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<b>Sponsor/company:</b>	sanofi-aventis	<b>ClinialTrials.gov Identifier:</b>	NCT
<b>Generic drug name:</b>	Fexofenadine	<b>Study Code:</b>	M016455A_4139
		<b>Date:</b>	11/Mar/2008
<b>Title of the study:</b>	Single center, randomized, double-blind, crossover study comparing the effects of single-dose fexofenadine HCl 180 mg, cetirizine 10 mg, and placebo on cognitive performance in naval flight personnel		
<b>Investigator(s):</b>	CAPT Charles Vacchiano, CRNA, Ph.D. Aerospace Medical Research Laboratory Naval Air Station, Pensacola, FL		
<b>Study center(s):</b>	Single center		
<b>Study duration and dates:</b>	15 September 2003 to 28 January 2005	<b>Phase of development:</b>	IV
<b>Objectives:</b>	<p><u>Primary objective</u> To compare the effects of fexofenadine HCl 180 mg, cetirizine HCl 10 mg, and placebo on computerized scores derived from the Aeromedical Vigilance Task (AVT), a computerized objective measure of attention, accuracy, and reaction time in healthy naval flight personnel. The primary endpoint was the AVT overall (average of the 18 blocks) mean change from baseline in total number of errors (commission errors + omission errors). In addition, the safety of these single-dose treatments was also to be assessed.</p> <p><u>Secondary objectives</u> To evaluate the change from baseline between fexofenadine HCl 180 mg and cetirizine HCl 10 mg in total number of errors under each normobaric hypoxic condition, as well as over the entire 60-minute duration AVT. Additional secondary objectives were to evaluate the change from baseline between fexofenadine HCl 180 mg, cetirizine HCl 10 mg, and placebo in the following measures at ambient atmospheric conditions, under each normobaric hypoxic condition, and over the entire 60 minute AVT:</p> <ul style="list-style-type: none"> <li>• Computerized scores of accuracy derived from the AVT for number of hits, omission errors, commission errors, and correct rejections;</li> <li>• Computerized scores of speed derived from the AVT for overall maximum mean hit reaction time and mean hit reaction time;</li> <li>• Computerized scores of variability derived from the AVT for overall hit reaction time standard error;</li> <li>• Computerized scores of attention derived from the AVT for risk taking (<math>\beta</math>) and d prime (<math>d'</math>);</li> <li>• A self-rated visual analog scale (VAS) score for drowsiness, a subjective assessment of drowsiness, in healthy naval flight personnel.</li> </ul> <p>In addition, the objective measurements of cognitive function and the subjective assessment of drowsiness in healthy naval flight personnel were to be correlated. Placebo comparisons for all endpoints were also to be reported.</p>		

<b>Study design:</b>	<p>This was a single-center study conducted by Captain Charles Vacchiano, CRNA, PhD, at the Aerospace Medical Research Laboratory, Naval Air Station, Pensacola, FL. This was a single-dose, randomized, double-blind, placebo-controlled, 3-period crossover study. Subjects were to perform a neuropsychological test (AVT) that focused on cognitive skills important for naval aviation, and were to complete a self-rated VAS, a subjective measure of drowsiness.</p> <p>These tests were to be administered at the Naval Aerospace Medical Research Laboratory in Pensacola, FL.</p>
<b>Number of subjects planned:</b>	A total of 72 subjects were to be enrolled and treated with study medication.
<b>Inclusion criteria:</b>	<p>Subjects meeting all of the following criteria were to be considered for enrollment into the study:</p> <ul style="list-style-type: none"> <li>• Male or female naval flight personnel =18 years of age;</li> <li>• CogScreen-Aeromedical Edition (CogScreen-AE) Logistic Regression Probability Value &lt;0.6 at the baseline screening visit;</li> <li>• Normal SaO2 (&gt;95%) as measured by pulse oximetry;</li> <li>• Female subjects of non-childbearing potential (i.e., surgically sterile or at least 1 year postmenopausal).</li> </ul>
<b>Treatments:</b>	<p>Visit 1 (Baseline): single dose of single-blind placebo;</p> <p>Visits 2, 3, and 4 (Treatment): single-dose, double-blind fexofenadine HCl 180 mg, cetirizine HCl 10 mg, and placebo in complete, randomized crossover design. A total of 7 to 12 days were to separate baseline and treatment visits.</p>
<b>Efficacy data:</b>	Efficacy was to be evaluated based on the subjects' performance on a neuropsychological test (the AVT) that measured cognitive skills important for naval aviation, and on a self-rated VAS that subjectively assessed drowsiness.
<b>Safety data:</b>	Safety was to be evaluated based on adverse events, electrocardiograms, physical examinations including vital signs, and clinical laboratory data.
<b>Statistical procedures:</b>	<p>The primary efficacy variable was the change from baseline in the average number of AVT errors under ambient atmospheric conditions (average of the totals of Blocks 1 through 18). The total number of AVT errors in a given block was defined as the sum of the number of commission errors and the number of omission errors within a block.</p> <p>The variables used to define the primary efficacy variable included the following:</p> <ul style="list-style-type: none"> <li>• Baseline average number of AVT errors under ambient atmospheric conditions (computed using Visit 1 data). The total number of AVT errors from each of Blocks 1 through 18 was averaged, giving the baseline average number of AVT errors under ambient atmospheric conditions.</li> <li>• Average number of AVT errors under ambient atmospheric conditions computed for each of Visits 2, 3, and 4 separately. The total number of AVT errors from each of Blocks 1 through 18 was averaged, giving the average number of AVT errors under ambient atmospheric conditions.</li> <li>• Change from baseline in the average number of AVT errors under ambient atmospheric conditions (average number of AVT errors under ambient atmospheric conditions) minus (baseline average number of AVT errors under average atmospheric conditions).</li> </ul> <p>Secondary efficacy analyses investigated changes in the following measures under various atmospheric conditions:</p> <ul style="list-style-type: none"> <li>• Accuracy measures</li> <li>• Speed measures</li> <li>• Variability measures</li> <li>• Attention measures</li> <li>• VAS measures.</li> </ul>
<b>Interim analysis:</b>	No interim analysis was performed for this study.

