Abstracts & Posters

AAAAI Annual Meeting 2019
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ALK

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Dear AAAAI delegate

ALK welcomes you to the AAAAI 2019 Annual Meeting in San Francisco, CA.

As the world leader in allergy immunotherapy (AIT), we are proud to present a total of seven abstracts. Two of the abstracts focus on house dust mite (HDM) allergy, specifically the impact of SQ HDM SLIT-tablet on sleep quality and on the consistent treatment effect of SQ HDM SLIT-tablet in subjects polysensitized to HDM, tree and/or grass.

Three abstracts use pooled data from the extensive clinical development programs of SQ timothy grass, ragweed, birch, and HDM SLIT-tablets to evaluate the common immunologic mechanisms among the SLIT-tablets and the impact of baseline allergen specific IgE on efficacy and safety.

Another abstract reports the safety and tolerability of a subcutaneous immunotherapy (SCIT) updosing regimen of 7 injections. Finally, one abstract reports the results of a systematic review and meta-analysis evaluating the effect of pharmacotherapy and AIT versus placebo on nasal symptoms in adults with perennial allergic rhinitis.

ALK is committed to sustain, develop and disseminate AIT 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
North America and International Markets

Effect of House Dust Mite SLIT-Tablet Treatment on Quality of Sleep in Allergic Rhinitis Patients

P869

H. Jacobi[1], D. Rehm[1], H. Nolte[2], K.F. Andersen[1], P. Demoly[3]

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Introduction

Symptoms of allergic rhinitis with or without conjunctivitis (AR/C) can cause substantial sleep impairment and sleep problems, which worsen with increased severity of symptoms.[1,2] House dust mite (HDM) sublingual immunotherapy (SLIT) tablet (12 SQ-HDM, ALK, Denmark) has been shown to be effective in treating HDM AR/C and asthma in DBPC trials.[3-6] This post-hoc analysis investigated the effect of treatment with SQ HDM SLIT-tablet on sleep in subjects with HDM AR/C.

Methods

Adult subjects (18–65 y) with moderate-to-severe HDM AR/C were treated for up to 1 year with 12 SQ-HDM (n=318), 6 SQ-HDM (n=336), or placebo (n=338) in a previously described Phase 3 trial (EudraCT: 2011-002277-38).[3] Only results from the US Food and Drug Administration and European Medicines Agency approved dose of 12 SQ-HDM are reported. Subjects were provided with free allergy rescue medication throughout the treatment period. At baseline and during the course of the trial, subjects completed the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ).[7] The RQLQ measures 3 sleep parameters scored from 0 (not troubled) to 6 (extremely troubled):

- LACK of a good night's sleep
- WAKE up during night
- DIFFICULTY getting to sleep

For the purpose of this analysis, scores <3 were categorized "mildly affected" and scores ≥3 "moderately/severely affected". The RQLQ sleep domain score was analyzed using an analysis of covariance (ANCOVA). Sleep severity was analyzed by means of a logistic regression model.

Results

At baseline, approximately 65% of subjects had moderately/severely affected sleep (**Figure 1**). During the efficacy evaluation period, the adjusted mean RQLQ sleep domain score was significantly better with 12 SQ-HDM (1.29) compared with placebo (1.53; p=0.02).

Figure 1. Percentage of subjects with mildly affected or moderately/severely affected sleep at baseline.

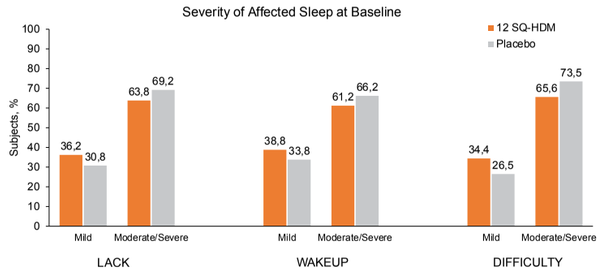
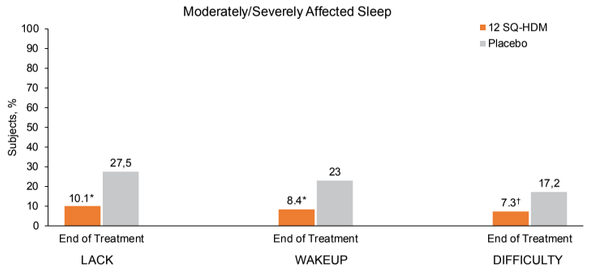


Figure 2. Estimated proportions of subjects with moderately/severely affected sleep at baseline who remained moderately/severely affected at end of treatment. *p<0.001; †p=0.006 vs placebo.



Funding: Support for this analysis was funded by ALK, Hørsholm, Denmark. Medical writing assistance was provided by Erin P. Scott, PhD of Scott Medical Communications, LLC.

Only 7.3%–10.1% of subjects with moderately/severely affected sleep impairment at baseline remained in that category following treatment with the 12 SQ-HDM tablet (**Figure 2**). This improvement was significantly higher than that observed following treatment with placebo:

- LACK: 12 SQ-HDM, 10.1%; Placebo, 27.5%; p<0.001
- WAKEUP: 12 SQ-HDM, 8.4%; Placebo, 23.0%; p<0.001
- DIFFICULTY: 12 SQ-HDM, 7.3%; Placebo, 17.2%; p=0.006

Only 1%–7% of subjects with mildly affected sleep impairment at baseline shifted to the moderate/severe category at end of treatment, with no difference between placebo and 12 SQ-HDM groups.

