

90-53 A double-blind, placebo-controlled comparison of venlafaxine and once-daily venlafaxine XR in patients with major depression

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Objective: Compare the efficacy and safety of venlafaxine and once-daily venlafaxine extended release (XR) with that of placebo in outpatients with major depression.

Methods: This was a randomized, double-blind, placebo-controlled comparison of the efficacy and safety of venlafaxine and venlafaxine XR. Outpatients with DSM-III-R major depression were randomly assigned to venlafaxine 37.5 mg twice daily, venlafaxine XR 75 mg once daily, or placebo for a maximum of 12 weeks. If the response was inadequate after 2 weeks, the dosage of venlafaxine or venlafaxine XR could be increased to 150 mg daily. Of 278 patients evaluated, 87 received venlafaxine XR, 92 venlafaxine, and 99 placebo.

Results: Venlafaxine XR was superior ($p < 0.05$) to placebo at weeks 2, 3 and 4 and continuing through week 12 for all primary efficacy variables. Similarly, venlafaxine was superior ($p < 0.05$) to placebo beginning at week 2 on the HAM-D total and depressed mood item, week 3 on the MADRS total, and week 6 on the CGI severity scales. Venlafaxine XR exhibited superiority ($p < 0.05$) over venlafaxine at week 12 for all primary efficacy variables. The most common adverse event with venlafaxine XR was nausea, which was highest during the first 2 weeks with a rapid decrease thereafter.

Conclusions: Venlafaxine XR is effective and well tolerated for the treatment of major depression at once daily doses ranging from 75 to 150 mg.

90-54 Effects of once-daily extended release (XR) venlafaxine on anxiety in patients with major depression

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Objective: Evaluate the effects of once-daily venlafaxine extended release (XR) and venlafaxine on symptoms of anxiety in patients with depression and associated anxiety.

Methods: Study 1 was a 12-week, randomized, double-blind, placebo-controlled trial. Patients received venlafaxine 37.5 mg twice daily, venlafaxine XR 75 mg once daily, or placebo. The venlafaxine or venlafaxine XR dose could be increased to 150 mg daily after 2 weeks to increase the response. Study 2 was an 8-week, randomized, double-blind, placebo-controlled trial. Patients received venlafaxine XR 75 mg once daily or placebo. The venlafaxine XR dose could be increased to a maximum of 225 mg/day. Moderate or greater anxiety was defined as a HAM-D anxiety-psycho item score ≥ 2 and severe anxiety was a score ≥ 3 .

Results: Study 1: Among patients with moderate or greater anxiety ($n = 252$) or severe anxiety ($n = 96$) at baseline, a significant reduction ($p \leq 0.05$ to ≤ 0.001) in the HAM-D anxiety-psycho item scores occurred with venlafaxine XR compared with placebo from weeks 4 through 12. A similar response was observed with venlafaxine. Study 2: Among patients with moderate or greater anxiety ($n = 161$) or severe anxiety ($n = 60$) at baseline, a significant reduction ($p \leq 0.05$ to ≤ 0.001) in HAM-D anxiety-psycho item scores occurred with venlafaxine XR compared with placebo from weeks 1 through 8.

Conclusion: Venlafaxine XR is effective for the reduction of symptoms of anxiety at doses of 75 to 225 mg/daily in depressed outpatients with associated anxiety.

90-55 Prescribing patterns of selective serotonin reuptake inhibitors in primary care in the United Kingdom

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The aim of this study was to investigate the prescribing of selective serotonin reuptake inhibitors (SSRIs) for the treatment of depression during the Defeat Depression Campaign.

Method: Cross sectional data for prescriptions for SSRIs for patients with a diagnosis of depression were obtained from a large primary care computerised database (750,000 patients) for four consecutive twelve month periods ending June 1993, 1994, 1995 and 1996.

Results: Analysis of the prescribing patterns of SSRIs shows that their prescribing patterns are consistent over time. 100% of prescriptions for

SSRIs are in effective doses. Dosing patterns suggesting titration to higher doses are evident during the study period, showing the least dose titration with fluoxetine and the greatest with sertraline. This pattern of prescribing may have both clinical and economic implications.

