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<b>Study No.:</b> S3B10903	
<b>Title:</b> An Open-Label, Non-Randomized, Single-Dose Study of the Pharmacokinetics of Alosetron 1mg in Children 6-11 Years of Age With Non-Constipated Irritable Bowel Syndrome	
<b>Rationale:</b> Based on the prevalence of IBS in children and adolescents, it was anticipated that Alosetron might be used in the pediatric population, and might provide a meaningful therapeutic benefit for this group. Data on the use of Alosetron in a pediatric population had to be obtained in order to support safe pediatric use of Alosetron. This study was conducted in order to provide pharmacokinetic data on Alosetron in children 6 to 11 years of age. This study also examined the safety and tolerability of Alosetron in children.	
<b>Phase:</b> I	
<b>Study Period:</b> 17 Mar 2000 to 24 May 2000	
<b>Study Design:</b> A single-dose, open-label, non-randomized study. The duration of the study was up to approximately 4 weeks per subject.	
<b>Centres:</b> This study was conducted at 3 centers in the United States (US)	
<b>Indication:</b> Non-Constipated Irritable Bowel Syndrome (IBS)	
<b>Treatment:</b> Following a screening Visit ( $\leq 14$ days prior to dosing), subjects received a single dose of an oral solution containing 1mg alosetron (GR68755C)/5mL.	
<b>Objectives:</b> The primary objective of this study was to determine the systemic exposure of a 1mg dose of alosetron administered to pediatric subjects aged 6 to 11 years.	
<b>Statistical Methods:</b> Twenty-four subjects were planned to be enrolled in the study (12 females, and 12 males). Since this was an observational study, 24 subjects would have provided an adequate assessment of the pharmacokinetics (PK) of alosetron in children. However, due to the small sample size (n=5), no formal statistical analyses were performed to compare the age and gender groups.	
<b>Pharmacokinetic Analysis:</b> Serum alosetron concentrations at each time point, and PK parameters (area under the plasma concentration-time curve from time 0 to infinity [AUC $\infty$ ], maximum observed plasma concentration [C $_{max}$ ], time of observed maximum concentration [T $_{max}$ ], and drug half-life [t $_{1/2}$ ]) were summarized using descriptive statistics. For the geometric mean of each PK parameter, 95% confidence intervals (CI) were constructed. Data are presented for all subjects and by gender/age group (6 to 7 year old girls and 8 to 9 year old boys). In May, 2000, Glaxo Wellcome (GW) decided to put the study on hold. This decision was made as a consequence of issues concerning the instability of the alosetron oral solution. Investigators were advised on 26 May 2000 not to enroll new subjects until further notice from GW. This study was terminated prior to achieving the planned enrollment of 24 patients. The early termination of the trial occurred as the result of a decision by GW on 28 November 2000, to discontinue the Alosetron clinical development program. Following this decision, GW immediately initiated an orderly cessation of all ongoing trials.	
<b>Study Population:</b> Male and female subjects aged 6 to 11 years with non-constipated IBS as defined by the Rome criteria for IBS. Females were to be pre-menarchal.	
<b>Number of Subjects:</b>	<b>Alosetron 1mg</b>
Planned, N	24
Dosed, N	5
Completed, n (%)	5 (100)
Total Number Subjects Withdrawn, N (%)	0
Withdrawn Due to AEs, n (%)	0
Withdrawn Due to Lack of Efficacy, n (%)	0
Withdrawn for Other Reasons, n (%)	0
<b>Demographics:</b>	<b>Alosetron 1mg</b>
N (Safety)	5
Females:Males	2:3
Mean Age in Years (SD)	7.8 (0.8)
Mean Weight in kg (SD)	27.00 (7.55)
Caucasian, n (%)	3 (60)

<b>Alosetron PK Parameters Following a Single 1mg Oral Dose</b>
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PK Parameter	Age 6-7 (N=2 females) Geo. Mean (95% CI)	Age 8-9 (N=3 males) Geo. Mean (95% CI)	Total (N=5) Geo. Mean (95% CI)
AUC <sub>∞</sub> (ng•h/mL)	34.94 0.33, 3676.11	20.12 2.98, 136.09	25.09 10.86, 57.95
C <sub>max</sub> (ng/mL)	16.79 0.10, 2810.23	10.08 1.69, 60.23	12.36 5.54, 27.60
T <sub>max</sub> (h) <sup>a</sup>	0.99 0.98-1.00	1.03 1.00-1.17	1.00 0.98-1.17
t <sub>1/2</sub>	0.80 0.04, 14.71	0.97 0.87, 1.08	0.90 0.71, 1.14
Median (Min-Max)			
<b>Safety results:</b> Adverse events were monitored and recorded from screening through to telephone follow-up.			
<b>Adverse Events:</b>		<b>Alosetron 1mg</b>	
N (Safety)		5	
Subjects With AEs, n (%)		2 (40)	
<b>Serious Adverse Events (SAEs), n (%) [# considered by the investigator to be related, possibly related, or probably related to study medication]:</b>			
Subjects With SAEs, n (%)		0	
<b>Conclusion:</b> See publication below.			
<b>Publications:</b>  Symptom Severity in Women with Diarrhea-Predominant IBS (D-IBS) VZ Ameen, SH Gordon, AT Heath and EG Carter  Response to Conventional Therapy in Women with Moderate to Severe Diarrhea-Predominant IBS (D-IBS) VZ Ameen, SH Gordon, AT Heath, EG Carter			

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