References

1. Leger D, et al. *Arch Intern Med.* 2006;166(16):1744-1748.
2. Meltzer EO, et al. *Allergy Asthma Proc.* 2009;30(3):244-254.
3. Demoly P, et al. *J Allergy Clin Immunol* 2016;137(2):444-451.
4. Nolte H, et al. *J Allergy Clin Immunol.* 2016;138(6):1631-1638.
5. Okubo KM, K, et al. *J Allergy Clin Immunol.* 2017;139(6):1840-1848.e1810.
6. Virchow JC, et al. *JAMA.* 2016;315(16):1715-1725.
7. Juniper EF, et al. *J Allergy Clin Immunol.* 1999;104(2 Pt 1):364-369.

Conclusions

Treatment with 12 SQ-HDM significantly improved quality of sleep for the group of subjects who were affected by poor sleep at the start of the trial. At the end of treatment both treatment groups showed improved sleep quality, but improvement was more pronounced in actively treated subjects. Access to free rescue medication likely also improved sleep in placebo-treated subjects.

Disclosure of presenting author: H. Jacobi is an employee of ALK.

Poster Number: 869
Session Number: 4213
Session Title: Rhinitis and Immunotherapy
Poster Hall Location: Moscone Center South, Exhibition Level, Hall B
Presentation Date: Monday, February 25, 2019
Presentation Time: 9:45-10:45am

Efficacy of house dust mite sublingual immunotherapy-tablet in tree and/or grass poly-sensitized subjects

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Rationale

House dust mite (HDM) SLIT-tablet (12 SQ-HDM, ALK, Denmark) has been shown to be effective in treating HDM allergic rhinitis and asthma in several large DBPC trials. This post-hoc analysis investigates if treatment with the SQ-HDM SLIT-tablet also shows efficacy in HDM allergic subjects sensitized to tree and/or grass during relevant periods of pollen exposure.

Methods

Subjects from a Phase III trial (EudraCT: 2011-002277-38; placebo: N=338, 12 SQ-HDM: N=318) with moderate-severe HDM allergic rhinitis were treated for up to 1 year (Demoly *et al.* 2016;JACI;137:444-51). This post-hoc analysis evaluated efficacy (Total Combined Rhinitis Score [TCRS] during pollen seasons [April to July]) in HDM allergic subjects with or without tree/grass pollen sensitization.

Results

The "tree/grass" group comprised 294 subjects (Placebo: N=159; 12 SQ-HDM: N=135) while the "non-tree/grass" group comprised 362 subjects (Placebo: N=179; 12 SQ-HDM: N=183). Overall, the two treatment groups had similar efficacy profiles throughout the trial period including the tree and grass pollen seasons (tree/grass: 1.23 [14%], p=0.0219; non-tree/grass: 1.19 [14%], p=0.0212).

Conclusions

The SQ-HDM SLIT-tablet shows consistent treatment effect in tree/grass and non-tree/grass sensitized subjects irrespective of pollen seasons. This suggests that patients with tree and grass sensitizations also benefit from a reduced burden to HDM symptoms with SQ-HDM SLIT-tablet during the pollen seasons.

Oral Abstract: 605
Session Number: 3606
Session Title: Allergic Rhinitis and Sublingual Immunotherapy
Location: Moscone Center South
Presentation Date: Sunday, Feb 24, 2019
Presentation Time: 2:00-3:15 PM

HOUSE DUST MITE SLIT-TABLET

The class of fast-dissolving tablets for sublingual allergen immunotherapy induce comparable serological IgE and IgG4 responses

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Rationale

Fast-dissolving tablets for sublingual allergen immunotherapy (SLIT) are now globally available and cover the three major allergies grass, house dust mite, and ragweed. This allows for comparative evaluation of immunological responses to treatment on a global scale across SLIT-tablet development programs.

Methods

Data collected during 8 placebo-controlled, phase III studies covering 2509 patients was used for analysis. In all trials, allergen-specific IgE and IgG4 (sIgE and sIgG4) were measured using ImmunoCAP. Active treatment comprised fast-dissolving Zydis-formulation (SLIT-tablets) for allergic rhinitis and/or allergic asthma due to the following allergens: house dust mite (4 trials), grass (2 trials), and ragweed (2 trials).

Results

Across trials and allergens, active treatment groups show comparable levels of changes in immunological responses of sIgE and sIgG4. For all trials, the largest average increase in sIgE was observed within the first three months whereas sIgG4 continuously increased during the first year of treatment. For placebo-treated patients, a minor increase in antibody titers in relevant pollen seasons was observed. Looking at individual measurements, consistency was further demonstrated by similar distribution profiles of changes in sIgE and sIgG4 during the early and late phase of treatment, respectively (**Figure 2**). There is some overlap in the individual response between placebo and SLIT-tablet groups in the range of 0 to 0.3 log10 for IgE and 0 to 2.5 log10 for sIgG4, suggesting that sIgE and sIgG4 levels cannot distinguish a response between active and placebo treatment in some subjects at the lower range.

There were no differences in immunologic response based on race (ie, white vs Asian).

Conclusions

During the first year and across trials, changes in sIgE and sIgG4 demonstrate a high level of similarity despite underlying heterogeneity in enrolled patients, tablet treatments, and geographical location including Europe, North America, and Japan. This indicates a common immunological mechanism for the entire class of fast-dissolving SLIT-tablets. On a subject level there is overlap between active SLIT-tablet and placebo in the lower ranges of the immunologic response that suggest smaller changes must be interpreted with caution.

