



Contact: Anne Bancillon + 33 (0)6 70 93 75 28

**STUDIES EVALUATING ELOXATIN[®]-BASED REGIMENS
IN GASTROINTESTINAL CANCERS PRESENTED AT THE 42nd ANNUAL MEETING
OF THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO)**

Atlanta, GA, June 5, 2006 – Sanofi–aventis announced today key results from three studies evaluating Eloxatin[®] (oxaliplatin injection) in various gastrointestinal tumor types (colorectal, pancreatic and gastric cancers). These results were presented at the 42nd Annual Meeting of the American Society of Clinical Oncology (ASCO) in Atlanta, Georgia.

Final analysis of TREE-study demonstrates that Eloxatin[®]-based chemotherapy combined with bevacizumab provided significant improvement in overall survival (OS) for patients with advanced colorectal cancer.

Results from this study evaluating the use of Eloxatin[®]-based regimens plus bevacizumab demonstrate a greater than two year median overall survival (OS) among patients with metastatic colorectal cancer, the longest survival results seen to date in this patient population. The research findings were presented on Monday, June 5, during an oral scientific presentation.

In the TREE-study, two successive cohorts (TREE-1 and TREE-2) were investigated. The TREE-1 study contained three arms, evaluating Eloxatin[®] combined with three different ways to deliver fluoropyrimidine chemotherapy (intravenous infusion, intravenous bolus and oral). TREE-2 evaluated the same three regimens in combination with the vascular epithelial growth factor inhibitor bevacizumab. The two cohorts of patients were included from the same centers and investigators, and the inclusion and exclusion criteria, as well as the base cytotoxic chemotherapy regimens were identical in each cohort.

The median overall survival results from the TREE-1 cohort, 18.2 months [95% C.I.14.5 – 21.6 months] are in line with previous studies looking at Eloxatin[®] in combination with fluoropyrimidine alone¹. The median overall survival in the TREE-2 cohort was 24.4 months [21.4–26.8 months]. The safety results revealed no unexpected toxicity, and are also in line with previously presented data on the combination of Eloxatin[®]-based chemotherapy and bevacizumab². Overall, the incidence of any grade 3/4 severe toxicity (TREE-1 vs. TREE-2 respectively) were as follows: FOLFOX 75% vs. 66%, bFOL 42% vs.59%, CapeOx 73% vs. 54%. The addition of bevacizumab in TREE2 caused more grade 3/4 hypertension, impaired wound healing, and bowel perforation in each arm.

“The results of this study demonstrate for the first time that median survival for patients with advanced colorectal cancer can extend beyond two years,” said Howard S. Hochster, M.D., FACP, principal investigator and professor at the New York University School of Medicine. *“Oxaliplatin-based chemotherapy is already the standard treatment for these patients, and now the TREE-2 results show that adding bevacizumab to this regimen delivers increased overall survival for these patients.”*

About TREE-2

The randomized multicenter TREE-2 (A Randomized, Prospective Study Comparing Three Regimens of oxaliplatin Plus Fluoropyrimidine and Bevacizumab for Evaluation of Safety and Tolerability in First-Line Treatment of Patients with Advanced Colorectal Cancer) is the first study evaluating the safety and tolerability of bolus, infusional, and oral fluoropyrimidine + oxaliplatin-based regimens combined with bevacizumab for the first-line treatment of metastatic colorectal cancer.

In the TREE-2 study, 213 adults aged 18 or older with metastatic colorectal cancer were treated with one of three oxaliplatin-containing chemotherapy regimens: oxaliplatin plus infusional 5-fluorouracil/leucovorin (FOLFOX), oxaliplatin plus bolus 5FU (bFOL), and oxaliplatin plus Capecitabine (CapeOx), all used in combination with bevacizumab.

¹Goldberg R, et al. J Clin Oncol 2004;22:23-30.

