HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TAXOTERE safely and effectively. See full prescribing information for TAXOTERE.

TAXOTERE (docetaxel) injection, for intravenous use
Initial U.S. Approval: 1996

WARNING: TOXIC DEATHS, HEPATOTOXICITY, NEUTROPENIA, HYPERSENSITIVITY REACTIONS, and FLUID RETENTION

See full prescribing information for complete boxed warning.

- **Treatment-related mortality increases with abnormal liver function, at higher doses, and in patients with NSCLC and prior platinum-based therapy receiving TAXOTERE at 100 mg/m^2 (5.1)**
- **Avoid use of TAXOTERE if bilirubin > ULN, or if AST and/or ALT >1.5 × ULN concomitant with alkaline phosphatase >2.5 × ULN. LFT elevations increase risk of severe or life-threatening complications. Obtain LFTs before each treatment cycle (5.2)**
- **Do not administer TAXOTERE to patients with neutrophil counts <1500 cells/mm^3. Obtain frequent blood counts to monitor for neutropenia (4, 5.3)**
- **Severe hypersensitivity, including fatal anaphylaxis, has been reported in patients who received dexamethasone premedication. Severe reactions require immediate discontinuation of TAXOTERE and administration of appropriate therapy (5.5)**
- **Contraindicated if history of severe hypersensitivity reactions to TAXOTERE or to drugs formulated with polysorbate 80 (4)**
- **Severe fluid retention may occur despite dexamethasone (5.6)**

----------INDICATIONS AND USAGE----------

TAXOTERE is a microtubule inhibitor indicated for:

- **Breast Cancer (BC)**: single agent for locally advanced or metastatic BC after chemotherapy failure; and with doxorubicin and cyclophosphamide as adjuvant treatment of operable node-positive BC (1.1)
- **Non-small Cell Lung Cancer (NSCLC)**: single agent for locally advanced or metastatic NSCLC after platinum therapy failure; and with cisplatin for unresectable, locally advanced or metastatic untreated NSCLC (1.2)
- **Castration-Resistant Prostate Cancer (CRPC)**: with prednisone in metastatic castration-resistant prostate cancer (1.3)
- **Gastric Adenocarcinoma (GC)**: with cisplatin and fluorouracil for untreated, advanced GC, including the gastroesophageal junction (1.4)
- **Squamous Cell Carcinoma of the Head and Neck (SCCHN)**: with cisplatin and fluorouracil for induction treatment of locally advanced SCCHN (1.5)

----------DOSAGE AND ADMINISTRATION----------

Administer in a facility equipped to manage possible complications (e.g., anaphylaxis). Administer intravenously (IV) over 1 hr every 3 weeks. PVC equipment is not recommended. **Use only a 21 gauge needle to withdraw TAXOTERE from the vial.**

- BC locally advanced or metastatic: 60 mg/m^2 to 100 mg/m^2 single agent (2.1)
- BC adjuvant: 75 mg/m^2 administered 1 hour after doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2 every 3 weeks for 6 cycles (2.1)
- NSCLC: after platinum therapy failure: 75 mg/m^2 single agent (2.2)
- NSCLC: chemotherapy naive: 75 mg/m^2 followed by cisplatin 75 mg/m^2 (2.2)
- HRPC: 75 mg/m^2 with 5 mg prednisone twice a day continuously (2.3)
- GC: 75 mg/m^2 followed by cisplatin 75 mg/m^2 (both on day 1 only) followed by fluorouracil 750 mg/m^2 per day as a 24-hr IV (days 1-5), starting at end of cisplatin infusion (2.4)
- SCCHN: 75 mg/m^2 followed by cisplatin 75 mg/m^2 IV (day 1), followed by fluorouracil 750 mg/m^2 per day as a 24-hr IV (days 1-5), starting at end of cisplatin infusion; for 4 cycles (2.5)
- SCCHN: 75 mg/m^2 followed by cisplatin 100 mg/m^2 IV (day 1), followed by fluorouracil 1000 mg/m^2 per day as a 24-hr IV (days 1-4); for 3 cycles (2.5)

