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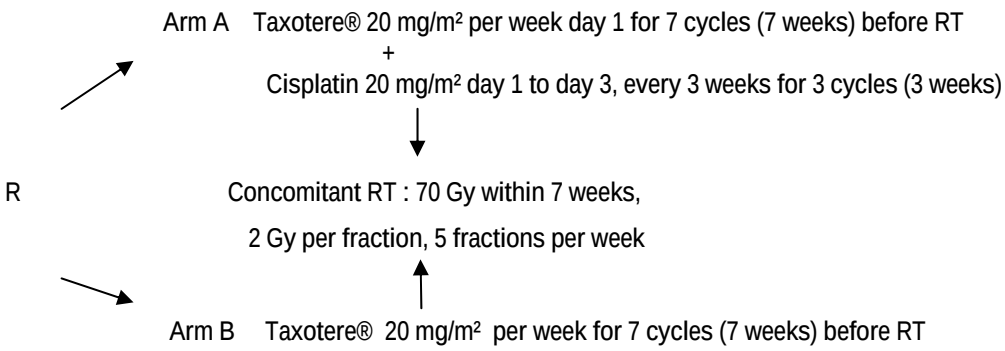
Prescribing decisions should be made based on the approved package insert in the country of prescription

Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00521521
		Study Code:	TAX_FR1_236
Generic drug name:	Docetaxel	**Date:**	28 January 2009

Protocol no.	TAX_FR1_236
Study title	A randomized phase II study of concomitant chemotherapy (docetaxel with or without cisplatin) and radiotherapy (RT) in first-line treatment of locally advanced head and neck cancer (LAHNC).
Sponsor	SAF
Research Coordinator/Country	Professeur Jean-François MORERE Hôpital Avicenne 125, boulevard Stalingrad 93000 BOBIGNY Docteur Thierry BOUILLET Hôpital Avicenne 125, boulevard Stalingrad 93000 BOBIGNY
Centers	8 centres
Country	France
Phase	Phase II randomized with direct individual benefit
Study period	Date first patient enrolled: 16/07/2001 Date last patient enrolled: 17/02/2005 Last patient out : 24/05/2005
Study objectives	Primary: To determine efficacy in term of response rate Secondary: To evaluate safety profile of RTCT association , time to progression and overall survival
Methodology	Open-label, randomized phase II study
Number of patients	90 patients (45 per arm) were expected From July 2001 to March 2005, 86 patients were included and 82 were treated in this Phase II study Arm A (docetaxel cisplatin) : 35 Arm B (docetaxel) : 38
Inclusion criteria	1. Patients (pts) with histolologically proven squamous carcinoma, locally advanced (T3 or T4) or resecable disease but patient's refusal ; primary site : buccal cavity, hypopharynx, oropharynx, larynx

	2. WHO performance status < 2. 3. Age ≥ 18 years and ≤ 70 years 4. Informed consent form obtained, signed and dated before specific protocol procedures. 5. No prior chemotherapy or radiotherapy 6. Normal Hematological, renal and liver functions
Exclusion criteria	1. Prior chemotherapy or radiotherapy 2. Prior surgery 3. History of prior malignancies, except for cured non-melanoma skin cancer, curatively treated in-situ carcinoma of the cervix or other cancer curatively treated and with no evidence of disease for at least five years. 4. Symptomatic peripheral neuropathy Grade ≥ 2 5. Other serious concomitant illness or medical conditions: Congestive heart failure or angina pectoris except if it is medically controlled. Previous history of myocardial infarction within 1 year from study entry, uncontrolled hypertension or arrhythmias. History of significant neurological or psychiatric disorders including dementia or seizures. Active infection requiring IV antibiotics. 6. Hypersensitivity to docetaxel, cisplatin, or any of its excipients. 7. Concomitant use of phenytoin, carbamazepin, barbiturates, or rifampicin. 8. Mental condition rendering the patient unable to understand the nature, scope, and possible consequences of the study. 9. Patient unlikely to comply with protocol, i.e., uncooperative attitude, inability to return for follow-up visits, and not likely to complete the study.
Exposure to treatment	

