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:**	NCT00782041
		Study Code:	L_8311
Generic drug name:	Oxaliplatin	**Date:**	24 October 2008

Title of the study:	Phase II study of oxaliplatin in combination with 5 -fluorouracil(5-FU) and folinic acid (FA) in patients who have failed first-line treatment for locally advanced or metastatic cervical cancer		
Investigator(s):	Assoc.Prof. Dr.Vicharn Lorvidhaya, Faculty of Radiation, Chiangmai University, Chiangmai, Thailand		
Study center(s):	Monocentric		
Publications (reference):	NA		
Study period: Date first patient/subject enrolled: 23-Jan-2003 Date last patient/subject completed: 07-Aug-2003		Phase of development: Phase II	
Objectives:	Primary Study Endpoint: Response rate - RECIST (uni-dimensional) criteria Secondary Study Endpoint(s): Progression free survival Overall survival Tolerance safety		
Methodology:	*Open-label, Non-randomisation, Non-comparator*		
Number of patients/subjects:	Planned: 33-36	Randomized: NA	Treated: 11 Completed: 5
Evaluated:	Efficacy: - To evaluate response rate, in each treatment arm. - To evaluate the progression-free survival. - To evaluate the overall survival.	Safety: - To investigate safety using NCI-CTC criteria version 2 by adverse events happened and laboratory parameters	Pharmacokinetics: NA

Diagnosis and criteria for inclusion:	Eligibility criteria: - Have Locally advanced/metastatic squamous or adenocarcinoma of the cervix - Prior therapy with cisplatin allowed - First-line treatment may have been surgery,radiotherapy or chemotherapy either as a single agent or multi-modality therapy - Must have measurable disease - Histologically Proven Carcinoma of the cervix - No known allergy to one of the study drugs - No peripheral neuropathy > grade2 - ECOG PS <=2 - No other serious concomitant illness - Fully recovered from any prior therapy - Patient and doctor have signed informed consent - Age >18 - Lab: ANC >1500 mm^3, Platelets > 100000 mm^3, Creatinine <= 1.5 x Normal value, Bilirubin <= 1.5 x Normal value, SGPT (ALT) <= 2.5 x Normal value
Investigational product: Dose: Administration:	Oxaliplatin: Oxaliplatin is presented as a whitish freeze-dried powder packaged in glass vials. It is reconstituted by adding water for injection or 5% glucose solution and then diluting in an infusion solution. 5-Fluorouracil, , Folinic acid (racemic): commercially available formulation The protocol is 2 weekly regimen as • Oxaliplatin 85 mg/m^2 over 3 hours at D1 and D15 • 5-FU 2,000 mg/m^2 over 4 hours at D1 • and Folinic acid 20 mg/m^2 Bolus at D1 IV

Duration of treatment: Treatment will be administered until disease progression, unacceptable toxicity, patient refusal, or treatment delay > 3 weeks Patient will be considered to be on-study for the duration of treatment and during 30 days following treatment discontinuation.	Duration of observation: All included patients will be followed up recovery from residual toxicities/ AEs. Whenever possible, follow-up will be continue until death.

Reference therapy: Dose: Administration:	NA NA NA
Criteria for evaluation:	
Efficacy:	To evaluate response rate, in each treatment arm. To evaluate the progression-free survival. To evaluate the overall survival.
Safety:	To investigate safety using NCI-CTC criteria version 2
Statistical methods:	The primary efficacy endpoint will be Response rate. The objective response rate using RECIST (uni-dimensional) criteria will be determined with its 95 % confidence interval. The secondary efficacy endpoint(s) will be Progression free survival, Overall survival and Tolerance safety. The progression-free survival (or the time to progression) and the overall survival will be analyzed according to the Kaplan-Meier method. The safety evaluation will be based on the review of NCI-CTC grading and descriptive statistics (listings, summary tables, and data plots). Appropriate hypothesis tests may be performed on parameters of interest if possible trends are observed in the summary statistics. The worst grade of prelisted toxicity will be summarized by patient and by cycle in each treatment group. Grade 3-4 toxicities *will be summarized* by patient and by cycle in each treatment group.

Summary:	Early on during routine monitoring a discrepancy between planned and delivered dose of experimental treatment was detected. Patients should have received a 2-weekly regimen of oxaliplatin based therapy instead patients were dosed with a 3-weekly regimen. This was deemed to be a major protocol violation and as such, and in agreement with the investigator, the study was closed. Due to too few patients being treated no conclusion can be drawn from this study.
Efficacy results:	<u>Response Rate</u> 11 patients were enrolled and a total of 59 cycles of chemotherapy were administered. A total of 5 cases were able to be evaluated for response: • 4 cases were evaluated as Progressive Disease • 1 case as Stable Disease The remaining 6 cases were excluded from the analysis: • 3 cases had treatment refused by the patinet • 2 cases had a treatment delay > 3 weeks • 1 case was lost to follow-up <u>Time to progression</u> • TTP 6 months - 1 case • TTP 5 months - 1 case • TTP < 3 months - 3 cases
Safety results:	In terms of the limited safety data that was collected the following adverse events were reported: • Neuropathy-sensory: Grade 1 = 4 events, Grade 2 = 9 events • Fatigue: Grade 1 = 3 events, Grade 2 = 1 event • Alopecia: Grade 1 = 4 events • Nausea/ Vomiting and Diarrhea: Grade 2 = 1 event, Grade 3 = 1 event • Neutropenia: Grade 2 = 3 events • Thrombocytopenia: Grade 2 = 3 events • Anemia: Grade 2 = 2 events • Platelet: Grade 1 = 1 event • Partial Bowel Obstruction 1 event Only 1 SAE was reported as being Grade 4 as defined by NCI-CTC criteria version 2. This was reported as severe vomiting and extreme fatigue which in the investigator's opinion was possibly related to the combination effect from the chemotherapy.
Date of report:	29-Sep-2008