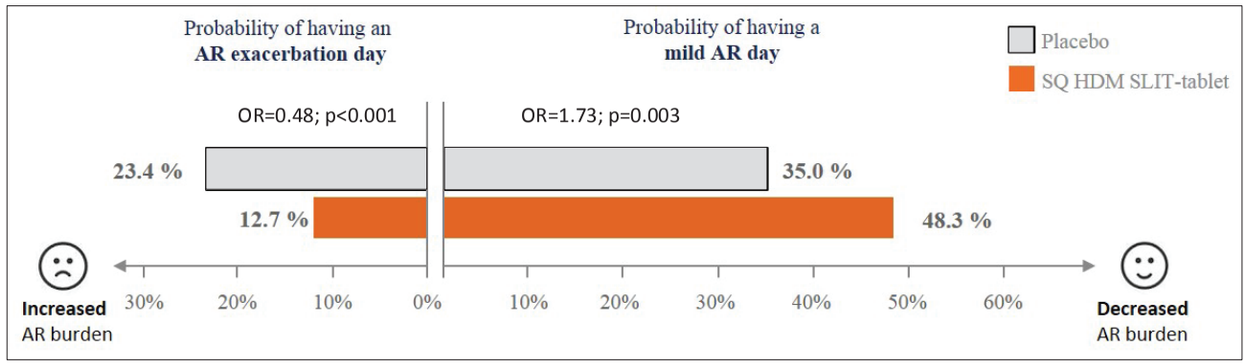


Figure 2: Probability of having an AR exacerbation day or a mild AR day for Placebo and SQ HDM SLIT-tablet treated patients during the 8 week efficacy evaluation period. AR: allergic rhinitis.

- A rhinitis exacerbation day was a day with an allergic rhinitis symptom score of 6, or 5 with one individual symptom scored 3 (i.e. symptom that caused interference with daily life)
- A mild day was a day with no individual symptom scored higher than 1 (i.e. symptom caused minimal awareness) and no antihistamine use

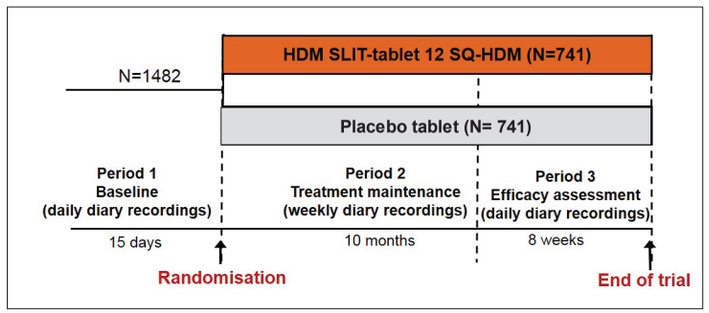


Figure 1: Trial design

References

1: Demoly P., Emminger W., Rehm D., et al. Effective treatment of house dust mite–induced allergic rhinitis with 2 doses of the SQ HDM SLIT-tablet: Results from a randomized, double-blind, placebo-controlled phase III trial. J Allergy Clin Immunol 2016;137(2):444-51
2: Nolte H., Bernstein D.I., Nelson H.S. et al. Efficacy of house dust mite sublingual immunotherapy tablet in North American adolescents and adults in a randomized, placebo-controlled trial. J Allergy Clin Immunol 2016;138:1631-8
3: Demoly P, Kleine-Tebbe J, Rehm D. Clinical benefits of treatment with SQ house dust mite sublingual tablet in house dust mite allergic rhinitis. Allergy. 2017;00:1–3. https://doi.org/10.1111/all.13155

Conclusion

Treatment with 12 SQ-HDM significantly reduced the patients probability for having rhinitis exacerbation days and increased the probability for having mild days. These findings illustrate the clinical relevance of the SQ HDM SLIT-tablet in patients with moderate-to-severe HDM allergic rhinitis.

