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MEETING ABSTRACT

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A prospective, randomized, double-blind, placebo-controlled trial to investigate the effects of dextroamphetamine or zolpidem on attention and reaction time in healthy males

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Background: Driving and handling of machinery under the influence of medicines may be associated with a significant risk. However, legally acceptable intakes regarding the use of medicines are not defined and a subjective assessment by an authorized physician determines the individual physical and mental suitability. Thus, in contrast to established legal limits that exist for alcohol consumption, there is a gap in the standardization of tests and in the potentially acceptable concentration of medicines in the body to support physician's discrimination of the status of handling ability. This study has been designed to investigate (i) whether the changes in psychomotoric performance can be objectively measured in healthy people after intake of model drugs that are known to impair or enhance subject's concentration, and (ii) whether changes in psychomotoric performance are related to drug concentration in the body in order to establish minimally acceptable plasma concentrations.

Methods: In this randomized and double-blind phase I study, the effect of single doses of the investigational drug was analyzed in 60 healthy males allocated to one of 3 parallel groups: 20 subjects received dextroamphetamine (30 mg), zolpidem (5 mg) or placebo. Differences in reaction time from baseline were assessed with a computer test (Psytest; continuous attention, reaction time and working memory) at 3 h and 8 h after intake of the medication. Concentrations of the biologically active substances in blood plasma and in body sweat were measured. The subjective drug effect was assessed with the Drug Effect Questionnaire (DEQ) and the Barratt Impulsiveness Scale (BIS-15) questionnaire.

Results: Four out of 48 participants reported tachycardia and/or palpitations as adverse reactions. In this subgroup, mean arterial pressure (MAP) increased from 92 ± 5 mmHg (mean ± SD) at pre-dose to 106 ± 10 mmHg and pulse rate from 70 ± 21 bpm to 75 ± 28 bpm at three hours after dosing, respectively. This was paralleled by an increase in average error rate in the Psytest® from 2.5 ± 2.1 to 2.8 ± 2.1 and a decrease in omission rate from 8.3 ± 6.2 to 5.5 ± 3.9 omissions per test, respectively.

Discussion: Development of standardized methods to characterize psychomotoric effects of medicines may help to establish guidelines for handling of machinery and concomitant use of drugs. An acceptable upper limit of drug concentration that does not affect individual's physical or mental performance may be defined by using appropriate standardized tests during drug development.

Keywords: cognition – psychomotoric performance – reaction time – attention – Psytest

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