Poster Number: 868
Session Number: 4213
Session Title: Rhinitis and Immunotherapy
Poster Hall Location: Moscone Center South, Exhibition Level, Hall B
Presentation Date: Monday, February 25, 2019
Presentation Time: 9:45-10:45am

P.S. Andersen[1], C. Lundegaard[1], H.H. Ipsen[1], K. Ohashi-Doi[2], H. Nolte[3], T. Stranzl[1]

[1]ALK, Hørsholm, Denmark; [2]Torii, Tokyo, Japan; [3]ALK, Bedminster, NJ, USA

Introduction

Allergy immunotherapy (AIT) induces tolerance to allergens in part by stimulating production of allergen-specific IgG4 that inhibits IgE-facilitated binding of allergen-IgE complexes.[1] AIT also induces an early increase in specific IgE followed by a decrease over time.[2] Fast-dissolving tablets for sublingual allergen immunotherapy (SLIT) are now globally available and cover the three major allergies grass, house dust mite (HDM) and ragweed. This allows for comparative evaluation of immunological responses to treatment on a global scale across SLIT-tablet development programs.

Methods

Sera from subjects were collected during 8 randomized, double-blind, placebo-controlled phase 3 SLIT-tablet clinical trials (2 timothy grass; 2 ragweed; 4 HDM) conducted in North America, Europe and Japan. Active treatment comprised fast-dissolving Zydis-formulation SLIT-tablets for allergic rhinitis with or without conjunctivitis and/or allergic asthma. Subjects included in the analysis were aged ≥18 years and had at least 2 immunologic assessments at scheduled visits. In all trials, allergen-specific IgE and IgG4 (sIgE and sIgG4) were measured using ImmunoCAP. Results are shown for the most potent SLIT-tablet dose used in each trial and placebo.

Results

A total of 2509 subjects were included in the analysis. Across trials and allergens, active treatment groups showed comparable levels of changes in immunological responses of sIgE and sIgG4 (**Figure 1**). For all trials, the largest average increase in sIgE was observed within the first three months whereas sIgG4 continuously increased during the first year of treatment (**Figure 1**). For placebo-treated patients, a minor increase in antibody titers in relevant pollen seasons was observed (**Figure 1**).

Funding: Support for this analysis was funded by ALK, Hørsholm, Denmark. Medical writing assistance was provided by Erin P. Scott, PhD of Scott Medical Communications, LLC.

Disclosure of presenting author: P.S. Andersen is an employee of ALK.

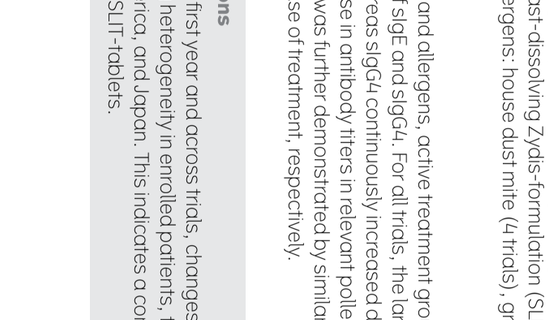

Figure 1. Allergen-specific IgE and IgG4 levels over time in response to house dust mite (HDM) SLIT-tablet, grass SLIT-tablet, ragweed SLIT-tablet, seasonal allergen placebo, and HDM placebo. Results are from the most potent SLIT-tablet doses evaluated in each trial.

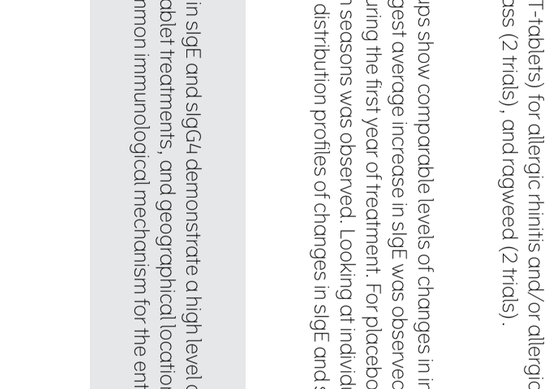

Figure 2. Distribution profile of changes from pretreatment in A) IgE early in treatment (first visit after 4 weeks of treatment) and B) IgG4 late in treatment (≥ week 25).

References

1. James LK, et al. *J Allergy Clin Immunol.* 2011;127(2):509-516.e501-505.
2. Matsuoka T, et al. *Allergol Int.* 2013;62(4):403-413.

Association between baseline specific IgE levels and adverse events with sublingual immunotherapy tablets

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Rationale

Adverse events (AEs) associated with sublingual immunotherapy (SLIT)-tablets used to treat allergic rhinoconjunctivitis and/or asthma occur at a rate of approximately 57%-83%, most of which are mild-to-moderate. Biomarkers that could identify patients at risk of more severe reactions would be useful. Baseline specific IgE data from 11 trials of timothy grass, ragweed, house dust mite (HDM), and tree SLIT-tablets were evaluated for associations with frequency and severity of first-reported AEs.

Methods

Specific IgE (kUA/L) was divided into Class 0/1/2 (<3.5), Class 3 (3.5-17.4), Class 4 (17.5-49), Class 5 (50-99), or Class 6 (≥100). Patients' first-reported AEs were classified as none, mild, moderate, or severe.

