Synopsis – Study 10413

Title of Study A double-blind, multicentre, randomised, parallel-group, placebo-controlled study assessing the efficacy and safety of escitalopram in post-myocardial infarction patients suffering from depressive symptoms
Investigators 6 investigators in 3 countries *Signatory investigator* – Sidney Kennedy, MD, University of Toronto, Ontario, Canada
Study Centres 6 centres – 1 in Denmark, 4 in Estonia, and 1 in Norway
Publications None (as of the date of this report)
Study Period *First patient first visit* – 26 October 2004 *Last patient last visit* – 15 August 2005
Objectives • *Primary objective*: – to assess the efficacy and safety of 8 weeks of escitalopram treatment on depressive symptoms in post-myocardial infarct (MI) outpatients • *Secondary objectives*: – to assess the efficacy of escitalopram – to assess the safety and tolerability of escitalopram – to assess quality of life – to evaluate resource utilisation
Methodology • Multinational, multicentre, randomised, double-blind, parallel-group, placebo-controlled study. • Patients were randomised (1:1) to 24 weeks of double-blind treatment with escitalopram or placebo. Patients randomised to escitalopram received a fixed dose of 10 mg/day for the first 8 weeks of the study; for the remainder of the study (Weeks 9 to 24), the dose was flexible (10 or 20 mg/day), adjusted according to the patient's response to treatment, as judged by the investigator. • All patients who completed 24 weeks of double-blind treatment entered a 1-week, double-blind, down-taper period (Week 25). • A safety follow-up visit was scheduled 30 days after completion of the study or after withdrawal from the study. Study completion was at Week 24. • The study was terminated due to insufficient patient enrolment. For patients who had not completed the study, the investigators were advised to stop treatment immediately and to determine the appropriate treatment for each individual patient.

Number of Patients Planned and Analysed

- 290 patients were planned for enrolment: 145 in the placebo group and 145 in the escitalopram group.
- Patient disposition is tabulated below:

	Placebo		Escitalopram		Total	
	n	(%)	n	(%)	n	(%)
Patients randomised	10		9		19	
Patients treated (all-patients-treated set (APTS)):	10		9		19	
Patients completed	2	(20)	2	(22)	4	(21)
Patients withdrawn	8	(80)	7	(78)	15	(79)
Primary reason for withdrawal:						
Adverse event(s)	0	(0)	2	(22)	2	(11)
Protocol violation	0	(0)	1	(11)	1	(5)
Administrative or other reason(s)	8	(80)	4	(44)	12	(63)

Diagnosis and Main Inclusion Criteria

Outpatients, who:

- had a Symptom Checklist – 90 item – Revised (SCL-90-R) Depression subscale score ≥20 at screening and at baseline
- were between 40 and 75 years of age (extremes included)
- had been admitted for chest pains (or other MI symptom) with a diagnosis of evolving MI not less than 3 weeks and not more than 24 weeks prior to screening, as evidenced by either an elevation of biochemical markers of MI (troponin and creatine kinase-MB fraction) or electrocardiogram (ECG) changes that were unequivocally consistent with an acute, evolving MI, that is, development of a significant Q-wave in at least two continuous leads

Investigational Product, Dose and Mode of Administration, Batch Number

Escitalopram – 10 or 20 mg once daily; tablets, orally; batch Nos. 2022410 and 2019557

Duration of Treatment

24 weeks of double-blind treatment followed by 1 week of down-tapering

Reference Therapy, Dose and Mode of Administration, Batch Number

Placebo – once daily; tablets, orally; batch Nos. -703-02 and -001-02

Criteria for Evaluation – Safety

Adverse events (AEs), vital signs, and ECGs (rhythm, QRS complex, ST-segment, and T-wave inversion)

Statistical Methods

- The analysis set used was the APTS, which included all randomised patients who took at least one dose of investigational medical product (IMP).
- Only descriptive statistics were used in this study.

Demography of Study Population

- Ten patients were women and 9 were men. All the patients were Caucasian, except 1 (*other*). The mean age of the patients was 61 years (range 44 to 75 years) (APTS; Table 2).
- There were no clinically relevant differences in age, sex, weight, or BMI between the treatment groups (APTS; Tables 2 and 3).
- At baseline, there were no clinically relevant differences between the placebo and escitalopram groups with respect to medical history or the use of concomitant medication (Listings 2 and 3 respectively).

Efficacy Results

The limited number of enrolled patients resulted in insufficient data for any meaningful analyses.

Safety Results

- The adverse event incidence is summarised below:

	Placebo		Escitalopram	
	n	(%)	n	(%)
Patients treated	10		9	
Patients who died	0		0	
Patients with serious AEs (SAEs)	0		1	(11)
Patients with AEs	6	(60)	7	(78)
Total number of AEs	11		13	

n = number of patients; % = percentage of patients within treatment group

- A total of 9 patients were exposed to escitalopram with a mean duration of 88 days (median 57 days; range 2 to 170 days) and a total exposure of 2.2 patient years (Table 4).
- Six (60%) patients in the placebo group and 7 (78%) patients in the escitalopram group had AEs.
- One SAE was reported: 1 patient in the escitalopram group had 1 SAE (atrial fibrillation). [redacted] She had escitalopram for 15 days when she had palpitations and an ECG showed atrial fibrillation (up to 150 bpm). Twelve days later, she had *recovered with sequelae* and was discharged from the hospital. The event was considered *not related* to IMP by the investigator and the patient completed the study. For further details regarding the patient with hypersensitivity, see *Narratives of Serious Adverse Event and Withdrawal due to Adverse Event*, page 43.
- Two patients in the escitalopram group withdrew from the study due to AEs (Table 5). The AEs leading to withdrawal were insomnia and hypersensitivity. Both events were considered *probably related* to IMP by the investigator. For further details, see *Narratives of Serious Adverse Event and Withdrawal due to Adverse Event*, page 43.
- The system organ classes with the highest incidences (≥20%) of treatment-emergent AEs (TEAEs) were cardiac disorders and nervous system disorders in the escitalopram group and cardiac disorders and respiratory, thoracic, and mediastinal disorders in the placebo group (Table 6).
- There were no discernible trends within or between treatment groups with regard to vital signs (Listing 7).
- For 1 patient (in the placebo group), the ECG showed a change in rhythm with unspecific QRS changes. For 3 patients (1 in the escitalopram group and 2 in the placebo group), the ECGs showed *non-specific changes*. For the remaining 15 patients, the ECGs were *unchanged* from those at baseline (Listing 8).

Conclusions

- Escitalopram was safe and well tolerated in patients who had recently had an MI.
- Due to the small number of patients enrolled, no conclusions regarding efficacy could be drawn.

Date of the Report

15 August 2006

This study was conducted in compliance with the principles of *Good Clinical Practice*.