Methods: Pooled analyses of all company-sponsored, acute-phase, placebo-controlled, fixed-dose trials using the Hamilton Depression Rating Scale (HDRS) conducted to evaluate the effect of citalopram, paroxetine, or sertraline in adult major depression (n=2859). The single item depressed mood, which has proven a more sensitive measure to detect an antidepressant signal than the conventional one, i.e. the sum score of all HDRS items, was designated primary effect parameter

Results: Doses below or at the lower end of the dose range usually recommended (citalopram: 10-20mg, paroxetine: 10mg; sertraline: 50mg) were superior to placebo but inferior to higher doses. In contrast, among doses above these, there was no indication of a dose-response relationship. The effect size after exclusion of suboptimal doses was of a more respectable magnitude (0.5) than that usually attributed the antidepressant effect of the SSRIs. With respect to the depressed mood item, high-dose and low-dose both outperformed placebo already after one week.

Conclusions: The observation that low doses are less effective than higher ones challenges the oft-cited view that the effect of the SSRIs is not dose-dependent and hence not caused by a specific, pharmacological antidepressant action. We suggest that inclusion of suboptimal doses in previous meta-analyses has led to an underestimation of the efficacy of these drugs. Moreover, the finding that both low-dose and high-dose SSRI reduce depressed mood more effectively than placebo already during the first week of treatment may have implications for our understanding of the mechanism of action of these drugs.

PS82

Does Serum Amyloid ß-Protein predict the Response to Antidepressant treatment in Major Depression?

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Abstract

Objective: Recent studies demonstrated changes of serum and plasma amyloid ß-protein (Aβ) levels in patients with depression. Although the change of serum levels of Aβ has been suggested as a risk factor for future onset of Alzheimer's disease, the relationship between Aβ levels and treatment response in patients with depression is still unclear. Our objective of this study is to assess whether serum levels of Aβ may predict the response to antidepressant treatment in patients with major depression.

Methods: Serum Aβ40 and Aβ42 levels at admission were evaluated in 120 patients with major depressive disorder. All patients were treated with antidepressant. Depressive symptoms were assessed using the Hamilton rating scale for depression at admission, 4-weeks after treatment and at the time of clinical remission. The relationship between serum levels of Aβ and 4-weeks response rate was analyzed using multiple regression analysis controlling age, gender, severity of depression and number of depressive episodes.

Results: Serum levels of Aβ40 (β=-0.147, p=0.143), Aβ42 (β=-0.003, p=0.977) and Aβ40/42 ratio (β=0.085, p=0.396) were not significantly associated with 4-weeks response rate. Similar results were shown in elderly patients (>60 years).

Conclusions: Serum levels of Aβ may not predict the response to antidepressant treatment in patients with major depression. Further studies which controlled antidepressant type and dose will be needed.

PS83

Impact of Vortioxetine on Functional Capacity in MDD Patients with Subjective Cognitive Dysfunction: A Post-hoc Analysis of the University of California San Diego Performance-Based Skills Assessment

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Abstract

Background: *Post-hoc* analyses of study NCT01564862 evaluated the effect of flexible-dose vortioxetine (10-20mg) on functional capacity in adults with MDD using the UCSD Performance-Based Skills Assessment (UPSA).

Methods: Adults with MADRS≥26 who self-reported symptoms of cognitive dysfunction were enrolled in this double-blind, placebo-controlled, active-reference study. Change from baseline to Week 8 in both UPSA and MADRS were compared to placebo (ANCOVA, modified intent-to-treat). Analyses were performed in patient subgroups based on severity of functional impairment (baseline UPSA≤75, ≤70). Clinically relevant improvements in functional capacity were evaluated using pre-defined cutoffs for UPSA improvement (≥5, ≥7, ≥10). Path analysis determined the proportion of direct *versus* indirect effects of vortioxetine on UPSA. Analyses of remission from depressive symptoms and functional improvement (MADRS total score ≤10 and UPSA ≥75) were also conducted.

Results: 602 patients were randomly assigned to treatment. Statistically significant increases in functional capacity for vortioxetine *versus* placebo in the UPSA composite score, were seen in all patients (vortioxetine, n=175, Δ+8.0; placebo, n=166, Δ+5.1: $p<0.001$), in patients with baseline UPSA≤75 (n=62, Δ+14.9; n=73, Δ+9.9, $p=0.003$) and UPSA≤70 (n=41, Δ+16.7; n=46, Δ+10.8: $p=0.010$). Patients treated with duloxetine showed no significant improvement in functional capacity ($p=0.637$). More vortioxetine patients were responders: ΔUPSA≥7 (n=85, 48.6%; n=59, 35.5%: $p=0.015$) and ΔUPSA≥10 (n=66, 37.7%; n=46, 27.7%: $p=0.049$). Both vortioxetine and duloxetine significantly improved depressive symptoms *versus* placebo based on the MADRS ($p<0.05$; $p<0.001$, respectively). Path analysis of UPSA revealed that 96.9% of the effect of vortioxetine was direct and not due to improvement in depressive symptoms. For composite efficacy analysis (MADRS≤10 and UPSA≥75), vortioxetine was significantly superior to placebo (22.3% *versus* 10.2%, $p=0.005$), but duloxetine (16.0%) was not ($p=0.124$).

Conclusion: Vortioxetine, but not duloxetine, significantly improved functional capacity *versus* placebo on the UPSA. These results emphasize the distinct profile of vortioxetine in MDD patients with cognitive dysfunction.

Funding: This study was funded by H. Lundbeck A/S and Takeda Pharmaceutical Company, Ltd.

PS84

Comparison of risk for development of mania or hypomania between Venlafaxine monotherapy group and Olanzapine augmentation group with Originally diagnosed as Unipolar depressive disorder during 7-year follow up: naturalistic study, retrospective review.