<p><b>Results – Study subjects and conduct:</b></p>	<p>A total of 125 subjects were screened and enrolled into the study. Of those, 89 subjects were enrolled in the single-blind phase of the study, and a total of 81 subjects were randomized to a double-blind study treatment sequence at a single site. All randomized subjects were treated with study medication. Thus, a total of 81 subjects were randomized and exposed to single doses of at least one of the 3 study treatments (fexofenadine HCl 180 mg, cetirizine HCl 10 mg, and placebo) in a crossover fashion (double-blind safety-evaluable population). Seven of the 81 randomized subjects withdrew before the planned end of study. The most common reason for withdrawal was lost to follow-up. The per-protocol population, defined as all subjects who completed the study without a major protocol violation, consisted of 74 subjects.</p> <p>Duration of each treatment was considered to be one day (a single dose). A total of 74 subjects received single doses of all 3 treatments; 7 additional subjects received single doses of either one or 2 treatments prior to withdrawal. The age range of subjects in the study was from 21 years of age to 46 years of age. A majority of subjects were male, white, and 23 years of age and older.</p>
<p><b>Results – Efficacy:</b></p>	<p>The per-protocol analyses of the primary efficacy variable (average AVT number of errors [commission errors plus omission errors] under ambient atmospheric conditions) demonstrated no statistically significant increases overall in the number of errors in either active treatment compared with placebo, or for fexofenadine HCl compared with cetirizine HCl.</p> <p>At normobaric hypoxic conditions of 10,000 feet and 15,000 feet, as well as over the entire 60 minutes, the overall average AVT number of errors significantly increased for cetirizine HCl over placebo. In addition, at normobaric hypoxic conditions of 10,000 feet, the overall average number of errors significantly increased for cetirizine HCl over fexofenadine HCl.</p> <p>Analyses of the overall change in average number of correct hits indicated that at normobaric hypoxic conditions of 10,000 feet and 15,000 feet and over the entire 60 minutes, there were significantly fewer correct hits for subjects taking cetirizine HCl compared with placebo. Other accuracy measures that were analyzed included change in average AVT number of omission errors, number of commission errors, and number of correct rejections. Overall average number of omission errors increased significantly for subjects taking cetirizine HCl compared with placebo at normobaric hypoxic conditions of 10,000 feet and 15,000 feet, as well as over the entire 60 minutes; while for subjects taking cetirizine HCl compared with fexofenadine HCl, overall average number of commission errors increased significantly and average number of correct rejections decreased significantly at normobaric hypoxic conditions of 10,000 feet.</p> <p>Analyses of speed measures included change from baseline in average AVT maximum mean hit reaction time and mean hit reaction time. Findings were similar in both analyses, which demonstrated statistically significantly greater overall maximum mean hit reaction time and mean hit reaction time for cetirizine HCl over placebo at normobaric hypoxic conditions of 10,000 feet.</p> <p>Overall maximum mean hit reaction time was also significantly greater for cetirizine HCl at hypoxic conditions of 15,000 feet.</p> <p>Analyses of risk taken and d prime (attention measures) were performed under ambient atmospheric conditions and over the entire 60 minutes. There were no significant changes in risk taken (changes towards increased caution versus increased impulsiveness) under these conditions when treatments were compared. On the other hand, results of analyses of d prime showed a significant change towards less attentiveness for subjects taking cetirizine HCl over placebo for the entire 60-minute period.</p> <p>Analyses of change from baseline in VAS scores immediately before receiving study medication, immediately prior to AVT, and immediately following AVT did not reveal any significant increase in drowsiness for either active treatment compared with placebo, or fexofenadine HCl compared with cetirizine HCl. There did appear to be a stronger correlation, however, between number of errors and VAS scores for fexofenadine HCl at all 3 time points under all atmospheric conditions compared with the other treatments.</p>

<b>Results – Safety:</b>	<p>The following conclusions regarding the safety of fexofenadine HCl in healthy subjects: There were no treatment-emergent adverse events reported during the study and no clinically relevant changes from baseline to the end of the study were observed with respect to vital signs. The frequency of individual vital signs PCAs/LPCAs during the study was low. Overall, fexofenadine HCl was well tolerated in this study.</p>
<b>Date of report:</b>	25-Jul-2005