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Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00259363
		Study Code:	L_8330
Generic drug name:	Oxaliplatin	**Date:**	08/04/ 2008

Title of the study:	L_8330: Phase I-II study of preoperative oxaliplatin-FU and radiotherapy for patients with rectal cancer		
Investigator(s):	Dr. Eugenio Marcuello Gaspar – HOSPITAL DE LA SANTA CREU I SANT PAU, BARCELONA		
Study center(s):	The study was performed within several Departments of 2 Spanish hospitals: Hospital de la Santa Creu i Sant Pau (Barcelona) – Dpt. Of Medical Oncology, Dpt. Of Radiotherapeutic Oncology, Surgery Service and Hospital Sant Joan de Reus (Tarragona) – Dpt. Of Medical Oncology.		
Publications (reference):	NA		
Study period: Date first patient enrolled: 25-may-2002 Date last patient completed: 30-jun-2006		**Phase of development:** I-II	
Objectives:	Primary objective - Phase I: To determine the Maximum Tolerated Dose, dose limiting toxicity and Recommended Dose of the proposed flowchart, among the Oxaliplatin dose levels in this study for the neoadjuvant treatment of the Rectal Cancer. - Phase II: To determine the efficacy of the treatment in terms of clinical and pathologic clinical rates of the treatment flowchart at the recommended dose established at Phase I.		
Methodology:	*Open, non-randomized*		
Number of patients	Planned: 46	Randomized: NA	Treated: 42
Evaluated:		Safety: 46	

Diagnosis and criteria for inclusion:	Same criteria at Phase I and at Phase II: - ECOG: 0-2 - Life expectedness greater than 3 months. - Histological rectal adenocarcinoma confirmation. 6. T3 N0-2 and M0 Preoperative stages, bulky tumors, ,tumors at risk in R1 ó R2 surgery or preoperative T4 stage or non resectable tumors. 7. Tumor can be placed until 12 cms above pectin line from the anal margin 8. Chemotherapy naive (6 months before of the inclusion) . Pelvic radiotherapy is forbidden.
Investigational product: Dose:	Oxaliplatin

Dose level	**Oxaliplatin**	**5-FU**	**Radiotherapy**
	Days 1, 15, 29	1-7, 8-14, 15-21, 22-28, 29-35	1-5, 8-12, 15-19, 22-26, 29-33
1	65 mg/m^2	225 mg/m^2/day	180 cGy/day
2	75 mg/m^2	225 mg/m^2/day	180 cGy/day
3	85 mg/m^2	225 mg/m^2/day	180 cGy/day

Administration:	i.v.
Duration of treatment: See reference above	Pre-operative QRT: 5 weeks Surgery: 6-8 weeks after QRT Post-operative QRT: 6 months
Duration of observation:	Every 3 months
Reference therapy: Dose: Administration:	Oxa 60 mg/m2/15 days, 5-FU 225 mg/m2/ day 5 weeks during radiotherapy (RT) 45 Gys/25 days
Criteria for evaluation:	Clinical Response Rate. Tumor Regression Rate (by Grade)
Statistical methods:	Two steps Simon´s Method The primary end point is the response rate The study was designed to achieve 50% of response. If the response is less than 40%, the study´ll be early finished. To achieve 60% of response, the sample size required to detect this response was 46 patients

Efficacy Results	**Clinical response** PR: 66% CR:10% NR: 24% **Tumor Regression Grade** Grade 1: 10% Grade 2: 38% Grade 3: 28% Grade 4: 24%
Safety Results	**Grade II/IV Toxicity** Asthenia:11% Neutropenia/fever: 0% Anaemia: 2,4% Neutropenia: 2,4% Dermatitis: 2,4% Cystitis: 2,4% Stomatitis: 2,4% Rectal mucositis: 15% Diarrhea:17% Nausea and vomiting : 2,4%
Summary:	Results: Phase I : Level 1: 6 pts treated. 2 pts had CTC-Grade 3 diarrhoea and 1 pt grade 3 rectitis, considered as DLT and leading to chemoradiotherapy discontinuation. Level 0(OXA 60 mg/m² and 5FU 225 mg/m²): 3 pts treated and none had grade 3-4 toxicity, being this dose level considered as MTD. There was not neurologic toxicity greater than grade 1. All 9 pts completed radiotherapy, but 3 pts on dose level 1 did not complete third OXA dose and up to 2 weeks of 5FU. All 9 pts underwent radical surgery, without operative mortality. Overall response rate was > 80%. 4 pts (44%) had a major down-staging (2 pT0N0M0 and 2 pT2N0M0). Conclusions: This combined treatment appears feasible and effective. OXA 60 mg/m²/15 days x 3 doses should be the recommended dose for phase II studies. 6 additional pts have been included in the trial for a better characterisation of the safety profile of the combination and recommended dose for Phase II Oxa 60 mg/m2/15 days, 5-FU 225 mg/m2/ day 5 weeks during radiotherapy (RT) 45 Gys/25 days. Phase II: The tumor response rate was 76% and half of the patients demonstrated a major pathological tumor regression. This strategy may enhance the rate of curative surgery and permit sphincter preservation in 2/3 of patients
Date of report:	31-March-2008