was designed to extend these studies with a comprehensive multimodal intervention (Plasticity-based Adaptive Cognitive Remediation, PACR) composed of auditory, visual, executive function, and social cognition exercises. A large multi-site trial was designed to assess the safety and efficacy of PACR for the treatment cognitive impairment in schizophrenia, and was of the size, methodological rigor, and duration required for regulatory clearance as a medical device by the US Food and Drug Administration (FDA).
Methods: 150 patients with DSM-IV-TR diagnosed schizophrenia from 11 sites across the United States were enrolled into the trial based upon the MATRICS guidelines for cognitive enhancement trials. Patients were stratified based upon baseline cognitive performance on the MATRICS Consensus Cognitive Battery (MCCB), and randomized to receive treatment with 130 one-hour sessions of PACR or a control condition of video games 4-5 times per week over the course of 6 months. PACR is a set of eleven computerized cognitive training exercises designed to improve the speed and accuracy of information processing and neuromodulatory function. Each module involves an adaptive procedure to ensure learning, stimulus sets designed to generalize to real-world function, and a "game" wrapper that encourages controlled engagement of neuromodulatory systems. Treatment response was measured with two co-primary outcome measures: the MCCB for cognition, and the University of California, San Diego Performance Based Skills Assessment (UPSA-2) to measure functional capacity. Each outcome measure was analyzed separately using a mixed effects longitudinal linear model with subject as a random effect and the following fixed effects: site, treatment (PACR and control), week (week 0, 13 and 26), and treatment by week interaction. The primary contrast of interest was PACR versus control at Week 26.
Results: There were no significant differences between groups on demographic or clinical factors at baseline. Patients were aged 43 +/-12 years of age, with MCCB composite scores of 29+/-13 and UPSA-2 scores of 87+/-15. Of the 75 patients randomized to each treatment group, 44 completed treatment with PACR while 58 completed treatment in the computer game condition ($P = .05$). Useful field of view, but not auditory time order judgment, used as positive controls for target engagement, demonstrated significant improvement with PACR compared to the control condition. Changes in MCCB and UPSA-2 were small, and did not differ significantly between treatment groups.
Discussion: In contrast to previous studies assessing the effect of plasticity-based computerized cognitive remediation limited to the auditory system and verbal learning, the current larger study of a more comprehensive program consisting of exercises targeting auditory, visual, executive function, and social cognition did not demonstrate significant improvement in cognitive performance measures. Possible explanations include lack of target engagement, negative interference between auditory and visual training, and overall program efficacy. Additional analyses will focus on demographic and clinical measures that distinguished responders from non-responders, the relationship between "treatment engagement" markers and treatment response, and the reasons for the increased drop-out rate in patients randomized to the PACR intervention.

T59. Long-term safety and durability of effect of aripiprazole lauroxil in a one year schizophrenia extension study

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Background: Aripiprazole lauroxil (AL; ARISTADA™, Alkermes, Inc.) a long-acting injectable (LAI) antipsychotic is approved for the treatment of schizophrenia. We report on efficacy and safety outcomes from a 1-year extension study of long-term treatment with AL.
Methods: This 1-year AL treatment extension study enrolled subjects ($n = 478$, safety population) from two sources: de novo subjects with chronic stable schizophrenia; and rollover subjects who had completed a double-blind, 12-week, placebo-controlled study. De novo subjects received monthly injections of AL 882 mg, and rollover (placebo or AL) subjects received monthly injection with either AL 441 mg or AL 882 mg depending on their assigned treatment in the preceding placebo-controlled study. Subjects who are first assigned to active AL also received daily oral aripiprazole (15 mg) for 3 weeks. The key primary and secondary objectives were to characterize the safety, and to evaluate the durability of therapeutic effect of AL during long-term treatment of subjects with stable schizophrenia.
Results: Of 478 (de novo [$n = 242$], rollover [$n = 236$]) enrolled subjects, 462 had evaluable post-baseline data. At baseline, the mean (SD) age was 39 (12) years, 58% were male, 64% were white, 19% were black, 17% were Asian, and the mean (SD) PANSS total score was 61 (14). High proportions of subjects received ≥ 9 (76%) or ≥ 13 injections (69%) of AL. Of the 110 and 368 patients enrolled in the 441 mg and 882 mg AL study arms, respectively, 32% of patients discontinued in each study arm. Drug-related adverse events were reported in 29 (26%) and 112 (30%) of subjects in the 441 and 882 mg AL arms. Treatment-emergent adverse events observed in $\geq 5\%$ of subjects were insomnia (8%), and increased weight (5%). Serious drug-related adverse events were reported only in the 882 mg arm [3 subjects ($< 1\%$)]. Overall incidence of Parkinsonism and akathisia based on the movement scale were 7% and 5%, respectively. The majority of patients (77%) gained ≤ 5 kg over 16 months, and, at any post-baseline visit, 88 subjects (18%) had a weight increase of $\geq 7\%$. Overall response ($\geq$30% decrease in PANSS total score from baseline to Day 365 or, CGI-I of 2 or 1) was achieved by 51% of subjects at endpoint. Overall, the mean (SD) change from baseline in PANSS total score at study endpoint was -8 (10) and in CGI-S was -0.4 (0.7). The mean (SD) reduction in PANSS total for the placebo to 441 mg AL subject group was -19 (15) and the placebo to 882 mg AL subjects was -12 (12).
Discussion: Treatment of subjects with schizophrenia for ≥ 1 year with AL demonstrated continued safety and additional therapeutic effect. As most safety extension studies have the limitation of selecting for responders, about half the study subjects were treated de novo. The low drop out/high retention of this study supports the high overall safety and tolerability of AL for patients with schizophrenia. Further, the low proportion with weight gain supports the beneficial metabolic profile of the treatment with AL LAI. This study supports continued reduction in symptoms with maintenance AL with over half of completers meeting response criteria.

T60. The importance of vulnerability factors in at-risk mental state of psychosis individuals

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Background: Stressors such as major life events or prevailing stress have been found to influence the onset and course of schizophrenic psychoses.[1] They are thought to exert their effects by interacting with preexisting vulnerability indicators, leading to vicious circles which in turn provoke frank psychoses.[2] Accordingly, the identification of indicators of heightened vulnerability for psychoses and relevant stressors may have important consequences to our understanding of the aetiology of these disorders. Various indicators of heightened vulnerability to psychosis and relevant stressors have been identified. However, it has scarcely been assessed prospectively to what extent these vulnerability factors are indeed more prevalent in individuals with an at-risk mental state (ARMS) for psychosis. Moreover, it remains largely unknown whether any of these contribute to the prediction of psychosis development in ARMS individuals.
Methods: In total, 28 healthy control subjects, 86 first-episode psychosis patients and 127 ARMS individuals were recruited as part of the prospective 'Früherkennung von Psychosen' (FePsy; English: early detection of psychosis) study.[3] The relative frequencies of 13 distinct vulnerability factors for psychoses were compared between healthy control subjects, psychoses patients, those individuals with an ARMS with subsequent transition to psychosis (ARMS-T; $n = 31$) and those without subsequent transition (ARMS-NT; $n = 55$). Survival analyses were conducted to determine associations between time to transition to psychosis and vulnerability factors in all 127 ARMS individuals.
Results: The vulnerability factors "difficulties during school education or vocational training" and "difficulties during employment" were more commonly present in ARMS and first-episode psychosis