Janssen-Ortho Inc., Canada
MEDICAL AFFAIRS

SYNOPSIS

Name of Sponsor/Company:	Janssen Ortho Inc.	Individual Study Table Referring to Part of the Dossier **n/a**	(for National Authority Use only)
Name of Finished Product:	[Pr]Pariet*	Volume: n/a	
Name of Active Ingredient:	Rabeprazole sodium	Page: n/a	
Title of Study:		A randomized, controlled, parallel-group, open-label study to evaluate different dosing regimens of rabeprazole in controlling nocturnal heartburn symptoms in patients with gastroesophageal reflux disease	
Investigators:		Coordinating Investigator: Dr. David G. Morgan (Hamilton, ON). Principal Investigators: Dr. Ford Bursey (St. John's, NL), Dr. Lawrence Cohen (Toronto, ON), Dr. Howard Conter (Halifax, NS), Dr. Robert Davies (Oshawa, ON), Dr. Carlo Fallone (Montreal, QC), Dr. Dana Farina (Halifax, NS), Dr. Subhas Ganguli (Hamilton, ON), Dr. James Gray (Vancouver, BC), Dr. Gilles Jobin (Montreal, QC), Dr. Allan Kelly (Edmonton, AB), Dr. Jacques Lenis (Longueuil, QC), Dr. Michael O'Mahony (Sarnia, ON), Dr. Henryk Pluta (Abbotsford, BC), Dr. Terry Ponich (London, ON), Dr. Brian Ramjattan (St. John's, NL), Dr. Jean Roy (Les Saules, QC), Dr. Thomas Sylwestrowicz (Saskatoon, SK), Dr. Alan Weiss (Vancouver, BC).	
Study centre(s):			
Publication (reference)		TBD	
Studied period (years):		Phase of development:	Phase IIIb
	(date of first enrolment)		30 July 04
	(date of last completed)		20 September 05
Objectives:		The primary objective of this study is to assess the efficacy of rabeprazole 20mg once daily in the evening, 10mg twice daily and 20mg once daily in the morning, in controlling nocturnal heartburn symptoms in patients with gastroesophageal reflux disease (GERD).	
Methodology:		**STUDY DESIGN:** This is a multicentre, randomised, controlled, parallel-group, open-label study in GERD patients. Subjects will be screened and enter a 2-week run-in phase to document heartburn symptoms while on their current therapy, during which they will complete a daily diary of symptoms and antacid use. Subjects who have troublesome nocturnal heartburn episodes, but adequate daytime heartburn symptom control (as defined) will enter an 8-week treatment phase where they are randomised to one of the rabeprazole regimens: 20mg once daily in the evening ("QPM"), 10mg twice daily ("BID")or 20mg once daily in the morning ("QAM"), plus antacids as required. Subjects will continue to complete a daily diary, including heartburn symptoms, compliance with study regimen and antacid use. Health-related quality of life (HRQoL) and productivity assessments will be administered at the start and at specified timepoints throughout the treatment period. Subjects will return for study visits at 4 and 8 weeks after initiation of study treatment regimen for review of diaries, completion of HRQoL and productivity instruments, review of concomitant medications and adverse events, and collection and dispensing of medication.	
		STUDY POPULATION: Subjects with a history of symptomatic GERD who have adequate control of daytime heartburn symptoms, but have troublesome nocturnal heartburn symptoms (see definitions) despite current acid suppression therapy. Determination of eligibility for the treatment phase of the trial will be done at the end of the 2-week run-in phase and will be based on a "heartburn score" derived from the incidence and severity of heartburn episodes. At the end of the run-in phase, subjects who meet heartburn symptom criteria will enter the treatment phase and continue on either rabeprazole 20mg once daily in the evening, 10mg twice daily or 20mg once daily in the morning; all doses taken ½-hour before meals. Adequate daytime heartburn control is defined as ≤3 daytime episodes during 7 consecutive days of the run-in period, only one of which can be rated as severe or very severe (score of ≥3 on the 5-point Likert scale) and a maximum total daytime heartburn score during the 7-day period = 5. "Troublesome" nocturnal heartburn symptoms will be defined as a nocturnal heartburn score of ≥4 during the 2-week run-in period.	

