Clinical Trial Synopsis

EudraCT number	**2009-016959-21**
Trial identification	
Full title of the study	Randomized, controlled, double-blind, placebo-controlled study of the efficacy of the homeopathic product BRN-01 in the treatment of hot flashes in menopausal women *(Etude contrôlée, randomisée en double aveugle versus placebo de l'efficacité de la spécialité homéopathique BRN-01 dans le traitement des bouffées de chaleur de la femme ménopausée)*
Abbreviated title	LHO
Sponsor protocol code	BRN-C-2009-03
Investigational medicinal products (IMP identification)	Homeopathic medicinal product BRN-01 (ACTHEANE®) Actaea racemosa 4CH Arnica montana 4CH, Glonoinum 4CH, Lachesis mutus 5CH Sanguinaria canadensis 4CH
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	Pr Jean Claude COLAU 92151- FR
Research Location and Sites	FR – 35 investigative sites (gynecologists)
Member State Concerned	AFSSAPS (ANSM) - France
Results Information	
Actual start date of recruitment	03 JUN 2010
Global end of trial date	(*date of the end of participation of the last person included in the research*) 21 JUL 2011
Planned number of subjects to be included- Country	120 (France)
Number of subjects enrolled - Country	108 (France)
Clinical Trial Phase	III
Clinical Trial duration	13 months
Publication reference	Colau JC, Vincent S, Marijnen P, Allaert FA. Efficacy of a non-hormonal treatment, BRN-01, on menopausal hot flashes: a multicenter,

	randomized, double-blind, placebo-controlled trial. Drugs R D. 2012 Sep 1;12(3):107-19. doi: 10.2165/11640240-000000000-00000. PMID: 22852580; PMCID: PMC3585763. https://pubmed.ncbi.nlm.nih.gov/22852580/
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	Menopausal hot flashes (HFS)
Main objective of the trial	The main objective of this study was to evaluate the efficacy of the homeopathic treatment BRN-01 (ACTHEANE®) versus placebo in the **treatment of hot flashes** experienced by menopausal women. This efficacy was evaluated by the reduction of the hot flash score (HFS).
Secondary's Objectives of the trial	The secondary objectives were to assess: * The improvement in quality of life by the HFRDIS score (Hot Flash Related Daily Interference Scale) * The number of nocturnal awakenings related to night sweats * The time to a significant reduction in the hot flash intensity score * The reduction of the discomfort induced by hot flashes * The tolerance of the treatment * The compliance of the subjects * The evolution of the average dosage during the study * The satisfaction with the homeopathic trial treatment
Principal Inclusion Criteria	Female subject who: * consulted spontaneously for hot flashes that started less than 2 years ago * whose hot flashes had an impact on social or professional life of at least 40 mm on a visual analog scale of 0 to 100 mm * whose frequency of hot flashes was at least 5 flashes per day on average during the 48 hours preceding the inclusion consultation * whose hot flashes were related to physiological menopause only * who agreed not to use any other therapeutic strategy for hot flashes other than the one provided for in the protocol for the duration of the clinical trial
Principal Exclusion Criteria	Female subject who: * was receiving or had ever received hormone replacement therapy (HRT); * was taking or had taken in the last 15 days a β-alanine treatment (Abufène®); * was taking phytoestrogens, food supplements or vitamin E to relieve hot flashes and/or vasomotor disorders or having taken them in the last 15 days; * was taking or had taken in the last week homeopathic treatments for the relief of hot flashes and/or vasomotor disorders or likely to interact with the study treatment

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	* were undergoing or had undergone acupuncture for the relief of hot flashes in the last 15 days; * had a menopause that had been artificially induced by surgery, chemotherapy or radiotherapy * had hot flashes of iatrogenic origin * presented with an associated pathology that may cause hot flashes * presented with one of the following contraindications - known hypersensitivity to one of the components of the homeopathic medicine under study; - known intolerance to galactose or fructose - known deficiency of Lapp lactase, sucrase-isomaltase; - known glucose or galactose malabsorption syndrome
Trial Status:	**Completed**
Statistical Analysis Description	The statistical analysis was carried out on the intent-to-treat (ITT) population, defined as all patients who took at least one dose of the study treatment and had a least one post-enrollment evaluation. In the case of missing data, the analysis took into account the last evaluation available according to the last-observation-carried-forward (LOCF) technique. The safety analysis was carried out on all patients who took at least one dose of the study treatment. Quantitative data are described as the number, mean, and SD. Qualitative data are described as the absolute and relative frequencies with 95% confidence intervals (CIs). Comparisons of means were carried out by analysis of variance (ANOVA) or by using the Kruskal-Wallis test if the distribution was not normal. Comparisons of percentages were carried out using the w2 test or Fisher's exact test if the conditions for use of the w2 test were not fulfilled. Where appropriate, comparisons over time were performed using the Student's t-test. All statistical analyses were carried out using SAS (version 9.2) software, with a level of statistical significance fixed at alpha = 0.05. For details see Colau *et al.*

Summary – research Findings

Homeopathic medicines have a place among the non-hormonal therapies for the treatment of hot flashes during the menopause.
The objective of this study was to evaluate the efficacy of the nonhormonal treatment BRN-01 (ACTHEANE®) in reducing **hot flashes** in menopausal women.
This was a multicenter, randomized, double-blind, placebo controlled study carried out between June 2010 and July 2011. The study was conducted in 35 active centers in France (gynecologists in private practice). One hundred and eight menopausal women, ± 50 years of age, were enrolled in the study. The eligibility criteria included menopause for <24 months and ± 5 hot flashes per day with a significant negative effect on the women's professional and/or personal life.
Treatment was either BRN-01 tablets (ACTHEANE®), a registered homeopathic medicine containing Actaea racemosa (4CH), Arnica montana (4CH), Glonoinum (4CH), Lachesis mutus (5CH), and Sanguinaria canadensis (4CH), or identical placebo tablets, prepared by Laboratoires Boiron according to European Pharmacopoeia standards. Oral treatment (2 to 4 tablets per day) was started on day 3 after study enrollment and was continued for 12 weeks.

The main outcome measure was the hot flash score (HFS) compared before, during, and after treatment. Secondary outcome criteria were the quality of life (QoL) [measured using the Hot Flash Related Daily Interference Scale (HFRDIS)], severity of symptoms (measured using the Menopause Rating Scale), evolution of the mean dosage, and compliance.
All adverse events (AEs) were recorded.

One hundred and one women were included in the final analysis (intent-to-treat population: BRN-01, n = 50; placebo, n = 51). The global HFS over the 12 weeks, assessed as the area under the curve (AUC) adjusted for baseline values, was significantly lower in the BRN-01 group than in the placebo group (mean –SD 88.2 – 6.5 versus 107.2 – 6.4; p = 0.0411). BRN-01 was well tolerated; the frequency of AEs was similar in the two treatment groups, and no serious AEs were attributable to BRN-01.

In conclusion, BRN-01 seemed to have a significant effect on the HFS, compared with placebo. According to the results of this clinical trial, BRN-01 may be considered a new therapeutic option with a safe profile for hot flashes in menopausal women who do not want or are not able to take hormone replacement therapy or other recognized treatments for this indication.
For details see Colau *et al*, 2012

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