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: Study to Evaluate the Efficacy and Safety of Single Intravenous Doses of Onicit® (Palonosetron) 0.25 mg in the Prevention of Acute and Delayed Nausea and Vomiting Associated with Moderate and Highly Emetogenic Chemotherapy in Colombia (P04935).

Unique Identifier: NCT00684463

Studied Period: 7 MAY 2007 to 22 FEB 2008 | **Clinical Phase:** 4

Objective(s): The aim of this study was to evaluate the efficacy and safety of a single intravenous dose of palonosetron 0.25 mg which is indicated to prevent early or delayed chemotherapy induced nausea and vomiting (CINV) in case of high or moderate emetogenic chemotherapy in Colombian patients.

The objectives of this study were:

- To measure the complete response (CR) defined as no vomiting and no rescue therapy, after chemotherapy administration when palonosetron is given 30 minutes prior to chemotherapy.

Secondary objectives of this study were:

- To measure the effectiveness of palonosetron in helping subjects achieve CR and complete control (CC), defined as a complete response but without presence of nausea.
- To measure number of emetic episodes, time to first emetic episode, time to administration and need for rescue therapy, time to treatment failure.
- Safety

Methodology: 2-Center, Interventional, Single Group Assignment, Open Label, Uncontrolled, Efficacy Study.

Number of Subjects: Only 59 patients (8 male, 51 female; mean age 51.7) were included, the number of patients was smaller than the estimate for the sample (152 patients) due to a low rate of recruitment..

Diagnosis and Criteria for Inclusion: Subjects diagnosed with cancer and then requiring chemotherapy participated in this trial.

The most frequent diagnosis of participants was breast cancer (38 patients). 21 patients (35.6%) presented concomitant diseases, the most frequent were arterial hypertension (15 patients), and type 2 Diabetes Mellitus (5 patients).

The drugs used most were: ciclofosfamide (35 patients) and doxorubicin (34 patients). Owing to emetic risk, 48 patients (81.4%) received regimens moderately emetogenic and 6 (10.2%) regimens highly emetogenic. Only one patient had a monotherapy regimen and 27 subjects (45.8%) had regimens with more than two drugs.

Test Product, Dose, Mode of Administration: Subjects received a single intravenous infusion dose of palonosetron (0.25 mg) over 30 minute infusion. The infusion was given 30 minutes before chemotherapy.

Duration of Treatment: Subjects received a single intravenous infusion dose of palonosetron 30 minutes prior to chemotherapy and were evaluated during the first 3 hours (acute phase), at 24 hours, and 8 days after chemotherapy was administered.

Reference Therapy, Dose, Mode of Administration: N/A

Criteria for Evaluation: The primary outcome measure was the number of subjects having achieved CR 24 hours after administration of chemotherapy. Number of subjects achieving CC was also measured. CC and CR measures were evaluated for the first 3 hours, at 24 hours, and 8 days after chemotherapy.

Statistical Methods: The descriptive analysis was made by central tendency and dispersion measures for continuous variables and proportions for categorical variables. Results are reported in tables and figures in the full report. Efficacy (complete response and complete control) was evaluated in percentage terms. Efficacy was assessed three times (first 3 hours, at 24 hours and 8 days after). To determinate if significant differences in the efficacy between the three assessments existed; we performed the repetitive Cochran Q test and Mc Nemar Ji square between pars of moments.

We estimated the total percentage change over the allocated time to find out the proportion of patients which changed groups (responders to non-responders or vice-versa) by the following formula:

$$p = \frac{1}{N(T-1)} \sum_{i=1}^{N} ci \quad ; \quad SD = \sqrt{\frac{p(1-p)}{N}}$$

P is the total percentage change, *N* the number of subjects, *T* the number of measurements and *ci* the number of changes for a patient (i) within the allocated time.

To determinate which factors were associated with non-complete response, we calculated crude and adjusted Odds Ratio (OR), by logistic regression for longitudinal data (logistic Generalized estimating equations). All statistical analysis adopted two-side test in this study for an error I type of 5%. All statistical analyses were performed using SPSS version 15.0 and STATA 10 software.

SUMMARY-CONCLUSIONS:

RESULTS:

Efficacy:

Nausea/Vomiting: During the acute phase, after having received Palonosetron, 100% (59 patients) of patients had no vomiting; consequently they did not require additional medication. Nausea was presented in two patients (3.4%) and they did not need additional medication for control of nausea.

At 24 hours 22 patients presented vomiting (37.3%) and 7 of them were given additional medication. The number of vomiting episodes varied between 1 and 10. The average was 3±2 and the median of two episodes. During the same period 27 patients presented nausea (45.8%) and 7 of them also required additional therapy.

At 8 days 24 patients presented vomiting (40.7%) and 9 of them used additional medication. The number of vomiting episodes varied between 1 and 10. The average was 3±2 and a median of two episodes. Nausea was presented in 27 patients (40.7%) and 9 of them also required additional therapy.

CR and CC: For the acute phase 100% (59 patients) and 97% (57 patients) (CI 95%; 92% to 100%) of subjects had complete response and complete control respectively. At 24 hours the percentage of complete response decreased to 63% (37 patients) (CI 95%; 50% to 75%) and the percentage of complete control also decreased to 51% (30 patients) (CI 95%; 38% to 64%). At 8 days the percentage of complete response went down slightly to 59% (35 patients) (CI 95%; 46% to 72%) while complete control percentage increased slightly to 56% (33 patients) (CI 95%; 43% to 69%).

The efficacy of medication was assessed as complete response and complete control. It shows significant differences between the acute phase, at 24 hours and at 8 days ($p<0.001$, Cochran Q test); the proportion of responders decreases significantly with time. However, the comparison of complete response and complete control between 24 hours and 8 days did not show significant differences ($p=0.670$ and $p=0.54$ respectively, Mc Nemar ji-square test).

The total percentage change was 58% for complete response (CI 95%; 46% to 71%), it indicates that there is a significant change in the proportion of patients with complete response during the follow up. Significantly, the total percentage change for complete control was 44% (CI 95%; 31% to 57%). As well as Cochran Q test, the change is due to the decrease in the proportion of patients with complete response and complete control at 24 hours compared with the acute phase, when complete response was 100% and complete control 97%.

Follow up time	No vomiting n (%)	No nausea n (%)	No rescue therapy n (%)
Acute phase (first 3 hours)	59 (100%)	57 (97%)	59 (100%)
24 hours	37 (63%)	32 (54%)	52 (88%)
Day 8	35 (59%)	35 (59%)	50 (85%)

Safety:

Three mild adverse events were reported: two episodes of non-clinically significant leucopenia and an episode of headache.

CONCLUSIONS:

- A single dose of palonosetron (0.25 mg) IV administered 30 minutes before chemotherapy is effective and safe to prevent nausea and vomiting induced by chemotherapy in both acute (<24 hours) and delayed (>24hours) cases for Colombian patients who received highly and moderately emetogenic chemotherapy.

Date of the Report: 11 AUG 2009