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Study No: S3BH02				
Title: A randomised, double-blind, placebo-controlled, cross-over study to investigate the effect of alosetron (GR68755C) on basal jejunal water and electrolyte transport in healthy male subjects.				
Rationale: Reduction of intestinal secretion may have a role in reducing the severity of diarrhoea and thus the need for oral or intravenous fluid replacement therapy as a consequence of infectious diarrhoeas. This study was performed to evaluate the effects of alosetron (GR68755C) on water and electrolyte secretion in the human jejunum in healthy subjects.				
Phase: I				
Study Period: January 1993 – May 1993.				
Study Design: A single-centre, randomised, double-blind, placebo-controlled, two-way crossover study.				
Centres: One centre in the UK.				
Indication: None.				
Treatment: Subjects received single dose oral alosetron 4 mg or placebo in two separate study sessions. There was a 7 to 28-day washout period between the two treatments.				
Objectives: To examine the effects of alosetron on basal water and electrolyte transport in the jejunum of healthy subjects.				
Statistical Methods: Statistical analysis of water and electrolyte transport was performed using parametric methods, where the analysis included a test for carry-over effect. In the absence of carry-over effect in the parametric analysis all subjects' data were included in the analysis, with the factors subject, period and treatment in the model. Estimate of the adjusted treatment effect and a 95% confidence interval were determined. Where the carry-over effect existed and was significantly different between treatment groups then the data were presented graphically, and data from the first treatment period were analysed. All subjects who received at least one dose of study medication were included in the safety population. The pharmacodynamic (PD) population included all subjects who had had at least one post-treatment PD assessment.				
Study Population: Healthy male subjects, aged 18 – 35 years.				
Number of Subjects:				
Planned N		10		
Dosed N		10		
Completed n (%)		9 (90)		
Total Number Subjects Withdrawn N (%)		1 (10)		
Withdrawn due to Adverse Events n (%)		0		
Withdrawn due to Lack of Efficacy n (%)		0		
Withdrawn for Other Reasons n (%)		1 (10)		
Demographics				
N (ITT)		10		
Males		10		
Mean Age in Years (SD)		24.8 (5.2)		
Mean Weight in kg (SD)		73.2 (7.2)		
White n (%)		10 (100)		
Pharmacodynamic Endpoints: The primary comparison was the effect of alosetron and placebo on water transport across the mucosa of the jejunum. Transport of sodium, potassium, chloride and bicarbonate was also estimated.				
Water Transport (mL/cm/h)				
Treatment sequence	Alosetron Mean (SD) n=3	Placebo Mean (SD) n=4	Treatment difference n=3	Overall Treatment difference (95% CI) 1.900 (-0.367, 4.167)
P/A	4.920 (3.265) n=5	3.620 (0.963) n=5	1.300 (2.989) n=5	
Sodium Transport (mmol/cm/h)				
Treatment sequence	Alosetron Mean (SD)	Placebo Mean (SD)	Treatment difference	Overall Treatment difference ¹ (95% CI)

A/P	0.187 (0.205) n=3	0.580 (0.109) n=4	0.270 (0.191) n=3	0.357 (0.081, 0.633)
P/A	0.536 (0.172) n=5	0.460 (0.121) n=5	0.076 (0.209) n=5	

1. analysis using Period 1 values only due to statistically significant carry-over effect, p = 0.072

Potassium Transport (mmol/cm/h)

Treatment sequence	Alosetron Mean (SD)	Placebo Mean (SD)	Treatment difference	Overall Treatment difference (95% CI)
A/P	0.028 (0.004) n=3	0.018 (0.011) n=4	0.015 (0.001) n=3	0.017 (-0.017, 0.050)
P/A	0.034 (0.052) n=5	0.016 (0.013) n=5	0.018 (0.046) n=5	

Chloride Transport (mmol/cm/h)

Treatment sequence	Alosetron Mean (SD)	Placebo Mean (SD)	Treatment difference	Overall Treatment difference ² (95% CI)
A/P	2.533 (3.696) n=3	0.175 (0.096) n=4	2.367 (3.581) n=3	0.200 (-0.100, 0.500)
P/A	0.240 (0.270) n=5	0.220 (0.268) n=5	0.020 (0.370) n=5	

2. non-parametric analysis, treatment effect is the median difference

Bicarbonate Transport (mmol/cm/h)

Treatment sequence	Alosetron Mean (SD)	Placebo Mean (SD)	Treatment difference	Overall Treatment difference ² (95% CI)
A/P	0.440 (0.080) n=3	0.323 (0.043) n=4	0.123 (0.107) n=3	0.010 (-0.100, 0.110)
P/A	0.282 (0.094) n=5	0.344 (0.079) n=5	-0.062 (0.096) n=5	

2. non-parametric analysis, treatment effect is the median difference

Safety results: Adverse events were monitored throughout the study.

Adverse Events:	Alosetron	Placebo
N (ITT)	10	10
No. subjects with AEs n (%)	2 (20)	1 (10)
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:

No Publication

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