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:**	NCT00263029
		Study Code:	L_8479
Generic drug name:	Oxaliplatin	**Date:**	22/01/ 2008

Title of the study:	Preoperative Radiotherapy/ Oxaliplatin/ Capecitabine Treatment For Unresectable Locally-advanced rectal cancer (PROCTFUL)	
Investigator(s):	Name : Dr. Ray TT Chan Address : Department of Clinical Oncology, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong Remarks: Dr. Ray TT Chan is currently in private practice.	
Study center(s):	One center Queen Mary Hospital, Hong Kong	
Publications (reference):	In submission	
Study period: Date first patient enrolled: 12 June 2002 Date last patient completed: 02 March 2007		**Phase of development:** Phase 2
Objectives:	Primary objective: • To determine the efficacy in down-staging by neoadjuvant chemoradiation using oxaliplatin and capecitabine: This rate is represented by the surrogate endpoints of response rates*, both clinical and pathological, of the primary rectal cancer observed after the chemoradiotherapy. • To determine the histologically confirmed complete resection rate (R0 rate). **The clinical response rate in the present study is to be assessed by comparison between serial MRI (or less preferably CT) before and after the neoadjuvant concomitant therapy (coded mT-stage e.g. mT3 or mT4 before and after treatment) and the pathological response rate is to be assessed by the pathological examination of the resected specimen. As it is not appropriate to compare the latter with the pre-treatment clinical T-stage obtained on imaging, only the complete pathological response rate is to be reported and no correlation between the remaining incomplete pathological response rate with the clinical response rate is to be attempted.* Secondary objective(s): • To determine the disease free survival (DFS) and overall survival (OS) rate of this combination regimen of oxaliplatin, capecitabine and pelvic region radiotherapy at 24 months and 36 months.	

<table>
<tr><td></td><td>

To assess the toxicity profile (NCI CTC v2.0) of the combination based on the adverse events and abnormal laboratory values recorded during and up to 4 weeks after treatment. Late toxicity will be recorded up to 36 months after radiotherapy.
To determine the failure pattern: the local recurrence rate, the abdominal recurrence rate and the distant recurrence rate at 24 and 36 months.
In relevant patients, the sphincter-sparing rate is to be recorded.
In all patients, the sphincter function is to be assessed by the the MSKCC anal sphincter function criteria.
To determine the compliance with the planned dose of chemotherapy.
To determine the compliance with the planned dose of radiotherapy.

</td></tr>
<tr><td>Methodology:</td><td>Single-centre, single-arm, non-randomized, phase II trial</td></tr>
<tr><td>Number of patients:</td><td>Planned: 28 | Randomized: N/A | Treated: 18</td></tr>
<tr><td>Evaluated:</td><td>Efficacy/Pharmacodynamics: 18 | Safety: 18 | Pharmacokinetics: N/A
<table>
<tr><th>Parameter</th><th>Assessment</th><th>Evaluable patients</th></tr>
<tr><td>Efficacy</td><td>Response rate</td><td>Clinical RR: 17 patients
Pathological RR: 18 patients</td></tr>
<tr><td></td><td>R0 rate</td><td>18 patients</td></tr>
<tr><td></td><td>3-year disease-free survival</td><td>18 patients</td></tr>
<tr><td></td><td>3-year overall survival</td><td>18 patients</td></tr>
<tr><td>Safety</td><td>Toxicity</td><td>18 patients</td></tr>
</table>
</td></tr>
<tr><td>Diagnosis and criteria for inclusion:</td><td>Rectal adenocarcinoma (clinically stage mT3 or mT4), either considered (1) inoperable, or (2) locally advanced, where histologically confirmed curative resection is considered unlikely.</td></tr>
<tr><td>Investigational product:
Dose:

Administration:</td><td>Oxaliplatin (+ Radiotherapy and Capecitabine)
Oxaliplatin 60mg/m² on the date of radiotherapy (completed within 2 hours prior to radiotherapy).
Remarks: Capecitabine 750mg/m² bid 10 doses/ week (The 1st dose is to be taken in the evening before the first fraction of radiotherapy)

Oxaliplatin as 2-hours intravenous infusion</td></tr>
<tr><td colspan="2">Duration of treatment:
5-6 weeks coinciding with the planned radiotherapy

Duration of observation:
3-years</td></tr>
</table>

Reference therapy: Dose: Administration:	N/A N/A N/A
Criteria for evaluation:	
Efficacy: Or Pharmacodynamics:	Response rate (both clinical and pathological) of the primary rectal cancer observed after the chemoradiotherapy. Histologically confirmed complete resection rate (R0 rate) 3-years disease-free-survival 3-years overall survival
Safety:	Adverse events reported by the patient/subject or noted by the investigator and standard hematology and blood chemistry, and rating according to NCI CTC version 2
Pharmacokinetics:	N/A
Pharmacokinetic sampling times and bioanalytical methods:	N/A
Statistical methods:	Statistical analyses is performed by intention to treat. Descriptive statistics is provided according to the nature of variables: • Size, mean, standard deviation, minimum and maximum, median and quartiles for quantitative variables. • Size and absolute frequencies for qualitative variables. Time to events is illustrated with survival curves using the Kaplan-Meier Method.
Summary:	17 of the 18 subjects had complete (R0) resection. High grade pathologic response was observed in 17 of the 18 patients and down-staging and complete pathologic response was recorded in 78% and 22% of patients respectively. Survival and relapse-free survival at 3-year were 78% and 61% respectively. Treatment-related toxicities were manageable with no grade 4 toxicities and grade 3 anaemia, urinary frequency, tenesmus and diarrhea, alone or in combination, were seen in 4 patients.

<table>
<tr><td>Efficacy results:
or
Pharmacodynamic results:</td><td>
<table>
<tr><td>Assessment</td><td>Results</td></tr>
<tr><td>Response rate (RR)</td><td>Clinical RR (N=17): 9 partial response (53%) and 8 static disease (47%).
Pathologic RR (N=18): 4 complete responses (22%) and 14 “down-staging*” (78%).
*a reduction in size by ≥ 50% on impression-response scoring</td></tr>
<tr><td>R0 rate</td><td>N=17(94%)</td></tr>
<tr><td>3-year disease-free survival (DFS)</td><td>Median DFS: not yet reached
3-year DFS: 61%</td></tr>
<tr><td>3-year overall survival</td><td>Median OS: not yet reached
3-year OS: 78%</td></tr>
</table>
</td></tr>
<tr><td>Safety results:</td><td>
<table>
<tr><th>Toxicity (G3)</th><th>No. of patients</th><th>% of cycles</th></tr>
<tr><td>Diarrhoea</td><td>1</td><td>2%</td></tr>
<tr><td>Tenesmus</td><td>3</td><td>4%</td></tr>
<tr><td>Urinary frequency</td><td>1</td><td>2%</td></tr>
<tr><td>Haemoglobin</td><td>1</td><td>2%</td></tr>
</table>
No specific serious GI/ haematological toxicities
Skin toxicity: G2 local radiation dermatitis (33%)
No hand-foot-syndrome
Sensory neuropathy:
Reversible G1 (50%), G2 (6%)
Overall well tolerated.
SAE: 3 (1 anaphylactic reacti on, 1 rash and fever, 1 poor wound healing)
</td></tr>
<tr><td>Pharmacokinetic results:</td><td>N/A</td></tr>
<tr><td>Date of report:</td><td>28 Dec 2007</td></tr>
</table>