Protocol Number: LP-CT-PALO-202002

Study Title	A Randomized, Dose-ranging, Open-label, Parallel Group Study to Assess the Efficacy, Safety and Pharmacokinetics of Palonosetron HCl Buccal Film *versus* IV Palonosetron 0.25 mg (ALOXI®) for the Prevention of Chemotherapy-induced Nausea and Vomiting in Cancer Patients Receiving Moderately Emetogenic Chemotherapy
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Protocol Number	LP-CT-PALO-202002
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SYNOPSIS

Study Number:	LP-CT-PALO-202002
Name of Investigational Product:	Palonosetron HCl Buccal Film (LP035)
Title of Study:	A Randomized, Dose-ranging, Open-label, Parallel Group Study to Assess the Efficacy, Safety and Pharmacokinetics of Palonosetron HCl Buccal Film *versus* IV Palonosetron 0.25 mg (ALOXI®) for the Prevention of Chemotherapy-induced Nausea and Vomiting in Cancer Patients Receiving Moderately Emetogenic Chemotherapy
Indication:	Prevention of acute and delayed nausea and vomiting associated with moderately emetogenic cancer chemotherapy
Development Phase:	2
Objectives:	To compare the efficacy, safety and pharmacokinetics of single dose of Palonosetron HCl Buccal Film 0.25 mg or 0.5 mg to IV palonosetron 0.25 mg in the prevention of chemotherapy-induced nausea and vomiting in cancer patients receiving moderately emetogenic chemotherapy
Study Population:	The study population will consist of male or female adult chemotherapy naïve (i.e. no history of cytotoxic chemotherapy) or non-naïve patients with histologically or cytologically confirmed solid tumors, scheduled to receive MEC.
Study Design:	This is a randomized, open-label, multicenter, parallel group, dose-ranging efficacy, safety and pharmacokinetic study. Patients will be randomized into three treatment groups.
Number of Subjects:	22 subjects will be randomized into three treatment groups, 8 subjects in 0.25 mg LP035 group, 8 subjects in 0.5 mg LP035 group, 6 subjects in 0.25 mg ALOXI® group. Palonosetron PK will be assessed in a subgroup of patients in 12 patients, 4 patients per group.
Study Duration:	Patients not included in the PK subgroups, will stay on the study for a maximum of 16 days including an up to 7-days screening period, 6 days on study (control phase) and a follow-up patient visit or telephone call 3 days after control phase. Patients involved in the PK subgroups will stay on the study for a maximum of 18 days including an up to 7-days screening period, 8 days on study (6 days control phase, and an additional 2 days PK phase) and a follow-up patient visit or telephone call 3 days after the PK phase.
Treatment Groups:	Divided into 3 groups: **Test Drug (Group A):** Palonosetron HCl Buccal Film 0.25 mg, administered on Day 1, 8 subjects; **Test Drug (Group B):** Palonosetron HCl Buccal Film 0.5 mg, administered on Day 1, 8 subjects; **Reference (Group C):** IV palonosetron 0.25 mg (ALOXI®), administered on Day 1 6 subjects.
Criteria for Inclusion:	For inclusion in the study, patients must fulfill all of the following criteria: 1. Provide written informed consent; 2. Male or female, aged ≥ 18 years; 3. With histologically or cytologically confirmed malignant disease; 4. Patients and patients' partners using reliable contraceptive measures;

