Table 11 - Clinically Important Treatment Emergent Adverse Reactions Regardless of Relationship to Treatment in the Gastric Cancer Study

	TAXOTERE 75 mg/m^2 + cisplatin 75 mg/m^2 + fluorouracil 750 mg/m^2 n=221		Cisplatin 100 mg/m^2 + fluorouracil 1000 mg/m^2 n=224	
Adverse Reaction	**Any %**	**G3/4 %**	**Any %**	**G3/4 %**
Anemia	96.8	18.2	93.3	25.6
Neutropenia	95.5	82.3	83.3	56.8
Fever in the absence of infection	35.7	1.8	22.8	1.3
Thrombocytopenia	25.5	7.7	39.0	13.5
Infection	29.4	16.3	22.8	10.3
Febrile neutropenia	16.4	N/A	4.5	N/A
Neutropenic infection	15.9	N/A	10.4	N/A
Allergic reactions	10.4	1.8	5.8	0
Fluid retention*	14.9	0	4.0	0.4
Edema*	13.1	0	3.1	0.4
Lethargy	62.9	21.3	58.0	17.9
Neurosensory	38.0	7.7	24.6	3.1
Neuromotor	8.6	3.2	7.6	2.7
Dizziness	15.8	4.5	8.0	1.8
Alopecia	66.5	5.0	41.1	1.3
Rash/itch	11.8	0.9	8.5	0.0
Nail changes	8.1	0.0	0.0	0.0
Skin desquamation	1.8	0.0	0.4	0.0
Nausea	73.3	15.8	76.3	18.8
Vomiting	66.5	14.9	73.2	18.8
Anorexia	50.7	13.1	54.0	11.6
Stomatitis	59.3	20.8	61.2	27.2
Diarrhea	77.8	20.4	49.6	8.0
Constipation	25.3	1.8	33.9	3.1
Esophagitis/dysphagia/ odynophagia	16.3	1.8	13.8	4.9
Gastrointestinal pain/cramping	11.3	1.8	7.1	2.7
Cardiac dysrhythmias	4.5	2.3	2.2	0.9
Myocardial ischemia	0.9	0.0	2.7	2.2
Tearing	8.1	0	2.2	0.4
Altered hearing	6.3	0	12.5	1.8

Clinically important TEAEs were determined based upon frequency, severity, and clinical impact of the adverse reaction.
*Related to treatment

- Head and Neck Cancer

Combination therapy with TAXOTERE in head and neck cancer

Table 12 summarizes the safety data obtained from patients that received induction chemotherapy with TAXOTERE 75 mg/m^2 in combination with cisplatin and fluorouracil followed by radiotherapy (TAX323; 174 patients) or chemoradiotherapy (TAX324; 251 patients). The treatment regimens are described in Section 14.6.

Table 12 – Clinically Important Treatment Emergent Adverse Reactions (Regardless of Relationship) in Patients with SCCHN Receiving Induction Chemotherapy with TAXOTERE in Combination with cisplatin and fluorouracil followed by radiotherapy (TAX323) or chemoradiotherapy (TAX324)

	TAX323 (n=355)				**TAX324 (n=494)**			
	TAXOTERE arm (n=174)		**Comparator arm (n=181)**		**TAXOTERE arm (n=251)**		**Comparator arm (n=243)**	
Adverse Reaction (by Body System)	**Any %**	**G3/4 %**	**Any %**	**G3/4 %**	**Any %**	**G3/4 %**	**Any %**	**G3/4 %**
Neutropenia	93.1	76.3	86.7	52.8	94.8	83.5	84.2	56.0
Anemia	89.1	9.2	87.8	13.8	90.0	12.4	86.0	9.5
Thrombocytopenia	23.6	5.2	47.0	18.2	27.5	4.0	30.9	10.7
Infection	27.0	8.6	26.0	7.7	23.1	6.4	27.6	5.3
Febrile neutropenia*	5.2	N/A	2.2	N/A	12.1	N/A	6.6	N/A
Neutropenic infection	13.9	N/A	8.3	N/A	11.7	N/A	8.3	N/A
Cancer pain	20.7	4.6	16.0	3.3	17.1	8.8	20.2	11.1
Lethargy	40.8	3.4	38.1	3.3	61.4	4.8	55.6	10.3
Fever in the absence of infection	31.6	0.6	36.5	0	29.5	3.6	27.6	3.3
Myalgia	9.8	1.1	7.2	0	6.8	0.4	7.0	1.6
Weight loss	20.7	0.6	26.5	0.6	14.3	1.6	14.0	2.1
Allergy	6.3	0	2.8	0	2.0	0	0.4	0
Fluid retention**	20.1	0	14.4	0.6	13.1	1.2	7.0	1.6
Edema only	12.6	0	6.6	0	12.0	1.2	5.8	1.2
Weight gain only	5.7	0	6.1	0	0.4	0	0.8	0.4
Dizziness	2.3	0	5.0	0.6	15.9	4.0	15.2	1.6
Neurosensory	17.8	0.6	10.5	0.6	13.9	1.2	14.4	0.4
Altered hearing	5.7	0	9.9	2.8	12.7	1.2	18.5	2.5
Neuromotor	2.3	1.1	3.9	0.6	8.8	0.4	10.3	1.6
Alopecia	81.0	10.9	43.1	0	67.7	4.0	43.6	1.2
Rash/itch	11.5	0	6.1	0	19.9	0	16.0	0.8
Dry skin	5.7	0	1.7	0	4.8	0.4	3.3	0
Desquamation	4.0	0.6	5.5	0	2.4	0	4.5	0.4
Nausea	47.1	0.6	51.4	7.2	76.5	13.9	79.8	14.0
Stomatitis	42.5	4.0	47.0	11.0	65.7	21.1	67.5	27.2
Vomiting	26.4	0.6	38.7	5.0	56.2	8.4	62.6	10.3
Diarrhea	32.8	2.9	23.8	4.4	47.8	7.2	40.3	3.3
Constipation	16.7	0.6	16.0	1.1	27.1	1.2	37.9	0.8
Anorexia	16.1	0.6	24.9	3.3	40.2	12.4	34.2	11.5

	TAX323 (n=355)				TAX324 (n=494)			
	TAXOTERE arm (n=174)		Comparator arm (n=181)		TAXOTERE arm (n=251)		Comparator arm (n=243)	
Adverse Reaction (by Body System)	**Any %**	**G3/4 %**	**Any %**	**G3/4 %**	**Any %**	**G3/4 %**	**Any %**	**G3/4 %**
Esophagitis/dysphagia/ Odynophagia	12.6	1.1	18.2	2.8	25.1	12.7	26.3	9.5
Taste, sense of smell altered	10.3	0	5.0	0	20.3	0.4	16.9	0.8
Gastrointestinal pain/cramping	7.5	0.6	8.8	0.6	14.7	4.8	10.3	1.6
Heartburn	6.3	0	6.1	0	12.7	1.6	12.8	0.8
Gastrointestinal bleeding	4.0	1.7	0	0	5.2	0.4	2.1	0.4
Cardiac dysrhythmia	1.7	1.7	1.7	0.6	6.0	2.8	4.5	2.5
Venous* **	3.4	2.3	5.5	1.7	3.6	2.4	4.9	3.7
Ischemia myocardial	1.7	1.7	0.6	0	1.6	1.2	1.2	1.2
Tearing	1.7	0	0.6	0	1.6	0	2.1	0
Conjunctivitis	1.1	0	1.1	0	1.2	0	0.4	0

Clinically important treatment emergent adverse reactions based upon frequency, severity, and clinical impact.
*Febrile neutropenia: grade ≥2 fever concomitant with grade 4 neutropenia requiring i.v. antibiotics and/or hospitalization.
**Related to treatment.
*** Includes superficial and deep vein thrombosis and pulmonary embolism

6.2 Post-marketing Experiences

The following adverse reactions have been identified from clinical trials and/or post-marketing surveillance. Because they are reported from a population of unknown size, precise estimates of frequency cannot be made.

Body as a whole: diffuse pain, chest pain, radiation recall phenomenon.

Cardiovascular: atrial fibrillation, deep vein thrombosis, ECG abnormalities, thrombophlebitis, pulmonary embolism, syncope, tachycardia, myocardial infarction.

Cutaneous: very rare cases of cutaneous lupus erythematosus and rare cases of bullous eruptions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, and Scleroderma-like changes usually preceded by peripheral lymphedema. In some cases multiple factors may have contributed to the development of these effects. Severe hand and foot syndrome has been reported.

