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Clinical Trial Synopsis

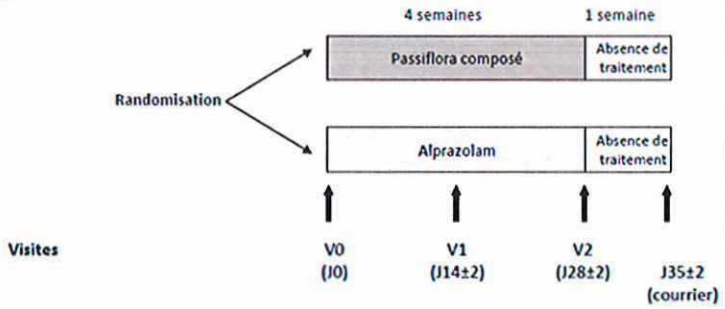
EudraCT number	2017-002263-17
Trial identification	
Full title of the study	Efficacy and safety of Passiflora Compose in patients newly diagnosed with adjustment disorder with anxiety, as first-line treatment, compared to alprazolam *(Efficacité et tolérance de Passiflora composé dans l'anxiété réactionnelle récente, en première intention, en comparaison de l'alprazolam.)*
Abbreviated title	PASSIANCE
Sponsor protocol code	BRN-C-2017-01
Investigational medicinal products (IMP identification)	Homeopathic medicinal product Passiflora Composé®
Sponsors	
Sponsor	BOIRON Laboratories
Sponsor Address	2 Avenue de l'Ouest Lyonnais 69510 Messimy FRANCE
Study Contact	Isabelle Chanel, Research & Development & Scientific & Medical Affairs Director BOIRON Laboratories ✉ isabelle.chanel@boiron.fr
Scientific Contact	Dr Alain GIACOMINO 37420-FR
Research Location and Sites	FR – 16 investigative sites
Member State Concerned	ANSM - France
Results Information	
Actual start date of recruitment	12 JAN 2018
Global end of trial date	(*date of the end of participation of the last person included in the research*) 27 JUN 2019
Planned number of subjects to be included- Country	282 (France)
Number of subjects enrolled - Country	104 (France)
Clinical Trial Phase	III

Clinical Trial duration	18 months
Publication reference	None.
General information about the trial	
Clinical Trial Type:	Therapeutic confirmatory
Design of the trial	Controlled – Randomized – Double blind - Parallel group – Comparator (Alprazolam)
Medical Condition	Adjustment disorder with anxiety *(Anxieté réactionelle récente)*
Main objective of the trial	The main objective of the study was to demonstrate the non-inferiority of Passiflora Composé (PC) in comparison to Alprazolam (APZ) in anxiety disorders after 4 weeks of treatment (efficacy objective).
Secondary's Objectives of the trial	The secondary objectives were : - **Efficacy** : o To evaluate the rate of responders to the treatment for anxiety or in remission of anxiety ; o to evaluate the evolution of anxiety component during treatment ; o to evaluate the evolution of the sleep disorders during treatment ; - **Safety** : o to evaluate changing in prescription during the follow-up ; o to evaluate the concomitant use of medicine ; o to evaluate the safety drug ; o to evaluate the rebound effect after stopping drug ; - **Others** : o to evaluate the evolution of the functional capacity of the patient during treatment ; o to evaluate the general impression of the doctor and of the patient for symptoms and the evolution of symptoms ; o to evaluate the treatment compliance.
Principal Inclusion Criteria	- Age ≥ 18 and ≤ 70 years ; - Patient having adjustment disorder with anxiety or trait anxiety ; - Hamilton score scale-anxiety (HAM-A) ≥ 18 at inclusion ; - Recent anxiety (inferior or equals to 3 months), with no pharmacological or psychological treatment ; - Disorders needing prescription of anxiolytic treatment with homeopathic medicine or benzodiazepine according to the doctor ; - Patient unable to understand information about study , to read information sheet and accepting to sign the informed consent.
Principal Exclusion Criteria	- Patient with anxiety disorder other than adjustment disorder with anxiety, major depressive disorder or all other mental pathology ; - Anxiety related to bereavement ; - Anxiety felt more than 3 months ; - Patient treated for anxiety with psychotropic substances or with psychotherapy in the last 3 months ; - History of alcohol abuse or drug abuse ; - Pregnancy or lactation, woman of childbearing potential not using a medically acceptable, highly effective method of birth control ; - Known hypersensitivity to one of the components of the study or contra-indication to one of the treatments ;

	- Participation in another clinical study or at exclusion period for another clinical trial
Trial Status:	Completed
Statistical Analysis Description	Details of the statistical methods are presented in the statistical analysis plan (version 1.0 - 12/11/2019). The analysis was performed with SAS software version 9.4 or later. The risk of first kind (α) was set at 5% in a two-sided situation, except for the non-inferiority analysis of the main objective where it was set at 2.5% in a one-sided situation. The inferential analyses were preceded by descriptive analyses. Quantitative variables were described by the number of values filled in, the number of missing data, the mean, the standard deviation, the median, the 1st quartile and 3rd quartile, the 95% confidence interval (IC95%), the minimum and the maximum. Categorical variables were described by the number of values filled in, the number of missing values, the frequency and the percentage per modality.

Summary – research Findings

The main objective of the PASSIANCE study was to demonstrate the non-inferiority of Passiflora Composé (PC) in comparison to Alprazolam (APZ) in anxiety disorders after 4 weeks of treatment (efficacy objective).



During the course of this study, the recruitment target was not met within the initial timeframe (8 months). Despite an extension of the recruitment period of 9 months, 104 patients were included instead of the 282 initially planned. The recruitment period was not extended again, and it was decided to conduct analysis with available data.

Demographic and other characteristics at inclusion showed no major difference between the two groups, PC and APZ. It was noted that Generalized Anxiety Disorder, representing the previous anxiety state, was more present in the PC group than in the APZ group but that on the other hand reactive anxiety was also more present in the PC group than in the APZ group at inclusion.
For the total HAM-A score or change in HAM-A score between V0 and V2, in the PP population, with the LOCF model (main analysis of the primary objective), **the non-inferiority of PC versus APZ was not demonstrated** because the upper bound of the 95% CI was greater than the non-inferiority threshold set at 2.8. Sensitivity analyses confirmed the result of the primary analysis.

Regarding the secondary endpoints, which were studied on an exploratory basis, a statistically significant difference was observed between V0 and V2 for the *HAM-A psychic sub-score* and a more favorable evolution of functional capacity for the PC group between V0 and V2. It was also be noted that a statistically significant difference was observed at V2 for the rate of patients in remission, but only in the ITT population.

The results related to clinical impression are "globally" more in favor of the APZ group than the PC group at V2, the results on the CGI-A scale being slightly more favorable to the PC group at V1.
Regarding compliance, the number of patients classified as "*good compliance*" was higher in the PC group than in the APZ group.

None of the treatments showed any specific safety issues. Although the percentage of patients with at least one AE was twice as high in the APZ group as in the PC group, the difference in occurrence was not statistically significant at the 5% level (p=0.0873). Similarly, no statistically significant difference between the PC and APZ groups was found for patients who had at least one AE by type, relationship to treatment and consequence on continuation of treatment.
Very few prohibited concomitant treatments were taken during the study in both groups. The same is true for treatments with a known effect on the central nervous system.
One SAE was reported in the APZ group (carbon monoxide poisoning). It resulted in the death of the patient but was not considered to be related to the treatment.

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Name & Function Signature : Date of Transmission	Isabelle Chanel Director of Research & Development & Scientific & Medical Affairs. 08 MAR 2023