Efficacy of the SQ HDM SLIT-tablet on nasal congestion symptoms; results from 2 DBPC trials

Stephen Tilles[1]; Jonathan Corren[2]; Bente Riis[3]; Hendrik Nolte[3]
[1]University of Washington, Seattle, WA, USA; [2]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [3]ALK, Denmark

Introduction

Nasal congestion has been reported as one of the most bothersome symptoms for patients with house dust mite (HDM) allergy. This abstract presents the clinical efficacy on nasal congestion from 2 double-blind, randomized, placebo-controlled trials conducted in North America (trial A, clinicaltrials.gov: NCT01700192) and Europe (trial B, EudraCT: 2011-002277-38).

Methods

Subjects (N=1482 in trial A, N=992 in trial B) with moderate-to-severe HDM allergic rhinitis were treated with the SQ HDM SLIT-tablet (ALK, Denmark) for up to 1 year. For both trials, the primary endpoint was average total combined rhinitis score (TCRS) during the last 8 weeks of treatment with active compared to placebo. As part of the TCRS, patients were asked daily about symptoms of blocked/stuffy nose. The scoring scale went from 0 (no symptoms) to 3 (severe symptoms). Quality of life was measured with Juniper's rhinoconjunctivitis quality of life questionnaire (RQLQ).

Results

In both trials, the nasal congestion score was significantly reduced in the active group (12 SQ-HDM) compared with placebo (trial A: estimate 0.1, 95%CI [0.1; 0.2], p<0.05, relative difference 19%; trial B: 0.16, 95%CI [0.04; 0.27], p<0.01, relative difference 15%). The overall RQLQ score was significantly improved in active versus placebo, and so was the blocked nose domain score (trial A: estimate: 0.30, 95%CI [0.15; 0.45], p<0.05; trial B: estimate: 0.23, 95%CI [0.03; 0.44], p<0.05).

Conclusion

Treatment with 12 SQ-HDM reduced the patient's probability for having rhinitis exacerbation days and increased the probability for having mild days. These findings illustrate the clinical relevance of the SQ HDM SLIT-tablet in adolescents and adults with moderate-to-severe HDM allergic rhinitis.

Efficacy of the SQ HDM SLIT-tablet on nasal congestion symptoms; results from 2 DBPC trials

S. Tilles[1], J. Corren[2], B. Riis[3], H. Nolte[3]
— 1: Clinical Professor, University of Washington, Seattle, WA, USA; 2: David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; 3: ALK, Denmark

Introduction

Nasal congestion has been reported as one of the most bothersome symptoms for patients with house dust mite (HDM) allergy. Here the clinical efficacy on nasal congestion from 2 double-blind, randomized, placebo-controlled trials conducted in North America (In-Field trial 1, clinicaltrials.gov: NCT01700192) (1) and Europe (In-Field trial 2, EudraCT: 2011-002277-38) (2) is presented.

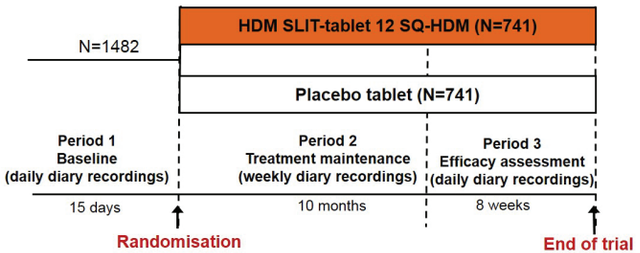


Figure 1: In-Field trial 1 design

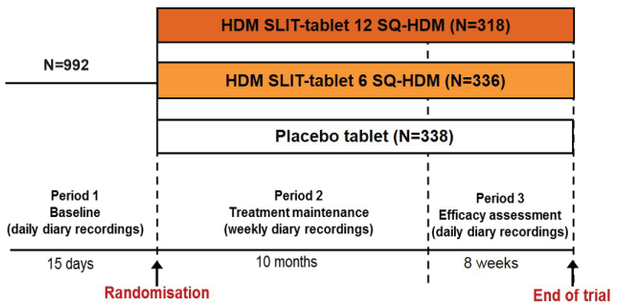


Figure 2: In-Field trial 2 design. For comparability with In-Field trial 1, only the SQ HDM SLIT-tablet 12 SQ-HDM group and the placebo group are included on this poster.

