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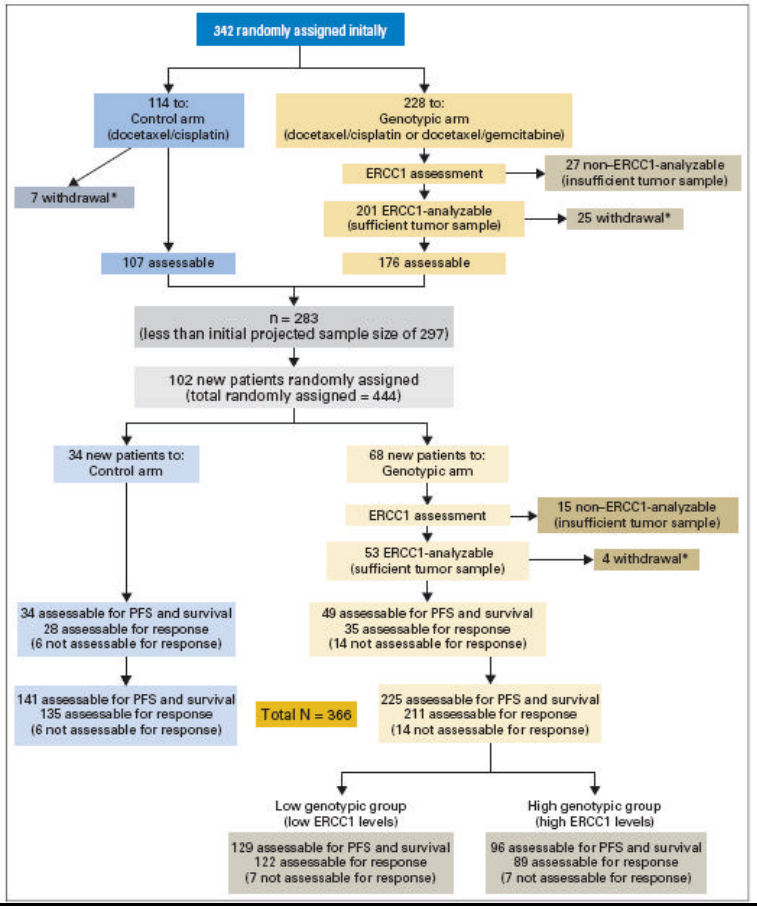
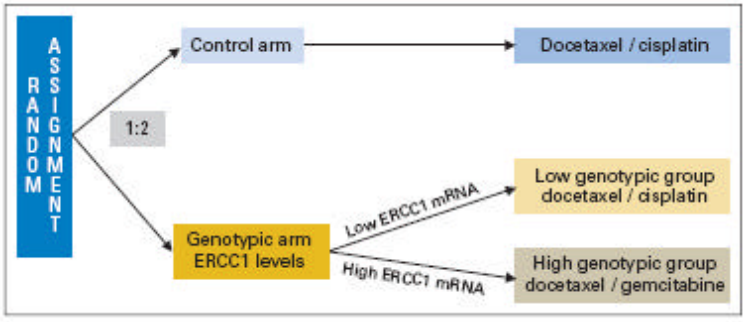
Prescribing decisions should be made based on the approved package insert in the country of prescription

Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00174629
		Study Code:	TAX_ES1_302
Generic drug name:	DOCETAXEL	**Date:**	04 August 2008

Title of the study:	Open-label, cooperative, randomized, multicenter phase III study on the use of cisplatin resistant genotype (ERCC1 over-expression) in tumor RNA to customize chemotherapy in Stage IV-IIIb (malignant pleural effusion) non-small cell lung cancer patients.
Coordinating Investigator:	Dr.R. Rosell H.Germans Trías i Pujol Dr.J.M. Sanchez H. 12 Octubre
Study center(s):	H.Germans Trias i Pujol, Barcelona I.Catalán de Oncología, Hospitalet H. Valle Hebrón, Barcelona H. Clínic i Provincial, Barcelona H. Arnau de Vilanova, Valencia H. General Universitario, Valencia Thorazklinik. Heidenberg, Alemania H. General Universitario, Alicante Hospital Ramón y Cajal, Madrid Fundación Jiménez-Díaz, Madrid Hospital Virgen del Rocío, Servilla H. de la Creu Roja, Hospitalet Hospital de Cruces, Baracaldo Hospital Lozano Blesa , Zaragoza Consorcio S. del Maresme, Mataró Clínica Puerta de Hierro, Madrid Hospital Carlos Haya, Málaga Hospital E. Santo, Sta Coloma I. Valenciano de Oncología, Valencia Hospital de Terrassa, Terrassa H. del Mar, Barcelona H. 12 de Octubre, Madrid Klinik und P. Für Onkologie, Zürich H. Virgen de la Victoria, Málaga
Publications (reference):	Journal of Clinical Oncology Volume 25 – Number 19 – July 1, 2007

