The study listed may include approved and non-approved uses, formulations, or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this registry, healthcare professionals should consult prescribing information for the product approved in their country.

Results presented here may include different data from those shown on http://clinicaltrials.gov/, which specifically identifies data to be disclosed, as mandated by US federal law.

Title of Study: Open-Label Clinical Trial to Assess the Efficacy, Tolerability and Safety of a Single IV Dose of Palonosetron 0.25 mg + Dexamethasone IV in the Prevention of Moderately Emetogenic Chemotherapy-Induced Nausea and Vomiting (CINV) (Protocol: P04594).

Study Center(s): Multicenter, 8 centers in 5 countries: MEXICO, VENEZUELA, PERU, El SALVADOR, GUATEMALA

Studied Period: 1 JAN 2008 to 31 AUG 08 | **Clinical Phase:** IV

Objective(s): The primary objective was to determine if a single intravenous (IV) dose of palonosetron 0.25 mg plus a single IV dose of dexamethasone 8 mg was effective to prevent nausea and vomiting induced by moderately emetogenic chemotherapy in subjects with cancer. Secondary objectives were to evaluate the following:

- Measure the proportion of patients who achieved a clinical response and of those who achieved complete control; Number of emetic episodes; Time to first emetic episode, to administration and need for rescue therapy; and to treatment failure.
- Measure the severity of nausea; Patient global satisfaction and Quality of life (QOL)

Methodology: Study conducted in accordance with Good Clinical Practices, including the archiving of essential documents. This was a Phase IV,open label, multicenter, multinational clinical study. It is a one arm study with 118 patients (both sexes) in adults with cancer disease naïve or non-naïve to chemotherapy, with Karnofsky index superior or equal to 70% in active chemotherapeutic treatment. The baseline procedures were documented at the screening visit (Day –7 to 0; Visit 1). Treatment Visits 2 were to have occurred on Day 1, when Palonosetron was administered. Subjects who qualified at the screening visit were assigned to the next treatment: Palonosetron 0.25 mg, IV single dose, 30 minutes prior to the administration of the major chemotherapeutic agent, plus single IV dose of dexamethasone 8 mg administered 15 minutes before chemotherapy (in the event of a shortage of IV dexamethasone, a single oral dose of dexamethasone 20 mg or a single IV dose of methylprednisolone 125 mg was administered). Patients had to receive a single dose of at least one of the following agents administered on Study Day 1: any dose of Dactynomicin, Carboplatin, Epirubicin, Idarubicin, Ifosfamide, Irinotecan, Lomustine; or Methotrexate >250 mg/m^2, or Cyclophosphamide <=1500 mg/m^2, or Mitoxantrone <15 mg/m^2, or Doxorubicin >= 20 mg/m^2, or Citarabin > 1 g/m^2, Melphalan > 50 mg/m^2 , Oxaliplatin > 75 mg/m^2 administered over 1 to 4 hours. The administration of the major chemotherapeutic agent (which is the most emetogenic agent according to the classification of Hesketh, et al., The Oncologist 1999, 4: 191-196) defined Study Day 1 and administration of this agent was not extended beyond 4 hours. The study medication was administered 30 minutes before administering the main chemotherapeutic agent plus one single IV dose of dexamethasone 8 mg administered 15 minutes before chemotherapy. An observational post-treatment follow up period was to have occurred on Day 2 – Visit 3 and on Day 6 to 8 –Visit 4. The patient received a 5-day diary. Patients received instructions on how to use the diary and the questionnaires included in it.

Efficacy was assessed by measurements of emetic episodes, use of rescue drug, severity of nausea, and patient satisfaction with the antiemetic treatment during intervals of 24 hours up to 120 hours. Efficacy end-points included once daily subject-assessed symptoms over the 6-8-days of follow-up, evaluating the response during the first 24h up to 120h, using the following questionnaires: FLIE 1 (Functional Living Index – Emesis) (0-24 hours), FLIE 2 (24-96 hours), VAS (Visual Analog Scale) filled in on days 2 to 5 of the study, and the Likert scale filled in on days 2 to 5 of the study.

A key safety variable was the proportion of patients who suffered nausea and vomiting in the first 24h after treatment. Other measures of safety included the, presence of symptoms, nausea and vomiting, at a relative long term, 24-96h.

It was anticipated that approximately 8 centers in different countries would give the treatment with a variable number of patients at each center. The sample size of subjects who would be assigned for this study was 118 subjects.

Number of Subjects: 118 (99 women, 19 men).

Diagnosis and Criteria for Inclusion: Patients scheduled to receive a single dose of at least one of the following agents administered on Study Day 1: any dose of Dactynomicin, Carboplatin, Epirubicin, Idarubicin, Ifosfamide, Irinotecan, Lomustine; or Methotrexate >250 mg/m^2, or Cyclophosphamide <=1500 mg/m^2, or Mitoxantrone <15 mg/ m^2, or Doxorubicin >= 20 mg/ m^2, or Citarabin > 1g/ m^2, Melphalan > 50 mg/ m^2 , Oxaliplatin > 75 mg/ m^2 administered over 1 to 4 hours. The administration of the major chemotherapeutic agent (which is the most emetogenic agent according to the classification of Hesketh, et al., The Oncologist 1999, 4: 191-196) defined Study Day 1 and administration of this agent should not extend beyond 4 hours. The presence of histologically or cytologically confirmed malignant disease, being näive or non-näive to chemotherapy, with a Karnofsky index >= 70%.

Test Product, Dose, Mode of Administration: Palonosetron hydrochloride (Onicit®) administered on a single dose of 0.25mg, IV, 30 min before initiating chemotherapy. Vial 5 mL. Solution for injection 0.25 mg.

Duration of Treatment: A first visit was performed for screening of patients on days -7-0. Palonosetron was administered on single dose on Day 1 and two additional visits were performed on days 2 and 6-8 to evaluate post-treatment follow-up.

Reference Therapy, Dose, Mode of Administration: None

Criteria for Evaluation: Efficacy and safety were assessed on 2 additional study visits. The patients' diaries were used to record the following: emetic episodes, use of rescue drug, severity of nausea, and to evaluate patient satisfaction with the antiemetic treatment during intervals of 24 hours up to 120 hours.

Statistical Methods: The results were shown globally, by sociodemographic and FLIE / Likert/ VAS results. Mann-Whitney test and Paired T test calculations were used to analyze the time for FLIE and Likert evaluations.

SUMMARY - CONCLUSIONS:

RESULTS:

Efficacy: 1. The primary and secondary objectives could not be evaluated due to missing data 2. Results on Likert Index, FLIE and VAS suggest that Palonosetron sustained a good quality of life related to nausea and vomiting of the end-points evaluated: Day 2 and Day 5, with no symptoms in most of the population studied.

Safety: Palonosetron, administered on a single-fixed dose of 0.25mg plus Dexamethasone in patients with chemotherapy, is a safe drug with minimal adverse events.

CONCLUSIONS:

- The primary and the secondary objectives from the study could not be evaluated because of failures in data collection.
- Palonosotron IV on a single-fixed dose of 0.25mg plus Dexamethasone, administered concomitantly with chemotherapeutic agents, induces a good quality of life related to nausea and vomiting.
- Palonosetron IV administered concomitantly with chemotherapeutical agents, and a single-fixed dose of 0.25mg plus Dexametasone, is a safe treatment with minimal adverse events.