Number of patients (planned and analyzed):	Planned: 190 enrolled, 115 randomised	Actual: 128 enrolled, 48 randomised.
Diagnosis and main criteria for inclusion:	**STUDY POPULATION:** Subjects with a history of symptomatic GERD who have adequate control of daytime heartburn symptoms, but have troublesome nocturnal heartburn symptoms (see definitions) despite current acid suppression therapy. Determination of eligibility for the treatment phase of the trial will be done at the end of the 2-week run-in phase and will be based on a "heartburn score" derived from the incidence and severity of heartburn episodes. At the end of the run-in phase, subjects who meet heartburn symptom criteria will enter the treatment phase and continue on either rabeprazole 20mg once daily in the evening, 10mg twice daily or 20mg once daily in the morning; all doses taken ½-hour before meals. Adequate daytime heartburn control is defined as ≤3 daytime episodes during 7 consecutive days of the run-in period, only one of which can be rated as severe or very severe (score of ≥3 on the 5-point Likert scale) and a maximum total daytime heartburn score during the 7-day period = 5. "Troublesome" nocturnal heartburn symptoms will be defined as a nocturnal heartburn score of ≥4 during the 2-week run-in period Main Inclusion Criteria: Subjects must have had a minimum three-month history of symptomatic GERD, with heartburn as the predominant symptom, and must report nocturnal heartburn symptoms (i.e., heartburn symptoms experienced during the night-time period, between 2200 and 0600h).Subjects must currently be taking a proton-pump inhibitor (PPI) or histamine-2 receptor antagonist (H2RA) at least four weeks prior to study admission. Randomisation Criteria—Maintenance Phase Subjects must have had satisfactory heartburn symptom control during the last week of the acute phase (determined by diary ratings: 0 days of severe heartburn, ≤ 1 day of moderate heartburn, and ≤ 3 days of mild heartburn in the 7 days prior to randomization) plus heartburn indicated 'satisfactorily controlled' or 'completely controlled' on the Heartburn Control Assessment completed on the last day of the acute-phase. Subjects must also have been 80% compliant (medication and diary completion) during the acute phase, and did not exceed maximum allowable antacid usage (defined as more than an average of 2 antacid tablets per day, or ≥ 5 antacid tablets for ≥ 4 consecutive days during the acute phase).	
Test product, dose and mode of administration, batch number:	Rabeprazole sodium: 10mg Lot numbers: 03LS01G (exp: Nov-05), 04AS55H (exp: Dec-05), 20mg Lot numbers: 03LS27G (exp: Nov-05) Maalox® Extra Strength: 1000mg Lot number: 323783 (exp: Nov-05)	
Duration of treatment:	Total duration (run-in+ maintenance phases): 10 weeks Run-in phase: Current acid suppressive therapy (H2 receptor antagonists or PPI) for 2 weeks. Maintenance phase: Patients will be randomized either Rabeprazole 20mg QAM, Rabeprazole 20mg QPM or Rabeprazole 10mg BID for two 4-week treatment periods (total 8 weeks).	
Reference therapy, dose and mode of administration, batch number	Not applicable	
Criteria for evaluation:		
Efficacy:	Efficacy variables: The following will be evaluated for each regimen: Nocturnal heartburn score, satisfaction with heartburn control (weekly satisfaction question from diary), Physician and Subject Overall Treatment Evaluations, HRQoL and productivity measures, rescue medication usage, subject compliance with study medication regimen, daytime heartburn score.	
Safety:	• Analysis of vital sign data (changes from baseline) • Adverse Events (AEs)	

