The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: PAR 279 MDUK/29060/III/83/12

Title: A Study to Assess the Effectiveness and Tolerance of Paroxetine by Double-Blind Comparison with Placebo and Mianserin

Rationale: This study was designed to compare the effectiveness of paroxetine (PAR) with both mianserin (MIA) and placebo (PBO) and to compare the side effect profiles of PAR with MIA and PBO. The subject numbers were unbalanced between the three groups due to the refusal of one ethical committee to administer PBO. A second protocol using only active treatments was written for the hospital refusing to administer placebo, but the data are combined into this report. Only a small number of subjects were recruited and the data was presented in a minor report.

Phase: III

Study Period: June 1983 to April 1986

Study Design: A 6-week, double-blind, double-dummy, prospectively randomised, three-way comparison. (The study was intended to be parallel-group but was not operated in this way due to the refusal of one ethics committee to permit use of placebo).

Centres: 2 centres in London, UK

Indication: Depression

Treatment: Following a two-week placebo washout period, subjects were randomised to receive PAR 30mg/day, MIA 30-90mg/day, or PBO for a 6-week treatment period. Subjects in the PAR group received 30mg/day from weeks 1-6 and subjects in the MIA group received 30mg/day for Days 1-3, and thereafter could be increased to 60 or 90mg/day as dictated by subject response. After the 6-week treatment period when the blind was broken, therapy could be continued according to the subject's response.

Objectives: The objectives of the study were the following: to compare the effectiveness of PAR in subjects with depression with PBO, to compare the effectiveness of PAR with MIA, and to compare the side effect profile of PAR with MIA.

Outcome/Efficacy Variable:
Hamilton Depression Rating Scale, Global Assessment and Final Assessment of Efficacy and Tolerance.

Secondary Outcome/Efficacy Variables:
None defined.

Statistical Methods: Student's t-test was used for parametric data, Mann Whitney U-test and Kruskal-Wallis test for scored data, and chi-squared test where appropriate.
All subjects entered were included in the intent-to-treat (ITT) population, which was the primary analysis population. The results were based on the extender dataset which consists of all subjects last on-treatment visits (excluding baseline).

Study Population: Male and female subjects18 to 70 years of age, who suffered from unipolar depression and who had a score of $\geq$15 on the 17-item HAMD score could be eligible for study entry. Furthermore, subjects needed to be suitable for 'tricyclic-like' therapy and could not have taken any other anti-depressant treatment for two weeks prior to study entry.

	PAR	**MIA**	**PBO**
Number of Subjects:	19	16	10
Planned, N	Not available	Not available	Not available
ITT	19	16	10
Entered active treatment, n	19	16	10
Completed, n (%)	12 (63)	11 (69)	6 (60)
Total Number Subjects Withdrawn, N (%)	7 (37)	5 (31)	4 (40)
Withdrawn due to Adverse Events n (%)	6 (32)	4 (25)	1 (10)
Withdrawn due to Lack of Efficacy n (%)	1* (5)	2* (13)	3 (30)
Withdrawn for other reasons n (%)	1 (5)	1 (6)	0 (0)
*Withdrawn for more than one cause			
Demographics	**PAR**	**MIA**	**PBO**
N (Randomised)	19	16	10
Females: Males	13:6	7:9	7:3

Mean Age (S.D.)	39.7 (18.2)	42.7 (18.4)	51.6 (17.3)
White, n (%)	18 (95)	13 (81)	9 (90)
Efficacy Results:			
HAMD Total score:	**PAR**	**MIA**	**PBO**
Mean Baseline	22.8	21.3	22.3
p-value MIA vs PAR	0.257		
p-value PBO vs PAR	0.746		
p-value overall vs PAR	0.516		
Mean Week 6	13.7	11.0	15.6
p-value MIA vs PAR	0.601		
p-value PBO vs PAR	0.394		
p-value overall vs PAR	0.440		
Global Impression	**PAR**	**MIA**	**PBO**
Median Baseline	3	3	3
Median Week 6	2	2	2
Final Assessment	**PAR**	**MIA**	**PBO**
Efficacy			
Worse	0	1	0
No change	3	3	3
Improved	12	12	5
Unassessable	4	0	2
Tolerance			
Poorly or not well	9	6	1
Fairly well to well	10	10	7
Unassessable	0	0	2
Secondary Outcome/Efficacy Variables: None			
Safety Results: On therapy AEs are events occurring on active treatment			
	PAR	**MIA**	**PBO**
N	19	16	10
Summary of Adverse Events by Body System	**n (%)**	**n (%)**	**n (%)**
Subjects with any AE(s), n (%)	18 (95)	15 (94)	8 (80)
Body System	9(47)	3(19)	2(20)
Cardiovascular System	3(16)	5(31)	1(10)
Digestive System	13(68)	9(56)	3(30)
Metabolic and Nutritional	0	4(25)	0
Musculoskeletal System	1(5)	3(19)	0
Nervous System	14(74)	12(75)	6(60)
Respiratory System	0	1(6)	0
Skin and Appendages	5(26)	1(6)	0
Special Senses	4(21)	3(19)	1(10)
Urogenital System	3(16)	0	1(10)
Serious Adverse Events - On-Therapy	**PAR**	**MIA**	**PBO**
Subjects with non-fatal SAEs, n (%) [related]	2 (11)	1 (6)	0 (0)
Confusion	1 (5)[1]	0 (0)	0 (0)
Dysarthria	1 (5)[1]	0 (0)	0 (0)
Trauma	1(5) [**not specified = ns**]	0 (0)	0 (0)
Tremor	1 (5)[1]	0 (0)	0 (0)
Hematemesis	0 (0)	1 (5)[**ns**]	0 (0)
Subjects with fatal SAEs, n (%) [related]	0 (0)	0 (0)	0 (0)

Conclusion: The number of subjects were too small to make any conclusions about efficacy and to detect any statistical significance. Both PAR and MIA had comparable side-effect profiles, although PAR was associated with more severe symptoms of insomnia and headache and a somewhat higher drop-out rate related to AEs.
Publications: No publication

Date Updated: 16-Mar-2005