These results are supplied for informational purposes only. *Prescribing decisions should be made based on the approved package insert in the country of prescription*			
Sponsor/company:	**sanofi-aventis**	**ClinialTrials.gov Identifier:**	
		Study Code:	**XRP6976F_3501**
Generic drug name:	**Docetaxel**	**Date:**	**November 9th, 2006**

Title	A Randomized phase III multicenter trial of neoadjuvant docetaxel (Taxotere) plus cisplatin plus 5-fluorouracil (5-FU) versus neoadjuvant cisplatin plus 5-fluorouracil in patients with locally advanced inoperable squamous cell carcinoma of Head and Neck
Period	FPI : Nov.21th, 2002 LPO : Mar.30th, 2005
Design	Randomized, non blinded, multicenter phase III
Objectives	Primary : To compare clinical response rate after 3 cycles of induction chemotherapy with Docetaxel, Cisplatin, 5-Fluorouracil (TPF) versus Cisplatin, 5-Fluorouracil (PF). Secondary : 1. To compare pathologic response rate in case complete response of primary site after 3 cycles of induction chemotherapy with Docetaxel, Cisplatin, 5-Fluorouracil (TPF) versus Cisplatin, 5-Fluorouracil (PF). 2. To compare clinical response rate, pathologic response rate, survival, time to treatment failure, progression free survival after concurrent chemoradiotherapy following induction chemotherapy.
Sample Size	Total 80 patients was initially planned. Actual number of 86 patients (43 patients on each arm) were enrolled by 7 centers in Korea.
Inclusion Criteria	1. Histologically or cytologically proven squamous cell carcinoma of the head and neck with locally advanced inoperable disease. 2. Primary tumor sites eligible: oral cavity, oropharynx, hypopharynx, larynx or nasopharynx. 3. Patients are required to have at least one (bi-or uni-dimensionally) measurable lesion. 4. Stage III or IV without evidence of distant metastases 5. Inoperable tumor evaluated by multidisciplinary team. 6. 18 ≤ age ≤ 70. 7. WHO performance status 0 or 1 8. Laboratory data ● hematology - neutrophil count ≥ 2.0 x 10^9/L - platelet count ≥ 100 x 10^9/L - hemoglobin ≥ 10 g/dl (6.2 mmol/L) ● hepatic function - total serum bilirubin ≤ 1 x UNL -ASAT (SGOT) , ALAT (SGPT) ≤ 2.5 x UNL

	-Alkaline phosphatase ≤ 5 x UNL -patients with ASAT and ALAT > 1.5 UNL associated with alkaline phosphatase > 2.5 UNL are not eligible for the study ● renal function - Serum creatinine ≤ 120 µmol/L (1.4 mg/dl), if values are > 120 µmol, creatinine clearance should be ≥ 60 ml/min 9. Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule, those conditions should be discussed with the patient before registration in the trial. 10. Signed informed consent prior to beginning protocol specific procedures
Exclusion criteria	1. Patients with distant metastases 2. Pregnant or lactating women. 3. Participation in another therapeutic clinical trial within 30 days prior to study entry. 4. Concomitant treatment with any other anticancer therapy 5. Previous Chemotherapy. 6. Previous radiotherapy for H&N cancer. 7. Previous surgery for H&N cancer (except incisional biopsy of primary site). 8. Concomitant treatment with corticosteroids (except premedication) in the last 3 months prior to study entry. However patients receiving chronic treatment with corticosteroids (> 3 months) at low dose (≤ 20 mg of prednisone or equivalent) for whichever reason are eligible. 9. Any concomitant drug having interaction with 5-Fluorouracil (example: cimetidine, allopurinol, folic or folinic acid). 10. Past or present medical history ● Past or present malignancies at other sites, with the exception of adequately treated *in situ* carcinoma of the cervix uteri, basal or squamous cell carcinoma of the skin or other cancer curatively treated with surgery and with no evidence of disease for at least 5 years. ● Symptomatic peripheral neuropathy ≥ grade 2 by NCIC-CTG criteria. ● Hearing problem ≥ grade 2 by NCIC-CTG criteria (except metastatic auditory problem by H&N cancer). ● Other serious concomitant illnesses - unstable cardiac disease despite treatment - myocardial infarction within 6 months prior to study entry - history of significant neurologic or psychiatric disorders - active uncontrolled infection - active peptic ulcer - history of chronic obstructive pulmonary 1-year hospitalization. 11. Calcemia above normal limits of the laboratory. However a patient with prior hypercalcemia which is controlled by the administration of biphosphonates is eligible provided that the biphosphonates have been initiated at least 3 months prior to study entry. 12. Patient with locally advanced operable carcinoma.
Treatment	Dosage 1. PF arm = Cisplatin : 75 mg/m², administered as one-hour IV infusion on day 1 followed by the continuous IV infusion of 5-FU 1000 mg/m²/day from day 1 to day 5. 2. TPF arm = docetaxel : 70 mg/m², one hour IV infusion on day 1 followed by cisplatin 75 mg/m²,one-hour IV infusion on day 1. Then the continuous IV infusion of 5-FU 750 mg/m²/day from day 1 to day 5 was injected. Chemoradiotherapy 1. Radiotherapy: After the end of chemotherapy with 4-7 weeks interval using either a conventional fractionation (1.8 Gy~2.0 Gy, 1x/day, total dose of 66~70.2Gy) or accelerated/hyperfractionated regimens of radiotherapy (2 x/day, total dose 74 Gy). 2. Chemotherapy: Cisplatin 30mg/m^2 , administered as one-hour IV infusion on radiotherapy day 1 and repeated until the end of radiotherapy.