	HDM	Placebo	Difference (%)#	95% CL	P-value
In-Field trial 1					
Blocked nose symptom score*	1.1	1.4	0.10 (19%)	0.20;0.10	<0.05
RQLQ – overall	1.56	1.84	0.28 (15%)	0.41;0.16	<0.001
RQLQ – nose domain score	2.06	2.36	0.30 (13%)	0.45;0.15	<0.001
In-Field trial 2					
Blocked nose symptom score	0.88	1.04	0.16 (15%)	0.27;0.04	0.008
RQLQ – overall	1.38	1.58	0.19 (13%)	0.37;0.02	0.031
RQLQ – nose domain score	1.81	2.04	0.23 (11%)	0.44;0.03	0.028

Table 1: Effect of sublingual immunotherapy with SQ HDM SLIT-tablet on nose symptoms, overall RQLQ score and RQLQ nose domain score. *: the primary endpoint in In-Field trial 1 was pre-defined as the Hodges-Lehmann estimate of the median TCRS values – all other values in the table are mean-based; #: difference between Active and Placebo

Methods

Patients (N=1482 in In-Field trial 1, N=992 in In-Field trial 2) with moderate-to-severe HDM allergic rhinitis were treated with the SQ HDM SLIT-tablet (ALK, Denmark) for up to 1 year. For both trials, the primary endpoint was average total combined rhinitis score (TCRS) during the last 8 weeks of treatment with active compared to placebo. As part of the TCRS, patients were asked daily about symptoms of blocked/stuffy nose. The scoring scale went from 0 (no symptoms) to 3 (severe symptoms). Quality of life was measured with Juniper's rhinoconjunctivitis quality of life questionnaire (RQLQ).

Results

In both trials, the nasal congestion score was significantly reduced in the active group (12 SQ-HDM) compared with placebo (In-Field trial 1: estimate 0.1, 95%CI [0.1; 0.2], p<0.05, relative difference 19%; In-Field trial 2: 0.16, 95%CI [0.04; 0.27], p<0.01, relative difference 15%). The overall RQLQ score was significantly improved in active versus placebo, and so was the blocked nose domain score (In-Field trial 1: estimate: 0.10, 95%CI [0.10; 0.20], p<0.05; In-Field trial 2: estimate: 0.23, 95%CI [0.03; 0.44], p<0.05).

References

1: Nolte H., Bernstein D.I., Nelson H.S. et al. Efficacy of house dust mite sublingual immunotherapy tablet in North American adolescents and adults in a randomized, placebo-controlled trial. J Allergy Clin Immunol 2016;138:1631-8
2: Demoly P., Emminger W., Rehm D., et al. Effective treatment of house dust mite–induced allergic rhinitis with 2 doses of the SQ HDM SLIT-tablet: Results from a randomized, double-blind, placebo-controlled phase III trial. J Allergy Clin Immunol 2016;137(2):444-51

Conclusion

Symptoms of nasal congestion, and quality of life were significantly improved in both trials. The results from the 2 DBPC trials provide independent substantiation of the efficacy of the SQ HDM SLIT-tablet on nasal congestion in patients with HDM allergic rhinitis.