²Giantonio B, et al. ASCO 2005 (Abstract 2)

ECOG 6201 study shows non-statistically significant survival increase when using fixed dose rate (FDR) gemcitabine (GEM) or a combination of gemcitabine with Eloxatin[®] (oxaliplatin injection) (GemOx) compared to the standard gemcitabine regimen in patients with locally advanced or metastatic pancreatic cancer.

Results from a study of advanced pancreatic cancer patients were presented on Sunday, June 4, during a scientific oral presentation. The study evaluated three regimens including a standard gemcitabine regimen, (1000 mg/m² IV over 30 minutes once weekly for 7 weeks followed by one week of rest for course one only). In all subsequent courses, patients received gemcitabine IV over 30 minutes on days 1, 8 and 15, with courses repeating every 4 weeks in the absence of disease progression or unacceptable toxicity.); a fixed dose rate (FDR) gemcitabine regimen (gemcitabine 1500mg/m² IV over 150 minutes on days 1, 8, and 15. Courses repeated every 4 weeks in the absence of disease progression or unacceptable toxicity.); or the GemOx regimen (gemcitabine 1000mg/m² IV over 100 minutes on day 1 and oxaliplatin100mg/m² IV over 120 minutes on day 2. Courses repeated every 2 weeks in the absence of disease progression or unacceptable toxicity.) Overall survival results for the three regimens evaluated in the study were 4.9 months, 6.0 months and 5.9 months, respectively (95% CI: 4.5-5.6, 5.4-6.9, 5.1-6.8 respectively).

The findings show that changing the gemcitabine mode of administration or combining gemcitabine with oxaliplatin does not provide a significant clinical benefit in this patient population.

About ECOG 6201

This multi-institutional trial included patients with measurable and non-measurable advanced, unresectable pancreatic cancer, normal organ function and performance status (PS) 0-2. Patients had not previously received chemotherapy. Patients were stratified by PS 0-1 versus 2 and locally advanced versus metastatic disease (cancer that has spread beyond the original tumor). The study was designed to detect a 33% difference in median survival (hazard ratio 1.33) with 81% power while

maintaining a significance level of 2.5% in a two-sided test for each of the two primary comparisons, assuming exponential failure and median survival of 6 months for the standard gemcitabine regimen, and 8 months for the experimental regimens.

The primary endpoint was overall survival of the two experimental arms versus the standard arm. Secondary endpoints were the evaluation of toxicity, response, patterns of failure, progression-free survival and quality of life. Median follow up was 12.2 months. Eight hundred and thirty two patients were randomized (53% men, 88% PS 0-1, 88% metastatic). The most common side effects were grade 3/4 severe myelosuppression (decrease in blood cell count) and fatigue.

REAL 2 trial shows improved overall survival in advanced stomach cancer with Eloxatin[®]-capecitabine combination.

Results of the Real 2 study evaluating four regimens for the treatment of advanced stomach cancer were presented on Monday, June 5, during a scientific oral presentation. The randomised multi-center phase III study evaluated the replacement of fluorouracil with capecitabine and of cisplatin with oxaliplatin in patients with advanced gastric (stomach) cancer.

The results of the REAL 2 trial showed that a chemotherapy regimen including Eloxatin[®] and capecitabine (EOX) significantly improves median overall survival (OS) over a traditional standard regimen of epirubicin, cisplatin and 5-FU (ECF) in patients with advanced gastric (stomach) cancer. The efficacy advantage of the EOX combination was associated with less grade 3/4 neutropenia: 28% for EOX regimen versus 42% for the ECF regimen (p<0.01).

The REAL 2 trial findings show that the EOX regimen significantly improved one-year survival 46.8% (95% CI: 40.4-52.9) for EOX versus 37.7% (95% CI: 31.8-43.6) for ECF, and median overall survival (OS) (11.2 months for EOX versus 9.9 months for ECF [HR: 0.80 (95% CI: 0.65-0.97)]).

