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**	**Clinicaltrials.gov Identifier:**	NCT00826852
		Study Code:	XRP6976B_6020
Generic drug name:	Docetaxel	**Date:**	23-July-2010

Title of the study:	Phase II Clinical Study Evaluating the Efficacy and Safety of Weekly Docetaxel and Four Weekly Carboplatin Therapy in the First-line Treatment of Advanced Non-Small Cell Lung Cancer		
Investigator(s):	Associate Professor Mustafa Özgüroğlu, M.D. ISTANBUL UNIVERSITY, CERRAHPAŞA FACULTY OF MEDICINE, DEPARTMENT OF MEDICAL ONCOLOGY,ISTANBUL,TURKEY		
Study center(s):	Istanbul University, Cerrahpaşa Faculty of Medicine, Department of Medical Oncology **Principal investigator:** Assoc. Prof.Dr. Mustafa Özgüroğlu Erciyes University, Faculty of Medicine, Department of Medical Oncology **Principal investigator**: Assoc. Prof.Dr. Özlem Er Uludağ University, Faculty of Medicine, Department of Medical Oncology **Principal investigator:** Prof.Dr. Türkkan Evrensel		
Publications (reference):	None		
Study period: Date first patient enrolled: 30 October 2003 Date last patient completed: 20 July 2009		**Phase of development:** II	
Objectives:	Primary: To assess the efficacy of the combination in terms of Objective (clinical and radiological) Response Rate Secondary: • To assess time to response, the duration of response • To assess the time to progression of the disease; assess the safety profile of the combination, and assess the survival time.		
Methodology:	Open-label, prospective, non-comparative, multicenter phase II clinical trial		
Number of patients:	Planned: 50 patients	Randomized: NA Enrolled: 49 patients	Treated: 48 patients
Evaluated:	Efficacy: 48 patients	Safety: 48 patients	

Diagnosis and criteria for inclusion:	Male or female patients aged ≤75 (minimum age 36, maximum age 75), with locally advanced or metastatic non-small cell lung cancer, diagnosed histologically and that had not been previously treated were enrolled to the study.
Investigational product:	The protocol treatment, as specified below, was repeated every 28 days and given as 6 cycles. Docetaxel Docetaxel was administered on day 1, 8 and 15 of treatment and docetaxel dosage was 30mg/m^2; was administered intravenously and the duration of infusion was 60 minutes. Carboplatin Carboplatin was administered on day 1 of treatment and the dosage was AUC 5; was administered intravenously and the duration of infusion was 60 minutes.
Duration of treatment: 24 weeks Patients who do not progress or develop unacceptable toxicity received 6 cycles of chemotherapy.	**Duration of observation:** Patients were monitored on every treatment day to capture possible adverse effects of the study drugs. First response evaluation was done at the end of 3 rd cycle and further evaluation was done at the end of 6th cycle. Each patient continued to be monitored after the discontinuation of treatment every 3 months until death, to assess relapse of disease (for patients responding to treatment), or progression of disease (for patients with stable disease).
Reference therapy:	NA
Criteria for evaluation: Efficacy:	**Clinical and laboratory assessments** Tumor response was determined according to the WHO criteria. Evaluation of the response was based on the observation of the recorded lesions at the time of patient inclusion (within 14 days of enrollment) and carried out at intervals and evaluation methods specified in the study protocol. **Assessment criteria.** -- The assessment of the response required the following criteria: patient receiving 3 complete cycles and two consecutive assessments of the disease, clinical or radiological, as appropriate. - The assessment of progression free survival (PFS): Time to progression was defined as the time from enrolment of the patient until the disease objectively progressed. For those patients who at the time of current assessment have not progressed, this parameter was calculated as the time from inclusion to the date of the last assessment. Similarly, for the patients who died without progression, this parameter was calculated as the time from the initiation of treatment to the date of death. The duration of response was also evaluated following the WHO/IUCC criteria. The assessment of complete response (CR): time to complete response to the treatment was determined as the first date patient evaluated as responded to treatment, and the last date at the time which progression is established. In case of partial response (PR), only the global duration of the response was calculated, the initial date being the date corresponding to the determination of the response. After completion of the protocol specified treatment, patients were followed every 3 months for the evaluation of progression or withdrawal from the study due to any cause, until death occurs. Laboratory testing was performed before treatment and once every 4 weeks, during each treatment cycle and the following parameters were examined: RBC, WBC and platelet count, differential, hemoglobin; AST, ALT, total bilirubin, alkaline phosphatase, and creatinine and serum electrolytes. The assessment of toxicity required 2 series of laboratory studies, with at least 1 week interval, and the physical examination performed before and after the treatment by the patient's doctor.

