AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Fixed Dose Combination Capsule of Esomeprazole 20 mg And Acetylsalicylic Acid (ASA) 81 mg
ACTIVE INGREDIENT: Esomeprazole And Acetylsalicylic Acid (ASA)

Study No: D961FC00008
An Open-Label, Randomized, Single-Center, 3-Way Crossover Study Comparing The Therapeutic Efficacy, Using Percentage of Time With Intragastric pH > 4 as Surrogate Endpoint, of Repeated Oral Administration of a Fixed Dose Combination Capsule of Esomeprazole 20 mg And Acetylsalicylic Acid (ASA) 81 mg With Free Combinations of ASA Tablet 81 mg And Esomeprazole 20 mg as a Capsule or Tablet in Patients At Risk of Gastrointestinal Events Using Low Dose ASA for Cardiovascular Protection

Developmental Phase: I
Study Completion Date: March 17, 2010 (decision date for study stop)
Date of Report: April 8, 2010

OBJECTIVES:

The primary objective of this study was to investigate whether a fixed dose combination (FDC) capsule of esomeprazole 20 mg and acetylsalicylic acid (ASA) 81 mg has equivalent therapeutic efficacy compared to each of 2 free combinations of ASA tablet 81 mg plus esomeprazole 20 mg either as a capsule [clinical trial capsule (CTC)] or a tablet [multiple unit pellet system (MUPS)] in patients at risk of gastrointestinal events using low dose ASA for cardiovascular protection. This assessment was to be based on the percentage of time with intragastric pH > 4 over the 24-hour period following Day 5 of repeated oral administration/dosing.

METHODS:

Subjects were to receive one of the following treatments at 0.00 hour on Days 1 to 5 of each study period, according to a randomization scheme:

- 1 Esomeprazole 20 mg/ASA 81 mg Fixed Dose Combination Capsule (Treatment dose = 20 mg of esomeprazole and 81 mg of ASA)
- 1 Esomeprazole Clinical Trial Capsule 20 mg and 1 ASA Enteric Coated Delayed Release Tablet 81 mg (Treatment dose = 20 mg of esomeprazole and 81 mg of ASA)
- 1 Esomeprazole MUPS Tablet 20 mg and 1 ASA Enteric Coated Delayed Release Tablet 81 mg (Treatment dose = 20 mg of esomeprazole and 81 mg of ASA)

This study was to consist of three 7-day periods separated by at least a 14-day washout period from the last dose of one period to the first dose of the subsequent period.
Subjects were to be institutionalized the day before Day 1 dosing and would remain in the clinic until after the post-dose meal on Day 1 dosing for each study period, at which time they would be able to leave the clinic (subjects would be given a diary to take home to record study-related activities). Subjects were to fast overnight for at least 10 hours before dosing on Days 2, 3, and 4. Subjects were to return to the clinic on Days 2, 3, and 4 for dosing and breakfast. On Days 2 and 3, subjects were to return to the clinic during the morning (i.e. 1.5 hours before the scheduled dosing). Subjects were to receive a standard breakfast within 5 minutes after dosing. On Day 4, subjects were to return to the clinic during the morning (i.e. 1.5 hours before the scheduled dosing) for dosing and breakfast as described for Days 2 and 3, and remain until approximately 4 hours post-dose. Subjects could then leave the clinic, to return in the early evening for their overnight stay before Day 5 procedures. Subjects would be be institutionalized until 24.00 hours after Day 5 dosing for each study period at which time they could leave the clinic. Subjects were required to return for a follow-up visit 5 to 7 days after completion of all clinical study activities.

Blood samples were to be drawn at screening and at the end-of-study examination. In addition, female subjects will have blood drawn at check-in for Day 1 of each study period for serum β-CG testing. 19.5 mL and 34.5 mL of blood was be taken from male and female subjects, respectively

Pharmacodynamics (PD): The following PD parameters were to be calculated on Day 5: percentage of time during the 24-hour recording period that intragastric pH is maintained > 4.0, percentage of time during the 24-hour period that intragastric pH is maintained > 3.0, and median 24-hour intragastric pH.

Symptom Analysis: GOS gastrointestinal (GI) assessment was to be done as the first assessment on Day 5 of each study period. The GOS was to be measured by a 7-point scale and reflects the subject's overall GI symptoms over the previous 2 days.

Statistics: A 95% confidence interval (CI) of the mean difference (FDC-free combination) in percentage of time with intragastric pH > 4 over the 24-hour period after Day 5 dosing was to be calculated. The acceptable range is within [-0.15*mean (free combination) to +0.15*mean (free combination)].

Safety Analysis: The incidences of all adverse events (AEs) were to be tabulated by treatment and subject number. Absolute values for vital signs, laboratory parameters and physical examinations were to be documented and values outside the normal range were to be flagged

RESULTS:

Due to the results of D961FC00007, it was no longer necessary to perform this study and this study was stopped prematurely. Prior to termination, sixteen patients signed consent and were screened for the study. No patients received medication or any intervention. No data was entered into the CRF and as such, there are no results for this study.