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Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT
		Study Code:	M016455A_4148
Generic drug name:	Fexofenadine	**Date:**	11/Mar/2008

Title:	A Single-Center, Randomized, Double-Blind, Placebo-controlled, Two-Way Crossover Study Designed to Evaluate the Efficacy of Fexofenadine HCl 180 mg for Preventing and Controlling Cat Allergy Symptoms
Investigator(s), study site(s):	The investigators was Robert B. Berkowitz, M.D., RxResearch, Woodstock, GA 30188 and the study was performed at Good Mews, 736 Johnson Ferry Road Suite A-3, Marietta, GA

Study duration and dates: The first subject was enrolled on 17 November 2003 and the last subject completed the study on 29 February 2004	**Phase of development:** IV

Objectives:	**Primary** - To determine the efficacy of fexofenadine (HCl) 180 mg versus placebo in preventing and controlling self-reported cat allergy symptoms in subjects who had a know allergy to cats and were exposed to high levels of *feline domesticus* allergen 1 (Fel d1) using a live cat challenge model. **Secondary** - To determine the efficacy of fexofenadine HCL 180 mg compared to placebo in subjects with a known allergy to cats as measured by the duration of time spent in the cat challenge room. - To determine the efficacy of fexofenadine HCL 180 mg compared to placebo in controlling individual symptoms in subjects who had a known allergy to cats and were exposed to high levels of Fel d1. - To determine the efficacy of fexofenadine HCL 180 mg compared to placebo in preserving peak nasal inspiratory flow (PNIF) in subjects who had a known allergy to cats and were exposed to high levels of Fel d1.
Study design:	This was a single-center, prospective, randomized, double-blind, placebo-controlled, two-way crossover study. A well-characterized and accepted live cat challenge model was used as a naturalistic method for exposing subjects to Fel d1. Eligible subjects were randomly assigned in a 1:1 ratio to a treatment sequence of either A-B or B-A (where A = fexofenadine HCL 180 mg and B = placebo). Subjects who tested positive for cat allergy symptoms during a priming cat exposure challenge were eligible to enter the treatment phase of the study. Baseline efficacy measures were obtained prior to the dispensing of study medication during both treatment periods. Cat challenges were initiated 1.5 hours following treatment with study medication.
Number of subjects planned:	It was planned to enroll a minimum of 100 subjects in order to achieve 70 completed subjects. Due to a high number of screen failures, a late study start, and an early start of the spring allergy season in Atlanta, the completed sample size was limited to 63 subjects.

Inclusion criteria:	Male or female; aged 12 years or older, with a known history of cat-induced allergic rhinitis for at least 2 years that required the use of allergy medication or had resulted in avoidance of cats.
Treatments:	Fexofenadine HCL (Allegra) 180 mg or placebo taken orally after completing assessments at baseline and 1.5 hours before initiating cat challenge.
Efficacy data:	Severity of the following individual symptoms on a 5-point scale from 0 (absent) to 4 (severe) at 5-minute intervals during the cat challenge was recorded: - Rhinorrhea (nasal discharge/runny nose or postnasal drip) - Itchy nose/palate/throat - Sneezing - Itchy/watery/red eyes - Nasal congestion Total symptom score (TSS) would be calculated as the sum of the first four individual symptoms excluding nasal congestion. Total time spent in cat challenge room. The following would be calculated from recorded data: - Change in TSS from baseline to 30 minutes following initiation of cat exposure challenge, or earlier in cases of premature termination. - Absolute and percent change in TSS and individual symptom scores from baseline to each time point of 5-minute intervals during cat challenge - Mean absolute and percent changes in TSS and individual symptom scores from baseline over the entire duration of exposure - Changes in PNIF measurements from baseline to each time point of 10-minute intervals during cat challenge, and the mean changes over the entire duration of exposure.
Safety data:	Occurrence of all adverse events/treatment-emergent adverse events and changes from baseline in Forced Expiratory Volume at 1 second (FEV1) and Peak Expiratory Flow Rate (PEFR).

