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Survival Benefit of Taxotere[®]-Based Regimens In Patients With Non Small Cell Lung Cancer

- Taxotere[®]-based regimens demonstrated significant superior overall survival over vinca-alkaloid-based regimens in the first-line treatment of advanced Non Small Cell Lung Cancer -

Paris, France, September 4, 2007 - Sanofi-aventis announced today that a meta-analysis of Individual Patient Data (IPD) including 2,867 patients from seven clinical trials demonstrated a significant overall survival (OS) benefit of Taxotere[®] (docetaxel Injection Concentrate) over vinca-alkaloid-based regimens in the treatment of first line advanced Non Small Cell Lung Cancer (NSCLC) patients. Efficacy results of this IPD meta-analysis, called DOCMA-LC (DOCetaxel Meta-Analysis in Lung Cancer), were presented today at the 12th World Conference on Lung Cancer in Seoul, South Korea, as a proffered paper.

The aim of DOCMA-LC was to assess the overall survival and tolerability as well as to validate surrogate endpoints from all randomized clinical trials (RCT) comparing Taxotere[®]-based chemotherapy to vinorelbine- or vindesine-based chemotherapy regimens in first-line treatment of advanced NSCLC. The findings of DOCMA-LC announced today confirm the significant superiority of Taxotere[®]-based regimens compared to vinca-alkaloid regimens in terms of overall survival (HR: 0.90; 95%CI [0.82;0.98]). A multivariate analysis strongly confirmed this benefit of Taxotere[®]-based regimens (HR: 0.88; 95%CI [0.80; 0.97]).

Tolerability also favoured Taxotere[®]- based regimens as mentioned in a previous published meta-analysis presented at ASCO (American Society of Clinical Oncology) 2006¹ and currently in press with the Journal of Thoracic Oncology. In the IDP meta-analysis, tolerability, as well as surrogate end-points, are still under analysis.

"This individual patient data meta-analysis provides the evidence that one third-generation agent, Taxotere[®], is significantly superior to vinca-alkaloid regimens, in the first-line treatment of patients with advanced NSCLC," said Jean-Yves Douillard, Professor and Head of the Department of Medical Oncology at the Centre R Gauducheau in Saint Herblain, France, and principal investigator of the meta-analysis.

About the study

Background

Taxanes and vinca-alkaloids are commonly used agents, in first-line therapy of advanced NSCLC. The TAX 326 study demonstrating a benefit in median Overall Survival (OS) of docetaxel-cisplatin over vinorelbine-cisplatin was the basis of the European and US registration of Taxotere[®] in first line advanced NSCLC. As some data in comparative studies have suggested consistent benefit in survival and safety, a meta-analysis was performed in order to assess this potential benefit of Taxotere[®]-based regimens in comparison with vinca-alkaloid-based regimens, in terms of Overall Survival (OS) and tolerability.

Aim

DOCMA-LC aimed to assess OS and tolerability and to validate surrogate endpoints from all randomized clinical trials (RCT) comparing Taxotere[®]-based chemotherapy to vinorelbine- or vindesine-based chemotherapy in first-line advanced NSCLC.

Method

MEDLINE, CANCERLIT and Cochrane Library searches were supplemented by information from clinical study reports and by manual searching of relevant meeting proceedings. All individual patients' data were collected and analyzed. Only randomized clinical trials (RCT) comparing Taxotere[®]-based chemotherapy to vinorelbine- or vindesine-based chemotherapy were included. Seven RCT trials yielded a total of 2,867 patients (Taxotere regimens: 1,638; vinca-alkaloid regimens: 1,229). Taxotere[®] was combined with a platinum compound in three trials, with gemcitabine in two trials and used as monotherapy in two trials. Vinorelbine-regimens were the comparators in six of the seven trials, and vindesine-regimen in one²⁻⁸. The methodological quality of each trial was classified according to the Jada score.¹⁰

Statistical analysis

The efficacy analysis was performed on an intent-to-treat basis. Analysis of survival was based on the pooling of individual logarithms of the Hazard Ratio (HR). Data were pooled by the inverse-variance weighting method.

Results

The first survival results¹ for all drug combinations favoured Taxotere[®] with an HR of 0.87 (95% CI, 0.79–0.96) for Taxotere[®] combined with a platinum agent; 0.89 (95% CI, 0.82–0.96) for nonplatinum-based Taxotere[®] regimens; 0.96 (95% CI, 0.81–1.13) for Taxotere[®] combined with gemcitabine; and 0.87 (95% CI, 0.69–1.09) for Taxotere[®] monotherapy.

The individual patient data meta-analysis (DOCMA-LC) confirmed the Taxotere[®] benefit in OS with a 10% reduction of the risk of death (HR: 0.90; 95%CI [0.82; 0.98]). The pooled estimate for overall survival showed an improvement in favour of Taxotere[®] whatever the data used.

Tolerability was assessed and also favoured Taxotere[®]-based regimens in a previous published and unpublished meta-analysis presented at ASCO 2006 and currently in press with the Journal of Thoracic Oncology⁹ and further tolerability, as well as surrogate end-points, are still under analysis in the IDP meta-analysis.