Gastrointestinal: abdominal pain, anorexia, constipation, duodenal ulcer, esophagitis, gastrointestinal hemorrhage, gastrointestinal perforation, ischemic colitis, colitis, intestinal obstruction, ileus, neutropenic enterocolitis and dehydration as a consequence to gastrointestinal events have been reported.

Hematologic: bleeding episodes. Disseminated intravascular coagulation (DIC), often in association with sepsis or multiorgan failure, has been reported. Cases of acute myeloid leukemia and myelodysplasic syndrome have been reported in association with TAXOTERE when used in combination with other chemotherapy agents and/or radiotherapy.

Hypersensitivity: rare cases of anaphylactic shock have been reported. Very rarely these cases resulted in a fatal outcome in patients who received premedication.

Hepatic: rare cases of hepatitis, sometimes fatal primarily in patients with pre-existing liver disorders, have been reported.

Neurologic: confusion, rare cases of seizures or transient loss of consciousness have been observed, sometimes appearing during the infusion of the drug.

Ophthalmologic: conjunctivitis, lacrimation or lacrimation with or without conjunctivitis. Excessive tearing which may be attributable to lacrimal duct obstruction has been reported. Rare cases of transient visual disturbances (flashes, flashing lights, scotomata) typically occurring during drug infusion and in association with hypersensitivity reactions have been reported. These were reversible upon discontinuation of the infusion.

Hearing: rare cases of ototoxicity, hearing disorders and/or hearing loss have been reported, including cases associated with other ototoxic drugs.

Respiratory: dyspnea, acute pulmonary edema, acute respiratory distress syndrome, interstitial pneumonia. Pulmonary fibrosis has been rarely reported. Rare cases of radiation pneumonitis have been reported in patients receiving concomitant radiotherapy.

Renal: renal insufficiency and renal failure have been reported, the majority of these cases were associated with concomitant nephrotoxic drugs.

7. DRUG INTERACTIONS

Docetaxel is a CYP3A4 substrate. *In vitro* studies have shown that the metabolism of docetaxel may be modified by the concomitant administration of compounds that induce, inhibit, or are metabolized by cytochrome P450 3A4.

In vivo studies showed that the exposure of docetaxel increased 2.2-fold when it was coadministered with ketoconazole, a potent inhibitor of CYP3A4. Protease inhibitors, particularly ritonavir, may increase the exposure of docetaxel. Concomitant use of TAXOTERE and drugs that inhibit CYP3A4 may increase exposure to docetaxel and should be avoided. In patients receiving treatment with TAXOTERE, close monitoring for toxicity and a TAXOTERE dose reduction could be considered if systemic administration of a potent CYP3A4 inhibitor cannot be avoided ***[see Dosage and Administration (2.7) and Clinical Pharmacology (12.3)]***

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category D.
[see Warnings and Precautions (5.7)]

8.3 Nursing Mothers

It is not known whether TAXOTERE is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from TAXOTERE, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

The safety and effectiveness of docetaxel in pediatric patients have not been established.

8.5 Geriatric Use

In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy in elderly patients.
In a study conducted in chemotherapy-naïve patients with NSCLC (TAX326), 148 patients (36%) in the TAXOTERE+cisplatin group were 65 years of age or greater. There were 128 patients (32%) in the vinorelbine+cisplatin group 65 years of age or greater. In the TAXOTERE+cisplatin group, patients less than 65 years of age had a median survival of 10.3 months (95% CI: 9.1 months, 11.8 months) and patients 65 years or older had a median survival of 12.1 months (95% CI: 9.3 months, 14 months). In patients 65 years of age or greater treated with TAXOTERE+cisplatin, diarrhea (55%), peripheral edema (39%) and stomatitis (28%) were observed more frequently than in the vinorelbine+cisplatin group (diarrhea 24%, peripheral edema 20%, stomatitis 20%). Patients treated with TAXOTERE+cisplatin who were 65 years of age or greater were more likely to experience diarrhea (55%), infections (42%), peripheral edema (39%) and stomatitis (28%) compared to patients less than the age of 65 administered the same treatment (43%, 31%, 31% and 21%, respectively).
When TAXOTERE was combined with carboplatin for the treatment of chemotherapy-naïve, advanced non-small cell lung carcinoma, patients 65 years of age or greater (28%) experienced higher frequency of infection compared to similar patients treated with TAXOTERE+cisplatin, and a higher frequency of diarrhea, infection and peripheral edema than elderly patients treated with vinorelbine+cisplatin.
Of the 333 patients treated with TAXOTERE every three weeks plus prednisone in the prostate cancer study (TAX327), 209 patients were 65 years of age or greater and 68 patients were older than 75 years. In patients treated with TAXOTERE every three weeks, the following TEAEs occurred at rates ≥10% higher in patients 65 years of age or greater compared to younger patients: anemia (71% vs. 59%), infection (37% vs. 24%), nail changes (34% vs. 23%), anorexia (21% vs. 10%), weight loss (15% vs. 5%) respectively.

In the adjuvant breast cancer trial (TAX316), TAXOTERE in combination with doxorubicin and cyclophosphamide was administered to 744 patients of whom 48 (6%) were 65 years of age or greater. The number of elderly patients who received this regimen was not sufficient to determine whether there were differences in safety and efficacy between elderly and younger patients.

Among the 221 patients treated with TAXOTERE in combination with cisplatin and fluorouracil in the gastric cancer study, 54 were 65 years of age or older and 2 patients were older than 75 years. In this study, the number of patients who were 65 years of age or older was insufficient to determine whether they respond differently from younger patients. However, the incidence of serious adverse reactions was higher in the elderly patients compared to younger patients. The incidence of the following adverse reactions (all grades, regardless of relationship): lethargy, stomatitis, diarrhea, dizziness, edema, febrile neutropenia/neutropenic infection occurred at rates ≥10% higher in patients who were 65 years of age or older compared to younger patients. Elderly patients treated with TCF should be closely monitored.

Among the 174 and 251 patients who received the induction treatment with TAXOTERE in combination with cisplatin and fluorouracil (TPF) for SCCHN in the TAX323 and TAX324 studies, 18 (10%) and 32 (13%) of the patients were 65 years of age or older, respectively.

These clinical studies of TAXOTERE in combination with cisplatin and fluorouracil in patients with SCCHN did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients. Other reported clinical experience with this treatment regimen has not identified differences in responses between elderly and younger patients.

8.6 Hepatic Impairment

Patients with bilirubin >ULN should generally not receive TAXOTERE. Also, patients with SGOT and/or SGPT >1.5 x ULN concomitant with alkaline phosphatase >2.5 x ULN should generally not receive TAXOTERE.

10. OVERDOSAGE

There is no known antidote for TAXOTERE overdosage. In case of overdosage, the patient should be kept in a specialized unit where vital functions can be closely monitored. Anticipated complications of overdosage include: bone marrow suppression, peripheral neurotoxicity, and mucositis. Patients should receive therapeutic G-CSF as soon as possible after discovery of overdose. Other appropriate symptomatic measures should be taken, as needed.

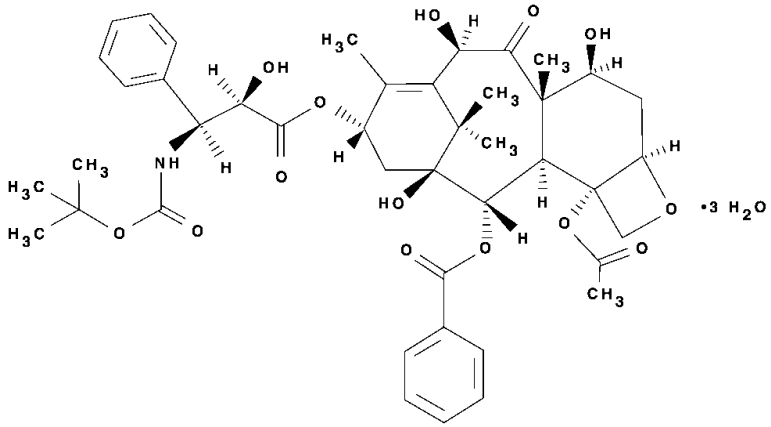
In two reports of overdose, one patient received 150 mg/m^2 and the other received 200 mg/m^2 as 1-hour infusions. Both patients experienced severe neutropenia, mild asthenia, cutaneous reactions, and mild paresthesia, and recovered without incident.

