Titre du résumé

Simultaneous blockade of α1b-adrenergic and 5HT2A-serotonergic receptors for the treatment of alcohol use disorder. Cocktail: a randomized, placebo-controlled proof-of-concept phase 2 trial.

Coordonnées des co-auteurs

Cocktail study group

Coordonnées de l'auteur principal qui sera le contact pour le Congrès de l'ALBATROS

H.-J. Aubin

AP-HP, Hôpitaux Universitaires Paris-Saclay, Inserm, CESP, 94800, Villejuif, France

Description précise des objectifs

The objective of the Cocktail study was to assess the efficacy and safety of a 12-week with the combination of cyproheptadine (C) and prazosin (P) (low dose C=8 mg/d and P=5mg/d; high dose C=12 mg/d and P=10mg/d) over placebo on the reduction of total alcohol consumption (TAC).

Matériel et méthodes

Main inclusion criteria: severe alcohol use disorder (AUD) (DSM5) and a WHO high-risk drinking level (RDL). Primary endpoint: change from baseline to month 3 in TAC.

Résultats et conclusions

154 subjects were randomized in the placebo group (N=54), the low dose group (LDG, N=54) and the high dose group (HDG, N=46). The mixed model for repeated measures failed to show a significant time*treatment effect on TAC change (p=0.128, ITT). However, Bayes-Factor was >6, allowing post-hoc analysis. The dose-effect relationship was significant in the per-protocol but not the ITT cohort. ITT TAC change was wider in the HDG vs. placebo (19.9 g/d, p=0.046, d=0.40). Subjects decreasing of at least 2 RDL were 20% (placebo) and 40% (HDG) (p=0.20), showing a number-needed-to-treat (NNT)=5 for the HDG. HDD change vs. placebo was significantly wider only in the HDG in the per-protocol cohort (5.74 HDD, p=0.024, d=0.45). There was a significant ITT age-adjusted increase of days abstinent in the HDG vs. placebo (p=0.011, d=0.53). HDG vs. placebo days abstinent change was 4.12 days (p=0.36, d=0.53). ITT OCDS and BDI score change showed no significant between-group difference; HDG vs. placebo OCDS score change was 1.60 (d=0.22), and HDG vs. placebo BDI score change was 1.58 (d=0.36). The most frequently reported treatment-emergent adverse events were vertigo, fatigue, dry mouth in the HDG. No serious adverse event was recorded in the HDG. In conclusion, even though this phase-2 study was underpowered, we consider that the results validate the concept of simultaneous blockade of α1 noradrenergic and 5HT2A-serotonergic receptors for the treatment of AUD.

Liens d'intérêt

Dr Aubin reported being member of advisory boards or DSMB for Bioprojet, CV Sciences, and Kinnov therapeutics, and has received sponsorship to attend scientific meetings, speaker honoraria or consultancy fees from Bioprojet, D&A Pharma, Ethypharm, Kinnov

Pharmaceuticals and Lundbeck. He is also member of the American Society of Clinical Psychopharmacology's Alcohol Clinical Trials Initiative (ACTIVE), which was supported in the last three years by Alkermes, Amygdala Neurosciences, Arbor Pharmaceuticals, Ethypharm, Indivior, Lundbeck, Mitsubishi, and Otsuka.
The study presented here was sponsored by Kinnov Therapeutics.