For all patients:

- Premedicate with oral corticosteroids (2.6)
- Adjust dose as needed (2.7)

----------DOSAGE FORMS AND STRENGTHS----------

- Injection: One-vial TAXOTERE: Single-dose vials 20 mg/mL and 80 mg/4 mL (3)

----------CONTRAINDICATIONS----------

- Hypersensitivity to docetaxel or polysorbate 80 (4)
- Neutrophil counts of <1500 cells/mm^3 (4)

----------WARNINGS AND PRECAUTIONS----------

- Second primary malignancies: In patients treated with TAXOTERE-containing regimens, monitor for delayed AML, MDS, NHL, and renal cancer. (5.7)
- Cutaneous reactions: Reactions including erythema of the extremities with edema followed by desquamation may occur. Severe cutaneous adverse reactions have been reported. Severe skin toxicity may require dose adjustment or permanent treatment discontinuation. (5.8)
- Neurologic reactions: Reactions including paresthesia, dysesthesia, and pain may occur. Severe neurosensory symptoms require dose adjustment or discontinuation if persistent. (5.9)
- Eye disorders: Cystoid macular edema (CME) has been reported and requires treatment discontinuation. (5.10)
- Asthenia: Severe asthenia may occur and may require treatment discontinuation. (5.11)
- Embryo-fetal toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception. (5.12, 8.1, 8.3)
- Alcohol content: The alcohol content in a dose of TAXOTERE Injection may affect the central nervous system. This may include impairment of a patient's ability to drive or use machines immediately after infusion. (5.13)
- Tumor lysis syndrome: Tumor lysis syndrome has been reported. Patients at risk should be well hydrated and closely monitored during treatment. (5.14)

----------ADVERSE REACTIONS----------

Most common adverse reactions across all TAXOTERE indications are infections, neutropenia, anemia, febrile neutropenia, hypersensitivity, thrombocytopenia, neuropathy, dysgeusia, dyspnea, constipation, anorexia, nail disorders, fluid retention, asthenia, pain, nausea, diarrhea, vomiting, mucositis, alopecia, skin reactions, and myalgia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact sanofi-aventis U.S. LLC at 1-800-633-1610 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Cytochrome P450 3A4 inducers, inhibitors, or substrates: May alter docetaxel metabolism. (7)

----------USE IN SPECIFIC POPULATIONS----------

- Lactation: Advise women not to breastfeed. (8.2)
- Females and Males of Reproductive Potential: Verify pregnancy status of females prior to initiation of TAXOTERE. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 01/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

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 11: 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 %**	**Grade 3/4 %**	**Any %**	**Grade 3/4 %**	**Any %**	**Grade 3/4 %**	**Any %**	**Grade 3/4 %**
Neutropenia	93	76	87	53	95	84	84	56
Anemia	89	9	88	14	90	12	86	10
Thrombocytopenia	24	5	47	18	28	4	31	11
Infection	27	9	26	8	23	6	28	5
Febrile neutropenia*	5	N/A	2	N/A	12	N/A	7	N/A
Neutropenic infection	14	N/A	8	N/A	12	N/A	8	N/A
Cancer pain	21	5	16	3	17	9	20	11
Lethargy	41	3	38	3	61	5	56	10
Fever in the absence of infection	32	1	37	0	30	4	28	3
Myalgia	10	1	7	0	7	0	7	2
Weight loss	21	1	27	1	14	2	14	2
Allergy	6	0	3	0	2	0	0	0
Fluid retention**	20	0	14	1	13	1	7	2
Edema only	13	0	7	0	12	1	6	1
Weight gain only	6	0	6	0	0	0	1	0
Dizziness	2	0	5	1	16	4	15	2
Neurosensory	18	1	11	1	14	1	14	0
Altered hearing	6	0	10	3	13	1	19	3
Neuromotor	2	1	4	1	9	0	10	2
Alopecia	81	11	43	0	68	4	44	1
Rash/itch	12	0	6	0	20	0	16	1
Dry skin	6	0	2	0	5	0	3	0
Desquamation	4	1	6	0	2	0	5	0
Nausea	47	1	51	7	77	14	80	14
Stomatitis	43	4	47	11	66	21	68	27
Vomiting	26	1	39	5	56	8	63	10
Diarrhea	33	3	24	4	48	7	40	3
Constipation	17	1	16	1	27	1	38	1
Anorexia	16	1	25	3	40	12	34	12

