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<b>Study No:</b> S3B10942		
<b>Title:</b> An open-label study of the pharmacokinetics of a single 1mg oral dose of alosetron in healthy Korean subjects.		
<b>Rationale:</b> Alosetron was developed for the treatment of irritable bowel syndrome (IBS). At the time of this study, clinical investigations had established the pharmacokinetics, safety and tolerability profile of alosetron in both healthy and patient caucasian subjects. This study was undertaken to provide data on the disposition of alosetron in Korean subjects.		
<b>Phase:</b> I.		
<b>Study Period:</b> 06 December 1999 to 21 December 1999.		
<b>Study Design:</b> Open-label, single-dose study in healthy Korean subjects.		
<b>Centres:</b> One centre in Australia.		
<b>Indication:</b> None.		
<b>Treatment:</b> Subjects received a single oral dose of alosetron 1 mg.		
<b>Objectives:</b> To evaluate the single dose pharmacokinetics of alosetron 1 mg in healthy Korean subjects.		
<b>Statistical Methods:</b> Area under the plasma concentration-time curve from time zero to infinity ( $AUC_{\infty}$ ), area under the plasma concentration-time curve from time zero to the last observation ( $AUC_{last}$ ), maximum plasma concentration ( $C_{max}$ ), terminal half-life ( $t_{1/2}$ ), terminal elimination rate constant ( $\lambda_z$ ), clearance uncorrected for bioavailability ( $CL/F$ ), and volume of distribution uncorrected for bioavailability ( $V/F$ ), with the exception of time to $C_{max}$ ( $t_{max}$ ), were log-transformed. Descriptive statistics, geometric mean estimates and 95% confidence intervals (CIs) were calculated for each gender. An analysis of variance (ANOVA) model was performed to evaluate the least squares estimates for each gender. The 95% CI for $t_{max}$ was estimated using a one-sample approach.		
<b>Study Population:</b> Healthy, non-smoking male and female subjects descended from four Korean grandparents, aged 18 – 50 years. Subjects were excluded if they were receiving or exposed to known or potential inducing/inhibiting agents of cytochrome P450 enzymes. Subjects were asked to eat a 'normal' Korean diet during the week before the study.		
<b>Number of Subjects:</b> Twenty-four subjects (12 male/12 female) were planned for this study. One subject withdrew consent after dosing, giving an incomplete pharmacokinetic profile. This subject was replaced. All 25 subjects who received alosetron were included in the safety population but only 24 subjects with complete pharmacokinetic profiling were included in the pharmacokinetic population.		
Planned N	24	
Dosed N	25	
Completed n (%)	24 (96)	
Total Number Subjects Withdrawn N (%)	1 (4)	
Withdrawn due to Adverse Events n (%)	0	
Withdrawn due to Lack of Efficacy n (%)	0	
Withdrawn for Other Reasons n (%)	1 (4)	
<b>Demographics</b>		
N (ITT)	25	
Females: Males	12 : 13	
Median Age in Years (range)	22.0 (18 – 45)	
Mean Weight in Kg (SD)	63.45 (10.37)	
Korean n (%)	25 (100)	
<b>Pharmacokinetics Endpoints:</b> Derived pharmacokinetic parameters are summarised in the following table.		
Parameter	Females (n=12)	Males (n=12)
$AUC_{\infty}$ (ng.h/mL) Geometric Mean (95% CI)	33.83 (24.95, 45.88)	16.92 (11.57, 24.76)
$C_{max}$ (ng/mL) Geometric Mean (95% CI)	11.81 (9.50, 14.96)	5.93 (4.20, 8.37)
$t_{max}$ (h) Estimated Median (95% CI)	1.02 (0.77, 1.26)	1.00 (0.99, 1.02)
$t_{1/2}$ (h) Geometric Mean (95% CI)	1.93 (1.57, 2.38)	1.88 (1.64, 2.16)
A retrospective ethnic comparison was carried out using data from a previous study with 29 Caucasian subjects (Study no. S3BB1011) . .		
<b>Comparison of serum alosetron pharmacokinetic comparators between Koreans (K) and Caucasians (C)</b>		

Parameter	K vs C	Ratio	90% CI
AUC <sub>∞</sub> (ng.h/mL)	Females	1.50	(1.11, 2.25)
	Males	1.84	(1.28, 2.62)
C <sub>max</sub> (ng/mL)	Females	1.59	(1.17, 2.18)
	Males	1.85	(1.35, 2.55)
t <sub>1/2</sub> (h)	Females	1.37	(1.16, 1.61)
	Males	1.37	(1.16, 1.61)
<b>Safety results:</b>			
<b>Adverse Events:</b>			
N (ITT)			25
No. subjects with AEs n (%)			11 (44)
Most Frequent AEs			
Headaches			7 (28)
Dizziness			2 (8)
Abdominal distension			2 (8)
<b>Serious Adverse Events n (%)</b>			
No. subjects with SAEs n (%)			0

<b>Publications:</b> No Publication
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