Efficacy Data	Efficacy will be estimated by the **overall response rate** (complete plus partial responses) in population of patients eligible and evaluable for response **Time to progression** will be calculated from the date of start treatment until progression. **Duration of response** will be calculated in the same manner, but only on responders. All patients will be evaluated for **Survival**. Survival will be measured from the randomization date to the date of death.
Safety Data	**The safety analysis** was performed on all patients who had received at least one dose of chemotherapy.
Statistical Procedures	**Statistical Considerations**: The required number of patients for this phase II study was determined according to a two-stage Simon design. The design parameters assessed the treatment to be insufficiently active if the objective response rate was less than 84% and sufficiently active if the objective response rate was at least 88%. A maximum of 84 evaluable patients needed to be included in the study, assuming an α error rate of 0.05 and a β error rate of 0.10. **The efficacy analysis** was performed on all treated patients. The 95% confidence limits were provided for response rates using the exact method. Time related parameters were analysed using the Kaplan-Meier method.
Summary:	**86 patients were included in this study**. This phase II study was conducted in two stages **In the first**, the patients were randomized to treatment with either • Arm A: docetaxel: 20 mg/m²/week, **per week day 1 for 7 cycles (7 weeks) before** RT + cisplatin : 20 mg/m²/day on day 1 to 3, every 3 weeks (3 cycles). or • Arm B: docetaxel : 20 mg/m²/week **for 7 cycles (7 weeks) before** Concomitant Radiotherapy Conventional 70 Gy, duration : 7 weeks In the first stage, **73 patients** were randomized : - 35 patients were randomized in the arm docetaxel/ciplatine; - 38 patients were randomized in the arm docetaxel alone. **In the second stage**, following the decision to stop the inclusions in arm A (Interim analysis) 13 patients were included. The results are presented in the tables following : - group « Tax/CDDP »: group A patients treated with Concomitant radio-chemotherapy (chemotherapy with docetaxel/cisplatin) - group « Randomized Taxotere® »: group B patients treated with Concomitant radio-chemotherapy(chemotherapy with docetaxel alone): patients randomized in the first stage before stopping Arm A. - group «All Taxotere® » or Taxotere® alone: all the patients treated with Concomitant radio-chemotherapy with docetaxel alone and the patients arm B randomized in the first stage of the study and the 13 patients included in arm B during the second stage (randomization stopped in Arm A). 82 patients were treated and were assessable for the safety for the intent-to-treat (ITT) population, 35 in Arm Tax/CDDP and 47 in Arm Taxotere® alone *Treatment Administration:* (4 patients did not receive treatment) The Taxotere® relative dose intensity per patient was 87% (n=35) for Tax/CDDP and 99% (n=47) for Taxotere® alone The cisplatin relative dose intensity per patient was 97% (n=35) for Tax/CDDP The patients who received 7 weeks of radiotherapy per protocol is respectively 82.9% in the arm Tax / CDDP and 97.9% in the arm Taxotere ® alone.

Efficacy Results

An interim efficacy analysis was planned for this study and the randomization in the arm A (Tax CDDP) was stopped for inefficacy (67.7% response rate => Amendment 3 – Arm a stopped). Only the response rate and overall survival are presented in this narrative report.

	Tax/CDDP	Taxotere®
Evaluable Patients	N=31	N=44
ORR (CR+PR)	21(67.8%)	39 (88.6%)
[CI95%]	[48.63 -83.32]	[75.44- 96.21]
Overall Survival (months)	18.98	36.76
[IC95%]	[15.11-not reached]	[20.57 –not reached]

Safety Results

Adverse Event per patient (ITT population)

Total patients treated = 82	**Taxotere® / CDDP**	**Taxotere®**
Number of patients with at least:	n=35 (231week)	n=47 (332 week)
1 AE	35 (100%)	47 (100%)
1 AE related to the treatment	34 (97.1%)	46 (97.9%)
1 AE grade 3 -4	30 (85.7%)	40 (85.1%)
1 AE grade 3 -4 related to the treatment	25 (71.4%)	35 (74.5%)
1 Serious AE	19 (54.3%)	11 (23.4%)
1 Serious AE related to the treat	14 (40.0%)	8 (17.0%)

Main toxicities per patient related to the treatment

	Tax/CDDP n=35 Number of pts (%)		All Taxotere® n=47 Number of pts (%)	
	Grade3-4	All grade	Grade3-4	All grade
Stomatitis	26 (74.2%)	31 (88.6%)	15(31.9%)	46 (97.8%)
Cutaneous toxicity	6 (17.1%)	25 (71.4%)	11 (23.4%)	40(85.1%)
Haematological Toxicity				
- Neutropenia	2 (5.9%)	11(31.4%)	-	2 (4.3%)
- Anemia	2 (5.9%)	26(74.3%)	-	22 (46.8%)
-Thrombocytopenia	1 (2.9%)	2(5.9%)	-	-
- Neutropenic infection	2 (5.9%)	4(11.4%)	1(2.1%)	4(8.5%)
Weight loss	3 (8.6%)	20 (57.1%)	6 (12.8%)	29(61.7%)

Date of report: October 2008