	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 %**	**Grade 3/4 %**	**Any %**	**Grade 3/4 %**	**Any %**	**Grade 3/4 %**	**Any %**	**Grade 3/4 %**
Esophagitis/dysphagia/ Odynophagia	13	1	18	3	25	13	26	10
Taste, sense of smell altered	10	0	5	0	20	0	17	1
Gastrointestinal pain/cramping	8	1	9	1	15	5	10	2
Heartburn	6	0	6	0	13	2	13	1
Gastrointestinal bleeding	4	2	0	0	5	1	2	1
Cardiac dysrhythmia	2	2	2	1	6	3	5	3
Venous* **	3	2	6	2	4	2	5	4
Ischemia myocardial	2	2	1	0	2	1	1	1
Tearing	2	0	1	0	2	0	2	0
Conjunctivitis	1	0	1	0	1	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 intravenous antibiotics and/or hospitalization.
**Related to treatment.
***Includes superficial and deep vein thrombosis and pulmonary embolism

6.2 Postmarketing Experience

The following adverse reactions have been identified from clinical trials and/or postmarketing surveillance. Because these reactions are reported from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Body as a whole: diffuse pain, chest pain, radiation recall phenomenon, injection site recall reaction (recurrence of skin reaction at a site of previous extravasation following administration of docetaxel at a different site) at the site of previous extravasation.

Cardiovascular: atrial fibrillation, deep vein thrombosis, ECG abnormalities, thrombophlebitis, pulmonary embolism, syncope, tachycardia, myocardial infarction. Ventricular arrhythmia, including ventricular tachycardia, in patients treated with docetaxel in combination regimens including doxorubicin, 5-fluorouracil and/or cyclophosphamide may be associated with fatal outcome.

Cutaneous: cutaneous lupus erythematosus, bullous eruptions such as erythema multiforme and severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome, toxic epidermal necrolysis and acute generalized exanthematous pustulosis, scleroderma-like changes (usually preceded by peripheral lymphedema), severe palmar-plantar erythrodysesthesia, and permanent alopecia.

Gastrointestinal: enterocolitis, including colitis, ischemic colitis, and neutropenic enterocolitis,

which may be fatal. Abdominal pain, anorexia, constipation, duodenal ulcer, esophagitis, gastrointestinal hemorrhage, gastrointestinal perforation, intestinal obstruction, ileus, and dehydration as a consequence of gastrointestinal events.

Hearing: ototoxicity, hearing disorders and/or hearing loss, including during use with other ototoxic drugs.

Hematologic: bleeding episodes, disseminated intravascular coagulation (DIC), often in association with sepsis or multiorgan failure.

Hepatic: hepatitis, sometimes fatal, primarily in patients with pre-existing liver disorders.

Hypersensitivity: anaphylactic shock with fatal outcome in patients who received premedication. Severe hypersensitivity reactions with fatal outcome with docetaxel in patients who previously experienced hypersensitivity reactions to paclitaxel.

Metabolism and nutrition disorders: electrolyte imbalance, including hyponatremia, hypokalemia, hypomagnesemia, and hypocalcemia. Tumor lysis syndrome, sometimes fatal.

Neurologic: confusion, seizures or transient loss of consciousness, sometimes appearing during the infusion of the drug.

Ophthalmologic: conjunctivitis, lacrimation or lacrimation with or without conjunctivitis, cystoid macular edema (CME). Excessive tearing which may be attributable to lacrimal duct obstruction. Transient visual disturbances (flashes, flashing lights, scotomata), typically occurring during drug infusion and reversible upon discontinuation of the infusion, in association with hypersensitivity reactions.