Study period: Date first patient/subject enrolled: August 2001 Date last patient/subject completed: January 2007			**Phase of development:** Phase III
Objectives:	**Primary objective:** Response rate experimental arm vs control arm **Secondary:** Safety, TTF and overall survival between experimental arm vs control arm		
Methodology:	Open-label, cooperative, randomized, multicenter trial		
Number of patients:	Planned: 462	Randomized: 444	Treated: 366
Evaluated:	Efficacy: 346	Safety:	



Diagnosis and criteria for inclusion:	Patients were eligible if they had stage IV or stage IIIB (with malignant pleural effusion) histologically confirmed NSCLC and if paraffin-embedded tumor tissue, either the tumor block or at least five sections mounted on slides, was available. Other eligibility criteria included an Eastern Cooperative Oncology Group performance status (PS) of 0 or 1; age _ 18 years; adequate hematologic function (hemoglobin_9 g/dL [5.6 mmol/L], neutrophil count_ 1,500/_L, and platelet count _ 100,000/_L); adequate renal function (serumcreatinine _1.5_the upper limit of normal); and adequate liver function (bilirubin _ 1.5_ the upper limit of normal, AST and ALT _ 5_ the upper limit of normal). Patients with clinically overt brain metastases and those who had received previous chemotherapy were excluded. Patients with Eastern Cooperative Oncology Group PS of 2 were also excluded, based on results of previous studies in which these patients had a high rate of serious adverse events and poor survival.
Investigational product:	
Dose:	Low ERCC1: docetaxel 75mg/m2 D1+ cisplatin 75 mg/m2 D1 every 3 weeks High ERCC1: docetaxel 75mg/m2 D1+ gemcitabine 1000 mg/m2 D1,8 every 3 weeks
Administration:	IV
Duration of treatment: Six cycles (one cycle=3 weeks) or until disease progression	**Duration of observation:** 12-36 months
Reference therapy:	Docetaxel 75mg/m2 D1+ cisplatin 75 mg/m2 D1 every 3 weeks
Dose:	Docetaxel 75mg/m2 D1+ cisplatin 75 mg/m2 D1 every 3 weeks
Administration:	IV
Criteria for evaluation:	
Efficacy:	Response rate, Overall survival, median PFS
Safety:	Febrile neutropenia, nausea, vomiting and peripheral neurotoxicity.
Statistical methods:	The primary end point was the overall response rate (complete plus partial responses). Assuming a one-sided level of significance of .05, an initial sample size of 297 patients was calculated to provide an80%power to detect at least a15%difference in response (30%v 45%).With an assumed dropout rate of 15%, the number of patients needed was 342. In addition, for exploratory analyses of outcome according to ERCC1 levels, the genotypic arm was subdivided into the low genotypic group (low ERCC1 levels) and high genotypic group (high ERCC1 levels), and three-way comparisons were made between the control arm and both genotypic groups. Response rates between the control and genotypic arms were compared with a one-sided Fisher's exact test. Analyses of secondary hypotheses and other exploratory analyses were performed using two-sided tests: Fisher's or_2 for categoric variables and t test for continuous variables. When multiple comparisons were made, P values were corrected by the Bonferroni inequality method.

Summary: Efficacy results:	**Objective Response Rate** Of the 346 patients assessable for response, 53 patients (39.3%; 95% CI, 31.4% to 47.8%) in the control arm and 107 patients (51.2%; 95% CI, 44% to 57.5%) in the genotypic arm achieved objective response (one-sided Fisher's exact test, P_.02). **Progression-Free and Overall Survival** Of the 366 patients on study, 324 patients (88.5%) experienced disease progression or died. Median progression-free survival for all patients was 5.8 months (95% CI, 4.9 to 6.6 months). Median progression-free survival was 5.2 months (95% CI, 4.4 to 6.0 months) in the control arm and 6.1 months (95% CI, 4.9 to 7.2 months) in thegenotypic arm (HR, 0.9; range, 0.7 to 1.1; P _ .30). Median progression-free survival was 6.7 months (95% CI, 5.7 to 7.8 months) in the low genotypic group, and 4.8 months (95% CI, 3.4 to 6.1 months) in the high genotypic group (Table 2). Patients in the low genotypic group also had a trend toward a lower risk of progression than those in the controlarm(HR, 0.79;95%CI, 0.61 to 1.03;P_.08). Median overall survival was 9.8 months (95% CI, 8.9 to 10.7 months) in the control arm and 9.9 months (95% CI, 8.7 to 11 months) in the genotypic arm (HR, 0.9; range, 0.7 to 1.2; P _ .59). Median survival was 10.4 months (95% CI, 7.9 to 12.8 months) in the low genotypic group, and 9.5 months (95% CI, 8.2 to 10.8 months) in the high genotypic group). One-year survival was 39% in the control arm, 40.4% in the genotypic arm, 44% in the low genotypic group, and 33% in the high genotypic group.
Safety results	The median number of completed 3-week treatment cycles was five (range one to eight) for the control and six (range one to 10) for the genotypic arm) Nausea, vomiting, and fatigue were the most commonly reported treatment-related adverse events. Peripheral neurotoxicity was more frequently observed in the low genotypic group. Febrile neutropenia occurred more frequently in the control arm than in the genotypic arm (p= .002)
Date of report	09-JUL-2008