Efficacy of SQ SLIT-tablets in mono- and poly-sensitized HDM, grass, and ragweed allergic subjects

H. S. Nelson[1]; J Kleine-Tebbe[2]; Hendrik Nolte[3]; Bente Riis[3]; S. Durham[4], D. I. Bernstein[5]
[1]National Jewish Health, Colorado, Denver, USA; [2]Allergy & Asthma Center Westend, Berlin, Germany; [3]ALK, Denmark; [4]Imperial College and Royal Brompton Hospital, London, UK; [5]Bernstein Clinical Research Center and University of Cincinnati College of Medicine, Cincinnati, USA

Introduction

Many allergic patients are poly-sensitized and the benefits of treatment with sublingual immunotherapy tablets (SLIT-tablet) targeting only one allergy have been debated. In 3 different patient cohorts we studied the effect of treating mono- and poly-sensitized allergic rhinitis/conjunctivitis (AR/C) subjects with SLIT-tablets containing house dust mite (HDM), grass, or ragweed allergens, respectively.

Methods

We performed analyses of pooled data from 10 DBPC SLIT-tablet AR/C trials: 2 HDM SLIT-tablet trials (N=1,762); 6 grass SLIT-tablet, 6 trials (N=2,299); and 2 ragweed SLIT-tablet trials (N=643). Efficacy was measured by total combined AR/C symptoms and medication scores (TCRS) and compared for mono-sensitized versus poly-sensitized subjects.

Results

The majority (78%) of the included subjects were poly-sensitized. SLIT-tablet treatments were similarly effective in improving TCRS in mono- and poly-sensitized HDM, grass or ragweed allergic subjects

Conclusions

Regardless of mono- or poly-sensitization, treatment with SLIT-tablets containing HDM, grass, or ragweed allergens yielded significant and similar improvements in TCRS. . The analyses support that for these 3 major allergies, SLIT-tablet treatment will be as effective in poly-sensitized as in mono-sensitized patients.

Efficacy of SQ SLIT-tablets in mono- and poly-sensitized HDM, grass, and ragweed allergic subjects

H.S. Nelson[1], J. Kleine-Tebbe[2], H. Nolte[3], B. Riis[3], S.R. Durham[4], D.I. Bernstein[5]
— 1: National Jewish Health, Denver, Colorado, USA; 2: Allergy & Asthma Center Westend, Berlin, Germany; 3: ALK, Denmark; 4: Imperial College and Royal Brompton Hospital, London, UK; 5: Bernstein Clinical Research Center and University of Cincinnati College of Medicine, Cincinnati, Ohio, USA

Introduction

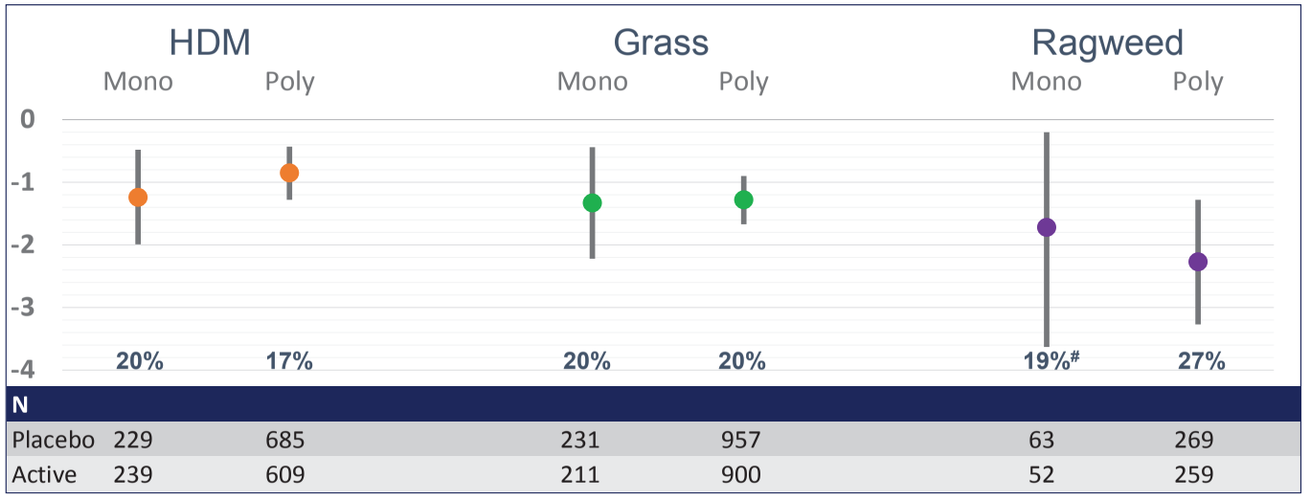
Many allergic patients are poly-sensitized and the benefits of treatment with sublingual immunotherapy tablets (SLIT-tablets) targeting only one allergy have been debated. In 3 different patient cohorts we studied the effect of treating mono- and poly-sensitized allergic rhinitis/conjunctivitis (AR/C) subjects with SQ SLIT-tablets containing house dust mite (HDM), grass, or ragweed allergens, respectively.