Respiratory: dyspnea, acute pulmonary edema, acute respiratory distress syndrome/pneumonitis, interstitial lung disease, interstitial pneumonia, respiratory failure, and pulmonary fibrosis, which may be fatal. Radiation pneumonitis in patients receiving concomitant radiotherapy.

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

Second primary malignancies: second primary malignancies, including AML, MDS, NHL, and renal cancer *[see Warnings and Precautions (5.7)]*.

Musculoskeletal disorder: myositis.

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), Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings in animal reproduction studies and its mechanism of action, TAXOTERE can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. Available data from case reports in the literature and pharmacovigilance with docetaxel use in pregnant women are not sufficient to inform the drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. TAXOTERE contains alcohol which can interfere with neurobehavioral development *[see Clinical Considerations]*. In animal reproductive studies, administration of docetaxel to pregnant rats and rabbits during the period of organogenesis caused an increased incidence of embryo-fetal toxicities, including intrauterine mortality, at doses as low as 0.02 and 0.003 times the recommended human dose based on body surface area, respectively *[see Data]*. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, miscarriage, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

TAXOTERE contains alcohol *[see Warnings and Precautions (5.13)]*. Published studies have demonstrated that alcohol is associated with fetal harm including central nervous system abnormalities, behavioral disorders, and impaired intellectual development.

Data

Animal data

Intravenous administration of ≥0.3 and 0.03 mg/kg/day docetaxel to pregnant rats and rabbits, respectively, during the period of organogenesis caused an increased incidence of intrauterine mortality, resorptions, reduced fetal weights, and fetal ossification delays. Maternal toxicity was also observed at these doses, which were approximately 0.02 and 0.003 times the daily maximum recommended human dose based on body surface area, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of docetaxel in human milk, or on its effects on milk production or the breastfed child. No lactation studies in animals have been conducted. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with TAXOTERE and for 1 week after the last dose.

8.3 Females and Males of Reproductive Potential

Based on findings in animals, TAXOTERE can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating TAXOTERE.

Contraception

Females

Based on genetic toxicity findings, advise females of reproductive potential to use effective contraception during treatment and for 2 months after the last dose of TAXOTERE.

Males

Based on genetic toxicity findings, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of TAXOTERE.

Infertility

Based on findings in animal studies, TAXOTERE may impair fertility in males of reproductive potential *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The alcohol content of TAXOTERE Injection should be taken into account when given to pediatric patients *[see Warnings and Precautions (5.13)]*.

The efficacy of TAXOTERE in pediatric patients as monotherapy or in combination has not been established. The overall safety profile of TAXOTERE in pediatric patients receiving monotherapy or TCF was consistent with the known safety profile in adults.

TAXOTERE has been studied in a total of 289 pediatric patients: 239 in 2 trials with monotherapy and 50 in combination treatment with cisplatin and 5-fluorouracil (TCF).

TAXOTERE Monotherapy

TAXOTERE monotherapy was evaluated in a dose-finding phase 1 trial in 61 pediatric patients (median age 12.5 years, range 1-22 years) with a variety of refractory solid tumors. The recommended dose was 125 mg/m^2 as a 1-hour intravenous infusion every 21 days. The primary dose limiting toxicity was neutropenia.

The recommended dose for TAXOTERE monotherapy was evaluated in a phase 2 single-arm trial in 178 pediatric patients (median age 12 years, range 1-26 years) with a variety of recurrent/refractory solid tumors. Efficacy was not established with tumor response rates ranging from one complete response (CR) (0.6%) in a patient with undifferentiated sarcoma to four partial responses (2.2%) seen in one patient each with Ewing Sarcoma, neuroblastoma, osteosarcoma, and squamous cell carcinoma.