Results

Overall, 9187 AEs were reported with SLIT-tablet treatment (n=5298 patients). The percentages of patients with any AE were 51.7%, 62.4%, 64.4%, 64.9%, and 67.5% for baseline IgE Classes 0/1/2, Class 3, Class 4, Class 5, and Class 6, respectively. Most AEs were mild. The percentages of patients with moderate/severe AEs were slightly higher for Classes 5 (11.7%) and 6 (10.6%) versus lower Classes (5.1%-7.9%). Patterns of slightly increasing AE frequency with increasing IgE levels were observed for seasonal SLIT-tablets, whereas AE frequencies with HDM SLIT-tablet were comparable among IgE classes. AE frequency decreased over time, with approximately 80% of all AEs occurring by week 5. Placebo-treated subjects with the highest baseline IgE classes (Class 3/4/5/6) had higher symptom and medication scores compared with Class 2, indicating a lower "placebo-effect" in subjects with higher baseline IgE levels.

Conclusions

The magnitude of baseline specific IgE corresponds with the frequency of AEs and appears to be a class effect of seasonal SLIT-tablets. The majority of AEs are mild and high IgE is not clearly associated with severe AEs. AE frequency decreases over time.

P871

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Introduction

Adverse events (AEs) associated with sublingual immunotherapy (SLIT)-tablets used to treat allergic rhinoconjunctivitis and/or asthma occur at a rate of approximately 57%-83%, most of which are mild-to-moderate.[1] Biomarkers that could identify patients at risk of more severe reactions would be useful. Baseline specific IgE data from 11 trials of timothy grass, ragweed, house dust mite (HDM), and tree SLIT-tablets were evaluated for associations with frequency and severity of first-reported AEs.

Methods

Specific IgE and first-reported treatment-emergent AE data were pooled and analyzed from 11 randomized, double-blind, placebo-controlled SLIT-tablet trials (4 timothy grass; 2 ragweed; 1 birch tree; 4 HDM). Subjects were categorized by baseline specific IgE (kU_A/L) into Class 2 (<3.5), Class 3 (3.5-17.4), Class 4 (17.5-49), Class 5 (50-99), or Class 6 (≥100). Subjects with less than specific IgE Class 2 at baseline were excluded from the trials. Subjects' first-reported treatment-emergent AEs were classified as none, mild, moderate, or severe.

Efficacy data were pooled and analyzed from 8 randomized, double-blind, placebo-controlled SLIT-tablet clinical trials (2 timothy grass; 2 ragweed; 1 birch tree; 3 house dust mite [HDM]). One HDM trial and the one tree trial were phase 2 trials where the clinical effect was assessed in environmental exposure chambers; the remaining trials were confirmatory phase 3 trials conducted as field studies in North America, Europe and Japan. Subjects were categorized by baseline specific IgE (kU_A/L) ≤3.5 (Class 2) and >3.5 (Class 3/4/5/6). Efficacy analyses were based on the primary efficacy endpoint of each trial: daily symptom score (DSS), daily medication score (DMS), total combined symptom and medication score (TCS), total combined rhinitis daily symptom and medication score (TCRS), total nasal symptom score (TNSS), or total combined nasal and ocular symptom score (TSS).

DMS, daily medication score; DSS, daily symptom score; EEC, environmental exposure chamber; HDM, house dust mite; SLIT, sublingual immunotherapy; TCS, total combined daily symptom and medication score; TCRS, total combined rhinitis daily symptom and medication score; TNSS, total nasal symptom score; TSS, total combined nasal and ocular score.

Funding: Support for this analysis was funded by ALK, Hørsholm, Denmark. Medical writing assistance was provided by Erin P. Scott, PhD of Scott Medical Communications, LLC.

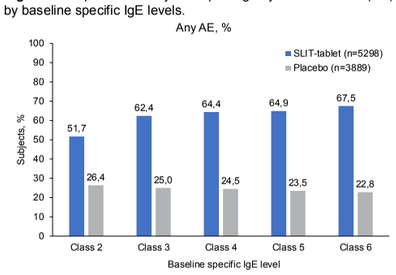
Disclosure of presenting author: H. Nolte is an employee of ALK.

Results

Overall, 9187 subjects were included in the analysis (SLIT-tablet, n=5298; placebo, n=3889); 12,757 AEs were reported with SLIT-tablet treatment.

There was a tendency in the SLIT-tablet group toward a slightly lower rate of AEs with Class 2 baseline IgE vs Classes 3 through 6 (**Figure 1**). The percentages of subjects with any AE in the SLIT-tablet group were 51.7%, 62.4%, 64.4%, 64.9%, and 67.5% for baseline IgE Class 2, Class 3, Class 4, Class 5, and Class 6, respectively (**Figure 1**).

Figure 1. Proportion of subjects reporting any adverse event (AE) by baseline specific IgE levels.



Most AEs were mild. The percentages of subjects with their first AE assessed as moderate/severe were slightly higher for Classes 5 (11.7%) and 6 (10.6%) versus lower Classes (4.0%-8.0%; **Figure 2A**). The pattern of slightly increasing AE frequency with increasing IgE levels was observed for seasonal SLIT-tablets, whereas AE frequencies with HDM SLIT-tablet were comparable among IgE classes (**Figure 2B**).

AE frequency decreased over time, with approximately 80% of all AEs occurring by week 5 (**Figure 3**).

Placebo-treated subjects with the highest baseline IgE classes (Class 3/4/5/6) had higher symptom and medication scores compared with Class 2, indicating a lower "placebo-effect" in subjects with higher baseline IgE levels (**Figure 4**).

