family is the 5-HT_6 receptor predominating in brain regions associated with cognition and behavior. The blockade of 5-HT_6 receptors leads to an improvement of cognitive performance in a wide variety of learning and memory paradigms. Our effective lead generation and optimization methods have resulted in a novel, potent and selective 5-HT_6 receptor antagonist SUVN-502 with Ki of 1.71 nM and exhibited antagonist like inhibition with EC_{50} of 0.103 μM. SUVN-502 is effective in animal models of cognition. In microdialysis studies, SUVN-502 enhanced brain acetylcholine and glutamate levels in rat ventral hippocampus and frontal cortex. SUVN-502 has completed all regulatory safety and toxicity studies. The objective of the present investigation is to assess the safety, tolerability and pharmacokinetics of ascending multiple oral doses of SUVN-502 in healthy subjects. **Methods:** A double-blind, placebo-controlled, randomized, ascending multiple-dose study was conducted with healthy male subjects. Adverse events, physical examinations, clinical chemistry examination, hematology, urinalysis and ECG were measured throughout the study. The plasma concentrations of SUVN-502 and its active metabolite M1 of SUVN-502 were analyzed by non-compartmental methods. **Results:** SUVN-502 was generally well tolerated upto highest dose administered. No serious adverse events occurred. No clinically significant changes or study medication related abnormalities were observed with respect to ECG's and laboratory evaluations. There were no clinically significant changes of vital sign parameters. **Conclusions:** SUVN-502 was safe and well tolerated at multiple doses of upto highest dose. SUVN-502 has the potential for best in the class candidate with a favorable pharmacokinetics, safety and toxicology profile. SUVN-502 completed human Phase I clinical studies (both Single Ascending Dose and Multiple Ascending Dose studies) and is ready to enter clinical proof of concept studies for cognitive dysfunction associated with Schizophrenia and Alzheimer's diseases.

P1-254 A SAFETY, TOLERABILITY AND PHARMACOKINETIC STUDY OF DIMEBON IN PATIENTS WITH ALZHEIMER'S DISEASE ALREADY RECEIVING DONEPEZIL

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Background: Dimebon is a novel drug in Phase 3 development for the treatment of Alzheimer's disease (AD). A previous study demonstrated improvement in cognition, function, and behavior in AD patients compared to placebo. The basis for its clinical effects is unknown; preclinical studies suggest dimebon may enhance mitochondrial function in the setting of cellular stress and promote neurite outgrowth. This study evaluated the safety and tolerability of dimebon in AD patients already treated with donepezil. **Methods:** AD patients stable on donepezil (10 mg daily) for at least 60 days and tolerating it well were randomized to dimebon (n=15) or placebo (n=9). The first 14 patients enrolled (9 dimebon, 5 placebo) underwent gradual within- patient dose-titration including 2.5 mg three times daily (TID) x 7 days, then 5.0 mg TID x 7 days, then 10 mg TID x 7 days, then 20 mg TID x 7 days. The next 10 patients (6 dimebon, 4 placebo) underwent more rapid dose-titration from 10 mg TID x 7 days to 20 mg TID x 7 days. Standard safety and tolerability assessments were collected, including PK of dimebon and donepezil. **Results:** All patients completed the treatment period except one placebo patient. No serious adverse events (AEs) or deaths occurred. 13/15 (87%) dimebon and 5/9 (56%) of placebo patients reported an AE. All dimebon AEs were mild in severity except 1 fall (moderate, without loss of consciousness) and 1 neuralgia (severe) both assessed as unrelated to study drug. AEs reported in at least 2 Dimebon patients and more frequently than in the placebo group were: fatigue (3/15, 20% vs. 0%), abdominal distension (2/15, 13% vs. 0%), dizziness (2/15, 13% vs. 1/9, 11%), fall (2/15, 13% vs. 0%), hyperkalemia (2/15, 13% vs. 1/9,11%), and nightmare (2/15,13% vs. 0%). These AEs were mild/moderate and resolved with continued treatment. Those patients who underwent the shortened titration period did not have an increased incidence of AEs as compared to those on the gradual titration. Co-administration of Dimebon and donepezil did not result in an increase in C_{max} or AUC of either drug. **Conclusions:** Dimebon was well-tolerated in this study of AD patients already treated with donepezil.

P1-255 THE TREATMENT COMPLIANCE WITH RIVASTIGMINE PATCH IN CLINICAL PRACTICE VERSUS TRIAL DATA: A CASE SERIES

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Background: Treatment compliance is challenging in many disease settings, and adherence to older oral cholinesterase inhibitors has been particularly poor. Patch therapy may offer benefits over oral treatments, including improved tolerability during initial months of treatment (titration phase) and consequently enhanced compliance. Trial data suggest rivastigmine transdermal patch is well tolerated and that relatively few patients discontinue due to common adverse events such as nausea or vomiting. Our objective was to determine whether low discontinuation rates due to nausea or vomiting, or skin irritation, were also seen in everyday clinical practice. **Methods:** This was a case series comprising patients who were prescribed rivastigmine patch 9.5 mg/24 h at the Central Institute of Mental Health in Mannheim, Germany. Patients were included over a 4 month period. Serious adverse events (SAEs) or discontinuations were recorded, and considered in light of those seen in the large 6-month clinical trial on which rivastigmine patch approval was based (Winblad et al, 2007). Due to the exploratory nature of this investigation, no formal statistics were applied. **Results:** The case series comprised 45 de novo patients receiving rivastigmine patch (mean age 79 years, range 54-95 years). One patient (2%) aged 80 years reported an SAE of paroxysmal atrial fibrillation (no discontinuation). Three discontinuations in patients aged 73 to 84 were reported: one (2%) due to skin irritation and two (4%) due to diarrhea (although one case of diarrhoea was attributed to viral infection). In comparison, in the published clinical trial, 8% of patients on rivastigmine patch 9.5 mg/24 h reported SAEs, 1% withdrew due to gastrointestinal events, and 2% withdrew due to skin irritation. **Conclusions:** Compared with clinical trial data, our centre saw similar rates of withdrawal due to skin irritation or gastrointestinal events. SAEs were not commonly reported. Consistent with published clinical trial, we conclude that discontinuations due to tolerability problems are relatively rare with rivastigmine patch, and that this might contribute to improved treatment compliance.

P1-256 ALOIS: ALZHEIMER'S AND COGNITIVE IMPROVEMENT STUDIES REGISTER, A FREE, ON-LINE REGISTER OF DEMENTIA AND COGNITIVE ENHANCEMENT TRIALS (HTTP://WWW.MEDICINE.OX.AC.UK/ALOIS/)

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Background: Multiple publication of clinical studies makes it difficult for researchers and the public to identify unique studies from reference lists and bibliographic searches. The Cochrane Dementia and Cognitive Improvement Group's Specialised Register has recently been extended to include reports of all trials of prevention strategies and cognitive enhancers, as well as of treatment and rehabilitation in dementia. It has also been made freely available on-line to the community of researchers and the public (http://www.medicine.ox.ac.uk/alois/). The objective of this project is to create and maintain a comprehensive, up-to-date study-based registry of all trials and to make this register freely available on-line. **Methods:** We developed highly sensitive search strategies for the retrieval of citations of studies of treatment, prevention, and cognitive enhancement. These were then run in major databases, trial registers and grey literature sources. Each RCT was read and data extracted. Duplicate publications were linked to the same trial record. Each record was linked to a published Cochrane review where appropriate. A user friendly, web interface for searching the database was created. **Results:** ALOIS contains records of 2,525 randomized