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:**	NCT00069888
		Study Code:	XRP6976J_2501
Generic drug name:	Docetaxel	**Date:**	17 July 2008

Title of the study:	A Multicenter, Open-Label, Phase II Trial of Adjuvant Taxotere® in Patients at High Risk of Relapse following Prostatectomy (Study Code: XRP6976J_2501)	
Investigator(s):	Mario Eisenberger, MD Johns Hopkins University 1650 Orleans Street Suite 1M51 Baltimore, MD 21231	
Study center(s):	Nine active study centers in the United States	
Publications (reference):	Adjuvant weekly docetaxel for patients with high risk prostate cancer after radical prostatectomy: A multi-institutional pilot study (Kibel AS, Rosenbaum E, Kattan MW, Picus J, Dreicer R, Klein EA, et al. J Urology 2007;177:1777-81.)	
Study period: Date first **patient/subject** enrolled: 01/Apr/2002 Date last **patient/subject** completed: 02/Jan/2007		**Phase of development:** Exploratory
Objectives:	Primary Objective: To assess the preliminary effects of 6 cycles of adjuvant, weekly Taxotere® (3 weeks on/1 week off) on the rate of progression free-survival (PFS) among prostate cancer patients at high risk of relapse following radical prostatectomy. Secondary Objectives: To determine the 3-year survival rate of prostate cancer patients at high risk of relapse following prostatectomy who are treated with 6 cycles of adjuvant, weekly Taoxtere (3 weeks on/1 week off). To determine the time to progression of disease for prostate cancer patients at high risk of relapse following prostatectomy who are treated with 6 cycles of adjuvant, weekly Taxotere (3 weeks on/1 week off). To determine the safety and tolerability of 6 cycles of adjuvant, weekly Taxotere (3 weeks on/1 week off).	
Methodology:	This was a multicenter, non randomized, single arm, open-label study.	

Number of patients/subjects:	Planned: 75 patients to enroll 70 evaluable patients	Enrolled: 77 patients	Treated: 77 patients
Evaluated:	Efficacy : 77 patients (intent-to-treat) 74 patients (per protocol)	Safety: 77 patients	
Diagnosis and criteria for inclusion:	Patients with pathologically confirmed adenocarcinoma of the prostate who were between 4 and 12 weeks postprostatectomy with an R_w' >2.84 and no radiographic evidence of metastasis; Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; adequate hematologic, renal, and hepatic function; no prior prostate cancer treatment (ie, systemic hormonal or chemotherapy or radiation therapy); and no concomitant alternative therapies for prostate cancer.		
Investigational product: Dose: Administration:	Taxotere (docetaxel) 35 mg/m² Intravenous infusion (30 minutes) on days 1, 8, and 15 of each 28-day cycle		
Duration of treatment: A total of six 28-day cycles	**Duration of observation:** Prestudy Period (up to 6 months, depending on prestudy evaluation); Treatment Period (a maximum of six 28-day cycles); and Follow-up Period (up to 3 years after radical prostatectomy to document disease progression)		
Reference therapy:	NA		
Criteria for evaluation:			
Efficacy:	The primary efficacy endpoint was the PFS rate at 2 and 3 years. This was derived from PFS, defined as the time interval from the date of surgery to the first occurrence of biochemical relapse (prostate specific antigen [PSA] ≥0.2 ng/mL and rising as determined by sequential PSA measurements obtained in accordance with the protocol schedule), clinical/radiological evidence of metastatic disease, or death due to any cause in the absence of prior biochemical relapse. Secondary efficacy endpoints included (1) the time to disease progression, defined as the interval from prostatectomy until the occurrence of disease progression (ie, PSA ≥0.2 ng/mL and rising), clinical/radiological evidence of metastatic disease, or death due to any cause in the absence of prior biochemical relapse and (2) the survival rate at 3 years.		
Safety:	Safety criteria included adverse events (AEs) reported by the patient or noted by the Investigator, and standard hematology and blood chemistry evaluations.		