In mice, lethality was observed following single IV doses that were ≥154 mg/kg (about 4.5 times the recommended human dose on a mg/m^2 basis); neurotoxicity associated with paralysis, non-extension of hind limbs, and myelin degeneration was observed in mice at 48 mg/kg (about 1.5 times the recommended human dose on a mg/m^2 basis). In male and female rats, lethality

was observed at a dose of 20 mg/kg (comparable to the recommended human dose on a mg/m^2 basis) and was associated with abnormal mitosis and necrosis of multiple organs.

11. DESCRIPTION

Docetaxel is an antineoplastic agent belonging to the taxoid family. It is prepared by semisynthesis beginning with a precursor extracted from the renewable needle biomass of yew plants. The chemical name for docetaxel is (2R,3S)-N-carboxy-3-phenylisoserine,N-*tert*-butyl ester, 13-ester with 5β-20-epoxy-1,2α,4,7β,10β,13α-hexahydroxytax-11-en-9-one 4-acetate 2-benzoate, trihydrate. Docetaxel has the following structural formula:



Docetaxel is a white to almost-white powder with an empirical formula of $C_{43}H_{53}NO_{14}$• $3H_2O$, and a molecular weight of 861.9. It is highly lipophilic and practically insoluble in water.

- **Two-vial formulation (Injection Concentrate and diluent)**

TAXOTERE (docetaxel) Injection Concentrate is a clear yellow to brownish-yellow viscous solution. TAXOTERE is sterile, non-pyrogenic, and is available in single-dose vials containing 20 mg (0.5 mL) or 80 mg (2 mL) docetaxel (anhydrous). Each mL contains 40 mg docetaxel (anhydrous) and 1040 mg polysorbate 80.

TAXOTERE Injection Concentrate requires dilution with diluent prior to addition to the infusion bag. A sterile, non-pyrogenic, single-dose diluent is supplied for that purpose. The diluent for TAXOTERE contains 13% ethanol in water for injection, and is supplied in vials.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Docetaxel is an antineoplastic agent that acts by disrupting the microtubular network in cells that is essential for mitotic and interphase cellular functions. Docetaxel binds to free tubulin and promotes the assembly of tubulin into stable microtubules while simultaneously inhibiting their disassembly. This leads to the production of microtubule bundles without normal function and to the stabilization of microtubules, which results in the inhibition of mitosis in cells. Docetaxel's binding to microtubules does not alter the number of protofilaments in the bound microtubules, a feature which differs from most spindle poisons currently in clinical use.

12.3 Human Pharmacokinetics

- Absorption:

The pharmacokinetics of docetaxel have been evaluated in cancer patients after administration of 20-115 mg/m^2 in phase I studies. The area under the curve (AUC) was dose proportional following doses of 70-115 mg/m^2 with infusion times of 1 to 2 hours. Docetaxel's pharmacokinetic profile is consistent with a three-compartment pharmacokinetic model, with half-lives for the α, β, and γ phases of 4 min, 36 min, and 11.1 hr, respectively. The initial rapid decline represents distribution to the peripheral compartments and the late (terminal) phase is due, in part, to a relatively slow efflux of docetaxel from the peripheral compartment. Mean total body clearance was 21 L/h/m^2.

- Distribution:

Mean steady state volume of distribution was 113 L. *In vitro* studies showed that docetaxel is about 94% protein bound, mainly to α_1-acid glycoprotein, albumin, and lipoproteins. In three cancer patients, the *in vitro* binding to plasma proteins was found to be approximately 97%. Dexamethasone does not affect the protein binding of docetaxel.

- Metabolism:

In vitro drug interaction studies revealed that docetaxel is metabolized by the CYP3A4 isoenzyme.

- Excretion:

A study of ^{14}C-docetaxel was conducted in three cancer patients. Docetaxel was eliminated in both the urine and feces following oxidative metabolism of the *tert*-butyl ester group, but fecal excretion was the main elimination route. Within 7 days, urinary and fecal excretion accounted for approximately 6% and 75% of the administered radioactivity, respectively. About 80% of the radioactivity recovered in feces is excreted during the first 48 hours as 1 major and 3 minor metabolites with very small amounts (less than 8%) of unchanged drug.

- Effect of Age and Gender:

A population pharmacokinetic analysis was carried out after TAXOTERE treatment of 535 patients dosed at 100 mg/m^2. Pharmacokinetic parameters estimated by this analysis were very close to those estimated from phase I studies. The pharmacokinetics of docetaxel were not influenced by age or gender.

- Hepatic Impairment:

The population pharmacokinetic analysis described above indicated that in patients with clinical chemistry data suggestive of mild to moderate liver impairment (SGOT and/or SGPT >1.5 times the upper limit of normal [ULN] concomitant with alkaline phosphatase >2.5 times ULN), total body clearance was lowered by an average of 27%, resulting in a 38% increase in systemic exposure (AUC). This average, however, includes a substantial range and there is, at present, no measurement that would allow recommendation for dose adjustment in such patients. Patients

with combined abnormalities of transaminase and alkaline phosphatase should, in general, not be treated with TAXOTERE.

Patients with severe hepatic impairment have not been studied. ***[see Warnings and Precautions (5.5) and Use in Specific Populations (8.6)]***

- Effect of Race:

Mean total body clearance for Japanese patients dosed at the range of 10-90 mg/m^2 was similar to that of European/American populations dosed at 100 mg/m^2, suggesting no significant difference in the elimination of docetaxel in the two populations.

- Effect of Ketoconazole:

The effect of ketoconazole (a strong CYP3A4 inhibitor) on the pharmacokinetics of docetaxel was investigated in 7 cancer patients. Patients were randomized to receive either docetaxel (100 mg/m² IV) alone or docetaxel (10 mg/m² IV) in combination with ketoconazole (200 mg orally once daily for 3 days) in a crossover design with a 3-week washout period. The results of this study indicated that the mean dose-normalized AUC of docetaxel was increased 2.2-fold and its clearance was reduced by 49% when docetaxel was co-administration with ketoconazole ***[see Dosage and Administration (2.9) and Drug-Drug Interactions (7)]***.

- Effect of Combination therapies:

- Dexamethasone: Docetaxel total body clearance was not modified by pretreatment with dexamethasone.
- Cisplatin: Clearance of docetaxel in combination therapy with cisplatin was similar to that previously observed following monotherapy with docetaxel. The pharmacokinetic profile of cisplatin in combination therapy with docetaxel was similar to that observed with cisplatin alone.

- Cisplatin and Fluorouracil: The combined administration of docetaxel, cisplatin and fluorouracil in 12 patients with solid tumors had no influence on the pharmacokinetics of each individual drug.

- Prednisone: A population pharmacokinetic analysis of plasma data from 40 patients with hormone-refractory metastatic prostate cancer indicated that docetaxel systemic clearance in combination with prednisone is similar to that observed following administration of docetaxel alone.

- Cyclophosphamide and Doxorubicin: A study was conducted in 30 patients with advanced breast cancer to determine the potential for drug-drug-interactions between docetaxel (75 mg/m²), doxorubicin (50 mg/m²), and cyclophosphamide (500 mg/m²) when administered in combination. The coadministration of docetaxel had no effect on the pharmacokinetics of doxorubicin and cyclophosphamide when the three drugs were given in combination compared to coadministration of doxorubicin and cyclophosphamide only. In addition, doxorubicin and cyclophosphamide had no effect on

docetaxel plasma clearance when the three drugs were given in combination compared to historical data for docetaxel monotherapy.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of docetaxel.

Docetaxel has been shown to be clastogenic in the *in vitro* chromosome aberration test in CHO-K_1 cells and in the *in vivo* micronucleus test in mice administered doses of 0.39 to 1.56 mg/kg (about $1/60^{th}$ to $1/15^{th}$ the recommended human dose on a mg/m^2 basis). Docetaxel did not induce mutagenicity in the Ames test or the CHO/HGPRT gene mutation assays. Docetaxel produced no impairment of fertility in rats when administered in multiple IV doses of up to 0.3 mg/kg (about $1/50^{th}$ the recommended human dose on a mg/m^2 basis), but decreased testicular weights were reported. This correlates with findings of a 10-cycle toxicity study (dosing once every 21 days for 6 months) in rats and dogs in which testicular atrophy or degeneration was observed at IV doses of 5 mg/kg in rats and 0.375 mg/kg in dogs (about $1/3^{rd}$ and $1/15^{th}$ the recommended human dose on a mg/m^2 basis, respectively). An increased frequency of dosing in rats produced similar effects at lower dose levels.

14. CLINICAL STUDIES

14.1 Breast Cancer

The efficacy and safety of TAXOTERE have been evaluated in locally advanced or metastatic breast cancer after failure of previous chemotherapy (alkylating agent-containing regimens or anthracycline-containing regimens).

