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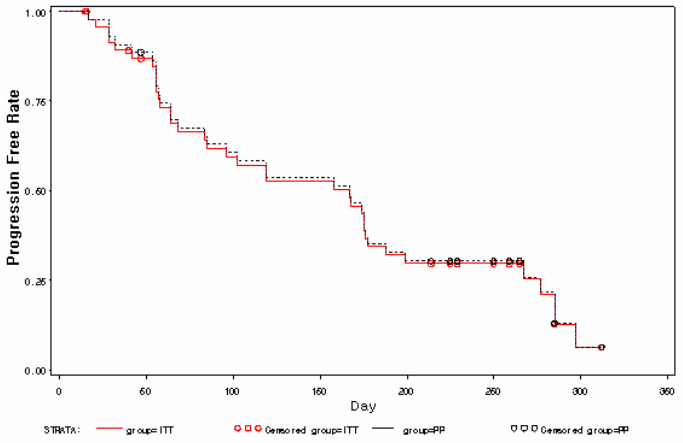
Sponsor/company:	**sanofi-aventis**	**ClinialTrials.gov Identifier:**	**NCT00261092**
		Study Code:	**PM_L_0126**
Generic drug name:	**oxaliplatin**	**Date:**	**26 December 07**

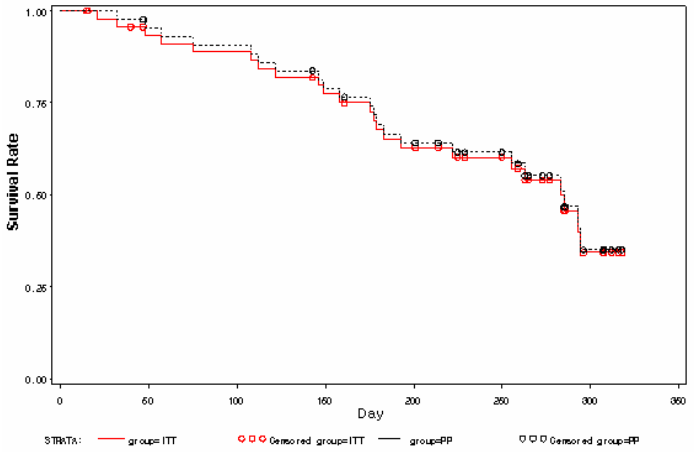
Title of the study:	Multicenter, open-lable, phase II, clinical study of oxaliplatin + gemcitabine combination therapy (GEMOX) in patients with advanced and metastatic pancreatic cancer: Phase II clinical study of GEMOX
Investigator(s): **Coordinating Investigators**	JunSuk Kim (Korea Univ. Kuro Hospital)
Study center(s):	13 centers Korea University Guro Hospital Korea University Anam Hospital Catholic University St. Vincent Hospital Korea Cancer Center Hospital Samsung Medical Center Keimyung University Dongsan Medical Center Yeungnam University Medical Center Catholic University, Gangnam St. Mary's Hospital Seoul National University Hospital Anyang Sacred Heart Hospital, Hallym University Asan Medical Center Yongdong Severance Hospital Veterans Hospital
Publications (reference):	NA

Study period: Date first patient/subject enrolled: 24-Oct-2005 Date last patient/subject completed: 30-Sep-2006	**Phase of development:** Phase II

Objectives:	The objective of this study is to assess whether the combination therapy of gemcitabine whose efficacy against pancreatic cancer is already well established and oxaliplatin whose efficacy is recognized through preclinical and clinical studies in the U.S., France, Belgium, Italy, etc. is safe in Korean patients and effective in terms of response rate as a primary objective. - Primary objective: response rate (based on RECIST criteria) - Secondary objective: Time to progression Overall survival Clinical benefit Quality of life, safety		
Methodology:	*Prospective, Non blinded*		
Number of patients/subjects:	Planned: 48	Randomized: NA	Treated: 48
Evaluated: Efficacy Safety: Physical & Laboratories examination	- Primary endpoint: response rate (based on RECIST criteria) - Secondary endpoint:: Time to progression Overall survival Clinical benefit Quality of life, safety		
Diagnosis and criteria for inclusion:	• Histologically confirmed adenocarcinoma of the pancreas		
Investigational product: Dose: Administration:	Eloxatin® Oxaliplatin 100mg/m² Day 1: 1000 mg/m² of gemcitabine injected intravenously at rate of 10 mg/m²/min. Day 2: 100 mg/m² of oxaliplatin injected intravenously for two hours. The above administration was repeated every two weeks.		
Duration of treatment: About 5 months ⇨ 7 cycles per patient (treatment is repeated in every 2 weeks) Maximum 16 cycles		**Duration of observation:** About 8 months. LPI : 13 Feb 2006, LPO : 30 Sep 2007 Observations from completion of each patient's treatment to LPO	

