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Study No: ARI10015		
Title: An Evaluation of the Absolute Bioavailability of GI198745 (dutasteride) Soft Gelatin Capsules Compared to GI198745 (dutasteride) Intravenous Solution in Healthy Volunteers.		
Rationale: Dutasteride (Dut) Soft Gelatin Capsule was clinically formulated as a soft gelatin capsule for oral administration. This study was conducted in man to determine the absolute bioavailability of the Dut Soft Gelatin Capsule compared with an IV solution given as an infusion over 2 hours.		
Phase: I		
Study Period: 08 Jul 1999 – 03 Sept 1999		
Study Design: This was an open-label, randomized, two period crossover study.		
Centres: 1 center in the US.		
Indication: None.		
Treatment: Following a 3-week screening period, volunteers were randomized to receive one of two treatments: either a single dose of Dut 0.5 mg Soft Gelatin Capsule or a 45 mL IV dose over 2 hours (approximately 0.004 mg/min: a dose of 0.5 mg). Following a 4 week washout period, the volunteer then received the alternate Dut treatment.		
Objectives: The primary objective was to estimate the absolute bioavailability of the Dut Soft Gelatin Capsule with respect to the Dut IV formulation.		
Statistical Methods: Power: Since the objective of this study was descriptive rather than comparative, no power or sample size calculations were appropriate. It was decided that 6 subjects would be adequate to meet the study objective.		
Pharmacokinetic: The primary objective was to estimate absolute bioavailability (ratio of AUC of Dut Soft Gelatin Capsule to AUC of the IV formulation). The ratios of the GI198745 Soft Gelatin Capsule formulation to the IV formulation were also calculated for secondary parameters AUC ₂₄ and AUC _{last} . Analysis of the three PK parameters were performed using analysis of variance allowing for effects due to sequence, subject (sequence), period, and formulation. The PK parameters were log transformed prior to analysis. Confidence intervals of the formulation ratios were estimated by exponentiating the log difference in least squares means and exponentiating the corresponding 90 and 95% confidence intervals about the differences. While no formal tests of normality were made, plots of the studentized residuals were made to verify the model assumptions of normality. In addition, standard summary statistics, n, mean, median, standard deviation, CV, minimum, maximum, calculated geometric mean and log standard deviation were produced for all PK parameters and GI198745 serum concentrations.		
Study Population: Healthy male volunteers aged between 18 and 55 years (inclusive) with a body mass index (BMI) of 19 to 29 kg/m ² (inclusive).		
Number of Subjects:	Soft Gelatin Capsule	IV
Planned N	6	6
Dosed N	6	6
Completed n (%)	6 (100)	5 (83)
Total Number Subjects Withdrawn N (%)	0	1 (17)
Withdrawn due to Adverse Events n (%)	0	0
Withdrawn due to Lack of	0	0

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Efficacy n (%)		
Withdrawn for Other Reasons n (%)	0	1
Demographics	All Subjects	
N (ITT)	6	
Females: Males	0:6	
Mean Age in Years (sd)	31 (8)	
Mean Weight in Kg (sd)	88.2 (12)	
White n (%)	6 (100)	
Pharmacokinetic (PK) Results:		
PK Parameters	Soft Gelatin Capsule (n=5)	IV (n=5)
AUC ₂₄ (ng.h/mL), mean (SD)	10.12 (7.04)	14.03 (8.08)
AUC _{last} (ng.h/mL), mean (SD)	18.53 (18.83)	27.88 (30.58)
AUC _∞ (ng.h/mL), mean (SD)	21.70 (21.89)	32.10 (34.09)
C _{max} (ng/mL), mean (SD)	1.27 (0.54)	2.11 (0.73)
t _{max} (h), median (range)	1.00 (1.0–3.0)	2.00 (2.0–2.0)
λ _z (h), mean (SD)	0.12240 (0.15071)	0.09280 (0.11956)
t _{1/2} (h), mean (SD)	20.72 (21.00)	25.49 (25.05)
Statistical treatment comparisons	Soft Gelatin Capsule (n=5)	IV (n=5)
AUC _∞ (ng.h/mL)		
Geometric LS mean	19.98	11.87
Geometric LS mean F ratio	0.59	
90% CI	(0.47, 0.75)	
AUC ₂₄ (ng.h/mL)		
Geometric LS mean	11.99	7.43
Geometric LS mean F ratio	0.62	
90% CI	(0.46, 0.84)	
AUC _{last} (ng.h/mL)		
Geometric LS mean	17.37	10.12
Geometric LS mean F ratio	0.58	
90% CI	(0.45, 0.75)	
Safety Results:		
Most Frequent Adverse Events (AEs) Affecting >1 Subject/Group- On Treatment	Soft Gelatin Capsule	IV
N	6	6
Subjects with AEs, n (%)	1 (17)	2 (33)
Serious Adverse Events (SAEs) - On Treatment n (%) [considered by the investigator to be possibly related, related or probably related to study medication]		
	Soft Gelatin Capsule	IV

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Subjects with Non-fatal SAEs, n (%)	0	0
Subjects with Fatal SAEs, n (%)	0	0

Date Updated: 21-Dec-2004

Publications:

No Publications