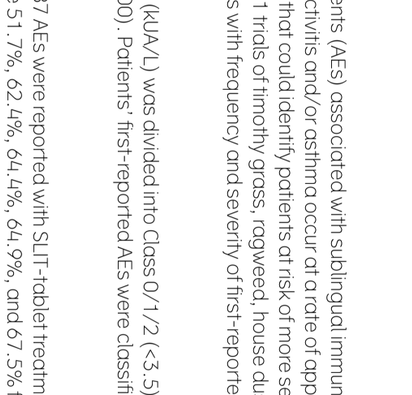


Figure 2. Proportion of first adverse events (AE) by severity and baseline specific IgE levels for A) all SLIT-tablets combined and B) HDM SLIT-tablets only.

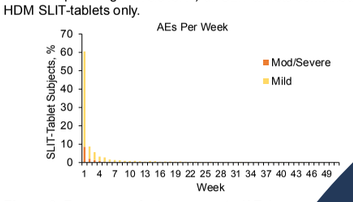


Figure 3. Frequency of adverse events (AEs) over time in the SLIT-tablet group. Data from one of the HDM trials (P001) is excluded as AEs were specifically solicited via daily questionnaire for the first 30 days in that trial.

Figure 4. Outcome analysis by baseline specific IgE levels. Results shown are estimates of primary endpoint (95% CI) by baseline specific IgE Class 3/4/5/6 relative to Class 2.

Reference

1. Bernstein DI, et al. *Postgrad Med*. 2017:1-8.

Conclusions

For the Class 2 IgE group, there is a slightly lower AE frequency distribution compared with the higher IgE classes; however, the AE frequency is constant in patients with Class 3, 4, 5, and 6 IgE. The majority of AEs are mild and high allergen specific IgE is not clearly associated with increased risk of severe AEs and therefore does not indicate a critical impact for clinical practice. AE frequency decreases over time. Subjects with the higher baseline IgE appear to be those who are in the most need of treatment.

Poster Number: 871
Session Number: 4213
Session Title: Rhinitis and Immunotherapy
Poster Hall Location: Moscone Center South, Exhibition Level, Hall B
Presentation Date: Monday, February 25, 2019
Presentation Time: 9:45-10:45am

A pooled post-hoc analysis of pre-treatment allergen specific IgE and SLIT-tablet efficacy

Stranzl T[1], Ipsen H[1], Lundegaard C[1], Ohashi-Doi K[2], Nolte H[3], Andersen PS[1]
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Rationale

Specific IgE sensitization is a common inclusion criteria in clinical trials evaluating sublingual immunotherapy (SLIT) tablets. Our aim was to evaluate the impact of pre-treatment specific IgE levels on clinical efficacy.

Methods

Data from 8 placebo-controlled, phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory Phase III trials conducted as field studies in North America, Europe and Japan. Presented efficacy analyses are based on the primary efficacy endpoint of each trial and investigate a potential difference in efficacy between subjects with pre-treatment specific IgE (kU/L) ≤3.5 (Class 2) and >3.5 (Class 3/4/5/6).

Results

For the active treatment groups, there was no consistent difference in efficacy outcomes between Class 2 and the combined group of Classes 3/4/5/6. In contrast, there was consistent reduced efficacy for Classes 3/4/5/6 over Class 2 in the placebo groups. An intra-Class group analysis comparing Class 2 active with Class 2 placebo, as well as Class 3/4/5/6 active with Class 3/4/5/6 placebo, showed a tendency to a larger treatment effect in subjects with IgE Class >2.

Conclusions

For all SLIT-tablet trials included in this analysis, we found a tendency of an increased treatment effect vs placebo for subjects with IgE Class 3/4/5/6, primarily driven by increased symptom and medication scores during the assessment period of Class 3/4/5/6 subjects compared with Class 2 subjects in the placebo group.

Poster Number: 867
Session Number: 4213
Session Title: Rhinitis and Immunotherapy
Poster Hall Location: Moscone Center South, Exhibition Level, Hall B
Presentation Date: Monday, February 25, 2019
Presentation Time: 9:45-10:45am

A Pooled Post-Hoc Analysis of Pre-Treatment Levels of Allergen Specific IgE and SLIT-Tablet Efficacy

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Introduction

Lack of biomarkers to assess responders and non-responders to allergy immunotherapy is an unmet need in the treatment of allergic rhinoconjunctivitis and asthma. Allergen specific IgE sensitization is a common inclusion criterion in clinical trials evaluating sublingual immunotherapy (SLIT)-tablets. Our aim was to evaluate the impact of pre-treatment specific IgE levels on the clinical efficacy of SLIT-tablets.

Methods

Efficacy data were pooled and analyzed from 8 randomized, double-blind, placebo-controlled SLIT-tablet clinical trials (2 timothy grass; 2 ragweed; 1 birch tree; 3 house dust mite [HDM]). One HDM trial and the one tree trial were phase 2 trials where the clinical effect was assessed in environmental exposure chambers; the remaining trials were confirmatory phase 3 trials conducted as field studies in North America, Europe and Japan. Subjects were categorized by baseline specific IgE (kU_A/L) ≤3.5 (Class 2) and >3.5 (Class 3/4/5/6). Efficacy analyses were based on the primary efficacy endpoint of each trial: daily symptom score (DSS), daily medication score (DMS), total combined symptom and medication score (TCS), total combined rhinitis daily symptom and medication score (TCRS), total nasal symptom score (TNSS), or total combined nasal and ocular symptom score (TSS). Primary endpoints were scored on different scales among the trials and results cannot be directly compared. Subjects included in the analysis were those aged 18 years and older.