Statistical methods:	The distribution of PFS was estimated and analyzed for the intent to treat (ITT) population (primary analysis) and the per protocol (PP) population (supportive analysis) using the Kaplan-Meier method. Median PFS was described with a 95% confidence interval (CI) computed using the Brookmeyer and Crowley method. The probability of being progression-free at 12, 24, and 36 months was derived (based on Kaplan-Meier estimates) from the analysis with 95% CI computed using the Greenwood formula. No interim analyses were planned for this study. Overall survival was estimated using the Kaplan-Meier method for the ITT population. Survival was characterized in terms of median survival with the 95% CI computed using the Brookmeyer and Crowley method and the probability of being alive at 12, 24, and 36 months (estimated by the Kaplan-Meier method) with the 95% CI computed using the Greenwood formula. Assessments of safety were based mainly on the incidence of AEs and on the number of laboratory values that fell outside predetermined ranges or worsened based on the National Cancer Institute Common Toxicity Criteria (NCI CTC).
Summary: Efficacy results:	The primary efficacy variable was the PFS rate estimate at 2 and 3 years after prostatectomy. The respective PFS rate estimates were 0.34 (95% CI: 0.237, 0.453) and 0.32 (95% CI: 0.210, 0.422) for the ITT population. For the PP population, the PFS rate estimates were 0.35 (95% CI: 0.240, 0.458) at 2 years and 0.32 (95% CI: 0.213, 0.427) at 3 years. For these analyses, biochemical relapse was defined as a PSA value ≥0.2 ng/mL and rising. An ad hoc analysis of PFS, using a different definition of biochemical relapse (ie, PSA value of ≥0.4 ng/mL), also was performed. The respective 2- and 3-year PFS rate estimates for the ITT population were 0.42 (95% CI: 0.305, 0.528) and 0.36 (95% CI: 0.249, 0.468), and for the PP population they were 0.43 (95% CI: 0.314, 0.541) and 0.37 (95% CI: 0.256, 0.480). A Cox Proportional Hazards Regression model was used to explore the association between disease characteristics and the PFS rate. Of the 5 covariates (ie, presurgery PSA value, surgical margin status, seminal vesicle involvement, pathologic Gleason sum, and lymph node involvement), only pathologic Gleason sum (p = .0174) and lymph node involvement (p = .0128) were statistically significantly associated with the PFS rate at the 5% significance level with respective hazard ratios (HRs) of 1.476 (95% CI: 1.071, 2.035) and 2.408 (95% CI: 1.206, 4.809). Median time to progression (determined using PSA ≥0.2 ng/mL and rising as the criterion for biochemical relapse) was similar for the ITT and PP populations. The respective median times were 14.07 months (95% CI: 11.97, 19.18) and 14.61 months (95% CI: 11.97, 21.15). The ad hoc analysis of median time to progression (determined using PSA ≥0.4 ng/mL as the criterion for biochemical relapse), also yielded similar results for the ITT and PP populations. The respective median times were 15.67 months (95% CI: 12.82, 25.11) and 15.90 months (95% CI: 13.15, 30.36). At 3 years after prostatectomy, median survival was not achieved since deaths were recorded for only 7 (9.09%) patients. The respective survival rate estimates (95% CI) at 1, 2, and 3 years were 0.97 (0.938, 1.010), 0.96 (0.917, 1.004), and 0.91 (0.842, 0.973).

Safety results:	Administration of docetaxel 35 mg/m² on a weekly schedule (days 1, 8, and 15 of each 28-day cycle) for up to 6 cycles appeared to be well-tolerated based on achieved exposure, TEAEs, hematology and blood chemistry laboratory values, and vital sign measurements. Sixty-seven (87.0%) patients completed all 6 cycles (ie, had at least 1 dose of docetaxel in each cycle). The respective, overall mean and median relative dose intensities were 0.983 and 0.987. The incidence of dose reductions, delays, and missed doses because of study drug-related toxicities was 5.2% (4 patients), 2.6% (2 patients), and 7.8% (6 patients), respectively. While all 77 patients (100.0%) experienced at least 1 treatment-related TEAE, most TEAEs were grade 1 or 2 (or mild or moderate in severity). In general, the TEAEs observed in this study are consistent with the docetaxel known safety profile. The most frequently reported treatment-related TEAEs (incidence ≥50%) included fatigue, dysgeusia, alopecia, nail disorder, and increased lacrimation. One or more grade 3 or 4 TEAE was reported for 22 (28.6%) patients, and 1 or more possibly or probably treatment-related, grade 3 or 4 TEAE was reported for 16 (20.8%) patients. The only treatment-related, grade 3 or 4 TEAEs reported in more than 1 (1.3%) patient each were fatigue and dyspnoea (3 [3.9%] patients) and capillary leak syndrome (2 [2.6%] patients). Six (7.8%) patients experienced at least 1 treatment-emergent SAE. Study drug was discontinued for 5 (6.5%) patients, and dosing was temporarily interrupted or otherwise adjusted for 25 (32.5%) patients. Seven (9.1%) patients died. Disease progression was the cause of death in 3 (3.9%) patients, and 2 (2.6%) patients died due to cardiac events that occurred approximately 6 months or longer after the last dose of study drug. One death that occurred approximately 1.5 years after the last dose of study drug was attributed to underlying, probably treatment-related pulmonary fibrosis. Another death (cause unknown) occurred 2 days after the last dose of study drug and was recorded as the outcome of a possibly treatment-related TEAE (acute abdomen). Shifts from baseline for hematologic laboratory variables were most marked for neutrophils and white blood cells and minimal for platelets. The incidence of grade 3 neutropenia was 2.6% (2 patients) and grade 3 decreases in WBC occurred in 8 (10.4%) patients. Shifts from baseline were observed for several blood chemistry variables. The only grade 3 elevations included SGPT (1 [1.3%] patient), sodium (2 [2.6%] patients), and glucose (11 [14.5%] patients). In addition, 2 (2.6%) patients had grade 4 glucose elevations. In several cases, hyperglycemia or diabetes mellitus was noted in the medical history. The observed incidence of hyperglycemia may be attributable to the requirement for dexamethasone administration before and after docetaxel administration. Further, blood samples may have been obtained under nonfasting conditions.
Date of report:	21-May-2008