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Study No: ARI10023		
Title: A double blind, randomized and placebo-controlled parallel group study to evaluate the safety and pharmacokinetics/pharmacodynamics of a single oral 0.5mg dose of dutasteride in healthy Korean male volunteers.		
Rationale: This study was designed to generate bridging data for dutasteride in Koreans. The clinical dose of dutasteride (0.5mg/day) is at the flat, upper and near maximal portion of the dose-response relationship for suppression of DHT. The data from other clinical studies of dutasteride (ARIA1001/1004/2001, 745-01) have shown that dutasteride is effective over the dose range from 0.5 to 40mg/day. Further to this, no significant ethnic differences have been observed in efficacy between individuals from different ethnic groups in the clinical studies conducted in foreign countries. Ethnic differences in pharmacokinetics have been reported for some drugs. For dutasteride major ethnic differences have not been observed and in consideration of its pharmacokinetic characteristics, none are to be expected. At the time of this study, information available indicated that the pharmacokinetics and pharmacodynamics of dutasteride were similar in Western and Japanese subjects. Nevertheless this study was conducted to examine the pharmacokinetics, pharmacodynamics and safety of a single dose of dutasteride in Koreans to support the registration of dutasteride in Korea. It was hoped that the results in healthy Koreans were broadly similar to those observed in Western subjects. It would then be anticipated that that the disposition and effects of dutasteride will be similar in Korean and Western patients. This study obtained basic clinical data for dutasteride in Korean people by characterizing the pharmacokinetics, pharmacodynamics and safety of a single 0.5mg dose in healthy male Korean subjects.		
Phase: Phase I		
Study Period: 2 Jan 2003 ~ 24 Feb 2003		
Study Design: A double blind, randomized, placebo-controlled parallel group single oral dose study.		
Centres: 1 center in Korea		
Indication: None		
Treatment: Study subjects were randomized to receive a single oral dose of dutasteride 0.5mg or placebo.		
Objectives: To evaluate the pharmacokinetics, pharmacodynamics and safety of dutasteride, after administration of single oral dose of 0.5mg to healthy male Korean subjects.		
Statistical Methods: PK parameters were summarised using descriptive statistics. Demographics of subjects prior to medication were compared using 'chi-square test' and 't-test' between a group of subjects who were given dutasteride and a control group who received a placebo. T-test was used to evaluate difference in value of blood glucose, ECG and vital signs at each required time point between groups. With time difference were calibrated, difference between groups were compared using ANOVA for repeated measurements. In order to evaluate the safety of the study drug, the rate of AE occurrence and 95% confidence interval were calculated. Severity of AE and relationship with study drug etc were evaluated. Laboratory test result and vital sign result evaluation were performed in order to evaluate safety		
Study Population: 40 healthy adult male subjects, 19~55 years of age less than 120kg and within 20% of ideal body weight completed the study. Subjects were excluded if there was a known hypersensitivity to any 5 α -reductase inhibitor or they had an active infection or a history of HIV infection. In addition, patients who were taking finasteride within 6 months preceding screening period of the study were excluded.		
Number of Subjects:	Dutasteride 0.5mg	Placebo
Planned N	30	10
Dosed N	30	10
Completed n (%)	30 (100)	10 (100)
Total Number Subjects Withdrawn N (%)	0	0
Withdrawn due to Adverse Events n (%)	0	0
Withdrawn due to Lack of Efficacy n (%)	0	0
Withdrawn for Other Reasons n (%)	0	0
Demographics	Group A	Group B

N (ITT)	30	10				
Females: Males	Male only	Male only				
Mean Age in Years (sd)	22.9 (2.7)	22.8 (1.8)				
Mean Weight in Kg (sd)	67.0(6.7)	69.5(7.4)				
Korean n (%)	30 (100)	10 (100)				
Pharmacokinetics (PK),pharmacodynamics (PD), PK/PD Endpoints: Safety parameters: Physical exam, Vital signs, ECG, Clinical laboratory tests and Aes Pharmacokinetic parameters: AUC _{last} , AUC _∞ , AUC _t , C _{max} , T _{max} and t _{1/2} Pharmacodynamic parameters: Maximum percent change in DHT concentration from pre-dose examination Amend heading as necessary eg remove PK or PD if not applicable to the study. Present outcome variable(s) with statistical annotation from synopsis/report. Format and presentation indication/study dependent. Use tables from report if available otherwise use text						
Dutasteride PK Parameters	Mean	SD	CV	Median	Min	Max
Tmax(hr)	1.72	0.89	51.66	2.00	0.50	4.00
Cmax(ng/mL)	2.57	0.95	37.02	2.43	1.04	5.36
AUClast(ng*hr/mL)	52.78	34.06	64.53	43.87	4.46	124.23
T1/2(Hr)	47.71	23.29	48.82	40.96	6.04	103.14
AUCinf(ng*hr/mL)	67.27	43.54	64.73	57.51	5.54	167.37
AUC_%Extrap(%)	21.42	6.96	32.48	22.23	9.43	39.04
Vz/F(L)	604.63	203.26	33.62	568.12	278.07	985.30
CL/F(L/hr)	13.99	17.48	124.98	8.69	2.99	90.24
MRTinf(hr)	64.85	33.22	51.23	58.46	7.38	142.19
Dutasteride PD Parameters	Maximal % change of DHT from baseline					
Mean	49.5					
Std	13.9					
Median	46.4					
Min	26.8					
Max	76.8					
Safety results:						
	Dutasteride (%)		Placebo (%)			
N (ITT)	30		10			
No. subjects with AEs n (%)	9 (30.0)		2 (20.0)			
Diarrhea	3 (10.0)		0			
Right arm rash	2 (6.7)		0			
Serious Adverse Events, 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		0			

Publications:
Abstract: Effect of srd5a2 genotype on pharmacodynamics of 5-alpha-reductase inhibitor analyzed by pk-pd modeling. Chung, J. MD, Cho, J. PhD, Lim, H. MD, Oh, D. OMD, Yi, S. MS, Jang, I. MD PhD, and Shin, S. MD PhD 105th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics 3/24/2004 Miami Beach, FL; USA

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