Methods

We performed post-hoc analyses of pooled data from 10 double-blind, placebo-controlled SQ SLIT-tablet allergic rhinitis/rhinoconjunctivitis (AR/C) trials in adults and adolescents (Table 1): 2 HDM SLIT-tablet trials (N=1,762); 6 grass SLIT-tablet trials (N=2,299); and 2 ragweed SLIT-tablet trials (N=643). At screening, subjects were tested (SPT and specific IgE) for allergy to the main allergen (HDM, grass or ragweed, depending on the trial) as well as a panel of other allergens. Based on these tests subjects were assigned to the mono-sensitized or poly-sensitized subgroups. Efficacy was measured by total combined AR/C symptoms and medication scores (TCRS) and compared for mono-sensitized versus poly-sensitized subjects.

Allergen	Geographical region	NCT/EudraCT number	Publication
HDM	USA	NCT01700192	Nolte et al. J Allergy Clin Immunol 2016
HDM	Europe	2011-002277-38	Demoly et al. J Allergy Clin Immunol 2016
Grass	Europe/USA	NA	Durham et al. J Allergy Clin Immunol 2006
Grass	Europe	NA	Dahl et al. Allergy 2006
Grass	Europe	2004-000083-27	Dahl et al. J Allergy Clin Immunol 2006
Grass	USA	NCT00421655	Murphy et al. J Negat Results in Biomed 2013
Grass	USA	NCT00562159	Nelson et al. J Allergy Clin Immunol 2011
Grass	USA	NCT01385371	Maloney et al. Ann Allergy Asthma Immunol 2014
Ragweed	USA	NCT00783198	Nolte et al. Ann Allergy Asthma Immunol 2013
Ragweed	USA/Europe	NCT00770315	Creticos et al. J Allergy Clin Immunol 2013

Table 1: Trials included in the analyses



N						
Placebo	229	685	231	957	63	269
Active	239	609	211	900	52	259

Figure 1: Comparison of efficacy in mono- and poly-sensitized subjects. Bars show absolute difference in TCRS (incl. 95% CI) for active vs. placebo for the three SLIT-tablets (HDM, grass, ragweed) for mono- and poly-sensitized subjects respectively. Numbers below zero favours active treatment. Percentages shown are the relative differences between active and placebo in TCRS. (TCRS: total combined AR/C symptoms and medication score ; #: Not significant)

Results

The majority (78%) of the subjects included in the trials were poly-sensitized (ranging from 68% to 89% in the individual trials). SQ SLIT-tablet treatments were similarly effective in improving TCRS in mono- and poly-sensitized HDM, grass or ragweed allergic subjects (Figure 1).

Conclusion

Regardless of mono- or poly-sensitization, treatment with SQ SLIT-tablets containing HDM, grass, or ragweed allergens yielded significant and similar improvements in TCRS. The analyses support that for these 3 major allergies, SQ SLIT-tablet treatment will be as effective in poly-sensitized as in mono-sensitized adult and adolescent patients.

