1 Synopsis

Name of Sponsor/Company: Allergopharma GmbH & Co. KG	Individual Study Table Referring to Part of the Dossier: Volume: Page:	(For National Authority Use only)
Name of Finished Product: Acaroid *D. pteron. 100%*		
Name of Active Ingredient: House dust mite allergoid preparation (*Dermatophagoides pteronyssinus*)		

Title of trial:

A multicentre randomised placebo-controlled double-blind clinical trial for evaluation of safety and efficacy of a specific immunotherapy with an aluminium hydroxide-adsorbed allergoid preparation of house dust mites of *Dermatophagoides pteronyssinus* in patients with rhinitis/rhinoconjunctivitis with or without allergic asthma bronchiale

Coordinating investigator:

[redacted]

Trial Centre(s): It was planned to open approx.. 60 trial sites in European countries and Russia. Until the premature termination of the study, 3 trial sites in Poland recruited patients.

Publication: None

Trial period:	**Phase of development:**
First patient, first visit: 16-June-2010 **Last patient, last visit:** 24-June-2010	III

Objectives:

To evaluate efficacy and tolerability of specific immunotherapy with an aluminium hydroxide-adsorbed allergoid preparation of major allergens of *Dermatophagoides pteronyssinus* in adolescent and adults with allergic rhinitis/rhinoconjunctivitis caused by house dust mites with or without controlled allergic asthma.

Methodology:

Multicentre, multinational, double-blind, placebo-controlled, randomised trial including 2 parallelgroups and 2 years duration. If efficacy could be demonstrated after the double-blind treatment period, active treatment was intended to be extended in open-label design for a third year of active treatment.

Number of patients (planned and analysed):

Planned: 206 patients were planned to be randomized.

Name of Sponsor/Company: Allergopharma GmbH & Co. KG	Individual Study Table Referring to Part of the Dossier: Volume: Page:	(For National Authority Use only)
Name of Finished Product: Acaroid *D. pteron. 100%*		
Name of Active Ingredient: House dust mite allergoid preparation (*Dermatophagoides pteronyssinus*)		

Analysed: 22 patients were included for screening. Due to the early termination of the trial before any randomization and treatment, no other than the All Patient Data Set was analysed descriptively.

All Patient Set (All): 22 patients.

Diagnosis and main criteria for inclusion:

Diagnosis:

IgE-mediated allergic diseases including symptoms of allergic rhinoconjunctivitis with or without controlled allergic bronchial asthma triggered by house dust mite allergens.

Inclusion criteria:

at screening:

- Male or female outpatients who are legally competent; written informed consent.
- Age: 12 - 60 years.
- IgE-mediated allergic rhinitis/rhinoconjunctivitis with or without asthma (controlled, acc. to GINA 2006) documented by:
- Skin prick test (SPT) wheal for *D. pter*. ≥5 mm in diameter ***and***
- Histamine (1% histamine) wheal ≥3 mm ***and***
- NaCl control reaction <3 mm ***and***
- Immunoassay result (central laboratory) >1.5 kU/L to *D. pter*. ***and***
- Main discomfort in the months October to December or over the entire year on exposure to house dust mites ***and***
- Treated with anti-allergic medications for at least 2 years before enrolment.

at entry to treatment period:

- Proven exposure to house dust mites demonstrated by positive house dust mite allergen determination in bed/upholstered furniture of the subject's living area.
- Only those subjects who demonstrate adequate symptoms in the subject diary. The required threshold for the AUC of the rhinitis symptom-medication-score (R-SMS) is to be determined at the screening review meeting.

Test product, dose and mode of administration, batch number:

Test product: House dust mite allergoid (*Dermatophagoides pteronyssinus 100%*) with buffered saline, adsorbed to aluminium hydroxide. The concentration is specified in therapeutic units (TU).

Mode of administration: Subcutaneous injection of following strengths: Strength A ([redacted]); Strength B ([redacted])

Name of Sponsor/Company: Allergopharma GmbH & Co. KG	Individual Study Table Referring to Part of the Dossier: Volume: Page:	(For National Authority Use only)
Name of Finished Product: Acaroid *D. pteron. 100%*		
Name of Active Ingredient: House dust mite allergoid preparation (*Dermatophagoides pteronyssinus*)		

Batch number: n.a. No patient received treatment with test product or placebo.

Duration of Treatment: 2 years double-blind (conditional 1 year open-label extension).

Reference therapy or comparator, dose and mode of administration, batch number:

Placebo in sterile suspension containing histamine dihydrochloride ([redacted] matching strength A, [redacted] matching strength B) for subcutaneous injection in the upper arm.

Criteria for evaluation:

Efficacy:

Primary endpoint:

- Change in the area under the curve (AUC) of the rhinitis symptom-medication-score
  (R-SMS) from the baseline period to after 2 years of double-blind treatment.

Secondary endpoints:

- Change in the AUC of the R-SMS from the baseline season to the season after 1 year of double-blind treatment.
- Immunologic changes: specific immunoglobuline G (IgG_1 & IgG_4).
- Well days based on rhinitis SMS (no medication intake & maximum 2 score points).
- Response status in terms of 40% improvement for the primary efficacy variable for an individual trial subject.
- Change of EQ-5D (before vs. after treatment).

Safety:

- Safety of treatment during the entire trial period will be assessed by clinical laboratory, vital signs and adverse events

Statistical methods:

The trial was planned as a confirmatory phase III pivotal trial. The primary endpoint is the change in the AUC of the R-SMS from the baseline period to after 2 years of double-blind treatment. The AUC of the daily R-SMS will be calculated from score data collected over 28 days. The statistical null hypothesis of no difference between the two treatment groups with regard to the absolute change in AUC will be tested in a confirmatory sense within the Full Analysis Set with the Wilcoxon-Mann-Whitney U-Test using a two-sided significance level of 0.05. The null hypothesis is rejected and the

Name of Sponsor/Company: Allergopharma GmbH & Co. KG	Individual Study Table Referring to Part of the Dossier: Volume: Page:	(For National Authority Use only)
Name of Finished Product: Acaroid *D. pteron. 100%*		
Name of Active Ingredient: House dust mite allergoid preparation (*Dermatophagoides pteronyssinus*)		

superiority of a treatment (placebo or active) is demonstrated if the p-value is less than the pre-specified significance level of 5%.

All further statistical tests were planned to be performed in an exploratory sense only.

Demography and baseline characteristics of trial population:

22 Patients (13 males/ 9 femals) were screened. No patient was randomized.

Summary – Conclusions:

The trial was discontinued prematurely during the screening phase due to a sponsor´s management decision.

For the all patients set the following parameters documentetd at screening were listed:

Informed consent date, visit dates, pregnancy test result, demographic data, in- exclusion criteria, allergy history, family history, medical history, blood samples, house dust sample reminder, vital signs, skin prick test, lung function, concomitant medication, study termination.

Efficacy results:

N.a. No evaluations of efficacy parameters were performed, since the trial had been discontinued prematurely before randomization.

Safety results:

Exposure to trial medication:

No patient received trial medication or placebo.

Adverse Events (AEs):

- Patients were only screened for being suitable to get enrolled into the trial. During the screening only routine procuedures like Skin Prick Test or lung function measurements were performed.
- There were no treatment-emergent adverse events (TEAEs) or serious adverse events (treatment emergent SAEs), since the trial had been discontinued before any treatment with the trial preparation or placebo.
- Procedural adverse events have not been reported.

Date of the report:

10-June-2016