TAXOTERE in Combination

TAXOTERE was studied in combination with cisplatin and 5-fluorouracil (TCF) versus cisplatin and 5-fluorouracil (CF) for the induction treatment of nasopharyngeal carcinoma (NPC) in pediatric patients prior to chemoradiation consolidation. Seventy-five patients (median age 16 years, range 9 to 21 years) were randomized (2:1) to TAXOTERE (75 mg/m^2) in combination with cisplatin (75 mg/m^2) and 5-fluorouracil (750 mg/m^2) (TCF) or to cisplatin (80 mg/m^2) and 5-fluorouracil (1000 mg/m^2/day) (CF). The primary endpoint was the CR rate following

induction treatment of NPC. One patient out of 50 in the TCF group (2%) had a complete response while none of the 25 patients in the CF group had a complete response.

Pharmacokinetics

Pharmacokinetic parameters for docetaxel were determined in 2 pediatric solid tumor trials. Following docetaxel administration at 55 mg/m^2 to 235 mg/m^2 in a 1-hour intravenous infusion every 3 weeks in 25 patients aged 1 to 20 years (median 11 years), docetaxel clearance was 17.3±10.9 L/h/m^2.

Docetaxel was administered in combination with cisplatin and 5-fluorouracil (TCF), at dose levels of 75 mg/m^2 in a 1-hour intravenous infusion day 1 in 28 patients aged 10 to 21 years (median 16 years, 17 patients were older than 16). Docetaxel clearance was 17.9±8.75 L/h/m^2, corresponding to an AUC of 4.20±2.57 μg·h/mL.

In summary, the body surface area adjusted clearance of docetaxel monotherapy and TCF combination in children were comparable to those in adults *[see Clinical Pharmacology (12.3)]*.

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.

Non-small Cell Lung Cancer

In a study conducted in chemotherapy-naive 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-naive, 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.

Prostate Cancer

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 treatment-emergent adverse reactions 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.

Breast Cancer

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.

Gastric Cancer

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.

Head and Neck Cancer

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

Avoid TAXOTERE in patients with bilirubin >ULN and patients with AST and/or ALT >1.5 × ULN concomitant with alkaline phosphatase >2.5 × ULN *[see Boxed Warning, Warnings and Precautions (5.2), Clinical Pharmacology (12.3)]*.

The alcohol content of TAXOTERE Injection should be taken into account when given to patients with hepatic impairment *[see Warnings and Precautions (5.13)]*.

10 OVERDOSAGE

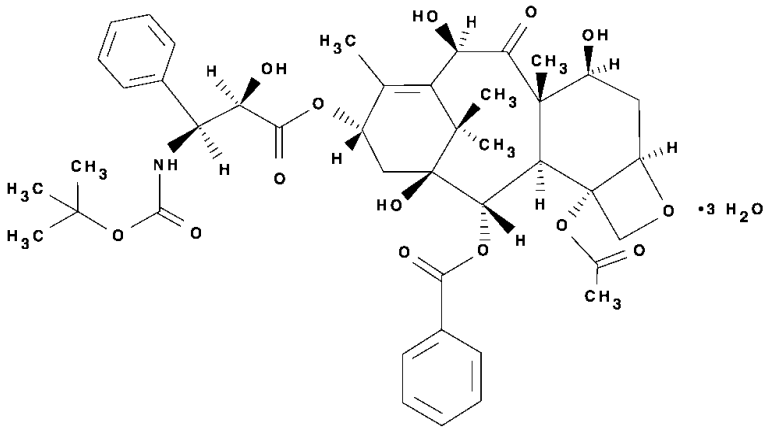
There is no known antidote for TAXOTERE overdosage. In case of overdosage, the patient should be kept in a specialized unit where vital functions can be closely monitored. Anticipated complications of overdosage include: bone marrow suppression, peripheral neurotoxicity, and mucositis. Patients should 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 intravenous doses that were ≥154 mg/kg (about 4.5 times the human dose of 100 mg/m^2 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 human dose of 100 mg/m^2 basis). In male and female rats, lethality was observed at a dose of 20 mg/kg (comparable to the human dose of 100 mg/m^2 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.

One-vial TAXOTERE (Injection)

TAXOTERE (docetaxel) Injection is a sterile, non-pyrogenic, pale-yellow to brownish-yellow solution at 20 mg/mL concentration.