Statistical procedures:	**<u>Demographic, Baseline, and Background Characteristics</u>** Standard baseline characteristics were summarized. **<u>Primary Efficacy</u>** The primary efficacy variable was the change from baseline to 30 minutes following initiation of cat challenge, or earlier in cases of premature termination, in TSS. Analysis of TSS was based on an analysis of variance (ANOVA) model for the study design. The efficacy parameter was analyzed by an ANOVA model with terms of treatment, period and sequence (carry-over effect), as fixed effect, and subject nested within sequence as a random effect to determine if any sequence (or carry-over) effect existed before a final model was selected for data analysis. If a significant sequence (or carry-over) effect was detected at a significance level of 0.001, then only the data collected from the first period was to be combined for analysis using a simple one-way ANOVA. In this case, pair-wise comparison among treatment groups was to be conducted using only the first period data. If no significant sequence (carry-over effects) was detected, an ANOVA model with terms of treatment and period as fixed effects, and subject nested within sequence as a random effect was to be performed. Pair-wise comparisons were carried out using appropriate statistical contrasts with two-sided significance level of 0.050. **<u>Secondary Efficacy</u>** If 2 or more subjects exited the cat challenge earlier than planned in one of the treatments, total time spent in cat challenge room would be analyzed using survival analysis. Kaplan-Meier curves and Wilcoxon matched pairs signed rank test would be used to test for differences between treatments for total time spent in cat challenge room. Stepwise Cox proportion hazards model with treatment sequence period as covariates would be used to analyze the total time spent in cat challenge room. Non-significant (*P* value >0.100) covariates would be dropped from the model. If less than 2 subjects exited the cat challenge earlier than planned, survival analysis would be abandoned, and the subjects who exited earlier than planned would be compared between treatments using Fisher's exact test. All other secondary efficacy parameters (absolute and percent changes from baseline to each time point and their mean changes over the exposure duration in TSS, individual symptom scores, and PNIF) were evaluated using the same method as that for the primary efficacy variable. **<u>Safety:</u>** Safety assessments were based on the frequency of adverse events and changes from baseline in FEV1 and PEFR.
Interim analysis:	No interim analysis was performed for this study.

Results – Study subjects and conduct:	**<u>Subject disposition:</u>** Two hundred and eleven subjects were screened and 66 subjects were randomized. One hundred and forty-five (68.7%) subjects were screen failures. Thirty-two subjects in the placebo/fexofenadine treatment sequence and 31 subjects in the fexofenadine/placebo treatment sequence completed the study. Three of the randomized subjects discontinued from the study. A total of 63 subjects completed the study. **<u>Demographics:</u>** There was a statistically significant difference in age between the placebo/fexofenadine and the fexofenadine/placebo sequence treatment groups. The average age of the placebo/fexofenadine group was 40 years and the average age of the fexofenadine/placebo group was 32 years. Overall, there were more female (80%) subjects than male (20%), and there were more black subjects (63%) than white subjects (35%) or those of other races (2%). **<u>Primary disease:</u>** There was a statistically significant difference in allergic rhinitis history between treatment sequence groups. The average year of allergic rhinitis history in the placebo/fexofenadine group was greater (20 years) compared to the fexofenadine/placebo treatment group (15 years).
Results – Efficacy:	There was a statistically significant difference between placebo and fexofenadine treatment in change from baseline in TSS at 30 MACC. Fexofenadine increased TSS from baseline less than placebo. There were no statistically significant differences in Fel d1 measurements between treatments. Fexofenadine reduced allergic rhinitis symptoms at most 5-minute intervals starting from 15 MACC compared to placebo throughout the duration of the cat challenge when expressed as a percent change in TSS from baseline. There were no statistically significant differences between treatments in total time spent in cat challenge room. All subjects who completed both treatment periods, except for one in the placebo treatment group, endured the entire 60 minutes exposure to cat challenge. Extending exposure time to cat challenge may have further differentiated effect of the fexofenadine compared to placebo reducing allergic rhinitis symptoms. There was a statistically significant difference between fexofenadine and placebo when comparing the individual symptoms scores of sneezes and nasal congestion. Fexofenadine treatment changed the absolute sneezes and nasal congestion scores less from pre-dose baseline compared to placebo. However, when comparing PNIF, there were no statistically significant differences between fexofenadine and placebo.
Results – Safety:	The overall incidence of treatment emergent adverse events (TEAEs) was low. Eight TEAEs were reported, 5 in the placebo group and 3 in the fexofenadine group. Only 6 subjects experienced TEAEs (4 during placebo treatment and 2 during fexofenadine treatment). There were no deaths and no serious adverse events (SAEs). There was only possibly related, mild in intensity, TEAE of somnolence that occurred after fexofenadine treatment. There were 2 permanent discontinuations from study medications due to an adverse event. Neither of the two AEs that resulted in discontinuation from the study was related to study medication. FEV1 and PEFR were measured in this study to compare lung function prior to and post cat challenge. There were no significant differences from baseline between treatment sequences in FEV1 level at any visit. FEV1 levels were not measured during cat challenge. A statistically significant difference in PEFR between treatments was observed at 30 MACC. PEFR decreased less from baseline in subjects treated with fexofenadine compared to the placebo treatment at 30 MACC.
Date of report:	11-Aug-2004