- Randomized Trials

In one randomized trial, patients with a history of prior treatment with an anthracycline-containing regimen were assigned to treatment with TAXOTERE (100 mg/m^2 every 3 weeks) or the combination of mitomycin (12 mg/m^2 every 6 weeks) and vinblastine (6 mg/m^2 every 3 weeks). 203 patients were randomized to TAXOTERE and 189 to the comparator arm. Most patients had received prior chemotherapy for metastatic disease; only 27 patients on the TAXOTERE arm and 33 patients on the comparator arm entered the study following relapse after adjuvant therapy. Three-quarters of patients had measurable, visceral metastases. The primary endpoint was time to progression. The following table summarizes the study results (See Table 13).

Table 13 - Efficacy of TAXOTERE in the Treatment of Breast Cancer Patients Previously Treated with an Anthracycline-Containing Regimen (Intent-to-Treat Analysis)

Efficacy Parameter	**Docetaxel (n=203)**	**Mitomycin/ Vinblastine (n=189)**	**p-value**
Median Survival	11.4 months	8.7 months	
Risk Ratio*, Mortality (Docetaxel: Control)	0.73		p=0.01 Log Rank
95% CI (Risk Ratio)	0.58-0.93		
Median Time to Progression	4.3 months	2.5 months	
Risk Ratio*, Progression (Docetaxel: Control)	0.75		p=0.01 Log Rank
95% CI (Risk Ratio)	0.61-0.94		
Overall Response Rate	28.1%	9.5%	p<0.0001
Complete Response Rate	3.4%	1.6%	Chi Square

*For the risk ratio, a value less than 1.00 favors docetaxel.

In a second randomized trial, patients previously treated with an alkylating-containing regimen were assigned to treatment with TAXOTERE (100 mg/m^2) or doxorubicin (75 mg/m^2) every 3 weeks. 161 patients were randomized to TAXOTERE and 165 patients to doxorubicin. Approximately one-half of patients had received prior chemotherapy for metastatic disease, and one-half entered the study following relapse after adjuvant therapy. Three-quarters of patients had measurable, visceral metastases. The primary endpoint was time to progression. The study results are summarized below (See Table 14).

Table 14 - Efficacy of TAXOTERE in the Treatment of Breast Cancer Patients Previously Treated with an Alkylating-Containing Regimen (Intent-to-Treat Analysis)

Efficacy Parameter	Docetaxel (n=161)	Doxorubicin (n=165)	p-value
Median Survival	14.7 months	14.3 months	
Risk Ratio*, Mortality (Docetaxel: Control) 95% CI (Risk Ratio)	0.89 0.68-1.16		p=0.39 Log Rank
Median Time to Progression	6.5 months	5.3 months	
Risk Ratio*, Progression (Docetaxel: Control) 95% CI (Risk Ratio)	0.93 0.71-1.16		p=0.45 Log Rank
Overall Response Rate Complete Response Rate	45.3% 6.8%	29.7% 4.2%	p=0.004 Chi Square

*For the risk ratio, a value less than 1.00 favors docetaxel.

In another multicenter open-label, randomized trial (TAX313), in the treatment of patients with advanced breast cancer who progressed or relapsed after one prior chemotherapy regimen, 527 patients were randomized to receive TAXOTERE monotherapy 60 mg/m^2 (n=151), 75 mg/m^2 (n=188) or 100 mg/m^2 (n=188). In this trial, 94% of patients had metastatic disease and 79% had received prior anthracycline therapy. Response rate was the primary endpoint. Response rates increased with TAXOTERE dose: 19.9% for the 60 mg/m^2 group compared to 22.3% for the 75 mg/m^2 and 29.8% for the 100 mg/m^2 group; pair-wise comparison between the 60 mg/m^2 and 100 mg/m^2 groups was statistically significant (p=0.037).

- Single Arm Studies

TAXOTERE at a dose of 100 mg/m^2 was studied in six single arm studies involving a total of 309 patients with metastatic breast cancer in whom previous chemotherapy had failed. Among these, 190 patients had anthracycline-resistant breast cancer, defined as progression during an anthracycline-containing chemotherapy regimen for metastatic disease, or relapse during an anthracycline-containing adjuvant regimen. In anthracycline-resistant patients, the overall response rate was 37.9% (72/190; 95% C.I.: 31.0-44.8) and the complete response rate was 2.1%.

TAXOTERE was also studied in three single arm Japanese studies at a dose of 60 mg/m^2, in 174 patients who had received prior chemotherapy for locally advanced or metastatic breast cancer. Among 26 patients whose best response to an anthracycline had been progression, the response rate was 34.6% (95% C.I.: 17.2-55.7), similar to the response rate in single arm studies of 100 mg/m^2.

14.2 Adjuvant Treatment of Breast Cancer

A multicenter, open-label, randomized trial (TAX316) evaluated the efficacy and safety of TAXOTERE for the adjuvant treatment of patients with axillary-node-positive breast cancer and no evidence of distant metastatic disease. After stratification according to the number of positive lymph nodes (1-3, 4+), 1491 patients were randomized to receive either TAXOTERE 75 mg/m^2 administered 1-hour after doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2 (TAC arm), or doxorubicin 50 mg/m^2 followed by fluorouracil 500 mg/m^2 and cyclosphosphamide 500 mg/m^2 (FAC arm). Both regimens were administered every 3 weeks for 6 cycles. TAXOTERE was administered as a 1-hour infusion; all other drugs were given as IV bolus on day 1. In both arms, after the last cycle of chemotherapy, patients with positive estrogen and/or progesterone receptors received tamoxifen 20 mg daily for up to 5 years. Adjuvant radiation therapy was prescribed according to guidelines in place at participating institutions and was given to 69% of patients who received TAC and 72% of patients who received FAC.

Results from a second interim analysis (median follow-up 55 months) are as follows: In study TAX316, the docetaxel-containing combination regimen TAC showed significantly longer disease-free survival (DFS) than FAC (hazard ratio=0.74; 2-sided 95% CI=0.60, 0.92, stratified log rank p=0.0047). The primary endpoint, disease-free survival, included local and distant recurrences, contralateral breast cancer and deaths from any cause. The overall reduction in risk of relapse was 25.7% for TAC-treated patients. (See Figure 1).

At the time of this interim analysis, based on 219 deaths, overall survival was longer for TAC than FAC (hazard ratio=0.69, 2-sided 95% CI=0.53, 0.90). (See Figure 2). There will be further analysis at the time survival data mature.

Figure 1 - TAX316 Disease Free Survival K-M curve

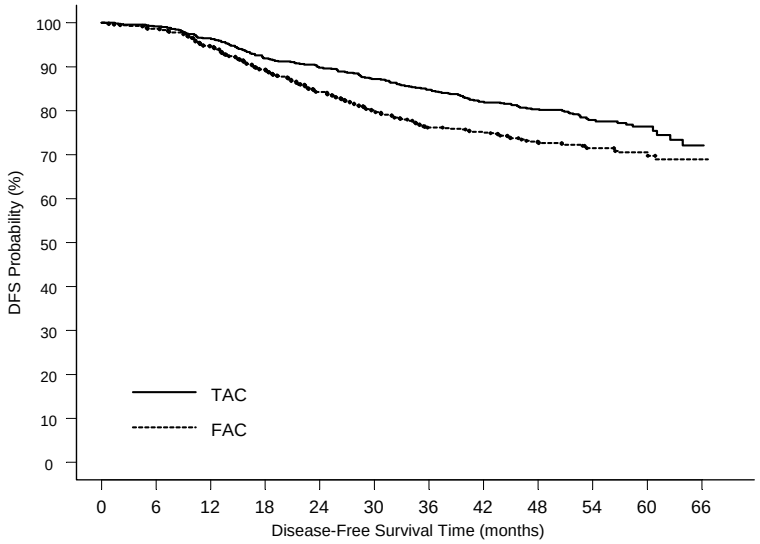
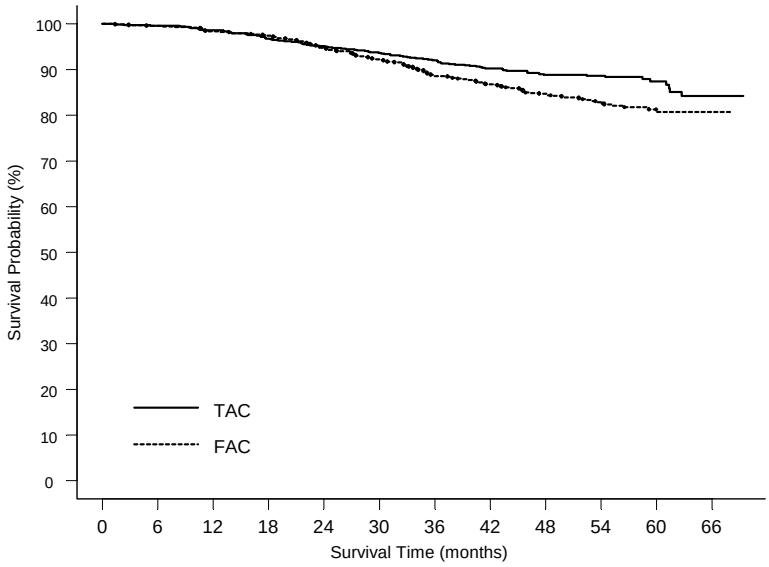


Figure 2 - TAX316 Overall Survival K-M Curve



The following table describes the results of subgroup analyses for DFS and OS (See Table 15).

