

P.2.a.004 Antidepressant combinations and monotherapy in the treatment of resistant depression: a randomised, open-label study

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Purpose of the study and Objectives: Use of antidepressant combination (CAD) is a popular, often used strategy to overcome resistance to treatment in resistant depressive patients. At least two double-blind studies comparing efficacy of CAD with antidepressant monotherapy (ADM) that had been administered from initiation of treatment demonstrated greater improvement of depressive symptoms for CAD comparing to ADM [1,2]. We also found superior higher efficacy of CAD in previous retrospective study [3]. This randomized, 6-week, open label study compared efficacy of ADM and CAD that were chosen according to clinical judgment of the attending psychiatrist with regard to the history of previous treatments and clinical guidelines in resistant inpatients in current clinical settings. We hypothesized that CAD would produce a greater therapeutic effect than ADM.

Methods: A total of 60 inpatients with depressive disorder (DSM-IV criteria) who previously did not respond to at least one antidepressant treatment, were randomly assigned to ADM (n=29) and CAD (n=31) treatments for 6 weeks. The primary outcome measure was score change in the Montgomery-Åsberg Depression Rating Scale (MADRS). We also evaluate clinical status of patients by Clinical Global Impression (CGI) and Beck Depressive Inventory-Short Form (BDI-SF). The response was defined as a $\geq 50\%$ reduction of MADRS score and the remission as the MADRS score equal or less than 10 points. The primary efficacy analyses were based on intent-to-treat (ITT) data set with the last observation analysis (LOAN) method. All tests were 2-sided and an exact significance level of 0.05 was adopted. The Prague Psychiatric Centre Institutional Review Board reviewed and approved this study and a written informed consent to participate in the research was obtained from all subjects.

Results: Mean change in total MADRS score from baseline to week 6 for patients treated by ADM was 13.2 ± 1.33 points (paired t-test: $t=8.25$, $df=28$, $p < 0.001$ and 14.51 ± 1.29 points (paired t-test: $t=8.4$, $df=3$, $p < 0.001$) for patients from CAD group, thus a non-significant between group difference (unpaired t-test: $t=-0.57$, $df=58$, $p=0.58$). The two-way repeated measures analysis of variance (RM-ANOVA) with the Greenhouse-Geisser adjustment confirmed significant effect of time ($F=89.16$, $df=3,270$, $p < 0.001$) but not effect of group ($F=0.427$, $df=1,58$, $p=0.51$) or group-time interaction ($F=0.953$, $df=3,270$, $p=0.4$). Post hoc analysis failed to find between-group differences within all visits as well. The similar pattern of results we found for CGI and BDI-SF. Response rates for ADM (48%) and CAD (58%, $p=0.61$) as well as remission rates (28 vs. 42%, $p=0.27$) and drop-out rates (ADM 3/29, CAD 6/31, $p=0.48$) did not differ between treatment groups (Fisher Exact Test).

Limitations: Relatively small sample size.

Conclusion: Both CAD and ADM treatments chosen according to clinical judgment of attending psychiatrist with respect to previ-

ous treatment produced clinically relevant reduction of depressive symptomatology in patients with resistant depression and their effect was comparable.

Trial Registration: www.isrctn.org: ISRCTN65259480

References

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P.2.a.005 Dosing of aripiprazole adjunctive therapy for Asian patients with major depressive disorder: a 24-week open label trial

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Introduction: Aripiprazole is the first atypical antipsychotic approved for adjunctive therapy in major depressive disorder, but the incidences of most common side effects, akathisia and restless, were up to 25% and 12%, respectively. The average dose of aripiprazole was 11.1 mg/day in previous studies of western countries [1,2,3]. Whether the Asia patients with lower body mass index (BMI) will be more sensitive to side effects or require lower dose of Aripiprazole need investigation.

Method: The 24-week open label trial was conducted in Taiwanese patients to evaluate the efficacy and tolerability of aripiprazole adjunctive therapy in major depressive disorder. The eligible subjects were patient who had received antidepressant treatment more than one month, and with Hamilton rating scale for depression (HAMD) more than 14. Aripiprazole 2.5 mg to 20 mg/day was augmented to antidepressant therapy. The outcome survey including psychiatrist ratings of HAMD, Montgomery Åsberg Depression Rating Scale (MADRS), Hamilton rating scale for Anxiety (HAMA); and patient subjective ratings of Inventory of Depressive Symptomatology (IDS), Depression and Somatic Symptoms Scale (DSSS), Beck Depression Inventory (BDI), Sheehan disability scale (SDS), and Medical Outcomes Study Short form-12 (SF-12) life quality.

Result: Forty patients, with 67.5% of female, average age of 46.7 ± 14.5 year old, and history of depression for 5.5 years, were enrolled. The baseline HAMD score was 21.5 ± 5.0 . The distribution of original antidepressant with serotonin specific reuptake inhibitor (SSRI), serotonin norepinephrine reuptake inhibitor (SNRI), norepinephrine and dopamine reuptake inhibitor (NDRI), and norepinephrine and specific serotonergic antidepressant (NASSA) was 33.3%, 45.5%, 9.1%, and 12.1%, respectively. Seven cases withdrawal from the study due to side effects or lost follow up, the response and remission rate among 33 cases with at least one visit after baseline was 75.8% and 39.4%, respectively. Nine cases (22.5%) withdrawal from the study due to side effects (akathisia, restless and poor sleep), had significantly lower BMI