SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: ACCOLATE™

ACTIVE INGREDIENT: zafirlukast (ICI 204,219)

Trial title (number): A Double-blind, Parallel Group Trial of Zafirlukast (ACCOLATE™) 20 mg bid in Combination With Cetirizine (ZYRTEC™) 10 mg at Bedtime Versus Cetirizine (ZYRTEC™) 10 mg at Bedtime for the Treatment of Subjects With Chronic Idiopathic Urticaria

Clinical phase: III
First patient recruited: 28 December 1998
Last patient completed: 30 August 1999
AstraZeneca approval date:

Principal investigator(s) and location (center number): Johnathan Bernstein MD, 844 Winton Rd, Cincinnati, OH 45231 (Center 001)

OBJECTIVES: The primary objective of this trial was to determine the efficacy of zafirlukast 20 mg bid as adjunctive therapy to antihistamine, for the treatment of chronic idiopathic urticaria. The secondary objective was to explore methods of assessing the treatment efficacy of chronic urticaria and statistically analyzing the same for use in later protocols.

This is an abbreviated clinical trial report. Data from this pilot trial are not intended for a new indication for the treatment of urticaria. Data from this trial are not needed to support any information included in the labeling.

METHODS

Design: This trial was a 3-week, randomized, double-blind, parallel-group trial comparing zafirlukast and cetirizine with zafirlukast-matching placebo (hereinafter referred to as placebo) and cetirizine, in subjects with chronic idiopathic urticaria. The double-blind period was preceded by a screening period during which eligible subjects were asked to discontinue all urticaria medication and to return (within 3 to 7 days) for a 7- to 10-day single-blind run-in period of placebo and cetirizine. It was expected that no more than 160 subjects would enter this trial to obtain 80 evaluable subjects.

Population: One hundred and sixty-seven patients were screened for this trial; 109 met the criteria and were randomized for treatment (55 zafirlukast and 54 placebo).

Key inclusion criteria: Eligible subjects were aged 12 years or older who had been diagnosed with chronic idiopathic urticaria.

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**Key exclusion criteria:** Patients were excluded from entrance into the trial if: they had a history of any cardiac or gastrointestinal disease, or any condition that might confound the results of the trial or place the patient at additional or unknown risk; required protocol-prohibited medication prior to or during the trial; or had any clinically significant laboratory abnormalities at screening. **Dosage:** AstraZeneca supplied the following trial medications: commercial zafirlukast (20-mg tablets [taken bid during the 3-week double-blind period]) formulation [F] number F7156; zafirlukast-matching placebo tablets F7173 (taken bid during the run-in and double-blind periods); cetirizine (10-mg tablets) F12492 (taken once daily in the evening during both the run-in and double-blind periods); and diphenhydramine (25-mg tablets) F12508 (used as rescue medication for the duration of the trial). **Key assessments:** Safety was assessed based on results of clinical laboratory tests, physical examinations, vital signs measurements, adverse event monitoring, and subjective symptomatology. Primary measures of efficacy were the 11-point Treatment Effectiveness Scale (rated from 0 to 10) and the Overall Condition Visual Analog Scale. **Statistical analyses:** No formal statistical analysis of safety data was performed for this trial. Safety data were summarized with descriptive statistics. Analysis of variance (ANOVA) methodology was used to summarize the primary efficacy variables. Summary tables of efficacy data are appended to this report.

**RESULTS**

**Demography:** A total of 109 patients were randomized into the trial; 11 subjects withdrew (4 zafirlukast and 7 placebo). Within treatment groups, most of the subjects were women (84%), the predominant ethnic group was white (82%), and most patients ranged in age from 18 to 55 years (84%). Baseline VAS and Effectiveness scores were similar between the groups. **Efficacy:** There were no consistent statistically significant differences between zafirlukast and placebo for the primary efficacy assessments performed for this trial. **Safety:** No deaths were reported. No serious adverse events or withdrawals due to adverse events occurred in the zafirlukast group. Two placebo-treated subjects had serious adverse events, 1 of which led to withdrawal, and 2 placebo subjects had nonserious adverse events leading to withdrawal. Adverse events were reported for 41.8% and 37.0% of zafirlukast- and placebo-treated subjects, respectively. The most commonly-reported adverse events were headache (10.9% versus 1.9%), abdominal pain (5.5% versus 5.6%), diarrhea (5.5% versus 3.7%), and somnolence (5.5% versus 1.9%), for zafirlukast versus placebo. Relatively few clinically significant changes in laboratory results occurred during the trial. For those laboratory results outside of the normal range, most were minor, or minor and present at baseline.

**CONCLUSIONS**

Zafirlukast 20-mg bid given with cetirizine (10 mg at bed time) was safe and well tolerated and not clinically different from treatment with cetirizine given with placebo. No new or unexpected adverse events were identified. There were no consistent statistically significant differences between zafirlukast and placebo for the efficacy assessments performed for this trial.