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

Sponsor: Sanofi **Drug substance(s):** XRP6976 (docetaxel)	**Study Identifiers:** UTN U1111-1131-0614, NCT02061631 **Study code:** DOCETL06445
Title of the study: Open label, non controlled, non randomized, interventional study to evaluate the response rate after induction therapy with docetaxel (T) and cisplatin (P) in unresectable locally advanced squamous cell carcinoma of head and neck (SCCHN)	
Study center(s): Three (3) study centers in Pakistan	
Study period: Date first subject/patient enrolled: 10/May/2014 Date last subject/patient completed: 05/Oct/2015	
Phase of development: Phase 2	
Objectives: **Primary Objective:** To evaluate the overall response (OR) rate (including complete response [CR] and partial response [PR]) of subjects treated with induction regimen docetaxel and cisplatin followed by chemoradiotherapy in patients with locally advanced head and neck cancer. **Secondary Objective**: To assess the safety and tolerability of induction regimen docetaxel and cisplatin followed by the chemoradiotherapy in patients with locally advanced head and neck cancer.	
Methodology: This was an open label, non controlled, non randomized and single arm study. The enrollment duration was approximately 18 months. The treatment duration for each patient was around six months. Patients included in the study were treated with induction regimen followed by chemo radiotherapy. Within the Induction Period there were three cycles (Docetaxel + Cisplatin) every 21 days. The post induction follow up was on day 21 after the third cycle. This was followed by the consolidation period consisting of radiotherapy for six weeks and cisplatin every week for four cycles. The post-consolidation follow up was at eight weeks after the consolidation period.	
Number of subjects/patients**:** Planned: 35 Treated: 35 **Evaluated:** Efficacy: 27 Safety: 35	

Diagnosis and criteria for inclusion:

The main inclusion criteria are as follows:

- Squamous cell carcinoma of head and neck (SCCHN) of oral cavity in stage III–IV without evidence of distant metastases.
- No prior chemotherapy or radiation therapy.
- Having at least one measurable lesion in one dimension.
- Age ≥18 and <65 years with Eastern Cooperative Oncology Group (ECOG) ≤1.
- Adequate organ function.
- Life expectancy >3 months.
- Informed written consent.

Study treatments

Investigational medicinal product(s): Docetaxel & Cisplatin

Formulation: Docetaxel: Each vial contains 20 mg/1 ml of docetaxel

Cisplatin: Each vial contains 50 mg cisplatin

Route(s) of administration: Intravenous

Dose regimen: One-hour intravenous infusion of docetaxel at 75 mg/m^2 followed by a 30 minute intravenous infusion of cisplatin at 75 mg/m^2. Patients were pre-medicated with oral dexamethasone at 8 mg twice daily for 3 days, commencing one day before docetaxel infusion.

Patients were premedicated with intravenous dexamethasone at 20 mg and either ondansetron or granisetron administered before cisplatin infusion. Either oral ondansetron 8 mg three times daily for 2 days or oral metoclopramide 0.5 mg/kg four times daily for 2 days, commencing 16 hours after cisplatin. Patients were given supportive G-CSF treatment beginning at the first cycle.

Docetaxel and cisplatin treatments were repeated every 21 days for three cycles

Chemoradiotherapy (CRT):

Intravenous cisplatin was administered at a dose of 30 mg/m^2 weekly starting concomitantly with conventional radiotherapy to the primary tumor and to the clinically positive nodes for a period of 6 weeks. Intravenous cisplatin was continued for four weeks.

Radiotherapy:

Gross disease dose was 60 Gy/30 fractions and sub clinical dose 45-50 Gy/30 fractions.

A boost of 4-6 Gy in 2-3 fractions to the gross tumor was optional.

Duration of treatment: The duration of treatment for each patient was around 6 months.

Duration of observation: The duration of observation for each patient was around 8 months.

Criteria for evaluation:

Efficacy:

Primary efficacy criteria

Proportion of patients who achieved complete response and partial response using the Response Evaluation Criteria in Solid Tumors (RECIST) criteria version 1.1 at 3 weeks after Cycle 3.

Secondary efficacy criteria

Proportion of patients who achieved CR and PR using the RECIST criteria version 1.1 at 8 weeks after completion of last cycle of CRT.

Safety:

Safety criteria

Incidence of serious and non-serious adverse events and nature of adverse events was recorded for each patient. The adverse events were classified based upon their occurrence and severity. The National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v4.03 was used to grade the adverse events.

Statistical methods:

Population characteristics were summarized using descriptive statistics such as mean, standard deviation and median for continuous variables, and frequencies and percentages for categorical variables. Efficacy population was the intent-to-treat (ITT) population. Safety population was the total treated population.

To determine proportion of patients, the sum of patients in each of the given six categories was divided by the ITT population. The categories were complete response (CR), partial response (PR), Stable disease (SD), progressive disease (PD), Unknown & Not done.

Summary:

Population characteristics: Thirty five patients were enrolled in this study. There were 24 (68.6 %) males. The overall mean and median age of these patients was 44.4±11.8 years and 45 years (range: 18 – 62 years) respectively. The mean and median age of male patients was 44.6± 10.3 years and 45 years respectively, and that of female patients was 43.9± 15.3 and 46 years respectively. TNM staging information showed that six (17.1%) patients had stage III disease and 29 (82.9%) patients had stage IV disease.

Efficacy results:

Primary efficacy endpoint: The overall response (OR) rate of the evaluable patients (n=27) was 88.9% (95% CI: 71.94 - 96.15). A complete response (CR) was not achieved by any patients and partial response (PR) was achieved by 24 (88.9%) of 27 patients. Stable disease (SD) and progressive disease (PD) were shown for 1 patient and 2 patients, respectively.

From the intent to treat analysis CR rate was not achieved by any patients and the OR rate was 68.6% (24 of 35).

Secondary efficacy endpoint: The OR rate of the evaluable patients (n=19) was 78.9% (95% CI: 56.7 – 91.5). A CR was achieved by two patients (10.5%) and a PR was achieved by 13 (68.4%) of 19 patients. Progressive disease (PD) were shown for four patients.

From the intent to treat analysis CR rate was 5.7 % (2 of 35) and the OR rate was 42.9% (15 of 35).

Safety results: During induction period, the most common hematological toxicity was leukopenia which occurred in eight patients, and three patients suffered from leukopenia of ≥Grade 3. The common non-hematologic toxicities (all grades) were nausea, stomatitis and alopecia which occurred in 21, 18, and 18 patients respectively.
During consolidation period, the most common adverse events (all grades) were alopecia, stomatitis and nausea which occurred in 14, 13, and 13 patients respectively.
Overall, there was one case of febrile neutropenia. Leukopenia, the most commonly reported hematological toxicity met the seriousness criteria in case of four patients. Nausea, vomiting and diarrhea of ≥Grade 3 occurred in one, three and five patients respectively.
During induction period, nephrotoxicity lead to the withdrawal of study treatment in one patient.
Overall, seven patients died during the study period. These fatal events were considered as not associated to the investigational drugs.

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