Statistical Methods:	Efficacy variables: Primary: The primary analysis was based on the mean nocturnal heartburn score observed after four weeks of drug administration for each of the three dosing regimens of rabeprazole. For each subject, the total nocturnal heartburn score was calculated as the sum of the nocturnal heartburn scores for the last 14 days of treatment in the period from Day 0 to Visit 3. The comparison of the treatments was done using an ANOVA model with the total nocturnal heartburn score (based on those last 14 days of treatment) as response and treatment group as main factor. If there were differences, then treatment differences were explored using adjustment for multiple comparisons. Secondary: ➢ Satisfaction with heartburn control (between regimens). A contingency table analysis was used to determine association between satisfaction and treatment group. ➢ Mean nocturnal heartburn score for each regimen at the end of treatment / 8 weeks of drug administration. This response was analyzed similar to the primary response. ➢ Mean incidence of nocturnal heartburn episodes for each regimen at 4- and 8-weeks. This response was analyzed similar to the primary response where the response will be the proportion of days with heartburn during the last 14 days of the four-week period. ➢ Median HRQoL (PAGI-SYM, PAGI-QOL) and productivity (WPAI-GH) scores at 4- and 8-weeks for each regimen. Between treatments differences of the change from baseline was be analyzed using the Kruskal-Wallis test. Within treatment differences of the differences from baseline was analyzed using the Wilcoxon's signed rank test. ➢ The Physician and Subject Overall Treatment Evaluation ratings at the end of treatment for each regimen. A contingency table analysis was used to determine association between rating and treatment group. ➢ Mean antacid (rescue medication) usage for each of the regimens. Main summary statistics was tabulated for the use of antacid medication, both for the run-in period and the treatment phase. ➢ Compliance with each regimen. Compliance with medications was based on whether the subject reported taking at least 80% of scheduled doses as prescribed. Treatment compliance will be compared using an ANOVA model. ➢ Mean daytime heartburn score, and mean incidences of daytime heartburn episodes at 4- and 8-weeks were calculated for each regimen. These variables were analyzed similar to the nocturnal variables. Safety: • Descriptive statistics and appropriate tests were used to summarize and analyze the Adverse Events (AEs) and the Vital Signs. AEs were summarized for each treatment regimen classified by body system class and WHO Dictionary preferred terminology. Mean, median, standard deviation, range, and change from baseline were calculated for vital sign data, by treatment regimen.