Results

For the SLIT-tablet treatment groups, there were no consistent differences in symptom and medication scores between Class 2 relative to the combined group of Classes 3/4/5/6 (**Figure 1**). In contrast, there were consistent increased symptom and medication scores (ie, "reduced efficacy") for Classes 3/4/5/6 relative to Class 2 in the placebo groups (**Figure 1**).

An intra-Class group analysis comparing Class 2 SLIT-tablet with Class 2 placebo, as well as Class 3/4/5/6 SLIT-tablet with Class 3/4/5/6 placebo, showed a tendency to a larger treatment effect in subjects with IgE Class 3/4/5/6 (**Figure 2**).

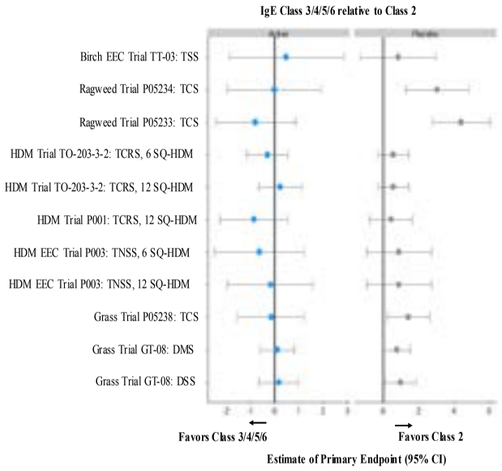

Figure 1. Outcome analysis by baseline specific IgE levels. Results shown are estimates of primary endpoint (95% CI) by baseline specific IgE Class 3/4/5/6 relative to Class 2.

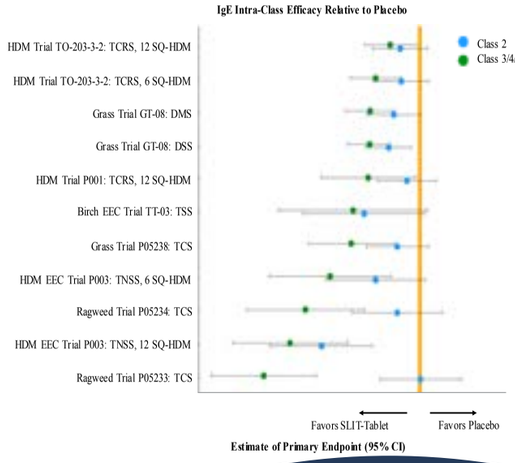

Figure 2. Outcome analysis by intra-Class baseline specific IgE levels. Results shown are estimates of primary endpoint (95% CI) in matched analysis (ie, Class 2 SLIT-tablet vs Class 2 placebo). Primary endpoints were scored on different scales among the trials and results cannot be directly compared.

DMS, daily medication score; DSS, daily symptom score; EEC, environmental exposure chamber; HDM, house dust mite; SLIT, sublingual immunotherapy; TCS, total combined daily symptom and medication score; TCRS, total combined rhinitis daily symptom and medication score; TNSS, total nasal symptom score; TSS, total combined nasal and ocular score.

Funding: Support for this analysis was funded by ALK, Hørsholm, Denmark. Medical writing assistance was provided by Erin P. Scott, PhD of Scott Medical Communications, LLC.

Conclusion

For all SLIT-tablet trials included in this analysis we found a tendency towards an increased treatment effect vs placebo for subjects with IgE Class 3/4/5/6, primarily driven by higher symptom and medication scores during the assessment period of Class 3/4/5/6 subjects compared with Class 2 subjects in the placebo group. Therefore, the placebo-effect appeared lower in subjects with higher IgE levels and may allow better signal detection in clinical trials.

Disclosure of presenting author: T. Stranzl is an employee of ALK.

Safety and tolerability of shortened updosing with 7 injections of subcutaneous allergen immunotherapy

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[1]ALK, Hamburg, Denmark; [2]Private ENT and Allergy Practice, Heidelberg, Germany; [3]ALK, Madrid, Spain; [4]ALK, Hørsholm, Denmark; [5]Hospital Clinico San Carlos, Allergy Department, Madrid, Spain

Rationale

Patients intended for allergen immunotherapy prefer fewer visits to the physician. Alutard SQ, a registered and widely used subcutaneous allergen immunotherapy (SCIT) product, is standardly updosed by 11 or more injections. The objective of this clinical trial was to investigate whether the safety and tolerability profile of a shortened updosing schedule to 7 injections is acceptable.

Methods

A partly randomized, parallel-group, controlled, multi-national trial was conducted in adolescents and adults (12-65 years). Subjects were treated with Alutard SQ grasses, birch, or house dust mites (HDM) and subjects receiving grass allergens were randomized to either updosing by 11 or 7 injections. Subjects receiving birch or HDM were updosed by 7 injections. The primary endpoint was the number of treatment related adverse events (TRAEs).

Results

340 subjects were treated (85 grass-11 injections; 85 grass-7 injections; 87 birch; 83 HDM). No major differences in the proportion of subjects with TRAEs were observed (grass-11: 76%, grass-7: 80%, birch: 76%, HDM: 84%). 1 (1%) subject discontinued due to TRAEs with grass-11 injections and 7 (8%) with grass-7 injections (birch: none, HDM 3 (4%) subjects). Severe TRAEs occured mainly in subjects treated with grass (11 injections: 7 (8%) subjects, 7 injections: 6 (7%) subjects). Treatment related SAEs occurred in 5 subjects: 4 with grass-11 injections and 1 with grass-7 injections. TRAEs were similar regardless of age group (adolescents: 71-86%, adults: 73-85%).