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Abstract

Objectives: To compare the risk for subsequent development of mania or hypomania between venlafaxine monotherapy group and Olanzapine augmentation group, the authors conducted a preliminary retrospective medical record review for patients originally diagnosed as unipolar major depression during 7-year follow-up period.

Methods: we selected samples from the patients who visited psychiatric outpatient clinic of Bongseng memorial hospital from August 1st 2006 to August 31st 2008. All patients were diagnosed as originally unipolar depressive disorder and prescribed venlafaxine alone (VLF) or olanzapine augmentation (OLZ+) from the first visit according to clinician's decision. We included consecutively 35 patients in each group and reviewed the development of mania or hypomania according to the DSM-IV-TR diagnostic criteria for 7-year follow up (F/U) period.

Results: In VLF group, symptom severity (CGI-S 3.9±0.7 vs 4.5±0.6) was lower, F/U duration (36.0±33.8 vs 62.6±41.0 months) was shorter and age at first visit (45.0±16.7 vs 57.2±12.4 years) was younger ($p < 0.01$) than OZP+ group. In VLF group, manic (2.9 vs 0.0 %) and hypomanic (8.6 vs 2.9 %) switch rate were higher than OZP+ group, but those were not statistically significant. Almost all cases were switched to manic or hypomanic in the early phase of F/U period (3 cases within 1 month and 1 case within 3 months) and revealed previous early onset or multiple non-treated brief mood episodes according to post-hoc meticulous history taking.

Conclusion: OLZ augmentation could be preventive option for manic or hypomanic switching in treatment of depressive disorder. We should be careful to detect manic or hypomanic switch in the early treatment phase of younger and non-treatment history patients with uncovered early onset or multiple brief mood episodes. Limitations of our study were small sample size, shorter duration of F/U period, no active periodic F/U check, older age of sample and unstructured design.

Key Words: manic switching, hypomanic switching, olanzapine augmentation, venlafaxine, unipolar depressive disorder.

PS85

Efficacy and Safety of Generic Escitalopram (Lexacure) in Patients with Major Depressive Disorder: A 6-week, Multi-center, Randomized, Rater-blinded, Escitalopram-comparative, Non-inferiority Study

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Abstract

Objectives: The primary aim of this non-inferiority study was to investigate the clinical effectiveness and safety of generic escitalopram (Lexacure) versus branded escitalopram (Lexapro) for patients with major depressive disorder (MDD).

Methods: The present study included 158 patients who were randomized (1:1) to receive a flexible dose of generic escitalopram (n = 78) or branded escitalopram (n = 80) over a 6-week single-blind treatment period. The clinical benefits in the two groups were evaluated using the MADRS), the 17-item HDRS, the CGI-S, and the CGI-I at baseline, Week 1, Week 2, Week 4, and Week 6. The frequency of adverse events (AEs) was also assessed to determine safety at each follow-up visit.

Results: The MADRS, HDRS, CGI-S, and CGI-I scores significantly decreased in both groups, and there were no significant differences between the groups. At Week 6, 28 patients (57.1%) in the generic escitalopram group and 35 patients (67.3%) in the branded escitalopram group had responded to treatment (as indicated by a ≥50% decrease from the baseline MADRS score; P = 0.126), and the remission rates (MADRS score: ≤10) were 42.9% (n = 21) in generic escitalopram group and 53.8% (n = 28) in the branded escitalopram group (P = 0.135). The most frequently reported AEs were nausea (17.9%), sleepiness/somnolence (7.7%), weight gain (3.8%), and dry mouth (2.6%) in the generic escitalopram group and nausea (20.0%), sleepiness/somnolence (3.8%), weight gain (2.5%), and dry mouth (2.5%) in the branded escitalopram group.

Conclusions: The present non-inferiority study demonstrated that generic escitalopram is a safe and effective initial treatment for patients with MDD and may also be considered as an additional therapeutic option for this population.

PS86

Kleptomania - a side-effect induced by venlafaxine

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Abstract

Objective: Venlafaxine is a dual serotonin and norepinephrine reuptake inhibitor (SNRI), widely used as treatment of major depressive disorder (MDD), social anxiety disorder, and generalized anxiety disorder. Venalfaxine is generally considered quite effective and safe, with commonly reported adverse reactions in clinical studies being nausea, dry mouth, headache and sweating.

Kleptomania is a rare impulse control disorder characterized by recurrent episodes of compulsive stealing, most commonly in the form of shoplifting. The stolen items are usually of trivial value, and not needed by the person stealing them. Kleptomanic behaviour during treatment with antidepressants was reported in several occasions, but was usually induced by serotonin selective reuptake inhibitors.

Methods: We present a clinical case of a 67 years old female patient treated with venlafaxine for MDD that developed kleptomania.

Results: Our patient was admitted to a psychiatric unit, presenting depressive symptoms that met ICD-10 criteria for a recurrent, severe MDD without psychotic features. Patient's leading symptoms were treated with venlafaxine and in subsequent weeks a clinically significant and subjective improvement was accomplished. After discharge, psychiatric outpatient treatment was continued. Eight months after her first hospital treatment, patient was readmitted: her depressive symptoms were recurring after she started to shoplift regularly and compulsively. As venlafaxine was discontinued and a new antidepressant, bupropion, was given, patient's compulsion vanished, leading to conclusion that kleptomania could have been induced by venlafaxine treatment. In the subsequent follow-ups, there were no signs of kleptomania. A good and stable remission of MDD was accomplished as well. Extensive diagnostic screening excluded all possible differential causes.

Conclusion: So far, kleptomania as side-effect of antidepressant treatment has been reported from several different sources. Possible pathophysiological causes are further discussed,