Each mL contains 20 mg docetaxel (anhydrous) in 0.54 grams polysorbate 80 and 0.395 grams dehydrated alcohol (50% v/v) solution, with citric acid for pH adjustment.

TAXOTERE is available in single-dose vials containing 20 mg (1 mL) or 80 mg (4 mL) docetaxel (anhydrous).

TAXOTERE Injection requires NO prior dilution with a diluent and is ready to add to the infusion solution.

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 Pharmacokinetics

Absorption

The pharmacokinetics of docetaxel has been evaluated in cancer patients after administration of 20 mg/m^2 to 115 mg/m^2 in phase 1 studies. The area under the curve (AUC) was dose proportional following doses of 70 mg/m^2 to 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 initial rapid distribution phase and the late (terminal) phase.

Distribution

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

Elimination

With extended plasma sampling up to 8 to 22 days post infusion, the estimated mean total body clearance was 18 L/h/m^2 (range of means: 14 to 23) and mean terminal elimination half-life was 116 hours (range of means: 92 to 135).

Metabolism

Docetaxel is metabolized by the CYP3A4 isoenzyme *in vitro [see Drug Interactions (7)]*.

Excretion

In three cancer patients urinary and fecal excretion accounted for approximately 6% and 75% of the administered radioactivity, respectively, within 7 days. About 80% of the radioactivity recovered in feces was excreted during the first 48 hours as 1 major and 3 minor metabolites with less than 8% as unchanged drug.

Specific Populations

Effect of Age: 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 1 studies. The pharmacokinetics of docetaxel was not influenced by age.

Effect of Gender: The population pharmacokinetics analysis described above also indicated that gender did not influence the pharmacokinetics of docetaxel.

Hepatic Impairment: The population pharmacokinetic analysis described above indicated that in patients with clinical chemistry data suggestive of mild to moderate liver impairment (AST and/or ALT >1.5 times 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 not be treated with TAXOTERE. Patients with severe hepatic impairment have not been studied *[see Warnings and Precautions (5.2), Use in Specific Populations (8.6)]*.

Effect of Race: Mean total body clearance for Japanese patients dosed at the range of 10 mg/m^2 to 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.

Drug Interaction Studies

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/m^2 intravenous) alone or docetaxel (10 mg/m^2 intravenous) 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 coadministered with ketoconazole *[see Dosage and Administration (2.7), 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 metastatic castration-resistant 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/m^2), doxorubicin (50 mg/m^2), and cyclophosphamide (500 mg/m^2) 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

Carcinogenicity studies with docetaxel have not been performed.

Docetaxel was genotoxic by an aneugenic mechanism 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 was not mutagenic in the Ames test or the CHO/HGPRT gene mutation assays.

Docetaxel did not reduce fertility in rats when administered in multiple intravenous 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 intravenous 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 Locally Advanced or Metastatic 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). Two hundred three 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 12.)

Table 12: 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) 95% CI (Risk Ratio)	0.73 0.58-0.93		p=0.01 Log Rank
Median Time to Progression	4.3 months	2.5 months	
Risk Ratio*, Progression (Docetaxel: Control)	0.75		p=0.01 Log Rank

Efficacy Parameter	Docetaxel (n=203)	Mitomycin/ Vinblastine (n=189)	p-value
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. One hundred sixty-one 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 13.)

Table 13: 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	45.3%	29.7%	p=0.004
Complete Response Rate	6.8%	4.2%	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% CI: 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% CI: 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 cyclophosphamide 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 intravenous 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