Conclusions

The date indicate that a 7-injection updosing schedule for Alutard SQ grass, trees and HDM in adolescents and adults has an acceptable safety and tolerability profile.

Poster Number: L34
Session Number: 4216
Session Title: Late Breaking Poster Session
Poster Hall Location: Moscone Center South, Exhibition Level, Hall B
Presentation Date: Monday, February 25, 2019
Presentation Time: 9:45-10:45am

Safety and tolerability of shortened up-dosing with 7 injections of subcutaneous allergen immunotherapy

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L34

Introduction

- Patients intended to be treated with allergy immunotherapy prefer fewer visits to the physician. Alutard SQ, a licensed and widely used subcutaneous allergen immunotherapy (SCIT) product, is standardly up-dosed by 11 or more injections.
- The objective of this clinical trial was to investigate whether the safety and tolerability profile of a shortened up-dosing schedule to 7 injections is acceptable.

Methods

- Partly randomized, parallel group, controlled, multi-national trial conducted in Germany and Spain (EudraCT 2017-000971-97) in adolescents and adults (12-65 years).
- Subjects were treated with Alutard SQ grasses and rye , birch or house dust mites (HDM), and subjects receiving grass allergens were randomized either to up-dosing by 11 or 7 injections (**Figure 1.** Trial design**, Figure 2.** Dosage schedules, volumes injected and concentrations used).
  Subjects receiving birch or HDM were up-dosed by 7 injections.
- The primary endpoint was the number of treatment related adverse events (TRAEs).

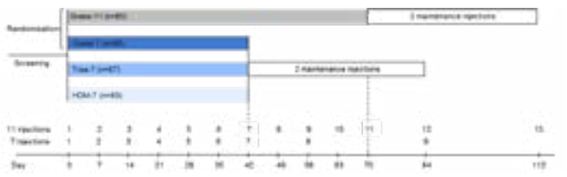

Figure 1. Trial design
Subjects received injections for up-dosing in 4 treatment groups. Subjects treated with grass allergens were randomized to an up-dosing schedule of 11 weekly injections (grass-11) with a duration of 70 days or of 7 injections (grass-7) with a duration of 42 days. Subjects treated with birch or HDM allergens were up-dosed by the 7-injection schedule (tree-7; HDM-7). Up-dosing was followed by 2 maintenance injections in all groups.

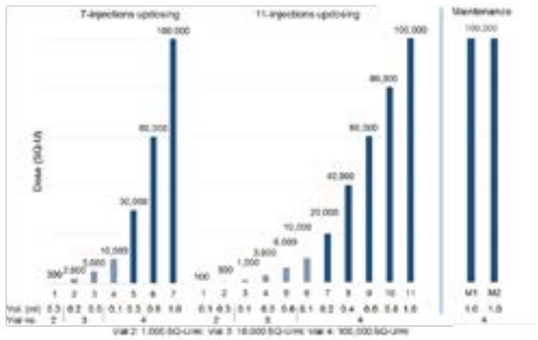

Figure 2. Dosage schedules, volumes injected and concentration used.
Subjects were up-dosed by a 7-injection or an 11-injection schedule followed by two maintenance doses. Doses were applied from vials with increasing concentrations (vial 2, 3, 4) by injecting the equivalent volume from the vial.

Results

- A total of 340 subjects were treated (grass-11: 85, grass-7: 85, tree-7: 87, HDM-7: 83)
- Primary endpoint: In total, 269 (79%) subjects experienced 2162 TRAEs.
- No major differences between treatment groups in the proportion of subjects with TRAEs were observed (grass-11: 76%, grass-7: 80%, tree-7: 76%, HDM-7: 84%).
- Most frequently reported TRAEs (≥5% of subjects in any group) were local reactions injection site swelling, injection site pruritus, injection site erythema (**Figure 3**).
- The following discontinuations due to TRAEs were observed: grass-11: 1 (1%) subject, grass-7: 7 (8%) subjects, tree-7: no subject, HDM-7: 3 (4%) subjects.
- Serious TRAEs occurred in 5 subjects (grass-11: 4 , grass-7: 1).
- TRAEs were similar, regardless of age group (adolescents: 71-86%, adults: 73-85%).

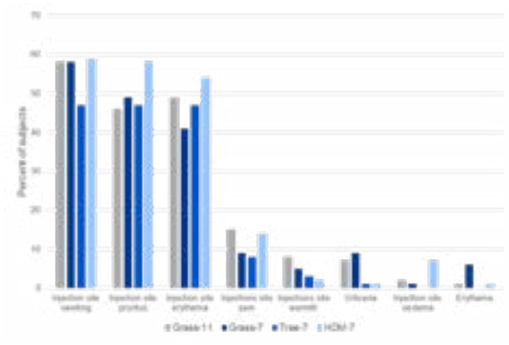

Figure 3. Most frequently reported treatment-related AEs (≥5% of subjects in any group)

Disclosure of presenting author: Dr. Wuestenberg is employee of ALK and holds stocks/stock options.

Conclusion

- The data indicate that a 7 injection up-dosing schedule for Alutard SQ grass, birch and HDM in adolescents and adults has an acceptable safety and tolerability profile.

