P11.24

Olanzapine-fluoxetine combination for treatment of psychotic depression

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Objective: Two parallel, 8-week double-blind trials, with an optional 48-week open-label extension, compared olanzapine-fluoxetine combination (OFC) to olanzapine (OLZ) or placebo (PLA) in psychotic depression (PD).

Method: 249 PD patients were randomized to OFC, OLZ or PLA treatment groups, and efficacy evaluated with the HAMD-24.

Results: Pooled data showed a significantly greater total score decrease with OFC than with OLZ or PLA (-18.3, -14.4, -11.4). OFC endpoint response (&61619;50% total score decrease) was significantly greater than OLZ or PLA (56%, 36%, 30%). 71% of acute OFC responders maintained response in the open-label phase. More OFC partial responders (&61619;25% total score decrease at 2 weeks) achieved full endpoint response compared with OLZ or PLA (64%, 35%, 32%). OFC median time to response was similar to OLZ, but faster than PLA (12, 12, 20 days). OFC remission rate and median time to remission was better (20%, 20 days) than OLZ (13%, 56 days) and PLA (11%, 24 days). OFC's safety profile was similar to OLZ.

Conclusion: OFC demonstrated greater acute improvement in depressive symptoms than OLZ or PLA, and 71% of acute OFC responders maintained response during the 48-week extension

P11.25

HPA axis activation in patients with few versus multiple episodes of depression

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Background: Activation of the hypothalamic–pituitary–adrenal (HPA) hormonal axis is commonly seen in affective disorders, but little is known about the outcome when correlated to illness course over a lifetime.

Methods: We evaluated the HPA axis in patients with treatment–refractory affective disorder by measuring adrenocorticotropin hormone (ACTH) and cortisol responses following administration of corticotropin-releasing-hormone (CRH) in 37 patients with treatment–refractory affective disorder and in 27 healthy volunteers. In retrospective life charts were recorded every previous illness episode for each patient.

Results: Seven of the patients had had one or two illness episodes ('pauciepisodic') and 30 had had three or more episodes ('multiepisodic'). The pauciepisodic patients had significantly larger peak and total ACTH responses to CRH compared to the multiepisodic patients as well as to the control group. Multiepisodic patients showed no difference compared to controls in ACTH secretion pre- and post-CRH. Cortisol secretion was the same in all three groups.

Conclusions: The pituary adrenocortical responses in pauciepisodic patients were higher than in multiepisodic patients and in volunteers. This suggests that the HPA axis in refractory multiepisodic affective disorders might change its original activity as illness proceeds.

P12. Dementia – Alzheimer type

P12.01

Dementia: neuroradiological imaging and neuropsychological testing are useful and necessitive extensions of clinical diagnostics

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Objective: The significance of extended diagnostics in dementia has been controversary discussed under the view of cost-effectiveness. The contribution of neuromaging and neuropsychological testing to diagnosis of dementia is evaluated.

Methods: Of 127 patients of a memory clinic the first clinical diagnosis, the diagnosis of neuroimaging and of neuropsychology are registered under equal criterias and compared with the final clinical diagnosis. The MRI-examination consists of standard-, FLAIR-, and special Hippocampus-oriented sequences. Power- and Speed-Tests are used by neuropsychology. Differentiation between demented vs. non-demented and vasculary vs. neuro-degenerative dementia (e.g. Alzheimer's disease) is made.

Results: Only 50,5% are demented patients. At 26% the results of extended clinical diagnostic are leading to changes of the final clinical diagnosis, compared with the first clinical examination. Statistical coherences can be found:

	ND/VD/XD		
	First clin. Exam.	Neuroradiol.	Psychology
Sensitivity	0.66/0.70/0.80	0.93/0.90/0.55	0.83/0.60/0.98
Specificity	0.90/0.83/0.90	0.89/0.79/0.96	0.88/0.94/0.98
PPV [%]	74/50/89	78/51/93	75/71/98

Contribution is given by neuropsychology to dementia-diagnosis (XD = non-demented) and by neuroimaging for the differentiation of vaskulary (VD) vs. neuro-degenerative (ND) dementia.

Conclusion: The extended diagnostics contribute to the diagnostic correctness, the contribution is complementary. Even with regard to cost-effectiveness, early secondary prevention, and therapy of the dementias neuroimaging and neuropsychological testing are essential.

P12.02

Alzheimer's disease diagnostics and the treatment at the psychiatric out-patients department

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Alzheimer's disease (AD) is a primary degenerative disease with multi-factorial etiology and with specific neuropathological and neurobiochemical changes.

AD is the most common form of dementia, 65% of all dementia of the population over 65 years of age have AD. Alzheimer's disease has an insidious star followed by a steady and quick progression of cognitive impairment, aphasia, agnosia, apraxis, are very quick.

Since we have no satisfactory biological marker for making the diagnosis of AD, clinical diagnosis is based on symptomatolgy, neuropsychological tests and computer tomography or magnetic nuclear imaging or PET, SPECT.