Table 15 - Subset Analyses-Adjuvant Breast Cancer Study

		Disease Free Survival		Overall Survival	
Patient subset	**Number of patients**	**Hazard ratio***	**95% CI**	**Hazard ratio***	**95% CI**
No. of positive nodes					
Overall	744	0.74	(0.60, 0.92)	0.69	(0.53, 0.90)
1-3	467	0.64	(0.47, 0.87)	0.45	(0.29, 0.70)
4+	277	0.84	(0.63, 1.12)	0.93	(0.66, 1.32)
Receptor status					
Positive	566	0.76	(0.59, 0.98)	0.69	(0.48, 0.99)
Negative	178	0.68	(0.48, 0.97)	0.66	(0.44, 0.98)

*****a hazard ratio of less than 1 indicates that TAC is associated with a longer disease free survival or overall survival compared to FAC.

14.3 Non-Small Cell Lung Cancer (NSCLC)

The efficacy and safety of TAXOTERE has been evaluated in patients with unresectable, locally advanced or metastatic non-small cell lung cancer whose disease has failed prior platinum-based chemotherapy or in patients who are chemotherapy-naïve.

- Monotherapy with TAXOTERE for NSCLC Previously Treated with Platinum-Based Chemotherapy

Two randomized, controlled trials established that a TAXOTERE dose of 75 mg/m^2 was tolerable and yielded a favorable outcome in patients previously treated with platinum-based

chemotherapy (see below). TAXOTERE at a dose of 100 mg/m^2, however, was associated with unacceptable hematologic toxicity, infections, and treatment-related mortality and this dose should not be used ***[see Boxed Warning, Warnings and Precautions (5.4), Dosage Adjustment During Treatment (2.7)].***

One trial (TAX317), randomized patients with locally advanced or metastatic non-small cell lung cancer, a history of prior platinum-based chemotherapy, no history of taxane exposure, and an ECOG performance status ≤2 to TAXOTERE or best supportive care. The primary endpoint of the study was survival. Patients were initially randomized to TAXOTERE 100 mg/m^2 or best supportive care, but early toxic deaths at this dose led to a dose reduction to TAXOTERE 75 mg/m^2. A total of 104 patients were randomized in this amended study to either TAXOTERE 75 mg/m^2 or best supportive care.

In a second randomized trial (TAX320), 373 patients with locally advanced or metastatic non-small cell lung cancer, a history of prior platinum-based chemotherapy, and an ECOG performance status ≤2 were randomized to TAXOTERE 75 mg/m^2, TAXOTERE 100 mg/m^2 and a treatment in which the investigator chose either vinorelbine 30 mg/m^2 days 1, 8, and 15 repeated every 3 weeks or ifosfamide 2 g/m^2 days 1-3 repeated every 3 weeks. Forty percent of the patients in this study had a history of prior paclitaxel exposure. The primary endpoint was survival in both trials. The efficacy data for the TAXOTERE 75 mg/m^2 arm and the comparator arms are summarized in Table 16 and Figures 3 and 4 showing the survival curves for the two studies.

Table 16 - Efficacy of TAXOTERE in the Treatment of Non-Small Cell Lung Cancer Patients Previously Treated with a Platinum-Based Chemotherapy Regimen (Intent-to-Treat Analysis)

	TAX317		**TAX320**	
	Docetaxel 75 mg/m^2 n=55	**Best Supportive Care/75 n=49**	**Docetaxel 75 mg/m^2 n=125**	**Control (V/I) n=123**
Overall Survival Log-rank Test	p=0.01		p=0.13	
Risk Ratio††, Mortality (Docetaxel: Control) 95% CI (Risk Ratio)	0.56 (0.35, 0.88)		0.82 (0.63, 1.06)	
Median Survival 95% CI	7.5 months* (5.5, 12.8)	4.6 months (3.7, 6.1)	5.7 months (5.1, 7.1)	5.6 months (4.4, 7.9)
% 1-year Survival 95% CI	37%*† (24, 50)	12% (2, 23)	30%*† (22, 39)	20% (13, 27)
Time to Progression 95% CI	12.3 weeks* (9.0, 18.3)	7.0 weeks (6.0, 9.3)	8.3 weeks (7.0, 11.7)	7.6 weeks (6.7, 10.1)
Response Rate 95% CI	5.5% (1.1, 15.1)	Not Applicable	5.7% (2.3, 11.3)	0.8% (0.0, 4.5)

* $p \leq 0.05$; † uncorrected for multiple comparisons; †† a value less than 1.00 favors docetaxel.

Only one of the two trials (TAX317) showed a clear effect on survival, the primary endpoint; that trial also showed an increased rate of survival to one year. In the second study (TAX320) the rate of survival at one year favored TAXOTERE 75 mg/m^2.

Figure 3 - TAX317 Survival K-M Curves - TAXOTERE 75 mg/m^2 vs. Best Supportive Care

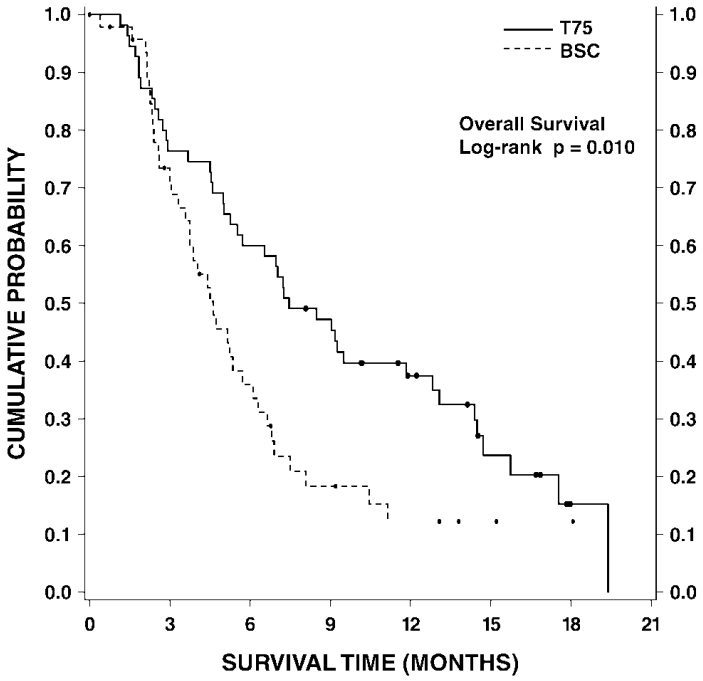
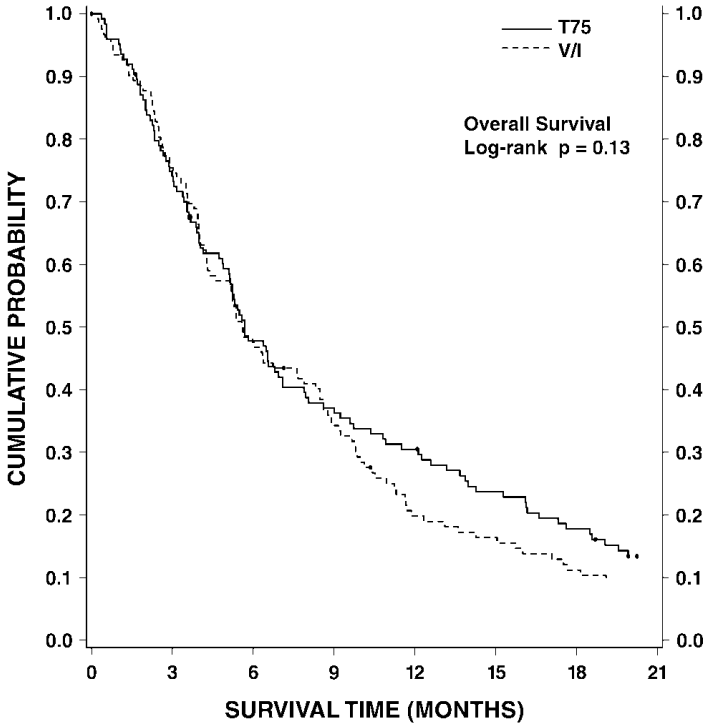


Figure 4 - TAX320 Survival K-M Curves - TAXOTERE 75 mg/m^2 vs. Vinorelbine or Ifosfamide Control



Patients treated with TAXOTERE at a dose of 75 mg/m^2 experienced no deterioration in performance status and body weight relative to the comparator arms used in these trials.

