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<b>Study No:</b> ARI19033				
<b>Title:</b> An open label, single dose, randomised, three period crossover study to investigate the relative bioavailability of dutasteride softgel vs. dutasteride tablet and dutasteride softgel vs. dutasteride capsule in healthy male volunteers				
<b>Rationale:</b> Dutasteride (GI198745) is a 5 $\alpha$ -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. The development of the formulations tested in this study was terminated due to a failure to demonstrate bioequivalence.				
<b>Phase:</b> Phase I				
<b>Study Period:</b> 15 Mar 2004 - 22 Jun 2004				
<b>Study Design:</b> This study was a single-center, open-label, active-comparator, randomized, 3- period, crossover study in healthy male subjects.				
<b>Centers:</b> One center in the USA.				
<b>Indication:</b> Benign Prostatic Hyperplasia				
<b>Treatment:</b> The 3 treatment arms of the study were single doses of 2 dutasteride formulations (0.5mg in capsule and tablet form) and the market product 0.5mg dutasteride. 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.				
<b>Objectives:</b> The primary objective was to assess the relative bioavailability of the 0.5mg capsule and 0.5mg tablet as compared with the currently-marketed 0.5mg softgel capsule. The secondary objective was to further assess the safety and tolerability of differing formulations of dutasteride.				
<b>Statistical Methods:</b> The sample size was calculated from the coefficient of variation (CV) of 0.09 for the natural log of AUC(0-24) derived from a previous dutasteride study (ARI10018). The CV of 0.44 for the natural log of Cmax was derived from the same study. With 24 evaluable subjects, equivalence of the natural log of AUC(0-t) can be demonstrated with 99% power with a related 90% confidence interval radius of 0. Using a CV of 44%, a 90% confidence interval radius of the natural log of Cmax for 24 subjects was projected as [0.209]. To insure at least 24 subjects complete, and assuming a 30% drop-out rate, at least 36 subjects were enrolled.				
No statistical methods were used to analyze the safety data.				
<b>Study Population:</b> Eligible subjects were healthy male subjects with no clinically significant diseases, between 18 and 55 years of age (inclusive). Concomitant use of medications prior to and during study was prohibited.				
<b>Number of Subjects</b>				
Planned, N		36		
Dosed, N		36		
Completed, n (%)		31 (86)		
Total Number Subjects Withdrawn, n (%)		5 (14)		
Withdrawn due to Adverse Events, n (%)		0		
Withdrawn due to Lack of Efficacy, n (%)		not applicable		
Withdrawn for other reasons, n (%)		5 (14)		
<b>Study Demographics</b>			<b>Study Population</b>	
N (ITT)		36		
Females: Males		0:36		
Mean Age in Years (sd)		32.6 (9.89)		
Mean Weight in Kg (sd)		83.8 (11.79)		
White n (%)		21 (58)		
<b>Pharmacokinetics</b> —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	32	32.1 (62.8)	2.0 (37.8)	3 (2-6)
<b>Safety results:</b> 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). Overall, all study subjects tolerated study drugs without any clinically significant or relevant events.	
<b>Adverse events</b>	<b>Marketed dutasteride formulation (Reference)</b>
N (Dosed)	32
No. Subjects with AEs, n (%)	5 (16)
Constipation	1(3)
Change of bowel habit	1(3)
Toothache	1(3)
Vomiting	1(3)
Dizziness	1(3)
Headache	1(3)
Fatigue	1(3)
Blood creatinine increased	1(3)
Pharyngolaryngeal pain	1(3)
Sputum discolored	1(3)
<b>Serious Adverse Events</b> , n (%) [n considered by the investigator to be related, possibly related, or probably related to study medication]:	
No. subjects with SAEs, n (%) -includes fatal and non-fatal events	0
<b>Publications:</b> No Publication	

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