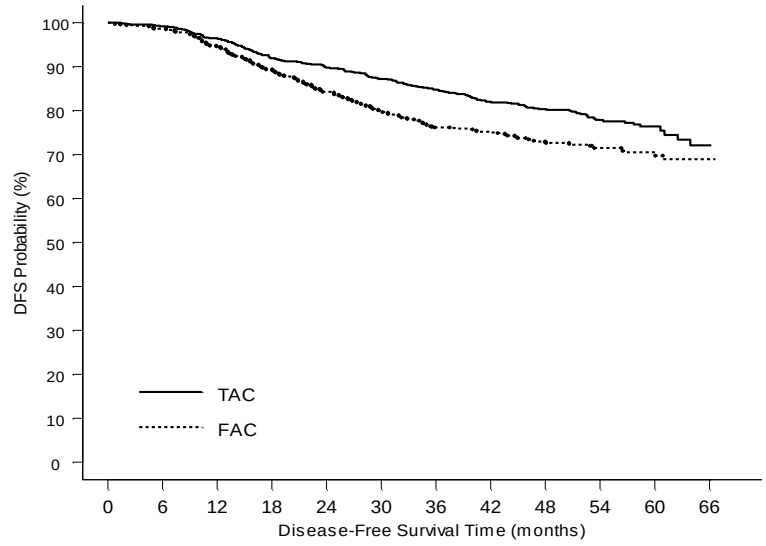
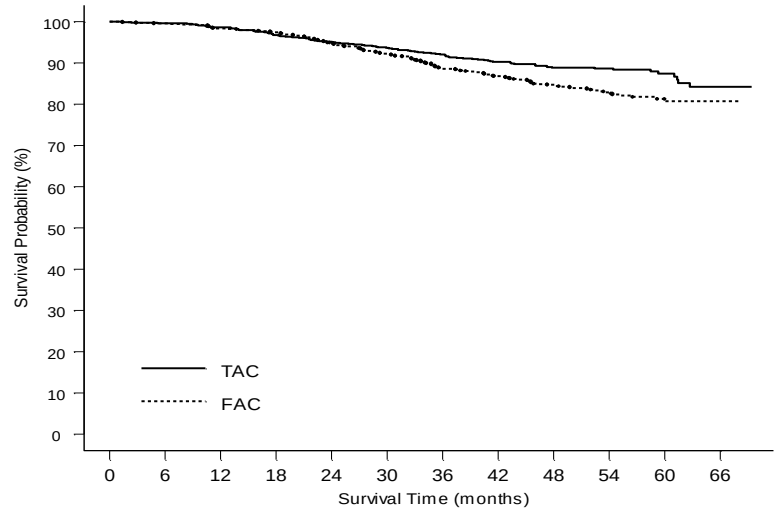


Figure 2: TAX316 Overall Survival K-M Curve



The following table describes the results of subgroup analyses for DFS and OS (See Table 14).

Table 14: Subset Analyses-Adjuvant Breast Cancer Study

Patient subset	Number of patients	Disease Free Survival		Overall Survival	
		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 naive.

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, Dosage and Administration (2.7), Warnings and Precautions (5.3)]*.

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 15 and Figures 3 and 4 showing the survival curves for the two studies.

Table 15: 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 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)	0.56		0.82	

	TAX317		TAX320	
	Docetaxel 75 mg/m^2 n=55	**Best Supportive Care n=49**	**Docetaxel 75 mg/m^2 n=125**	**Control (V/I*) n=123**
95% CI (Risk Ratio)	(0.35, 0.88)		(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)

*Vinorelbine/Ifosfamide
**p≤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 Versus Best Supportive Care