- Combination Therapy with TAXOTERE for Chemotherapy-Naïve NSCLC

In a randomized controlled trial (TAX326), 1218 patients with unresectable stage IIIB or IV NSCLC and no prior chemotherapy were randomized to receive one of three treatments: TAXOTERE 75 mg/m^2 as a 1 hour infusion immediately followed by cisplatin 75 mg/m^2 over 30-60 minutes every 3 weeks; vinorelbine 25 mg/m^2 administered over 6-10 minutes on days 1, 8, 15, 22 followed by cisplatin 100 mg/m^2 administered on day 1 of cycles repeated every 4 weeks; or a combination of TAXOTERE and carboplatin.

The primary efficacy endpoint was overall survival. Treatment with TAXOTERE+cisplatin did not result in a statistically significantly superior survival compared to vinorelbine+cisplatin (see table below). The 95% confidence interval of the hazard ratio (adjusted for interim analysis and multiple comparisons) shows that the addition of TAXOTERE to cisplatin results in an outcome ranging from a 6% inferior to a 26% superior survival compared to the addition of vinorelbine to cisplatin. The results of a further statistical analysis showed that at least (the lower bound of the 95% confidence interval) 62% of the known survival effect of vinorelbine when added to cisplatin (about a 2-month increase in median survival; Wozniak et al. JCO, 1998) was maintained. The efficacy data for the TAXOTERE+cisplatin arm and the comparator arm are summarized in Table 17.

All 3 regimens were administered in combination with prednisone 5 mg twice daily, continuously.

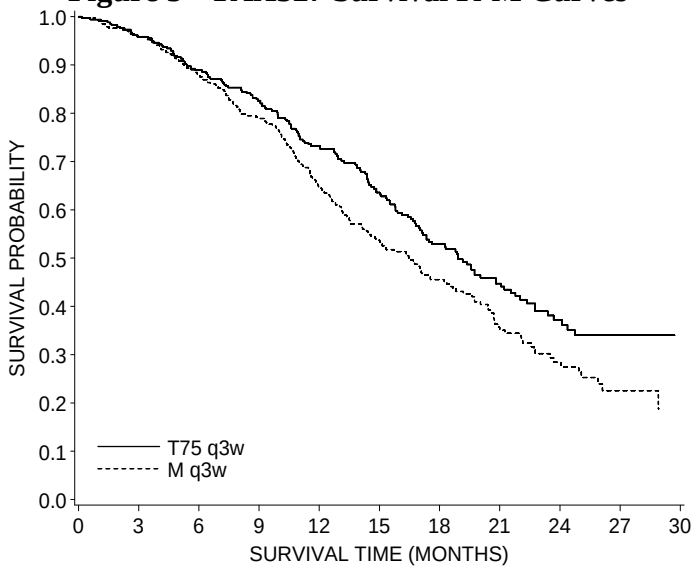
In the TAXOTERE every three week arm, a statistically significant overall survival advantage was demonstrated compared to mitoxantrone. In the TAXOTERE weekly arm, no overall survival advantage was demonstrated compared to the mitoxantrone control arm. Efficacy results for the TAXOTERE every 3 week arm versus the control arm are summarized in Table 19 and Figure 5.

Table 19 - Efficacy of TAXOTERE in the Treatment of Patients with Androgen Independent (Hormone Refractory) Metastatic Prostate Cancer (Intent-to-Treat Analysis)

	TAXOTERE every 3 weeks	**Mitoxantrone every 3 weeks**
Number of patients	335	337
Median survival (months)	18.9	16.5
95% CI	(17.0-21.2)	(14.4-18.6)
Hazard ratio	0.761	--
95% CI	(0.619-0.936)	--
p-value*	0.0094	--

*Stratified log rank test. Threshold for statistical significance = 0.0175 because of 3 arms.

Figure 5 - TAX327 Survival K-M Curves



14.5 Gastric Adenocarcinoma

A multicenter, open-label, randomized trial was conducted to evaluate the safety and efficacy of TAXOTERE for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who had not received prior chemotherapy for advanced disease. A total of 445 patients with KPS >70 were treated with either TAXOTERE (T) (75 mg/m^2 on day 1) in combination with cisplatin (C) (75 mg/m^2 on day 1) and fluorouracil (F) (750 mg/m^2 per day for 5 days) or cisplatin (100 mg/m^2 on day 1) and fluorouracil

(1000 mg/m^2 per day for 5 days). The length of a treatment cycle was 3 weeks for the TCF arm and 4 weeks for the CF arm. The demographic characteristics were balanced between the two treatment arms. The median age was 55 years, 71% were male, 71% were Caucasian, 24% were 65 years of age or older, 19% had a prior curative surgery and 12% had palliative surgery. The median number of cycles administered per patient was 6 (with a range of 1-16) for the TCF arm compared to 4 (with a range of 1-12) for the CF arm. Time to progression (TTP) was the primary endpoint and was defined as time from randomization to disease progression or death from any cause within 12 weeks of the last evaluable tumor assessment or within 12 weeks of the first infusion of study drugs for patients with no evaluable tumor assessment after randomization. The hazard ratio (HR) for TTP was 1.47 (CF/TCF, 95% CI: 1.19-1.83) with a significantly longer TTP (p=0.0004) in the TCF arm. Approximately 75% of patients had died at the time of this analysis. Overall survival was significantly longer (p=0.0201) in the TCF arm with a HR of 1.29 (95% CI: 1.04-1.61). Efficacy results are summarized in Table 20 and Figures 6 and 7.

Table 20 - Efficacy of TAXOTERE in the treatment of patients with gastric adenocarcinoma

Endpoint	**TCF n=221**	**CF n=224**
Median TTP (months)	5.6	3.7
(95%CI)	(4.86-5.91)	(3.45-4.47)
Hazard ratio†	0.68	
(95%CI)	(0.55-0.84)	
*p-value	0.0004	
Median survival (months)	9.2	8.6
(95%CI)	(8.38-10.58)	(7.16-9.46)
Hazard ratio†	0.77	
(95%CI)	(0.62-0.96)	
*p-value	0.0201	
Overall Response Rate (CR+PR) (%)	36.7	25.4
p-value	0.0106	

*Unstratified log-rank test

†For the hazard ratio (TCF/CF), values less than 1.00 favor the TAXOTERE arm.

Subgroup analyses were consistent with the overall results across age, gender and race.