PRIMARY (evaluable population): NTHB SCORE	QAM (N=15)	QPM (N=15)	BID (N=12)	*p*-value
Tbl TAB1. Mean nocturnal (NT) HB score after 4 weeks of study drug administration for each of the dosing regimens (i.e.: Mean total NT score for 14 days prior to Visit 3)	6.7	7.3	12.8	0.2330
SECONDARY ENDPOINTS (ITT): NTHB SCORE	**N=16**	**N=16**	**N=13**	
Tbl TAB1. Mean total NT score for 14 days prior to randomization visit (= baseline)	17.2	16.8	18.8	0.8845
Tbl TAB1. Mean total NT score for 14 days prior to Visit 3	8.1	6.9	12.0	0.4008
Tbl TAB1. Mean total NT score for 14 days prior to Final visit /Visit 4	6.0	4.6	12.0	0.1951
****Tbl TAB1a.*** Mean CHANGE in total NT score at baseline (period =14 days prior to randomization visit) compared to Visit 3 (week 4; period = 14 days prior to Visit 3) *i.e.: W0 – Wk 4*	-9.6 (p=0.0001)	-10.0 (p<0.0001)	-4.6 (p=0.2141)	0.2331 *Significance also tested within each regimen*
****Tbl TAB1a.*** Mean CHANGE in total NT score at baseline (period =14 days prior to randomization visit) compared to Final Visit (or week 8; period = 14 days prior to FV) *i.e.: W0 – Wk 8*	-11.2 (p=0.0003)	-11.1 (p<0.0001)	-4.6 (p=0.0064)	0.0351 *Significance tested within each regimen*
****Tbl TAB1a.*** Mean CHANGE in total NT score at Visit 3 (week 4; period = 14 days prior to Visit 3) compared to Final Visit (or week 8; period = 14 days prior to FV) *i.e.: W4 – Wk 8*	-2.5 (p=0.2952)	-1.8 (p=0.0328)	-3.7 (p=0.0342)	0.7548 *Significance tested within each regimen*
HB CONTROL & SATISFACTION	**N=15**	**N=16**	**N=15**	
Tbl TAB4,5a. Heartburn control "satisfactorily" or "completely" during last week of treatment: Visit 3	80.0%	100.0%	73.3%	P = 0.0972
	N=16	**N=14**	**N=13**	
Tbl TAB4,5a. Heartburn control "satisfactorily" or "completely" during last week of treatment: Final visit /Visit 4	87.5	92.9%	84.6%	P = 0.7928
	N=15	**N=16**	**N=15**	
****Tbl TAB5,5a.*** Satisfaction with heartburn control ("satisfied" or "very satisfied") during last week of treatment: Visit 3 (4weeks)	66.7	93.8%	60.0%	P =0.0750
	N=16	**N=14**	**N=13**	
****Tbl TAB5,5a.*** Satisfaction with heartburn control ("satisfied" or "very satisfied") during last week of treatment: Final visit /Visit 4 (8 weeks)	81.3	92.9%	69.2%	P =0.2886
COMPLIANCE	**N=16**	**N=16**	**N=13**	
****Tbl TAB 7.*** Study medication compliance:				
-Overall (Taking Medication) 4 weeks	100%	99.1%	99.5%	P=0.3775
-Regimen with respect to timing (meals as well as time of day) 4 weeks	97.8%	99.1%	96.2%	P=0.3857
	N=14	**N=17**	**N=13**	
-Overall (Taking Medication) 8 weeks	100%	99.5%	98.4%	P=0.4192
-Regimen with respect to timing (meals as well as time of day) 8 weeks	99.2%	99.5%	94.5%	P=0.2005
NT ANTACID USAGE	**N=15**	**N=16**	**N=14**	
Tbl TAB6. Mean (daily) NT antacid usage during 14 days prior to visit: randomization visit (= baseline)	0.8	0.5	0.6	0.5738
	N=14	**N=15**	**N=13**	
Tbl TAB6. Mean (daily) NT antacid usage during 14 days prior to visit: Visit 3	0.4	0.2	0.4	0.5012
	N=15	**N=12**	**N=13**	
Tbl TAB6. Mean (daily) NT antacid usage during 14 days prior to visit: Final Visit / Visit 4	0.3	0.1	0.4	0.3951
	N=14	**N=15**	**N=12**	
****Tbl TAB6a.*** Mean CHANGE in mean (daily) NT antacid usage at baseline (period =14 days prior to randomization visit) compared to Visit 3 (week 4; period = 14 days prior to Visit 3) *i.e.: W0 – Wk 4*	-0.40 (p=0.0017)	-0.38 (p=0.0157)	0.01 (p=0.9645)	0.0844 *Significance tested within each regimen*
	N=15	**N=12**	**N=12**	
****Tbl TAB6a.*** Mean CHANGE in mean (daily) NT antacid usage at baseline (period =14 days prior to randomization visit) compared to Final Visit (or week 8; period = 14 days prior to FV) *i.e.: W0 – Wk 8*	-0.47 (p=0.0239)	-0.36 (p=0.0513)	-0.07 (p=0.5056)	0.1962 *Significance tested within each regimen*
	N=14	**N=12**	**N=12**	
****Tbl TAB6a.*** CHANGE in mean (daily) NT antacid usage at Visit 3 (week 4; period = 14 days prior to Visit 3) compared to Final Visit (or week 8; period = 14 days prior to FV) *i.e.: Wk4 – Wk 8*	-0.15 (p=0.2523)	-0.02 (p=0.4382)	0.08 (p=0.3388)	0.2207 *Significance tested within each regimen*

