Clinical Trial Synopsis

EudraCT number	**2010-020810-27**
Trial identification	
Full title of the study	Multicenter randomized controlled clinical trial evaluating the efficacy of two homeopathic medicines (Dopamine 5 CH and Serotoninum muriaticum 5 CH) in children with ADHD aged 3 to 7 years (6 years / 11 months). *(Essai clinique contrôlé randomisé, multicentrique, évaluant l'efficacité de deux médicaments homéopathiques (Dopamine 5 CH et Serotoninum muriaticum 5 CH) chez l'enfant TDAH âgé de 3 à 7 ans (6 ans et 11 mois))*
Abbreviated title	**HYP-HOPE**
Sponsor protocol code	IB-08-03
Investigational medicinal products (IMP identification)	Homeopathic medicinal products: Dopamine 5 CH Serotoninum muriaticum 5 CH
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 Marie-France LE HEUZEY 75019- FR
Research Location and Sites	FR – 22 investigative sites (pediatric psychiatrists and neurologists)
Member State Concerned	AFSSAPS (ANSM) - France
Results Information	
Actual start date of recruitment	21 MAR 2011
Global end of trial date	(*date of the end of participation of the last person included in the research*) 03 JUL 2013
Planned number of subjects to be included- Country	112 (France)
Number of subjects enrolled - Country	97 (France)
Clinical Trial Phase	III

Clinical Trial duration	28 months
Publication reference	None
General information about the trial	
Clinical Trial Type:	Therapeutic confirmatory
Design of the trial	Multicentric - Controlled – Randomized –Double blind - Parallel group - Comparator (Placebo)
Medical Condition	Psychiatric disorders: Attention-Deficit/Hyperactivity Disorder (ADHD)
Main objective of the trial	The main objective of the study was to evaluate the efficacy of the combination of Dopamine 5 CH and Serotoninum muriaticum 5 CH, administered for 90 days, in children aged 3 to less than 7 years (on the day of inclusion) who have been diagnosed with **ADHD**.
Secondary's Objectives of the trial	The secondary objectives were to - evaluate the efficacy of the combination of Dopamine 5 CH and Serotoninum muriaticum 5 CH administered for 30 days on ADHD in children aged 3 to under 7 years (on the day of inclusion). - evaluate the improvement of the child's ADHD according to the investigator's judgment - assess changes in the child's sleep quality - assess the tolerance of the treatment
Principal Inclusion Criteria	o Male or female, o At least 3 years old and less than 7 years old on the day of inclusion in the study (6 years and 11 months), o Not receiving psychostimulant or psychotropic treatment on the day of inclusion, nor in the 3 months preceding inclusion, o With a diagnosis of ADHD established by a child psychiatrist on the basis of DSM-IV-R criteria, validated one by one during the inclusion visit, o T>65 on the Conners Global Index for Parents (CGI-P) o Parent(s) or legal guardian(s) understand and read French, o Written consent by the holders of parental authority (or the sole holder of full parental authority), o Parent(s) or holder(s) of parental authority affiliated to a Social Security system. See **Section E.3** for others
Principal Exclusion Criteria	o Mental retardation, o Pervasive developmental disorders including autism, o Characterized mood disorders, o Significant sensory deficit, o Receiving or likely to receive during the trial treatments not authorized by the protocol (psychotropic drugs, including methylphenidate (MPH) and other psychostimulants, other homeopathic treatment for ADHD)

	○ Concurrent chronic progressive disease (e.g., epilepsy, neurological or hormonal disease, asthma on long-term corticosteroid therapy), See **Section E.3** for others
Trial Status:	**Completed**
Statistical Analysis Description	Quantitative variables were described in terms of numbers, number of missing values, mean, standard deviation, extremes and median. Categorical variables were described in terms of number and percentage of data completed. Efficacy criteria were analyzed using the Chi-2 test or Fisher's exact test (if there were insufficient numbers) for categorical variables, the Mann Whitney test for ordinal variables, and the Student t test or Wilcoxon exact test (if distributions were not normal) for quantitative variables. All statistical tests were two-tailed, at the 0.05 significance level. - **Analysis Populations**: *FAS* (Full Analysis Set): all children who received at least one dose of treatment and had an on-treatment efficacy assessment (On-treatment = discontinuation of treatment less than 7 days before the primary endpoint assessment). *PP* (*Per Protocol*): all children who received at least one dose of treatment, had a treatment efficacy assessment and did not have major protocol deviations. *Tolerance*: all children who took at least one dose of study product. **- Efficacy:** Primary endpoint: The primary endpoint was the percentage of children responding to treatment after 90 days of treatment (D90). The percentages of responders were compared between the two groups by a Chi-2 test or Fisher's exact test (if insufficient numbers). This criterion was analyzed on the FAS and PP populations. The analysis of the two populations was the primary analysis. Other efficacy endpoints: The other efficacy endpoints were compared between the two treatment groups according to the general methodology defined. - **Tolerance:** Adverse events (AEs) including "treatment emergent" AEs were tabulated by organ system and preferred term (MedDRA dictionary). Body mass index (BMI) was calculated at each visit. Safety parameters were analyzed descriptively.

Summary – research Findings

This study did not allow to conclude on the efficacy of the combination of Dopamine 5 CH and Serotoninum muriaticum 5 CH compared to placebo, in the management of children under 7 years of age with diagnosed ADHD.
Nevertheless, we observe, according to a validated scale of assessment of hyperactivity by parents (Conners Global Index - Parents) a percentage of response to treatment of 27.3% whatever the

treatment group. Moreover, the investigators evaluated an improvement in almost half of the cases (48.9%) whatever the group studied after 3 months of treatment (global evaluation scale by the investigator).
Knowing that there is no drug treatment indicated in this pathology for children under 6 years of age in France, and considering its excellent tolerance, this combination of homeopathic drugs may represent a therapeutic alternative for health professionals and for parents reluctant to use other treatments. It could be associated with an accompanying therapy.

Finally, this study conducted in children under 7 years of age allowed to conclude that the initiation of Dopamine 5 CH and Serotoninum muriaticum 5 CH as a first-line treatment does not represent a loss of chance, within the framework of appropriate medical follow-up. It could even allow a gradual transition to a heavier drug treatment, if necessary.

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