Safety:	**Safety evaluation** - Adverse event reporting, according to, CTCAE Version 3.0 - Laboratory examination every 4 weeks, i.e. one cycle (RBC, WBC and platelet count, hemoglobin; creatinine clearance; AST, ALT, total bilirubin, creatinine, alkaline phosphatase). - ECG (if clinically indicated) **Special Equipment/Measures** None
Statistical methods:	**Efficacy:** The efficacy and safety parameters were summarized by usingdescriptive statistics (mean, ratio, median, standard deviation, confidence intervals). The analyses of the changes observed during the treatment period as compared with pretreatment period and various subgroups analysis were conducted through parametric or non- parametric tests depending on the character of the data (t-test, Fischer's exact test or MacNemar test). Limit of statistical significance has been determined as $P < 0.05$ (two- sided). Survival was calculated by Kaplan-Meier method.
SUMMARY Efficacy results:	This study is a national, multi-center, open label and single-arm phase II clinical study. Male or female patients aged ≤75 (Although no lower age limit was specified in the study protocol the youngest recruited patient was 36 years old when enrolled), diagnosed as locally advanced or metastatic non- small cell lung cancer (NSCLC) and previously not treated for NSCLC, with ECOG Performance Status 0-2 and at least one measurable lesion in two dimensions by means of CT scan were enrolled in this study. This study enrolled only metastatic patients and all enrolled patients had at least one metastasis at inclusion. A total of 49 patients were enrolled to the study, however, as one patient withdrew his/her consent during the treatment cycles, there were 48 evaluable patients (9 females and 39 males). Among 48 evaluated patients, one patient did not receive treatment and 47 patients received study treatment, as Docetaxel + Carboplatin which was repeated every 28 days and given as 6 cycles. Docetaxel was administered on day 1, 8 and 15 of treatment and the dose was 30mg/m $^{2.}$. Carboplatin was administered on day 1 of treatment and the dose was AUC 5; calculated by Calvert Formula [(Total dose (mg) = target AUC (mg/ml/min) x (CrCl + 25)(ml/min)]. Among 48 evaluated patients, 39 were male (81.3 %) and 9 were female (18.7 %), the youngest patient was at the age of 36 during inclusion and the oldest was at the age of 75. ECOG performance status evaluation at inclusion was mostly (75%) asymptomatic but ambulatory (PS 1). Asymptomatic patients (PS 0) made only 10.4 % of the enrolled population. (PS 0) Patients received a higher median number of treatment cycles (6 cycles) while patients with PS 1 status at inclusion received a median number of 3 treatment cycles. A total of 47 patients completed the first treatment cycle and 42 patients completed the second cycle. During the third treatment cycle 35 patients received docetaxel but only 34 received carboplatin. One less patient received the carboplatin dosage during the 4th treatment cycle (22 docetaxel/21 carboplatin). There were 19 patients who completed the 5th treatment cycle and only 14 patients completed the 6th cycle of the chemotherapy. Thirteen patients were withdrawn from the study treatment due to the progression after 3$^{rd\ cycle}$ of the treatment as per protocol requirements while only one patient remained under follow-up until death. The study was concluded on 20 July 2009 after death of this last patient. No complete response was reported during the study. Response rates were reported at two time points during the treatment phase, 3rd and 6th treatment cycles. A total of 27.3 of patients had partial response during the first evaluation; however, another 33.3 % had stable disease. Despite treatment, 39.4 % of patients were evaluated as progressed at the time of 3rd treatment cycle. During the second evaluation period

	partial response rate was 21.1% (4 patients); and stable disease was observed in 31.6 % of evaluable patients (n=6). However, 47.4 % of patients had progressive disease.
SUMMARY Safety results:	During the study period investigators recorded a total of 179 adverse events which were graded according to NCI-CTC criteria Version 3.0. There were 44 cases of Serious Adverse Events recorded. In 6 cases, the SAE's were recorded as death cases, however no reasons were specified. In 27 cases SAE's either required hospitalization or an intervention. For 6 SAE cases study treatment was either interrupted or dosage decreased (13.7%, one case of febrile neutropenia, one case of pancytopenia and one case of thrombocytopenia) and 8 cases study treatment was stopped and not re-initiated (18.2%, no hematological cases). Among hematological adverse events (n=37), there were 31 cases of Grade 1; 5 cases of Grade 2 and only one case of Grade 3 hematologic toxicities observed. Most common hematological toxicities were Grade 1 Leucopenia and Neutropenia. There were no grade 4 hematological toxicities observed. There were 114 cases of non-hematological toxicities reported. There were no Grade 4 toxicities observed. Grade 2 non-hematological toxicities was the most frequent toxicity observed (38,5%), In two cases peripheral neuropathy was observed (1.14 %). Most common non-hematological adverse events were diarrhea (5.14 %) and nausea (4.0%). These adverse events were rated as Grade 1 or 2. A total of 117 (59.5%) adverse events were reported as related to study drugs (docetaxel and/or carboplatin) while 45 (24.3%) of them were reported as not related.
Date of report:	07 July 2010