BOIRON
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Clinical Trial Synopsis

EudraCT number	2009-015722-11
Trial identification	
Full title of the study	Pilot study evaluating the value of Ruta graveolens 9 CH in patients with advanced cancer. (*Etude pilote évaluant l'intérêt de Ruta graveolens 9 CH chez des patients atteints de cancer à un stade avancé*)
Abbreviated title	ONCOMEO
Sponsor protocol code	BRN-C-2009-02
Investigational medicinal products (IMP identification)	Homeopathic medicinal product: Ruta graveolens 9 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	Pr Gilles FREYER 69495-FR
Research Location and Sites	FR – 1 investigative site
Member State Concerned	AFSSAPS (ANSM) - France
Results Information	
Actual start date of recruitment	15 MAY 2010
Global end of trial date	(*date of the end of participation of the last person included in the research*) 26 SEPT 2011
Planned number of subjects to be included- Country	30 (France)
Number of subjects enrolled - Country	31 (France)
Clinical Trial Phase	II
Clinical Trial duration	16 months
Publication reference	Freyer G, You B, Villet S, Tartas S, Fournel-Federico C, Trillet-Lenoir V, Hamizi S, Colomban O, Chavernoz N, Falandry C. Open-label uncontrolled pilot study to evaluate complementary therapy with Ruta graveolens 9c in patients with advanced cancer. **Homeopathy**. 2014 Oct;103(4):232-8. doi: 10.1016/j.homp.2014.06.001. Epub 2014 Jul 30. PMID: 25439039. https://pubmed.ncbi.nlm.nih.gov/25439039/

General information about the trial	
Clinical Trial Type:	Pilot
Design of the trial	Pilot – Monocentric - Open-label – Uncontrolled.
Medical Condition	Advanced cancer
Main objective of the trial	The main objective of this study was to evaluate the tumor response induced by Ruta graveolens 9 CH in patients with locally advanced or metastatic solid tumors who have already received all treatments defined standard in the pathology considered. In patients with tumor progression on imaging at the time of inclusion (calculated on the basis of the most recent evaluations), treatment that results in a tumor response of any duration (best tumor response defined according to RECIST criteria) or tumor stabilization lasting more than two months will be considered "beneficial". For patients with tumor stabilization on imaging at inclusion (but progressive markers), treatment that results in a tumor response of any duration (best tumor response as defined by RECIST criteria) will be considered "beneficial".
Secondary's Objectives of the trial	The secondary objectives were: - To evaluate the proportion of patients who showed an improvement in their WHO performance status (PS) during the study, as well as the average duration of this improvement - To evaluate the evolution of tumor markers every 4 weeks, when relevant, in patients treated with Ruta graveolens 9 CH - To measure the evolution of the quality of life of patients treated with Ruta graveolens 9 CH - To evaluate the tolerance of Ruta Graveolens 9 CH - To evaluate the overall survival of patients treated with Ruta graveolens 9 CH - To evaluate the progression-free survival of patients treated with Ruta graveolens 9 CH - To evaluate the compliance of Ruta graveolens 9 CH If a second cohort of patients was treated with Phenacetinum 4 CH, an evaluation of the treatment according to the same objectives was scheduled.
Principal Inclusion Criteria	- Age ≥ 18 years, - Life expectancy ≥ 3 months, - Performance by WHO status ≥ 2, - Histologically proven solid cancer tumor, locally advanced, not amenable to curative locoregional therapy or metastatic, - Measurable lesion according to RECIST criteria, - Progressive tumor disease according to the investigator's criteria (increase in tumor lesion size on imaging and/or increase in a tumor marker previously correlated with tumor mass and/or deterioration of the patient's clinical condition attributable to the evolution of his tumor pathology), - Radiological assessment evaluating the tumor disease, performed in the radiology department of the CHLS (France) and dated less than one month ago, - Biological tests less than two weeks old, including, if necessary, the

	evaluation of tumor markers, - Patient who has received all reference treatments for his tumor disease, - Patient able to participate in the follow-up of his treatment, See **Section E.3** for others
Principal Exclusion Criteria	- Anti-cancer treatment in the month prior to inclusion and throughout the protocol treatment, - Tumor of the hematopoietic system, - Uncontrolled brain metastases, carcinomatous meningitis, - Concomitant treatment with immunosuppressive drugs (corticosteroids, etc.) for more than one week, - Concomitant treatment with other alternative medicines, - Participation in another clinical trial (except observational studies), - Patient of childbearing age without effective contraception, - Pregnant or breast-feeding woman, - Serious psychiatric pathology, See **Section E.3** for others
Trial Status:	Completed
Statistical Analysis Description	Continuous variables were expressed as their mean, median, standard deviation (SD), or minimum and maximum. Discrete variables were expressed as group size, percentage and 95% confidence intervals (95%CI). The evolution of variables measured at repeated intervals was represented as means ± SD and percentages. The two global criteria, QoL and anxiety - depression, were compared using the non-parametric Wilcoxon's test. Comparisons were carried out between day 1 and the EOS, and between day 1 and weeks 8 and 16. If there were missing data, analysis took into account the last evaluation available according to the last-observation-carried-forward (LOCF) method. Continuous variables were compared with Wilcoxon's test and discrete variables with the chi2 test. The chi2 test was also used to compare the evolution of RECIST criteria. All tests were performed with an alpha-risk fixed at 5%, with the level of statistical significance set at $P < 0.05$. All statistical analyses were carried out using R2.14 software.

Summary – research Findings

Patients with advanced metastatic disease are often treated aggressively with multiple lines of chemotherapy, even in the last month of life. The benefit of such an approach remains uncertain.

The objective of the study was to investigate whether Ruta graveolens 9 CH homeopathic medicine can improve quality of life (QoL) and tumor progression in patients with advanced cancer.
This was a single-center, open-label, uncontrolled, pilot study.
Patients (>18-years, life-expectancy ‡3 months, performance status £2) with locally advanced solid tumors or metastases, previously treated with all available standard anti-cancer treatments were recruited. Oral treatment consisted of two 1-mL ampoules of Ruta graveolens 9CH given daily for a minimum of 8 weeks, or until tumor and/or clinical progression. Primary outcome was QoL measured using the EORTC QLQ-C30 questionnaire. Secondary outcome measures were anxiety/ depression measured using the Hospital Anxiety and Depression Scale (HADS), WHO performance status (PS), tumor progression assessed using RECIST criteria and tumor markers, survival, and tolerance.
Thirty-one patients were included (mean age: 64.3 years). Mean duration of treatment was 3.3 months (median: 2.1). QoL global health status improved significantly between baseline and week 8 ($P < 0.001$) and week 16 ($P = 0.035$) but was at the limit of significance ($P = 0.057$) at the end of the study. There was no significant change in anxiety/ depression or PS during treatment. Ruta

graveolens 9CH had no obvious effect on tumor progression. Median survival was 6.7months [95%CI: 4.8e14.9]. Ruta graveolens 9 CH was well-tolerated. Some patients treated with Ruta graveolens 9 CH had a transitory improvement in QoL, but the effectiveness of this treatment remains to be confirmed in further studies.

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Name & Function Signature : Date of Transmission	Isabelle Chanel Director of Research & Development & Scientific & Medical Affairs. 27 MAR 2023