Funding: This trial was sponsored by ALK, Hørsholm, Denmark

Meta-Analysis of the Efficacy of Pharmacotherapies and Allergy Immunotherapy for Adults with Perennial Allergic Rhinitis

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L25

Introduction

Treatments for perennial allergic rhinitis (PAR) include antihistamines, intranasal corticosteroids (INCS), leukotriene receptor antagonists, and allergy immunotherapy (AIT). This meta-analysis systematically evaluated the efficacy of pharmacotherapy and AIT versus placebo on nasal symptoms associated with PAR.

Methods

The meta-analysis protocol is registered in PROSPERO [CRD42018105632] per PRISMA guidelines.

Systematic review

Randomized, double-blind, placebo-controlled trials for adults with PAR were identified from systematic searches of PubMED/EMBASE through 5/18/2018. Pharmacotherapy trials were limited to those using products approved by the US Food and Drug Administration (FDA) and that are commonly recommended and well-studied. SLIT trials were limited to those using products approved by the FDA, which limited the analysis to SLIT-tablet trials. SCIT trials were limited to those using commercially-available or standardized products. Nasal provocation, environmental exposure unit, or cross-over trials were excluded. Trials that did not report total nasal symptom score (TNSS) in such a way that actual average daily sum score at the end of the primary assessment period could be directly evaluated or calculated were excluded. Risk of bias for each trial, and publication bias and heterogeneity across trials, were assessed.

Meta-analysis

The primary outcome was the mean numerical difference in TNSS between active treatment and placebo at the end of the primary assessment period. All TNSS data were converted to reflect the average daily sum on a scale of 0 to 12. Random-effect meta-analyses estimated the mean difference and corresponding 95% CI for each drug group weighted by inverse of trial variance.

AIT, allergy immunotherapy; INCS, intranasal corticosteroids; PAR, perennial allergic rhinitis; TNSS, total nasal symptom score; SCIT, subcutaneous immunotherapy; SLIT-tablet, sublingual immunotherapy tablet.

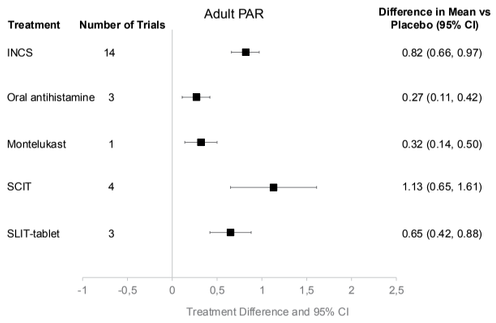
Disclosure of presenting author: E.O. Meltzer has served as a speaker or consultant for ALK, AstraZeneca, Boehringer-Ingelheim, GlaxoSmithKline, GossamerBio, Merck, Mylan, and Sanofi/Regeneron.

Results

From the pharmacotherapy searches, 774 records were screened and 18 records were ultimately used for PAR data abstraction. For the AIT searches, 593 records were screened and 7 records were used for PAR data abstraction. There was considerable heterogeneity among trials in disease severity, trial duration, and rescue medication use (allowed in all AIT trials, including active and placebo groups, not allowed in either active or placebo groups in 11 of the 14 pharmacotherapy trials that reported this information). Significant publication bias was noted for the INCS trials.

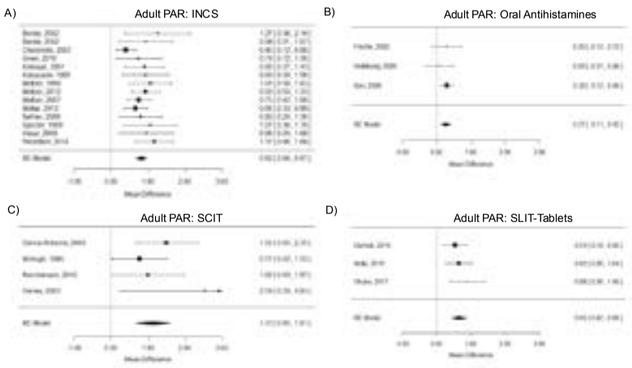
Mean difference in TNSS versus placebo (95% CI) for INCS was 0.82 (0.66, 0.97; 14 trials), for oral antihistamine was 0.27 (0.11, 0.42; 3 trials), for montelukast was 0.32 (0.14, 0.50; 1 trial), for SCIT was 1.13 (0.65, 1.61; 4 trials), and for SLIT-tablets was 0.65 (0.42, 0.88; 3 trials) (**Figure 1**). Forest plots for the individual trials in each drug group are shown in **Figure 2.**

Figure 1. Mean difference in total nasal symptom score (TNSS) between active treatment classes and placebo in adult perennial allergic rhinitis (PAR) trials.



Funding: Support for this analysis was funded by ALK, Hørsholm, Denmark. Medical writing assistance was provided by Erin P. Scott, PhD of Scott Medical Communications, LLC.

Figure 2. Mean difference in total nasal symptom score (TNSS) between active treatment classes and placebo in individual adult perennial allergic rhinitis (PAR) trials for A) INCS, B) oral antihistamines, C) SCIT, and D) SLIT-tablet.



Conclusions

All assessed pharmacologic and immunologic treatments significantly improved TNSS for adult PAR versus placebo. The effects of AIT on TNSS were in addition to the use of rescue medication in both active treatment and placebo groups. It is not possible to conclude differences in the relative effect of the different pharmacotherapies and AIT due to the substantial heterogeneity between trials and the overlapping confidence intervals. Head-to-head trials are needed for definitive comparisons because of methodological differences between AIT and pharmacotherapy trials.

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NOTES

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