Naturalistic studies reveal differences between drugs which may not be apparent in clinical trials. In particular, an effective dose may be achieved earlier in treatment with fluoxetine, and the incidence of side effects may be less. These are significant advantages which may simplify treatment and result in improved outcomes. Because sertraline is prescribed in higher doses, this may increase the cost of treatment significantly.

90-56 Meta-analysis of 2 European multicenter controlled trials with ademetionine (SAME) in major depression

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The antidepressant activity of Ademetionine (SAME), an endogenous methyl-donor, was tested in 2 double blind, controlled studies (MC1 and MC2). MC1 was a placebo-controlled trial and SAME (800 mg/day) was administered by i.v. route for 3 wks; MC2 compared i.v. SAME for 3 wks (800 mg/day) with i.v. Clomipramine (CIMI) (100 mg/day). The combined analysis of the results in pts with basal HAM-D ≥ 26 are shown in the table.

HAM-D scores (17 items) pre and post-treatment and % changes

		N	Pre-treatment mean \pm SD	Post-treatment mean \pm SD	% Δ
MC1	Placebo	35	30.0 \pm 3.2	21.7 \pm 9.7	27.6%
	SAME	40	29.9 \pm 4.0	17.7 \pm 8.6 [*]	40.8%
MC2	SAME	57	29.6 \pm 2.9	18.8 \pm 8.2	36.5%
	CIMI	65	29.3 \pm 3.5	15.0 \pm 6.8 [#]	48.8%

* $p = 0.05$ SAME vs placebo; # $p = 0.01$ CIMI vs SAME

In MC1 trial MADRS scores (mean \pm SD) decreased from 34.7 ± 6.1 to 20.6 ± 12.2 in the SAME group and from 34.8 ± 6.8 to 26.1 ± 12.6 in the placebo group ($p = 0.025$, SAME vs placebo); similarly the scores (mean \pm SD) of depressive core of HAM-D (items 1, 2, 3, 7 and 8) improved from 11.6 ± 1.8 to 6.2 ± 4.2 with i.v. SAME and from 11.5 ± 1.8 to 8.4 ± 4.2 with i.v. placebo ($p < 0.05$, SAME vs placebo). In the MC2 trial the drug-related adverse events and drop-outs for adverse events were significantly lower in SAME than in CIMI ($p < 0.05$). The review of these 2 studies shows that i.v. SAME has an intermediate antidepressant activity between i.v. placebo and i.v. CIMI and is better tolerated than CIMI.

90-57 Feasibility of one year treatment of depression by pharmacotherapy or pharmacotherapy plus psychotherapy

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Methods: Randomized study comparing pharmacotherapy (PhT) ($n = 57$) with combined therapy (CT, i.e. pharmacotherapy plus psychotherapy) ($n = 72$) in psychiatric outpatients (age 18-60 years) with DSM-III-R Major Depression and a 17-item HDRS baseline score of at least 14 points. In both conditions, patients were treated according to a pharmacotherapy algorithm (fluoxetine-amitriptyline-moclobemide). Pharmacotherapy was intended to be continued 1 year at full dose. In the CT condition, psychodynamic supportive psychotherapy protocol (23 sessions) was added to the pharmacotherapy. Efficacy was determined after 1/2 and 1 year according to remission rates (HDRS 0-7), response rates (50% reduction in HDRS scores) and CGI-Improvement scores. Feasibility was defined as taking the medication according to the algorithm.

Results: After 2, 6 and 12 months pharmacotherapy was feasible in 92%, 67% and 45% respectively. Remission rates in feasible versus not feasible treatment were: 37% versus 28% after 1/2 year and 59% versus 46% after 1 year. Response and improvement rates showed similar patterns. Feasibility was always greater in the CT condition.

Conclusions: Pharmacotherapy being feasible improves the efficacy after 1/2 and 1 year. Addition of psychotherapy enhances the feasibility of antidepressant therapy.