“The combination of a platinum compound and a fluoropyrimidine is the foundation for most if not all of the chemotherapeutic regimens used in the treatment of advanced gastric cancer,” said David Cunningham MD, FRCP, Department of Medicine, The Royal Marsden Hospital, UK and chief investigator of the REAL 2 trial. *“The REAL 2 trial findings demonstrate that the addition of the third generation platinum compound oxaliplatin and the oral fluoropyrimidine capecitabine to epirubicin resulted in an increase in overall survival compared to the standard regimen.”*

About REAL 2

The REAL 2 trial included 1,002 patients from 61 centers. After stratification for performance status (PS) and extent of disease, patients with histologically confirmed gastric (stomach) adenocarcinoma, squamous or undifferentiated carcinoma received one of four regimens: ECF = 263 patients; EOF (epirubicin, oxaliplatin, 5-FU) = 245 patients; ECX (epirubicin, cisplatin, capecitabine) = 250 patients or EOX = 244 patients. The dosing regimen was as follows: E 50 mg/m², C 60 mg/m² and O 130 mg/m² IV 3 weekly; F 200 mg/m² IV daily and X 625 mg/m² twice daily PO continuously for 8 cycles.

The primary endpoint of the study was overall survival. Demographics were balanced, 89% were PS 0-1, 77% metastatic, median age 63 (range 22-83), 81% were male and 40% gastric primaries. Median follow up was 17.1 months and 850 events have occurred.

The 2x2 comparisons primarily compared the fluoropyridine-containing arms (ECF + EOF versus ECX + EOX) and platinum-containing arms (ECF + ECX versus EOF + EOX). For the fluoropyrimidine comparison of 5-FU versus capecitabine the 1 year OS was 39.4% (median overall survival 9.6 months) versus 44.6% (median overall survival 10.9 months) [HR:0.86 (95% CI:0.80-0.99)]. For the platinum comparison of cisplatin versus oxaliplatin the 1 year OS was 40.1% (median overall survival 10.0 months) versus 43.9% (median overall survival 10.4 months) [HR:0.92 (95% CI: 0.80-1.1)]. Since the upper limit of the 95% CI for the hazard ratios of both comparisons excluded the non-inferiority margin of 1.23, it can be concluded that capecitabine is not inferior to 5-FU and oxaliplatin is not inferior to cisplatin in the first-line treatment of gastric cancers. In a comparison of survival by regimen, the median overall survival for ECF, EOF, ECX and EOX was 9.9, 9.3, 9.9 and 11.2 months respectively. EOX was associated with a significantly better median OS compared to ECF (p=0.02).

There were no significant differences in response rates comparing ECF to EOF, ECX and EOX (41%, 42%, 46%, and 48% respectively). In terms of safety, severe grade 3-4 non hematological toxicity was seen in 36%, 42%, 33% and 45%. Grade 3/4 (mainly grade 3) peripheral neuropathy was seen in 8.4% of the patients on the EOF arm and 4.4% in the EOX arm compared to less than 2% in the cisplatin-containing arms. Grade 3-4 neutropenia (low white blood cell count) was seen in 42%, 30% (p=0.008), 51% (p=0.043) and 28% (p=0.001) in the ECF, EOF, ECX and EOX arms respectively. There was no significant difference in the rate of febrile neutropenia between the arms.

About colorectal cancer

Colorectal Cancer is a leading cause of death. Every year, about one million new cases of colorectal cancer are diagnosed worldwide. About 194,000 new cases are detected in Europe and 150,000 in the United States. According to the American Cancer Society, colorectal cancer is the second leading cause of cancer-related death in the United States, accounting for 10% to 15% of all cancer deaths. Over a lifetime, about 1 in 18 people develop colorectal cancer and more than 56,000 people die from it in the United States each year. In Europe, 94,000 people die from colorectal cancer each year.

Colorectal cancer begins in the cells that line the colon or rectum. When these cancer cells spread away from the colon to distant locations in the body, the cancer is referred to as metastatic. Cancer cells may spread, or metastasize, through the blood or lymphatic system, or directly grow into tissues adjacent to the original cancer.