About Taxotere[®]

Taxotere[®] is currently approved in 5 different cancer types in Europe and the US:

- **In Breast Cancer**

In the United States and in Europe Taxotere[®] is approved to treat patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy. It is also approved in Europe in combination with doxorubicin for patients who have received prior cytotoxic therapy for this condition and in combination with capecitabine after failure of cytotoxic therapy which would have included anthracycline. In the adjuvant setting (post surgery) it is approved in the U.S. and in Europe in combination with doxorubicin and cyclophosphamide (TAC regimen) for the treatment of patients with operable, node-positive breast cancer. Finally, in Europe, Taxotere[®] is approved in combination with

trastuzumab for the treatment of patients with metastatic breast cancer- overexpressing HER2 receptor.

- **In Lung Cancer**

In the U.S. and in Europe, Taxotere[®], in combination with cisplatin, is approved for the treatment of patients with unresectable locally advanced or metastatic non-small cell lung cancer (NSCLC) who have not received prior chemotherapy, and it also is approved, as a single agent, for patients with unresectable locally advanced or metastatic NSCLC after failure of prior platinum-based chemotherapy.

- **In Prostate Cancer**

Taxotere[®] is approved for use in combination with prednisone as a treatment for androgen independent (hormone-refractory) metastatic prostate cancer in the U.S. and in Europe.

- **In Gastric (Stomach) Cancer**

The FDA and the Committee for Medicinal Products for Human Use (CHMP) of the European Agency for the Evaluation of Medicinal Products (EMA) approved in March 2006, the use of Taxotere[®] Injection Concentrate in combination with cisplatin and 5-fluorouracil for the treatment of patients with advanced stomach (gastric) cancer, including cancer of the gastro oesophageal (GE) junction, who have not received prior chemotherapy for advanced disease.

- **In Head and Neck Cancer**

In October 2006, the European Medicines Agency (EMA) and the FDA approved Taxotere[®] (docetaxel) Injection Concentrate in combination with cisplatin and fluorouracil for the induction treatment of patients with inoperable locally advanced squamous cell carcinoma of the head and neck (SCCHN).

References

1. Douillard J. Y , Fossella F., Georgoulas V., Pujol J. L.I, Kubota K., Monnier A., Takeda K., Cucherat M., Laporte S. *Comparison of docetaxel and vinca alkaloid, alone or in combination with other chemotherapy agents, in the first-line treatment of advanced non-small cell lung cancer (NSCLC): A meta-analysis.* J Clin Oncol, 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement), 2006: 7034
2. Fossella F, Pereira JR, von Pawel J, et al. *Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: The TAX 326 study group.* J Clin Oncol 2003;21:3016–3024
3. Douillard JY, Gervais R, Dabouis G, et al. *Sequential two-line strategy for stage IV non-small-cell lung cancer: docetaxel–cisplatin versus vinorelbine–cisplatin followed by crossover to single-agent docetaxel or vinorelbine at progression: final results of a randomized phase II study.* Ann Oncol 2005;16:81–89.
4. Kubota K, Watanabe K, Kunitoh H, et al. *Phase III randomized trial of docetaxel plus cisplatin versus vindesine plus cisplatin in patients with stage IV non-small-cell lung cancer: The Japanese Taxotere Lung Cancer Study Group.* J Clin Oncol 2004;22: 254–261.

5. Georgoulis V, Ardavanis A, Tsiadaki X, et al. *Vinorelbine plus cisplatin versus docetaxel plus gemcitabine in advanced non-small-cell lung cancer: A phase III randomized trial.* J Clin Oncol 2005;23:2937–2945.
6. Pujol JL, Breton JL, Gervais R, et al. *Gemcitabine–docetaxel versus cisplatin–vinorelbine in advanced or metastatic non-small-cell lung cancer: A phase III study addressing the case for cisplatin.* Ann Oncol 2005;16:602–610.
7. Kudoh S, Takeda K, Nakagawa K, et al. *Phase III study of docetaxel compared with vinorelbine in elderly patients with advanced non-small-cell lung cancer: Results of the West Japan Thoracic Oncology Group Trial (WJTOG 9904).* J Clin Oncol 2006;24:3657–3663.
8. Monnier A, Zatloukal P, Sifnerova H, et al. *Docetaxel (D) versus vinorelbine–cisplatin (VC) as front-line treatment for patients with advanced non-small cell lung cancer (NSCLC) and with a normal level of serum alpha 1 acid glycoprotein (AAG): Additional data on quality of life (QOL). Preliminary results.* Proc Am Soc Clin Oncol 2003 [Abstract 2680].
9. *Jada score* : This score incorporates assessments of randomization, proper generation and concealment of the treatment allocation sequence, blinding of patients and investigators, and completeness of follow-up (based on information for withdrawals and dropouts)

About sanofi-aventis

Sanofi-aventis is one of the world's leading pharmaceutical companies, 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, as amended. 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, intentions 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 “expects,” “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, 2006. Other than as required by applicable law, sanofi-aventis does not undertake any obligation to update or revise any forward-looking information or statements.