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REVIEW

Superiority of escitalopram to paroxetine in the treatment of depression

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Abstract

Post-hoc pooled analysis of data from two 6-month randomised controlled trials in patients with major depressive disorder (MDD) revealed superior efficacy and tolerability of escitalopram when compared with paroxetine. Escitalopram ($n=394$) produced a significantly ($p<0.01$) greater mean treatment difference of 2.0 points in primary endpoints, judged using the Montgomery–Åsberg Depression Rating Scale (MADRS) total score, compared with paroxetine ($n=383$). Significant differences were also observed in Clinical Global Impression (CGI) — severity (escitalopram, 2.1; paroxetine, 2.4; $p<0.01$) and CGI — improvement (escitalopram, 1.8; paroxetine, 2.0: $p<0.01$). In the sub-group of severely depressed patients (baseline MADRS ≥ 30), escitalopram showed further improved efficacy compared with paroxetine in all scores. This analysis supports previous observations of superior efficacy and tolerability of long-term escitalopram treatment (10 to 20 mg/day) compared with paroxetine (20 to 40 mg/day). Escitalopram is a good therapeutic option for the long-term treatment of MDD, particularly in severely depressed patients.

1. Introduction

Escitalopram, an allosteric serotonin reuptake inhibitor (ASRI) (Sanchez, 2006), is the therapeutically active S-stereoisomer of racemic citalopram and is significantly more effective than citalopram, which also includes the R-stereoisomer (Colonna et al., 2005; Lepola et al., 2004; Moore et al., 2005). Paroxetine is a selective serotonin reuptake inhibitor (SSRI) antidepressant. Escitalopram and paroxetine have both shown efficacy in the treatment of MDD (major depressive disorder) (Burke, 2002; Lepola et al., 2003; Kasper et al., 2007; Golden et al., 2002; Trivedi et al., 2004). Individual clinical trials involving direct comparison have shown superior efficacy for escitalopram when compared with citalopram, paroxetine and duloxetine (Khan et al., 2007; Wade et al., 2002; Boulenger et al., 2006; Moore et al., 2005).

This study is an analysis of pooled data from two previous studies (Baldwin et al., 2006; Boulenger et al., 2006) comparing

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Table 1 Summary data for the pooled analysis of MDD trials

Duration	Dose (mg/day)	Number of patients	Patients completed	Mean age (years)	Reference & inclusion criterion
27 weeks	ESC 10–20 [a]	165	143 [c]	45	Baldwin et al. (2006)
	PAR 20–40 [b]	158	123 [c]	45	MADRS ≥ 22
24 weeks	ESC 20	229	185	44	Boulenger et al. (2006)
	PAR 40	225	153	45	MADRS ≥ 30
Total		ESC = 394 PAR = 383			

ESC: escitalopram. PAR: paroxetine.
[a] Mean dose at Week 27: 13.9 mg/day.
[b] Mean dose at Week 27: 25.4 mg/day.
[c] Excluding patients withdrawn during taper down period.

escitalopram and paroxetine for the long-term treatment of MDD. Both studies showed a significantly greater treatment response for escitalopram in severely depressed patients, but the study reported by Baldwin and co-workers did not find that escitalopram was more efficacious in the overall patient group. The differences between these studies may be due to differences in the number of patients (323 patients, Baldwin et al., 2006; 454 patients, Boulenger et al., 2006) and differences in baseline severity of disease, determined by Montgomery–Åsberg Depression Rating Scale (MADRS) total score (MADRS ≥ 22, Baldwin et al., 2006; MADRS ≥ 30, Boulenger et al., 2006). Pooled analysis of data from randomised controlled trials is useful in evaluating the relative efficacy and acceptability of treatment over long periods. Combining original study data reduces the expense and time required to undertake additional trials whilst enhancing the accuracy of the original studies (Egger and Smith, 1997; Egger et al., 1997). Data from more than one study can be pooled (individual patient data) or analysed by meta-analysis (analysis of study outcome variables, such as odds-ratio or standardised mean). Pooled analysis of individual patient data is generally considered to have a greater statistical power than a meta-analysis (Thase, 2002). Pooled analysis therefore permits a more robust assessment of the efficacy and tolerability of escitalopram compared with paroxetine in the treatment of MDD and related disorders.