Figure 6 - Gastric Cancer Study (TAX325) Time to Progression K-M Curve

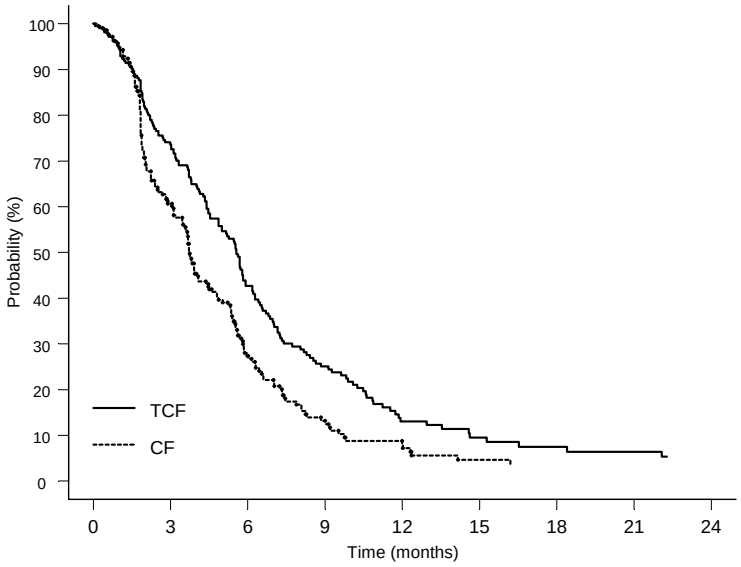
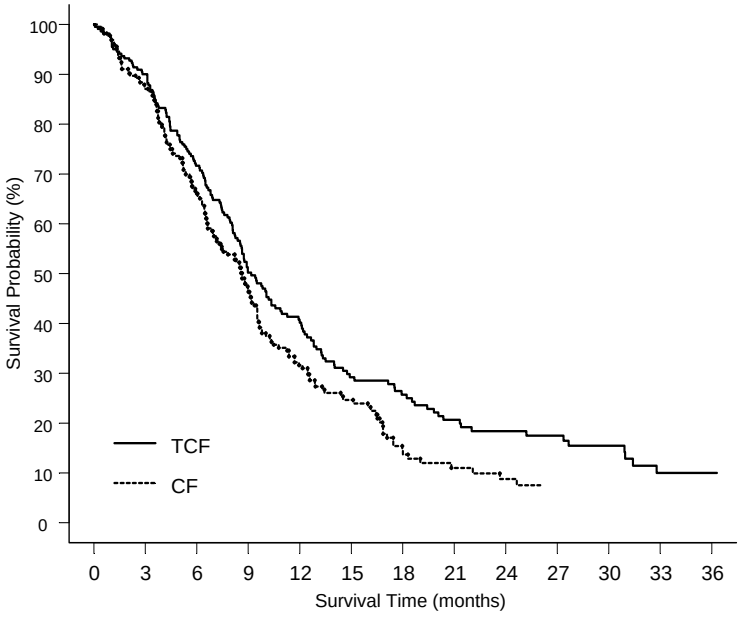


Figure 7 - Gastric Cancer Study (TAX325) Survival K-M Curve



14.6 Head and Neck Cancer

- Induction chemotherapy followed by radiotherapy (TAX323)

The safety and efficacy of TAXOTERE in the induction treatment of patients with squamous cell carcinoma of the head and neck (SCCHN) was evaluated in a multicenter, open-label, randomized trial (TAX323). In this study, 358 patients with inoperable locally advanced

SCCHN, and WHO performance status 0 or 1, were randomized to one of two treatment arms. Patients on the TAXOTERE arm received TAXOTERE (T) 75 mg/m^2 followed by cisplatin (P) 75 mg/m^2 on Day 1, followed by fluorouracil (F) 750 mg/m^2 per day as a continuous infusion on Days 1-5. The cycles were repeated every three weeks for 4 cycles. Patients whose disease did not progress received radiotherapy (RT) according to institutional guidelines (TPF/RT). Patients on the comparator arm received cisplatin (P) 100 mg/m^2 on Day 1, followed by fluorouracil (F) 1000 mg/m^2/day as a continuous infusion on Days 1-5. The cycles were repeated every three weeks for 4 cycles. Patients whose disease did not progress received RT according to institutional guidelines (PF/RT). At the end of chemotherapy, with a minimal interval of 4 weeks and a maximal interval of 7 weeks, patients whose disease did not progress received radiotherapy (RT) according to institutional guidelines. Locoregional therapy with radiation was delivered either with a conventional fraction regimen (1.8 Gy-2.0 Gy once a day, 5 days per week for a total dose of 66 to 70 Gy) or with an accelerated/hyperfractionated regimen (twice a day, with a minimum interfraction interval of 6 hours, 5 days per week, for a total dose of 70 to 74 Gy, respectively). Surgical resection was allowed following chemotherapy, before or after radiotherapy.

The primary endpoint in this study, progression-free survival (PFS), was significantly longer in the TPF arm compared to the PF arm, p=0.0077 (median PFS: 11.4 vs. 8.3 months respectively) with an overall median follow up time of 33.7 months. Median overall survival with a median follow-up of 51.2 months was also significantly longer in favor of the TPF arm compared to the PF arm (median OS: 18.6 vs. 14.2 months respectively). Efficacy results are presented in Table 21 and Figures 8 and 9.

Table 21 - Efficacy of TAXOTERE in the induction treatment of patients with inoperable locally advanced SCCHN (Intent-to-Treat Analysis)

ENDPOINT	TAXOTERE+ Cisplatin+ Fluorouracil n=177	Cisplatin+ Fluorouracil n=181
Median progression free survival (months) (95%CI)	11.4 (10.1-14.0)	8.3 (7.4-9.1)
Adjusted Hazard ratio (95%CI) *p-value	0.71 (0.56-0.91) 0.0077	
Median survival (months) (95%CI)	18.6 (15.7-24.0)	14.2 (11.5-18.7)
Hazard ratio (95%CI) **p-value	0.71 (0.56-0.90) 0.0055	
Best overall response (CR + PR) to chemotherapy (%) (95%CI)	67.8 (60.4-74.6)	53.6 (46.0-61.0)
***p-value	0.006	
Best overall response (CR + PR) to study treatment [chemotherapy +/- radiotherapy] (%) (95%CI)	72.3 (65.1-78.8)	58.6 (51.0-65.8)
***p-value	0.006	

A Hazard ratio of less than 1 favors TAXOTERE+Cisplatin+Fluorouracil
* Stratified log-rank test based on primary tumor site
** Stratified log-rank test, not adjusted for multiple comparisons
*** Chi square test, not adjusted for multiple comparisons

Figure 8 - TAX323 Progression-Free Survival K-M Curve

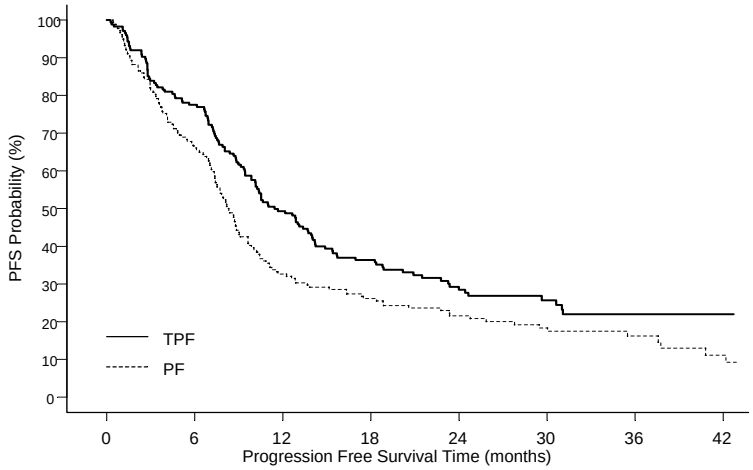
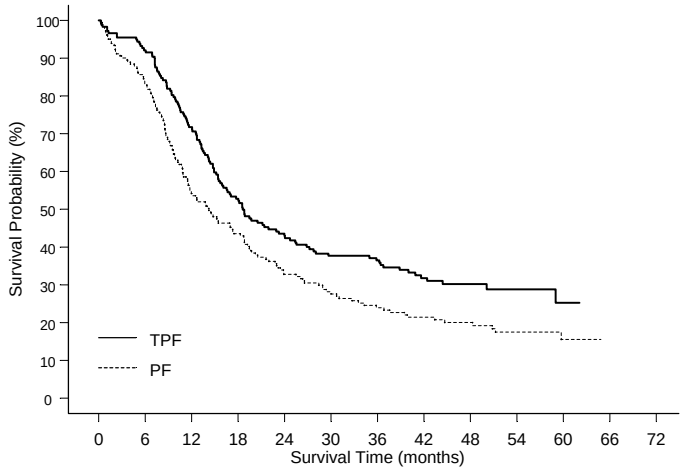


Figure 9 - TAX323 Overall Survival K-M Curve



- Induction chemotherapy followed by chemoradiotherapy (TAX324)

The safety and efficacy of TAXOTERE in the induction treatment of patients with locally advanced (unresectable, low surgical cure, or organ preservation) SCCHN was evaluated in a randomized, multicenter open-label trial (TAX324). In this study, 501 patients, with locally advanced SCCHN, and a WHO performance status of 0 or 1, were randomized to one of two treatment arms. Patients on the TAXOTERE arm received TAXOTERE (T) 75 mg/m² by IV infusion on day 1 followed by cisplatin (P) 100 mg/m² administered as a 30-minute to three-hour IV infusion, followed by the continuous IV infusion of fluorouracil (F) 1000 mg/m²/day from day 1 to day 4. The cycles were repeated every 3 weeks for 3 cycles. Patients on the comparator arm received cisplatin (P) 100 mg/m² as a 30-minute to three-hour IV infusion on day 1 followed by the continuous IV infusion of fluorouracil (F) 1000 mg/m²/day from day 1 to day 5. The cycles were repeated every 3 weeks for 3 cycles.