	Premedication Dexamethasone 8 mg (p.o, bid) was prescribed for 3days to experimental arm (TPF). Antibiotics (Ciprofloxacin) could be administered for prevention/treatment in case of listed below. - Febrile neutropenia or infection. - Grade 4 neutropenia (ANC<0.5). - When recovery from neutropenia is delayed on Day 28, Ciprofloxacin 500mg (p.o, bid) for 10 days was medicated. Premedication(both arms) Adequate hydration and administered antiemetics (5-HT_3 antagonist) before and after Cisplatin infusion. Duration of treatment Induction chemotherapy was given up to 3 cycles if there was no evidence of PD or unacceptable AE. Chemoradiotherapy was started from the last cycle of chemotherapy with using 4-7weeks interval and lasted until total target dose (66~70.2Gy for conventional fractionation or 74 Gy for hyperfractionated schemes) was reached.
Efficacy evaluation	1. Response assessment was performed after the administration of the 2nd cycle, 3rd cycle and at the end of cheomoradiotherapy with the same procedures used in the diagnosis and following modified WHO criteria. Eligibility to assess efficacy was considered when at least 2 cycles of chemotherapy had been received. In case PD before 2nd cycle was considered as "early progression" and eligible to assess efficacy. 2. Tumor assessment was performed after 2nd cycle and the patient responded as PD was dropped out. All other patients except PD after 2nd cycle, was reassessed clinical response after 3rd cycle and if response of primary tumor was complete response, biopsy was performed to evaluate pathological response. 3. 4 weeks later on chemoradiotherapy completion, overall tumor evaluation was performed. When the Patients with complete response which was partial response or stable disease after induction chemotherapy, underwent primary tumor biopsy. 4. Data related to progression free survival, median survival, overall survival was gathered through 6months follow-up with 3months interval from the last patient's end date of study.
Safety evaluation	1. Physical examination and recording adverse event followed NCI-CTC criteria. 2. Physical examination was performed at inclusion, every 3weeks during induction chemotherapy and at the end of chemotherapy (3 weeks after the last cycle) 3. Hematological tests was performed at inclusion, every 3weeks during induction chemotherapy (every week for 1st cycle) and at the end of chemotherapy. 4. Biochemistry was performed at inclusion, every cycle during chemotherapy and at the end of chemotherapy.
Statistical Analysis	Clinical response rate and pathologic response rate were compared by Chi-square test. Censored data like response duration and overall survival were analyzed using survival analysis methods (Kaplan-Meier and Log-rank test).

Results	For the efficacy result Clinical response rate (84.9%) in TPF arm was observed higher than PF arm (81.0%). Moreover, higher tendency was also shown in secondary efficacy variables such as response duration, overall survival and progression free survival. However, there was no statistical significance in every variable. For the safety result Every patient experienced at least more than 1 adverse event and most of these adverse events were evaluated possibly related to study drug. Frequency of serious adverse event in PF arm was observed lower than TPF arm.
Date of Report	May 30th, 2005