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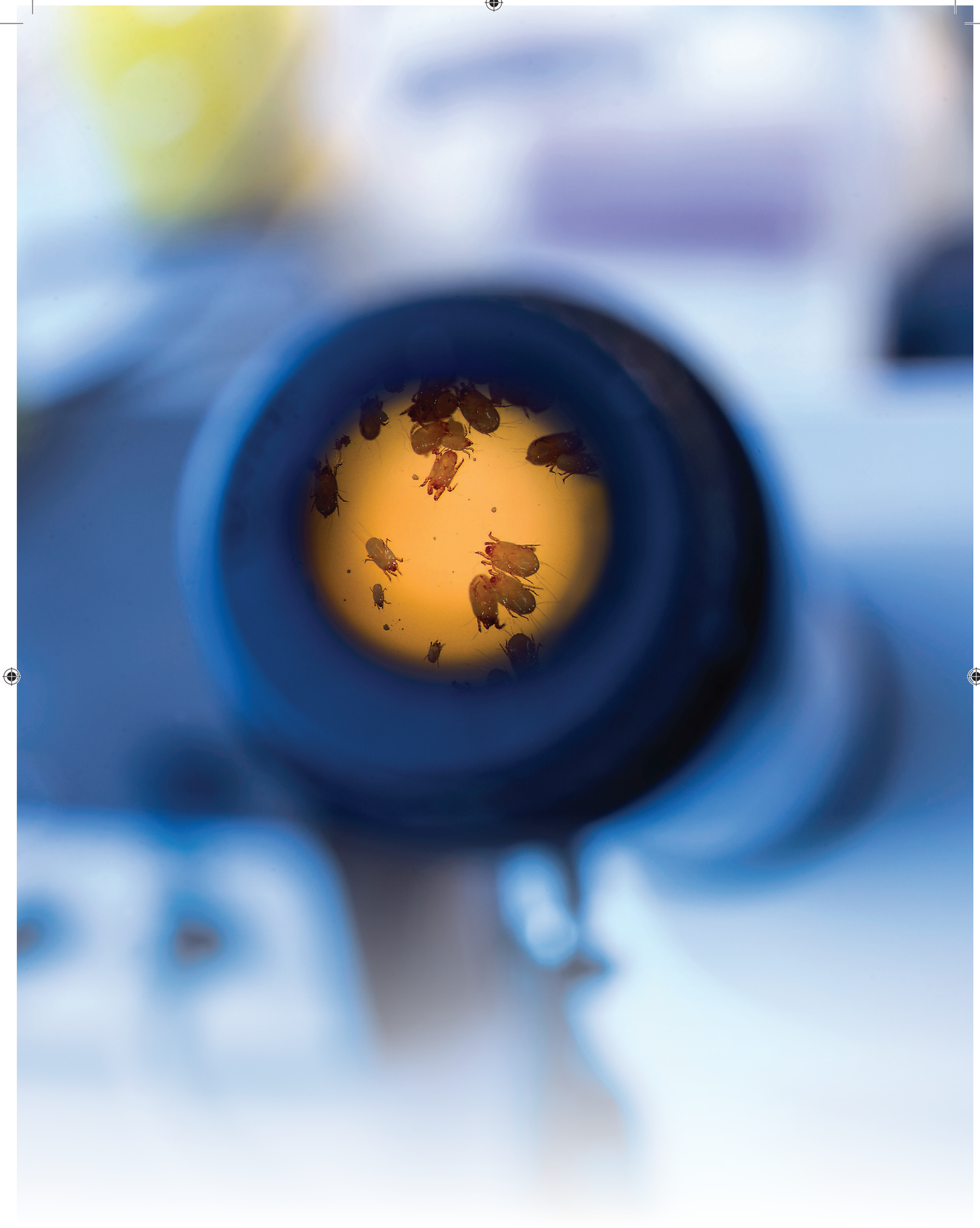

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