All patients in both treatment arms who did not have progressive disease were to receive 7 weeks of chemoradiotherapy (CRT) following induction chemotherapy 3 to 8 weeks after the start of the last cycle. During radiotherapy, carboplatin (AUC 1.5) was given weekly as a one-hour IV infusion for a maximum of 7 doses. Radiation was delivered with megavoltage equipment using once daily fractionation (2 Gy per day, 5 days per week for 7 weeks for a total dose of 70-72 Gy). Surgery on the primary site of disease and/or neck could be considered at anytime following completion of CRT.

The primary efficacy endpoint, overall survival (OS), was significantly longer (log-rank test, p=0.0058) with the TAXOTERE-containing regimen compared to PF [median OS: 70.6 versus 30.1 months respectively, hazard ratio (HR)=0.70, 95% confidence interval (CI)= 0.54 – 0.90]. Overall survival results are presented in Table 22 and Figure 10.

3. American Society of Health-System Pharmacists. (2006) ASHP Guidelines on Handling Hazardous Drugs. *Am J Health-Syst Pharm.* 2006;63:1172-1193

4. Polovich, M., White, J. M., & Kelleher, L.O. (eds.) 2005. Chemotherapy and biotherapy guidelines and recommendations for practice (2nd. ed.) Pittsburgh, PA: Oncology Nursing Society.

16. HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

- **Two vial formulation (Injection Concentrate and diluent)**

TAXOTERE Injection Concentrate is supplied in a single-dose vial as a sterile, pyrogen-free, non-aqueous, viscous solution with an accompanying sterile, non-pyrogenic, diluent (13% ethanol in water for injection) vial.

TAXOTERE 80 mg/2 mL (NDC 0075-8001-80)
TAXOTERE (docetaxel) Injection Concentrate 80 mg/2 mL: 80 mg docetaxel in 2 mL polysorbate 80 and Diluent for TAXOTERE 80 mg (13% (w/w) ethanol in water for injection). Both items are in a blister pack in one carton.

TAXOTERE 20 mg/0.5 mL (NDC 0075-8001-20)
TAXOTERE (docetaxel) Injection Concentrate 20 mg/0.5 mL: 20 mg docetaxel in 0.5 mL polysorbate 80 and Diluent for TAXOTERE 20 mg (13% (w/w) ethanol in water for injection). Both items are in a blister pack in one carton.

16.2 Storage

Store between 2 and 25°C (36 and 77°F). Retain in the original package to protect from bright light. Freezing does not adversely affect the product.

16.3 Handling and Disposal

Procedures for proper handling and disposal of anticancer drugs should be considered. Several guidelines on this subject have been published[1-4].

17. PATIENT COUNSELING INFORMATION

Patient Information Leaflet

Questions and Answers About Taxotere® Injection Concentrate

(generic name = docetaxel)

(pronounced as TAX-O-TEER)

What is Taxotere?

Taxotere is a medication to treat breast cancer, non-small cell lung cancer, prostate cancer, stomach cancer, and head and neck cancer. It has severe side effects in some patients. This leaflet is designed to help you understand how to use Taxotere and avoid its side effects to the fullest extent possible. The more you understand your treatment, the better you will be able to participate in your care. If you have questions or concerns, be sure to ask your doctor or nurse. They are always your best source of information about your condition and treatment**.**

What is the most important information about Taxotere?

• Since this drug, like many other cancer drugs, affects your blood cells, your doctor will ask for routine blood tests. These will include regular checks of your white blood cell counts. People with low blood counts can develop life-threatening infections. The earliest sign of infection may be fever, so if you experience a fever, tell your doctor right away.

• Occasionally, serious allergic reactions have occurred with this medicine. If you have any allergies, tell your doctor before receiving this medicine.

• A small number of people who take Taxotere have severe fluid retention, which can be life-threatening. To help avoid this problem, you must take another medication such as dexamethasone (DECKS-A-METH-A-SONE) prior to each Taxotere treatment. You must follow the schedule and take the exact dose of dexamethasone prescribed (see schedule at end of brochure). If you forget to take a dose or do not take it on schedule you must tell the doctor or nurse prior to your Taxotere treatment.

• If you are using any other medicines, tell your doctor before receiving your infusions of Taxotere.

How does Taxotere work?

Taxotere works by attacking cancer cells in your body. Different cancer medications attack cancer cells in different ways.

Here's how Taxotere works: Every cell in your body contains a supporting structure (like a skeleton). Damage to this "skeleton" can stop cell growth or reproduction. Taxotere makes the "skeleton" in some cancer cells very stiff, so that the cells can no longer grow.

How will I receive Taxotere?

Taxotere is given by an infusion directly into your vein. Your treatment will take about 1 hour. Generally, people receive Taxotere every 3 weeks. The amount of Taxotere and the frequency of your infusions will be determined by your doctor.

As part of your treatment, to reduce side effects your doctor will prescribe another medicine called dexamethasone. Your doctor will tell you how and when to take this medicine. It is important that you take the dexamethasone on the schedule set by your doctor. If you forget to take your medication, or do not take it on schedule, make sure to tell your doctor or nurse **BEFORE** you receive your Taxotere treatment. **Included with this information leaflet is a chart to help you remember when to take your dexamethasone.**

What should be avoided while receiving Taxotere?

Taxotere can interact with other medicines. Use only medicines that are prescribed for you by your doctor and **be sure** to tell your doctor all the medicines that you use, including nonprescription drugs.

What are the possible side effects of Taxotere?

Low White Blood Cell Count – Many cancer medications, including Taxotere, cause a temporary drop in the number of white blood cells. These cells help protect your body from infection. Your doctor will routinely check your white blood cell count and tell you if it is too low. Although most people receiving Taxotere do not have an infection even if they have a low white blood cell count, the risk of infection is increased.

Fever is often one of the most common and earliest signs of infection. Your doctor will recommend that you take your temperature frequently, especially during the days after treatment with Taxotere. If you have a fever, tell your doctor or nurse immediately.

Low Red Blood Cell Count – Taxotere can cause a drop in the number of red blood cells. These cells carry oxygen to different parts of the body. Your doctor will routinely check your red blood cell count and tell you if it is too low.

Other Blood Disorders – Changes in blood counts due to leukemia and other blood disorders may occur years after treatment with Taxotere.

Allergic Reactions – This type of reaction, which occurs during the infusion of Taxotere, is infrequent. If you feel a warm sensation, a tightness in your chest, or itching during or shortly after your treatment, tell your doctor or nurse immediately.

Fluid Retention – This means that your body is holding extra water. If this fluid retention is in the chest or around the heart it can be life-threatening. Shortness of breath may be a sign of fluid retention in the chest or around the heart. If you notice swelling in the feet and legs or a slight weight gain, this may be the first warning sign. Fluid retention usually does not start immediately; but, if it occurs, it may start around your 5th treatment. Generally, fluid retention will go away within weeks or months after your treatments are completed.

Dexamethasone tablets may protect patients from significant fluid retention. It is important that you take this medicine on schedule. If you have not taken dexamethasone on schedule, you must tell your doctor or nurse before receiving your next Taxotere treatment.

Gastrointestinal – Diarrhea has been associated with Taxotere use and can be severe in some patients. Constipation can also occur. Nausea and/or vomiting are common in patients receiving TAXOTERE. Severe inflammation of the bowel can also occur in some patients and may be life threatening.

Hepatic – Elevations in liver enzymes can occur.

Hair Loss – Loss of hair occurs in most patients taking Taxotere (including the hair on your head, underarm hair, pubic hair, eyebrows, and eyelashes). Hair loss will begin after the first few treatments and varies from patient to patient. Once you have completed all your treatments, hair generally grows back.

Your doctor or nurse can refer you to a store that carries wigs, hairpieces, and turbans for patients with cancer.

Every three-week injection of TAXOTERE for breast, non-small cell lung and stomach, and head and neck cancers
Take dexamethasone tablets, 8 mg twice daily.

Dexamethasone dosing:

Day 1 Date: _____ Time:_____ AM _____ PM

Day 2 Date: _____ Time:_____ AM _____ PM
(Taxotere Treatment Day)

Day 3 Date: _____ Time:_____ AM _____ PM

Every three-week injection of TAXOTERE for prostate cancer
Take dexamethasone 8 mg, at 12 hours, 3 hours and 1 hour before TAXOTERE infusion.

Dexamethasone dosing:

Date: _____ Time:_____

Date: _____ Time:_____
(Taxotere Treatment Day)
Time:_____

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