INCIDENCE OF NTHB EPISODES	QAM N=17	QPM N=16	BID N=15	*p*-value
Mean INCIDENCE of nocturnal heartburn episodes (proportion of days with heartburn during the last 14 days of the four-week period: baseline	9.3	8.4	7.8	*0.5496*
	N=16	N=16	N=13	
Mean INCIDENCE of nocturnal heartburn episodes (proportion of days with heartburn during the last 14 days of the four-week period: Visit 3	4.7	4.5	6.9	*0.3842*
	N=17	N=14	N=14	
Mean INCIDENCE of nocturnal heartburn episodes (proportion of days with heartburn during the last 14 days of the Eight-week period: Visit 4	4.4	2.9	5.1	*0.4878*
PAGI-SYM	**N=16**	**N=16**	**N=13**	
Tbl TAB EF9a Mean PAGI-SYM Total Score baseline	1.03	0.95	1.64	*0.0336*
Tbl TAB EF9a Mean PAGI-SYM Total Score 4-weeks	0.91	0.41	1.10	*0.0849*
Tbl TAB EF9c Mean PAGI-SYM Total Score 8-weeks	0.89	0.17	1.16	*0.0020*
Tbl TAB EF9a Mean subscore Heartburn and regurgitation subscales of the PAGI-SYM baseline	1.55	1.46	1.90	*0.4183*
Tbl TAB EF9a Mean subscore Heartburn and regurgitation subscales of the PAGI-SYM 4-weeks	1.02	0.51	1.35	*0.0413*
Tbl TAB EF9c Mean subscore for Heartburn and regurgitation subscale of the PAGI-SYM 8-weeks	0.87	0.34	1.44	*0.0195*
Tbl TAB EF9b Mean Change from baseline for PAGI-SYM Score 4-weeks	-0.12 (P=0.4332)	-0.53 (p=0.0001)	-0.55 (p=0.0942)	*0.6652*
Tbl TAB EF9d Mean Change from baseline for PAGI-SYM Score 8-weeks	-0.11 (p=0.4874)	-0.78 (p=0.0001)	-0.65 (p=0.0353)	*0.2438*
Tbl TAB EF9b Mean Change from baseline for Heartburn and regurgitation subscale of the PAGI-SYM 4-weeks	-0.54 (p=0.0612)	-0.96 (p=0.0002)	-0.55 (p=0.0840)	*0.3750*
Tbl TAB EF9d Mean Change from baseline for Heartburn and regurgitation subscale of the PAGI-SYM 8-weeks	-0.62 (p=0.0433)	-1.13 (p=0.0002)	-0.59 (p=0.1000)	*0.3039*
PAGI-QOL	**N=16**	**N=16**	**N=13**	
Tbl TAB EF10a Mean PAGI-QOL Total Score baseline	1.35	0.60	1.27	*0.0160*
Tbl TAB EF10a Mean PAGI-QOL Total Score 4-weeks	0.87	0.22	0.82	*0.0025*
Tbl TAB EF10c Mean PAGI-QOL Total Score 8-weeks	0.77	0.14	0.90	*0.0017*
Tbl TAB EF10a Mean subscore for daily activity subscale of the PAGI-QOL 4-weeks	0.73	0.16	0.75	*0.0396*
Tbl TAB EF10c Mean total score for the daily activity subscale of the PAGI-QOL 8-weeks	0.62	0.13	0.97	*0.0039*
Tbl TAB EF10b Mean Change from baseline PAGI-QOL Score 4-weeks	-0.48 (p=0.0214)	-0.38 (p=0.0005)	-0.45 (p=0.0171)	*0.7498*
Tbl TAB EF10d Mean Change from baseline PAGI-QOL Score 8-weeks	-0.54 (p=0.0079)	-0.46 (p=0.0007)	-0.56 (p=0.0479)	*0.8008*
Tbl TAB EF10b Mean Change from baseline for daily activity subscale of the PAGI-QOL 4-weeks	-0.40 (p=0.1055)	-0.31 (p=0.0010)	-0.32 (p=0.0127)	*0.9394*
Tbl TAB EF10d Mean Change from baseline for daily activity subscale of the PAGI-QOL 8-weeks	-0.45 (p=0.0920)	-0.34 (p=0.0010)	-0.32 (p=0.3180)	*0.6492*
WPAI-GH (% Activity Impairment Due to Health)	**N=16**	**N=16**	**N=13**	
Tbl TAB EF11a Mean WPAI-GH Total Score baseline	28.13	13.75	31.54	*0.0455*
Tbl TAB EF11a Mean WPAI-GH Total Score 4-weeks	23.75	5.00	24.62	*0.0319*
Tbl TAB 10a Mean Change from baseline WPAI-GH Score 4-weeks	-4.38 (p=0.7910)	-8.75 (p=0.0625)	-6.92 (p=0.5078)	*0.4970*
	N=17	**N=16**	**N=14**	
Tbl TAB EF11c Mean WPAI-GH Total Score 8-weeks	18.82	5.00	23.57	*0.0449*
Tbl TAB 10b Mean Change from baseline WPAI-GH Score 8-weeks	-7.65 (p=0.4775)	-8.75 (p=0.0938	-6.43 (p=0.4976)	*0.5560*
OVERALL TREATMENT EVALUATIONS N=48	**QAM N=17**	**QPM N=16**	**BID N=15**	
Tbl TAB EF12 Physician Global Impression of Change Scales scores at the end of treatment: Good or very good at 8-weeks	88.2%	93.8%	46.7%	*0.0031*
Tbl TAB EF12 Physician Global Impression of Change Scales scores at the end of treatment: No Change, Poor or Very Poor at 8-weeks	11.8%	6.3%	53.3%	
Tbl TAB EF13 Subject asked to rate the overall effect of the Pariet study medication regimen on NTHB control during the 8-week treatment period: Very good and good	88.2%	93.8%	46.7%	*0.0031*
Tbl TAB EF13 Subject asked to rate the overall effect of the Pariet study medication regimen on NTHB control during the 8-week treatment period: No Change, Poor or Very Poor	11.8%	6.3%	53.3%	

