

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No: ARI103880	
Title: An open label, single dose, randomized, three period crossover study to investigate the relative bioavailability of 0.5 mg of dutasteride from soft gelatin capsules (reference) vs. soft gelatin capsules containing two investigational formulations in healthy male volunteers.	
Rationale: Dutasteride (GI198745) is a 5 α -reductase inhibitor currently in use for treatment of BPH. This study was to evaluate the relative bioavailability of 2 investigational dutasteride formulations and collect safety and tolerability data on the different dutasteride formulations. Only safety data for the marketed formulation of dutasteride is being reported in this abbreviated summary. Data for the investigational formulations will be added, if and when they are approved and marketed	
Phase: I	
Study Period: 30 th March 2005-21 st June 2005	
Study Design: This study was a single-center, open-label, active-comparator, randomized, 3- period, crossover study in healthy male subjects.	
Centers: One center in the USA.	
Indication: Benign Prostatic Hyperplasia.	
Treatment: The 3 treatment arms of the study were single doses of 2 investigational dutasteride formulations and the marketed product 0.5mg dutasteride soft gelatin capsule. Doses were administered with approximately 240mL of tepid water under fasted conditions. Subjects were randomized to one of the 6 possible treatment sequences of a 3-period crossover.	
Objectives: The primary objective was to assess the relative bioavailability of 0.5mg soft gelatin capsules containing the investigational formulations as compared with the currently-marketed 0.5mg soft gelatin capsule.	
Statistical Methods: A sample size of 30 was based on study feasibility and evaluation of the variability of several previous studies. At least 39 subjects were enrolled to insure at least 30 subjects completed the study when a 20% drop-out rate was assumed. The coefficient of variation (CV) of 0.23 for the natural log of 72 hour AUC was derived from a previous dutasteride study (ARI19033). The CV of 0.24 for the natural log of Cmax was derived from the same study. Thirty subjects provide 95% power for each parameter to give an overall power across both Cmax and AUC(0-72) of 90% in terms of the two one-sided t-test.	
The pharmacokinetic parameters used to assess bioequivalence were AUC(0-72) and Cmax. AUC(0-72) and Cmax were analyzed separately by analysis of variance using a model appropriate to the study design including subject, sequence, treatment, and period. Effects associated with sequence, treatment, and period were assumed fixed. Effects associated with subject were assumed random. A point estimate and associated 90% confidence interval estimate for the difference between the 2 investigational formulations and the marketed product 0.5mgdutasteride soft gelatin capsule was constructed for each log-transformed PK parameter of interest. These point estimates and confidence intervals were then exponentially back-transformed to provide point estimates and associated 90% confidence intervals for the ratios of the PK mean of the test formulation to the reference formulation.	
Study Population: Healthy male subjects 18 -55 years of age, inclusive, with Body Mass Index between 19 and 24 kg/m ²	
Number of Subjects	
Planned, N	39
Dosed, N	37
Completed, n (%)	33 (90)
Total Number Subjects Withdrawn, n (%)	4 (11)
Withdrawn due to Adverse Events, n (%)	1 (3)
Withdrawn due to Lack of Efficacy, n (%)	not applicable
Withdrawn for other reasons, n (%)	3 (8)
Demographics	Population
N	37
Females: Males	0:37
Mean Age in Years (sd)	30.0 (8.88)
Mean Weight in Kg (sd)	82.7 (10.96)

White n (%)		26 (70)		
Pharmacokinetic Results: Geometric mean (CVb%) except for Tmax which is median (min-max)				
Formulation	N	AUC (0-72 hr) (ng•hr/mL)	Cmax (ng/mL)	Tmax (hr)
dutasteride 0.5 mg	35	26.3 (95)	2.48 (46)	1.0 (1.0, 6.0)
Safety results: A treatment-emergent adverse event (AE) or serious adverse event (SAE) was defined as an AE or SAE with onset on or after the start date of study medication but generally not after the follow-up visit 10-14 days following the last dose of study medication (third treatment session). Adverse events for the investigational formulations will be added to this summary, if and when they are approved and marketed. Overall, all study subjects tolerated study drugs without any clinically significant or relevant events.				
Adverse Events		Marketed 0.5mg dutasteride formulation (Reference)		
N (Dosed)		35		
No. subjects with AEs, n (%)		3 (9)		
Headache		2 (6)		
Vomiting		2 (6)		
Diarrhea		1 (3)		
Nausea		1 (3)		
Influenza like illness		1 (3)		
Rash		1 (3)		
Serious Adverse Events, n (%) [n considered by the investigator to be related, possibly related, or probably related to study medication]:				
Subjects with SAEs, n (%) -includes fatal and non-fatal events		0		
Publications: No Publications				

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