A RANDOMIZED, DOUBLE BLIND, PLACEBO- CONTROLLED EFFICACY STUDY OF HIGH-DOSE BACLOFEN IN ALCOHOL DEPENDENT PATIENTS: THE ALPADIR STUDY

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This study assessed the efficacy and safety of baclofen at the target dose of 180 mg/day for the maintenance of abstinence (primary endpoint) and the reduction of alcohol consumption (secondary endpoint) in alcohol dependent patients.

320 adult patients (158 baclofen and 162 placebo) were randomized after alcohol detoxification. After a 7-week titration, the maintenance dose was provided for 17 weeks, then tapered and stopped in 2 weeks. The mean baseline alcohol consumption was 95.5 g/day for baclofen patients and 93.6 g/day for placebo patients.

130 patients (40.6%) discontinued prematurely the study (59 baclofen and 71 placebo). In the baclofen group, the mean maintenance daily dose was 153.5 mg ± 40.5 (65.6% of patients at target dose of 180 mg). The percentage of abstinent patients from month 2 to month 6 (after a 4 week grace period), was low in both groups (baclofen: 11.9%; placebo: 10.5%), and showed no between-group difference (OR 1.20; 95%CI 0.58 to 2.50; p=0.619). An important reduction of alcohol consumption was observed at month 6 in both groups in terms of total alcohol consumption (TAC): -55.1 g/day for baclofen and -44.2 g/day for placebo, with no significant between-group difference (mean difference: 10.9 g/day; 95%CI -23.7 to 1.9,p=0.095). In the subgroup of patients with high drinking risk level (mean baseline TAC: baclofen patients: 123.6 g/day and placebo patients: 118.9 g/day), alcohol reduction was more important: -89.3 g/day for baclofen and -73.7 g/day for placebo, with no significant between-group difference (mean difference: 15.6 g/day, p=0.089). The OCDS score decrease was significantly greater in baclofen patients at month 6 (p=0.017). Other secondary endpoints (number of heavy drinking days per month, time to first drink/heavy drink, drinking risk level response, CGI, HAD and AlQoL9 scores, GGT and CDT) were all numerically in favor of baclofen but without reaching statistical significance.

Adverse events were more common with baclofen (somnolence, asthenia, dizziness and insomnia). No major safety concern was observed.

The reduction of alcohol consumption observed with baclofen was of clinical significance especially in high drinking risk level patients. A possible shift of patient's expectancies from abstinence towards reduction in the current French media context could explain low abstinence outcomes in this study.