Reference therapy: Dose: Administration:	NA NA NA
Criteria for evaluation:	- Primary endpoint: response rate (based on RECIST criteria) - Secondary endpoint: Time to progression Overall survival Clinical benefit Quality of life, safety
Safety:	1. It was considered that if the patient received cancer chemotherapy for at least one cycle, the patient was evaluable for the safety assessment. 2. The variables of safety assessment included description of death due to toxicity, early discontinuation of treatment due to toxicity, description of adverse events, serious adverse events (SAE), and assessment of toxicity using NCI-CTCAE v 3.0. 3. The others such as laboratory test results, degree of sensory neuropathy and weight were included in the safety assessment.
Statistical methods:	Primary endpoint: The objective response rate was provided and one-sided 95 % confidence interval was estimated. Secondary endpoint: 1. Time to progression was shown in a graph through Kaplan-Meier method and the median value and two-sided 95 % confidence interval were estimated. 2. Overall survival time was shown in a graph through Kaplan-Meier method and the median survivial time (50 percentile) and corresponding 95 % confidence interval were estimated. 3. For clinical benefit, the frequency analysis was performed in the subjects who showed clinical benefit regarding pain intensity, pain index and activities of daily living (ADL). The clinical benefit was summarized through mean, standard deviation, median and range of three scales. 4. For quality of life, the best scores of the overall QoL scale, five function scales and nine symptom scales obtained during the study were compared with baseline value. The quality of life of the patients who had shown PR, SD and PD as results of tumor assessment were compared. The quality of life of the subjects who lived shorter than the median survival and that of those who lived longer were also compared.

Summary:	1. Objective Response Rate Eight subjects (18.18 %) (95 % C.I.: 8.62 %, -) showed response (partial response: eight subjects). The objective response rates were same both in ITT population and PP population The objective response rate assessed by IRC was 27.27% (12 patients with SD) both in the ITT population and the PP population. 2. TTP and OS According to Kaplan-Meier estimate of time to progression, the median TTP time was 167 days (95 % C.I.: 84,177); 58 days for 75 % TTP time of the subjects and 277 days for 25 % TTP time. ITT population and PP population had the same results and the very similar survival curve until the disease progression. According to Kaplan-Meier estimate of overall survival time, the median survival time of ITT population was 283 (95 % C.I.: 193, -); 158 days for 75 % survival time of the subjects. The median survival time of PP population was 285 days (95 % C.I.: 193, -); 175 days for 75 % survival time of subjects. The survival time of 25 % could not be estimated. 3. Clinical Benefit and Quality of Life Among 44 subjects whose clinical benefit could be assessed, 16 subjects (36.36 %) showed the clinical benefit. Most of the scales indicated the quality of life after the treatment had significantly improved and maintained regardless of disease progression or survival time. Time to progression 

	Overall survival 

Safety results:	Adverse Events Safety assessment showed that 46 of 48 subjects (95.83 %) developed at least one adverse event. Among them, 42 subjects (87.50 %) developed the adverse events which had causal relationship with the study drug(ADR). Major adverse events related to 'gastrointestinal system' were 'nausea' (41 subjects, 85.42 %), 'anorexia' (32 subjects, 66.67 %), 'vomiting' (30 subjects, 62.50 %). The adverse events related to 'constitutional symptom' were 'fatigue' (18 subjects, 37.50 %), and 'temperature increase' (17 subjects, 35.42 %). The most common pain related adverse event was 'stomachache' (21 subjects, 43.75 %). And 'neurological' adverse event occurred in 21 subjects (43.75 %) and 'dermatological' adverse event in 20 subjects (41.67 %). For most of those adverse events, the relationship with the study drug could not be excluded. Grade 3 and 4 hematologic toxicities occurred as follows; neutropenia in 6.25%, anemia in 6.25% and thrombocytopenia in 2.1%. New or worsening adverse events were reported for 4 patients after the end of the study. The adverse event was 'Infection-other(septic cholangitis)' with 5th grade and 'Death NOS' with 5th grade. 'Muscule weakness-generalized' worsened from 1st grade to 5th grade after treatment. And there is 'Pain-NOS' with 3rd grade. All they were serious adverse event, but it wasn't considered to be possibly treatment-related. SAE The serious adverse events were observed in total of 18 subjects (37.50 %) at the completion of chemotherapy. Among them, the adverse events related to the study drug occurred in 10 subjects (20.83 %) and 'anorexia', 'nausea' and 'fever' occurred in two subjects, respectively. Four subjects died due to an adverse event. Among them, three subjects died of sepsis, general weakness and septic cholangitis respectively during the course of chemotreatment and one died due to unknown cause.
Date of report:	28-Jun-2007