2. Methods

2.1. Study design

Primary data were analysed from two randomised controlled trials lasting 6 months or longer (one 24-week and one 27-week trial) comparing escitalopram with paroxetine in patients with MDD. The data comprised the all-patients-treated set (APTS) (i.e., all patients treated with at least one dose of study medication), or the intent-to-treat (ITT) set, representing 394 patients treated with escitalopram and 383 with paroxetine (Table 1). This represents all Lundbeck- and Forest-sponsored studies comparing escitalopram and paroxetine in the treatment of patients with MDD.

2.2. Main entry criteria

Patients included in these trials fulfilled DSM-IV criteria for a current episode of MDD, following semi-structured interviews based on DSM-IV criteria, and had a minimum baseline MADRS total score ≥ 22 or ≥ 30 (Table 1). Participating patients had no uncontrolled medical illness and in one study (Boulenger et al., 2006), but not in the other (Baldwin et al., 2006), patients with comorbid anxiety disorders were included if MDD was the primary diagnosis. In both studies, patients were excluded if they were pregnant, breast-feeding, or without adequate contraception at time of screening; met DSM-IV criteria for any psychotic disorder, intellectual disability or any pervasive developmental or cognitive disorder; had a MADRS score ≥ 5 on item 10 (suicidal thoughts); were receiving treatment with antipsychotics, antidepressants, hypnotics, anxiolytics (except benzodiazepines in low doses for insomnia in the Baldwin et al., 2006 study), antiepileptics, barbiturates, chloral hydrate, or 5-HT_{1A} receptor agonists; were receiving electroconvulsive treatment; were receiving behavioural therapy or other forms of psychotherapy; had received treatment with any investigational drug within 30 to 90 days prior to entry; had drug or alcohol abuse (as defined by DSM-IV); had a history of severe drug allergy or hypersensitivity; or had a lack of response to more than one antidepressant treatment during the present depressive episode. Once enrolled into the study, patients were withdrawn if they were considered to be at significant risk of suicide, or if they scored ≥ 5 points on item 10 (suicidal thoughts) of the MADRS.

The pre-defined primary efficacy scale in each trial was the MADRS, using the principle of last-observation-carried-forward (LOCF) for missing values.

2.3. Allocation to treatment

Study medication was given as capsules of identical appearance. Patients who met the selection criteria at the baseline visit were assigned to double-blind treatment according to a computer-generated randomisation list. The details of the randomisation series were unknown to any of the investigators and were contained in a set of sealed opaque envelopes. At each trial centre, sequentially enrolled patients were assigned the lowest randomisation number available. All trial personnel and participants were blind to treatment assignment for the duration of the entire trial. Trials were conducted in accordance with the principles of *Good Clinical Practice* and the *Declaration of Helsinki*. Local ethics

Table 2 Patient baseline characteristics (pooled data, ITT)

	Escitalopram	Paroxetine
Number of patients, ITT	394	383
Women	69.5%	71.8%
Age ± SD (years)	44.3 ± 13.5	44.8 ± 13.0
Range	18 to 85	18 to 76
Weight ± SD (kg)	70.6 ± 15.3	71.1 ± 15.8
MADRS at baseline ± SD	32.8 ± 4.8	32.7 ± 4.7
CGI-S at baseline ± SD	4.8 ± 0.8	4.8 ± 0.8
Number of patients with MADRS ≥ 30	310	296

CGI-S: Clinical Global Impression – severity.
ITT: intent-to-treat set.
MADRS: Montgomery–Åsberg Depression Rating Scale.