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Prescribing decisions should be made based on the approved package insert in the country of prescription.

Sponsor / Company: Sanofi **Drug substance(s):** SSR411298	**Study Identifiers:** NCT01439919, U1111-1115-3390, 2011-002557-56 **Study code:** ACT11705

Title of the study:

A randomized, double-blind, parallel-group, placebo-controlled study to assess the clinical benefit of SSR411298 as adjunctive treatment for persistent cancer pain

Study center(s): 2 centers in US

Study period:

Date first patient enrolled: 11 January 2012

Date last patient completed: 14 February 2012

Phase of development: 2a

Objectives:

Primary objective

• To evaluate the efficacy of SSR411298 200 mg daily compared to placebo as adjunctive treatment for persistent cancer pain, as measured by the change from baseline (baseline = average pain intensity between Day -7 and Day -1 to end of treatment (end of treatment = average pain intensity during Week 4) in the Numeric Rating Scale (NRS)

Secondary objectives

• To evaluate the efficacy of SSR411298 200 mg daily compared to placebo as adjunctive treatment for persistent cancer pain, as measured by a variety of secondary efficacy endpoints (see below);

• To evaluate the tolerability and safety of SSR411298 as adjunctive treatment for persistent cancer pain;

• To characterize patient disease, in terms of cancer, cancer treatment, cancer pain and cancer pain treatment;

• To evaluate the pharmacokinetic (PK) exposure of SSR411298 as adjunctive treatment for persistent cancer pain;

• To assess endocannabinoid plasma concentrations.

Methodology:

Randomized, double-blind, parallel-group, placebo-controlled study

Number of patients:	Planned: 150	Screened: 5	Randomized: 0	Treated: 0
Evaluated:	Efficacy: 0	Safety: 0	Pharmacokinetics: 0	

The study was stopped after 5 subjects were screened due to other project prioritization within the company.

Diagnosis and criteria for inclusion:

Patients (≥18 years) with moderate or severe, persistent cancer pain who were receiving World Health Organization (WHO) Step 2 or 3 cancer pain treatment as background therapy.

Study treatments

Investigational medicinal product(s): SSR411298 or placebo

Formulation: tablet containing SSR411298 200 mg or placebo

Route(s) of administration: oral

Dose regimen: One tablet once daily in the morning with food

Patients continued to receive WHO Step 2 or 3 cancer pain treatment

Duration of treatment: was to be 4 weeks

Duration of observation: was to be 6 weeks (1-week screening to evaluate suitability to participate in the trial, in terms of cancer pain, cancer pain treatment, and screening safety evaluations, 4-week treatment and 1-week post-treatment follow-up to evaluate the potential rebound of pain and symptoms of withdrawal at the completion of the treatment period or in the event of early treatment discontinuation)

Criteria for evaluation:

Efficacy:

Primary: Change from baseline (baseline = average pain intensity between Day -7 and Day -1 to end of treatment (end of treatment = average pain intensity during Week 4) in NRS score (NRS is a daily assessment performed at the same time each day at the end of the day).

Secondary: Brief Pain Inventory Short-Form (BPI-SF), responder rate (reduction of ≥30% of pain intensity; reduction of ≥50% of pain intensity; composite of pain intensity and background therapy utilization), breakthrough pain frequency, background Therapy utilization (morphine-equivalent dose per day; adjuvant agent utilization; number of rescue medication doses per day), Hospital Anxiety and Depression Scale (HADS) for mood disorders, nausea visual analog scale (VAS), Bowel Function Index (BFI) for constipation), health care utilization (unscheduled hospitalizations, emergency department visits, healthcare provider office visits and sick leave days), patient satisfaction of pain relief (5-point Likert scale) and quality of life using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) version 3.

Safety:

Adverse events (AE) and other clinical parameters (e.g., vital signs, physical examination, clinical laboratories, electrocardiography), suicidality assessment (Columbia Suicide Severity Rating Scale [C-SSRS]), Drug Abuse and Liability Assessment (DALA), cognitive function tests (Digit-Symbol Substitution Test [DSST], Rey Auditory Verbal Learning Test [RAVLT], and 2-Digit Cancellation Test [2-DCT]) and pill dysphagia assessment.

Pharmacokinetics:

SSR411298 plasma concentrations, Endocannabinoid plasma concentrations and SAR250960 urine concentration

Statistical methods:

Analysis population

The primary efficacy analysis was to be performed using the intent-to-treat population, defined as all randomized patients who took at least one dose of investigational medicinal product and had at least one baseline and one post-baseline pain assessment on numeric rating scale (NRS), whatever the compliance to protocol procedures. Patients were to be analyzed in the treatment group as assigned by the central randomization system.

The safety analyses were to be performed using the safety population, defined as all randomized patients who took at least one dose of investigational medicinal product.

Primary analysis

The primary efficacy variable, the change from baseline in the NRS pain intensity, was to be analyzed using a mixed-effect model with repeated measures approach, under the missing at random framework.

The primary analysis was to provide an estimate of the treatment effect in the global population and in each subpopulation nociceptive or neuropathic cancer pain.

Safety

The tolerability and safety was to be assessed by adverse events and other clinical and para-clinical parameters (e.g., vital signs, physical examination, clinical laboratories, 12-lead electrocardiogram, suicidality assessment (Columbia Suicide Severity Rating Scale), drug abuse and liability assessment, and cognitive function (Digit-Symbol Substitution Test; Rey Auditory Verbal Learning Test and 2-Digit Cancellation Test).

Summary:

Population characteristics:

A total of 5 patients were screened. However, all five screened patients did not meet study inclusion/exclusion criteria therefore they were not eligible to participate in this study.

Efficacy results:

No efficacy was assessed as these patients did not meet study inclusion/exclusion criteria and were not eligible to be randomized.

Safety results:

No safety was assessed as these patients did not meet study inclusion/exclusion criteria and were not eligible to be randomized.

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