OVERALL TREATMENT EVALUATIONS Cont'd:	QAM N=17	QPM N=16	BID N=15	*p*-value
Tbl TAB EF14 Subject asked to rate overall satisfaction with Pariet study medication regimen during the 8-week treatment period: Very satisfied or satisfied	82.4%	93.8%	46.7%	*0.0070*
Tbl TAB EF14 Subject asked to rate overall satisfaction with their NTHB control during the 8-week period: Very Satisfied or Satisfied	76.5%	93.8%	46.7%	*0.0119*
DAYTIME HB SCORE	**N=16**	**N=16**	**N=15**	
Tbl TAB EF2B. Mean total DT score for 14 days prior to randomization visit (= baseline)	2.6	3.0	3.0	P=0.8332
	N=16	**N=16**	**N=13**	
Tbl TAB EF2B. Mean total DT score for 14 days prior to Visit 3	3.4	2.4	4.9	P=0.4485
	N=17	**N=14**	**N=13**	
Tbl TAB EF2B. Mean total DT score for 14 days prior to Final visit /Visit 4	3.2	2.0	3.4	P=0.7106
	N=15	**N=16**	**N=13**	
****Tbl TAB EF2c.*** Mean CHANGE in total DT score at baseline (period =14 days prior to randomization visit) compared to Visit 3 (week 4; period = 14 days prior to Visit 3) *i.e.: W0 – Wk 4*	0.9 (p=0.5006)	-0.6 (p=0.5746)	2.1 (p=0.2620)	P=0.3929 *Significance tested within each regimen*
	N=16	**N=14**	**N=13**	
****Tbl TAB EF2c.*** Mean CHANGE in total DT score at baseline (period =14 days prior to randomization visit) compared to Final Visit (or week 8; period = 14 days prior to FV) *i.e.: W0 – Wk 8*	0.9 (p=0.4780)	-1.0 (p=0.3294)	-0.6 (p=0.7526)	P=0.5706 *Significance tested within each regimen*
	N=16	**N=14**	**N=11**	
****Tbl TAB EF2c.*** Mean CHANGE in total DT score at Visit 3 (week 4; period = 14 days prior to Visit 3) compared to Final Visit (or week 8; period = 14 days prior to FV) *i.e.: W4 – Wk 8*	-0.4 (p=0.7442)	-0.8 (p=0.0279)	-2.2 (p=0.1370)	P=0.4623 *Significance tested within each regimen*
DT Heartburn Episodes	**N=16**	**N=16**	**N=15**	
Mean INCIDENCE of DT heartburn episodes (proportion of days with heartburn during the last 14 days of the four-week period: baseline	2.4	2.7	2.1	*P=0.7604*
Mean INCIDENCE of DT heartburn episodes (proportion of days with heartburn during the last 14 days of the four-week period: Visit 3	2.6	2.0	3.5	*P=0.6368*
Mean INCIDENCE of DT heartburn episodes (proportion of days with heartburn during the last 14 days of the Eight-week period: Visit 4	2.5	1.7	2.1	*P=0.8395*