A diagnosis of colorectal cancer is associated with a stage, which reflects the extent of the cancer and whether it has spread. Patients with colorectal cancer that has spread to distant organs or tissues are said to have advanced, or metastatic, colorectal cancer, also known as stage IV colorectal cancer. Patients with advanced colorectal cancer can now more confidently expect to live twice as long as they could only a few years ago.

About Pancreatic Cancer

Pancreatic cancer is the 9th most common cancer in Europe, the 10th in the US and the 6th in Japan. The incidence in 2004 was 31 860 cases in the US, 35 361 in Europe and 20 031 in Japan. In 2002, 38 854 patients died from pancreatic cancer in Europe, 30 324 in the US and 20 043 in Japan. The diagnosis is often made at an advanced stage and the median overall survival with standard treatment is around 6 months at this stage.

About Gastric (Stomach) Cancer

Stomach cancer is the 4th most common type of cancer worldwide with more than 934,000 new patients every year. It is also the second most common cause of cancer death worldwide; with more than 700,000 deaths annually. There were about 22,800 new cases of stomach cancer in the United States in 2005. In Europe, this number is over 143,000 patients. At diagnosis, most patients with stomach cancer have advanced disease with an expected two-year survival of only 11.5 percent.

About Eloxatin[®]

In Europe

Eloxatin[®] received approval in France for the second-line treatment of metastatic colorectal cancer in April 1996, and as a first-line treatment in April 1998. In July 1999, Eloxatin[®] was approved for the first-line treatment of advanced colorectal cancer in major European countries through the Mutual Recognition Procedure, France being the Reference Member State.

Eloxatin[®] successfully completed a Mutual Recognition Procedure in Europe in December 2003, which allowed the product to be marketed for the treatment of metastatic colorectal cancer in combination with 5-fluorouracil and folinic acid (i.e., in first- and second-line treatment).

In September 2004, the indication for Eloxatin[®] was extended in Europe, again through the Mutual Recognition Procedure, to include the "Adjuvant treatment of stage III (Dukes' C) colon cancer after complete resection of primary tumor."

In the United States

In the United States, Eloxatin[®], in combination with infusional 5-FU/LV, received approval on January 9, 2004, for the first-line treatment of advanced carcinoma of the colon or rectum (ie, first therapy for patients with metastatic colorectal cancer). This same Eloxatin[®]-based combination had initially (August 2002) received FDA approval for second-line treatment, (ie, therapy for previously treated patients with metastatic colorectal cancer).

On November 4, 2004, this Eloxatin[®]-based regimen was approved for the adjuvant treatment of stage III (Dukes' C) colon cancer after complete resection of the primary tumor.

Eloxatin[®] is currently not approved in pancreatic cancer or in stomach (gastric) cancer.



Eloxatin[®] was developed in association with Debiopharm SA and is currently marketed by sanofi-aventis in more than 60 countries.

About sanofi-aventis

Sanofi-aventis is the world's third largest pharmaceutical company, ranking number one in Europe. Backed by a world-class R&D organisation, sanofi-aventis is developing leading positions in seven major therapeutic areas: cardiovascular, thrombosis, oncology, metabolic diseases, central nervous system, internal medicine and vaccines. Sanofi-aventis is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995. Forward-looking statements are statements that are not historical facts. These statements include financial projections and estimates and their underlying assumptions, statements regarding plans, objectives and expectations with respect to future events, operations, products and services, and statements regarding future performance. Forward-looking statements are generally identified by the words "expect," "anticipates," "believes," "intends," "estimates," "plans" and similar expressions. Although sanofi-aventis' management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of sanofi-aventis, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include those discussed or identified in the public filings with the SEC and the AMF made by sanofi-aventis, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in sanofi-aventis' annual report on Form 20-F for the year ended December 31, 2005. Other than as required by applicable law, sanofi-aventis does not undertake any obligation to update or revise any forward-looking information or statements.

P r e s s r e l e a s e