Criteria for Inclusion:	5. Female patient of childbearing potential having a negative serum pregnancy test; 6. Be able to read, understand, and follow the study procedures and able to complete patient diary autonomously.
Exclusion Criteria:	Any of the following is regarded as a criterion for exclusion from the study: 1. Expect to be non-compliant with the study procedures; 2. Receive any investigational drugs within 30 days before the start of study treatment or schedule to receive a highly or moderately emetogenic chemotherapeutic agent; 3. Have a clinically unstable seizure disorder with seizure activity requiring anticonvulsant medication; 4. Have severe renal or hepatic impairment; 5. Have positive serology test results; 6. Have a known contraindication to 5-HT_3 receptor antagonists; 7. Treat with commercially available palonosetron formulations within 2 weeks prior to start of study treatment or enrollment in a previous trial investigating palonosetron; 8. Is allergic to palonosetron or any other 5-HT_3 antagonist; 9. Is currently a user of any recreational or illicit drugs (including marijuana) or has current evidence of drug or alcohol abuse or dependence as determined by the investigator; 10. Will be receiving stem cell rescue therapy in conjunction with study related course of emetogenic chemotherapy; 11. Has received or will receive total body irradiation or radiation therapy to the abdomen (includes the level of the diaphragm and below) or pelvis in the week prior to Treatment Day 1 and/or during the diary reporting period.
Study Treatments:	**Test Drug (Group A):** Administration of Palonosetron HCl Buccal Film 0.25 mg on Day 1, 60 ± 10 min before start of Chemotherapy. **Test Drug (Group B):** Administration of Palonosetron HCl Buccal Film 0.5 mg on Day 1, 60 ±10 min before start of Chemotherapy. **Reference (Group C):** IV palonosetron 0.25 mg (ALOXI®) administered on Day 1, 30 ±5 minutes before start of Chemotherapy, as an IV bolus over 30 seconds.
Schedule of Patient Visits:	Patients will undergo the following visits: • Screening: Visit 1 (Day -7 to Day -1); • Visit 2 (Day 1): chemotherapy and study drug administration; • Visit 3 (Day 2): 24 hours after the start of chemotherapy administration • Visit 4 (Day 6 [+2 days]/Day 8): 120 [up to 175] hours after start of chemotherapy administration • Visit 5 (Day 9 [± 1 day]/Day 11 [± 1 day]): follow-up [visit or phone contact].
Chemotherapy Regimens:	Any MEC (ASCO Guideline), taken on Day 1 is allowed. If more than one agent considered as MEC is administered on Day 1, the start time of the first agent is to be considered as the start of chemotherapy. Any chemotherapy agent of high or moderate emetogenicity during the period from Day 2 up to 120 hours after start of chemotherapy is not allowed.

Efficacy Assessments:	**Primary Endpoint:** Complete response (CR) (no emetic episode and no rescue medication) during the first 24 hours after chemotherapy.
Safety Assessments:	Safety assessments include the recording and assessing of all adverse events (AEs), vital signs, physical examinations (PE), clinical laboratory parameters, 12-lead electrocardiogram (ECG), buccal application site evaluation at 0.5 hour (for all subjects), 24 hours (for all subjects) post-dose and at Visit 4 (day 8 for PK subgroups, day 6-8 for non-PK subgroups).
Analysis Sets:	The full analysis set (FAS) is defined as all randomized patients who received the study medication and at least chemotherapy. The analysis based on the FAS is considered as primary analysis for all efficacy parameters. The per-protocol (PP) set is defined as all patients who completed Day 2 (primary endpoint) and who is compliant with the study protocol. Pharmacokinetic set (PKS) is defined as all subjects completing the study and for whom the pharmacokinetic profile can be adequately characterized. The safety set (SS) is defined as all patients treated and have at least one safety assessment after treatment. "Patients treated" is defined as any patient who received any study medication (palonosetron).
Pharmacokinetic:	Parameters: AUC_{0-t}, AUC_{0-inf}, C_{max}, Residual area, T_{max}, $T_{½\ el}$, and k_{el}.
Statistical Methods:	**Efficacy:** The primary analysis will be summarized by treatment arm. The number and proportion of patients will be presented by frequency table. For the response rate and for the difference in response rate between each Palonosetron HCl Buccal Film group and IV palonosetron group, 95% confidence interval (CI) will be provided. For the CR rate at 24 h, analyses will be carried out for both FAS and PP population; the other parameters will be analyzed only for FAS population. The subgroups will be analyzed based on FAS for the primary efficacy by age, gender, chemotherapy history, ethanol use, history of pregnancy-related morning sickness, history of motion sickness. The between-group treatment effect (with a nominal 95% CI) for the primary endpoint will be estimated within each category. **Safety:** The analysis of safety will be performed for the safety set. The result will be interpreted in a descriptive manner. Incidence of AEs will be calculated overall, by system organ and by preferred term. Physical examination, vital signs, 12-lead electrocardiogram and application site evaluation data will be listed and summarized. For vital signs, differences will be calculated compared to baseline. Laboratory data will be analyzed and described considering the age and/or gender dependent normal ranges of the local laboratory. Laboratory data will be summarized and listed. Marked abnormalities and assessments concerning clinical relevance for abnormal values will be included. Shift tables will be used for vital signs and laboratory data to evaluate categorical changes with respect to normal ranges.
Sponsor:	Xiamen LP Pharmaceutical Co., Ltd.