Exploratory Analysis

	Negative Endoscopy N=5	Erosive Endoscopy N=2	*p*-value
***Tbl Exp 1** Mean NTHB score at Randomisation	15.8	22.8	P=0.3312
***Tbl Exp 1** Mean NTHB score at Week 4	10.0	4.5	P=0.5612
***Tbl Exp 1** Mean NTHB score at Week 8	6.0	1.5	P=0.3660
***Tbl Exp 1** Mean change in NTHB score: W0-Wk4	-5.8	-18.3	P=0.0393
***Tbl Exp 1** Mean change in NTHB score: W0-Wk8	-9.8	-21.3	P=0.0091
***Tbl Exp 1** Mean change in NTHB score: W4-Wk8	-4.0	-3.0	P=0.8641

	Previous PPI	Previous H2RA	Previous PPI+H2RA	
	N=37	**N=5**	**N=3**	
***Tbl Exp 2** Mean NTHB score at Randomisation	16.4	25.3	11.7	P=0.1686
***Tbl Exp 2** Mean NTHB score at Week 4	9.2	10.2	1.7	P=0.4649
	N=39	**N=3**	**N=3**	
***Tbl Exp 2** Mean NTHB score at Week 8	8.0	1.0	6.7	P=0.6073
	N=37	**N=5**	**N=3**	
***Tbl Exp 2** Mean change in NTHB score: W0-Wk4	-7.2	-15.1	-10.0	P=0.2007
	N=39	**N=3**	**N=3**	
***Tbl Exp 2** Mean change in NTHB score: W0-Wk8	-8.2	-25.0	-5.0	P=0.0007
	N=36	**N=3**	**N=3**	
***Tbl Exp 2** Mean change in NTHB score: W4-Wk8	-2.7	-9.3	5.0	P=0.0230

***Tbl Exp 3** Spearman Correlation PAGI-QOL Daily Activity vs. PAGI-SUM Heartburn/Regurgitation Subscales: Baseline	R=0.38420 P=0.0070 N=48
***Tbl Exp 3** Spearman Correlation PAGI-QOL Daily Activity vs. PAGI-SUM Heartburn/Regurgitation Subscales: Visit 3	R=0.61680 P<0.0001 N=45
***Tbl Exp 3** Spearman Correlation PAGI-QOL Daily Activity vs. PAGI-SUM Heartburn/Regurgitation Subscales: Visit 4	R=0.61942 P<0.0001 N=48