In our practice we used clinical criteria for Alzheimer' disease described in the International Classification of Diseases, 10th

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revision/ICD-10 WHO, 1992 and Diagnostic and Statistical Manual of Mental Disorders/DSM-IV, APA, 1994.

P12.03

Intramuscular olanzapine: efficacy and safety in acutely agitated patients with dementia

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To investigate the efficacy and safety of rapid-acting intramuscular olanzapine in treatment of agitation in inpatients with dementia. Patients were randomized to receive up to 3 intramuscular injections within 24 hours: either 2.5-mg olanzapine (Olz2.5, n=71), 5.0-mg olanzapine (Olz5.0, n=66), 1.0-mg lorazepam (Lzp, n=68), or placebo (n=67).

Two hours after injection1, olanzapine and lorazepam improved scores significantly more than placebo on the PANSS Excited Component subscale (PANSS-EC) and Agitation–Calmness Evaluation Scale (ACES). Olz5.0 and Lzp also improved scores more on the Cohen–Mansfield Agitation Inventory. At 24 hours, both Olz groups continued to show statistical superiority over placebo on the PANSS-EC, but Lzp did not. Simpson–Angus and MMSE scores did not change significantly from baseline. Sedation (ACES >=8), adverse events, and laboratory analytes were not different from placebo for any treatment. QTc interval changes were not significantly different from placebo for any of the active treatments. No clinically and statistically significant changes were seen in any other vital signs, including orthostasis.

These results suggest that rapid-acting intramuscular injection of olanzapine may provide substantial benefit in treating dementia-related agitation.

P12.04

The DemTect®: a very sensitive screening instrument for mild dementia

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Objective: The Mini Mental State Examination (MMSE) has been criticized for lack of sensitivity in mild dementia. We compared the sensitivity of the MMSE and a new screening instrument, the DemTect®, in patients with mild vascular dementia (VD) and Alzheimer's dementia (AD).

Method: 31 control subjects, mean (±SD) age 65.0±10.6yrs, 28 VD patients (71.0±10.6yrs), and 36 AD patients (72.4±6.7yrs) with mild dementia according to the Clinical Dementia Rating scale were assessed with the DemTect® and the MMSE. Discriminant analyses were performed.

Results: Both dementia groups scored significantly ($p<.001$) worse than the controls in the DemTect® (mean [±SD] scores [maximum 18]: controls 16.1±1.3, VD 8.4±3.8, AD 5.6±2.6) and MMSE ([maximum 30]: controls 29.6±0.5, VD 25.1±4.7, AD 25.4±3.6). The sensitivity of the DemTect® was 95.2% for the VD and 95% for the AD patients, whereas the sensitivity of the MMSE was 58.3% for the VD and 74.5% for the AD patients. Specificity was >95% for both tests.

Conclusion: Compared to the MMSE, the DemTect® is a much more sensitive screening instrument in mild forms of vascular and Alzheimer's dementia.

P12.05

Efficacy of quetiapine in the treatment of behavioral symptoms in dementia

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Many patients with dementia, during the course of illness, shows psychiatric and behavioral symptoms. The most important are: delusions, allucination, aggressivity, irritability, depression, alteration of sleep/wake cycle and wandering. These symptoms, frequently are present in the early stage of illness and provoce distress to caregivers. The aim of our study is evaluate the frequency and severity of psychiatric and behavioral symptoms in 30 patient with mild and moderate Alzheimer's disease before and after treatment with 50- 200 mg/die of quetiapine. The behavioral symptoms are evaluate with the Neuropsychiatric Inventory and Behave-AD before the treatment and after 2, 4, 6 and 8 weeks. At the end of the study the behavioral and psychiatric symptoms are significantly reduce. This study confirm the efficacy of quetiapine in the treatment of behavioral disturbance in Alzheimer's disease. This finding is important, because a reduction of psychiatric symptoms in patient with dementia improve the quality of life and reduce the caregiver's distress.

P12.06

Cerebrospinal fluid 24S-hydroxycholesterol is increased in Alzheimer's disease compared to healthy controls

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Introduction: Experiments in cell cultures indicate that accumulation of cholesterol in hippocampal neurons results in an accelerated cleavage of APP into amyloidogenic components. Cholesterol is converted to 24S-hydroxycholesterol to be eliminated from the cerebrospinal fluid (CSF). To address potential effects of circulating plasma cholesterol on CSF 24S-hydroxycholesterol levels only patients and controls with cholesterol levels in the normal range were included.

Method: We investigated CSF concentrations of 24S-hydroxycholesterol in a group of 14 AD patients and 10 age-matched healthy controls without any cognitive deficits nor psychiatric or neurological disorders who showed normal plasma cholesterol levels in a range of 150–230 mg/dl.

Results: We found significantly elevated 24S-hydroxycholesterol CSF but not plasma levels in AD patients compared to healthy controls.

Conclusion: Our results demonstrate CSF 24S-hydroxycholesterol is increased in AD. This effect does not seem to be confounded by plasma cholesterol levels, since the latter did not significantly differ between groups.

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