Effect of Screening HB Score, Incidence and severity on Nocturnal HB score **N=44** (Type III SS) ***Tbl Exp 4***	PR>F
NTHB Score	0.3266
Incidence	0.2239
Severity	0.9891
Randomisation Group	0.1240

SAFETY

Screening phase (All subjects; N=128)	Not Randomized	QAM	QPM	BID	p-value
Tbl AE1. No. (%) with one or more AE	3 (3.75)	0 (0)	1 (5.88)	1 (6.67)	0.538
No. (%) with treatment stopped due to AE	0 (0)	0 (0)	0 (0)	0 (0)	
No. (%) with AE related to treatment	0 (0)	0 (0)	0 (0)	0 (0)	
No. (%) of related AE rated moderate or severe	0 (0)	0 (0)	0 (0)	0 (0)	
No (%) with SAE	0 (0)	0 (0)	0 (0)	0 (0)	
Tbl AE4. Most frequently reported:					
All less than 1% incidence (regardless of relationship to study drug)					
Ear pain, bladder infection, common cold, influenza, bronchitis, sore throat, muscle ache					

Post-randomization (study treatment) phase (All subjects; N=48)		QAM (n=16)	QPM (n=17)	BID (n=15)	p-value
Tbl AE5. No. (%) with one or more AE	--	4 (25)	6(35.3)	6(40.0)	0.691
No. (%) with treatment stopped due to AE	--	0 (0)	0 (0)	0 (0)	
No. (%) with AE related to treatment	--	0 (0)	3 (17.7)	2 (13.3)	
No. (%) of related AE rated moderate or severe	--	0 (0)	1 (5.9)	0 (0)	
No (%) with SAE	--	0 (0)	0 (0)	0 (0)	
Tbl AE8. Most frequently reported: **					
CNS	--				
• *Headache (overall incidence = 6.3%)*		0 (0)	2 (11.8)	1 (6.7)	
GI	--				
• *Diarrhea (overall incidence = 4.2%)*		0 (0)	2 (11.8)	0 (0)	

Vitals - *Tbl Vital 1*	QAM N=17	QPM N=16	BID N=15	p-value
Change in Weight	1.8 (p=0.1138)	-0.1 (p=0.9315)	0.0 (p=0.9145)	0.2680
Change in Pulse	1.2 (p=0.4619)	0.3 (p=0.8950)	1.5 (p=0.4832)	0.8814
Change in Systolic Blood Pressure	-0.8 (p=0.7179)	-2.1 (p=0.4994)	-4.5 (p=0.0504)	0.5698
Change in Diastolic Blood Pressure	-3.2 (p=0.1372)	-2.7 (p=0.3836)	-0.8 (p=0.6980)	0.7607

Discussion:	Mean (±SD) NT HB scores estimates at 4 weeks were QPM: 6.9±8.0, QAM: 8.1±10.4 and BID 12±12.6 (p=0.2330). There were changes at 4- and 8-weeks from baseline for all regimens with respect to mean NT HB score and antacid usage; changes were consistently larger for QAM and QPM regimens than for the BID regimen. The majority of patients in all regimens rated heartburn control "satisfactorily" or "completely controlled" at 4- and 8-weeks, as well as rated satisfaction with HB control as "satisfied" or "very satisfied" at these time points. Compliance with each regimen was excellent (>/=94%). All RAB regimens were safe and well tolerated.
CONCLUSION:	In many patients with NT HB, QAM or QPM regimens may provide better NT symptom control; however, further study is required to identify the best regimen.
Date of this report:	15-Feb-06, 2006 (Final) based on final listings dated 30-Nov-05

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