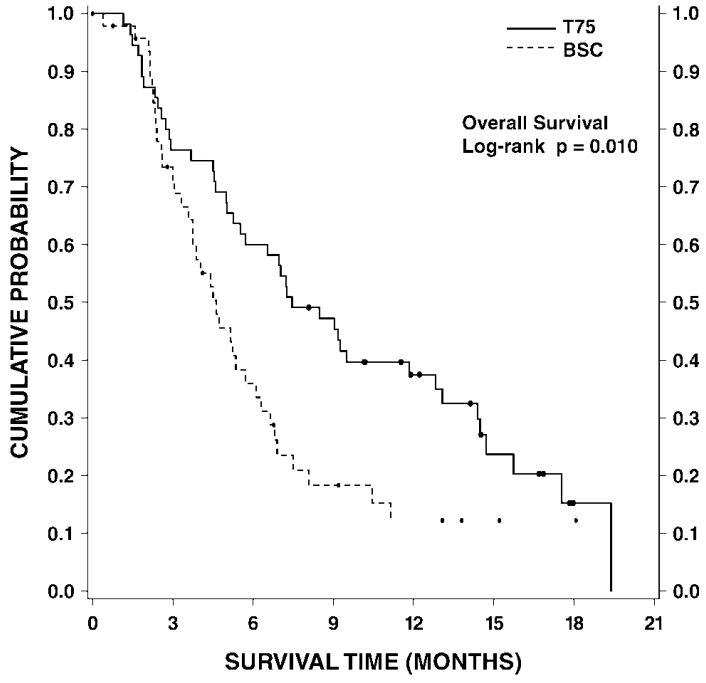
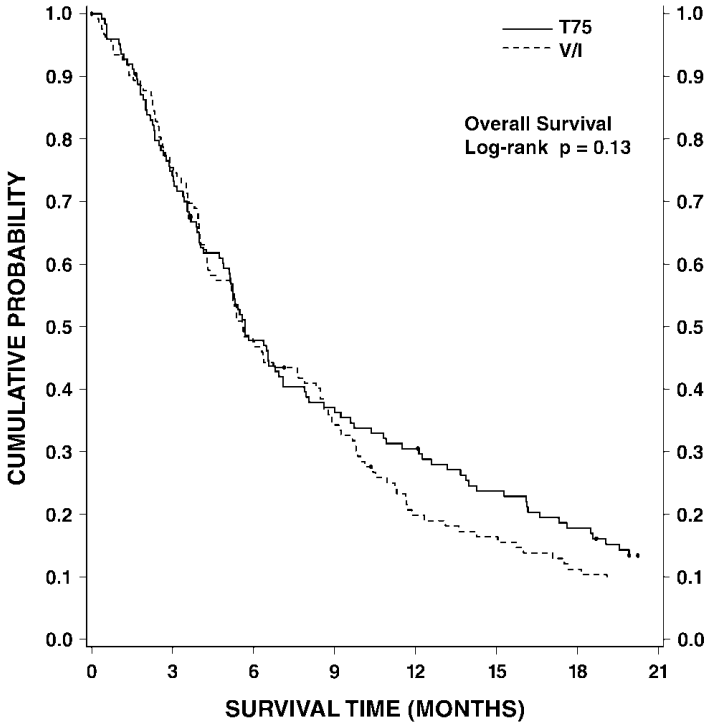


Figure 4: TAX320 Survival K-M Curves - TAXOTERE 75 mg/m^2 Versus Vinorelbine or Ifosfamide Control



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-Naive 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 to 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 16.

Table 16: Survival Analysis of TAXOTERE in Combination Therapy for Chemotherapy-Naive NSCLC

Comparison	**TAXOTERE + Cisplatin n=408**	**Vinorelbine + Cisplatin n=405**

Kaplan-Meier Estimate of Median Survival	10.9 months	10.0 months
p-value[a]	0.122	
Estimated Hazard Ratio[b]	0.88	
Adjusted 95% CI[c]	(0.74, 1.06)	

[a] From the superiority test (stratified log rank) comparing TAXOTERE+cisplatin to vinorelbine+cisplatin
[b]Hazard ratio of TAXOTERE+cisplatin versus vinorelbine+cisplatin. A hazard ratio of less than 1 indicates that TAXOTERE+cisplatin is associated with a longer survival.
[c]Adjusted for interim analysis and multiple comparisons.

The second comparison in the same three-arm study, vinorelbine+cisplatin versus TAXOTERE+carboplatin, did not demonstrate superior survival associated with the TAXOTERE arm (Kaplan-Meier estimate of median survival was 9.1 months for TAXOTERE+carboplatin compared to 10.0 months on the vinorelbine+cisplatin arm) and the TAXOTERE+carboplatin arm did not demonstrate preservation of at least 50% of the survival effect of vinorelbine added to cisplatin. Secondary endpoints evaluated in the trial included objective response and time to progression. There was no statistically significant difference between TAXOTERE+cisplatin and vinorelbine+cisplatin with respect to objective response and time to progression (see Table 17).

Table 17: Response and TTP Analysis of TAXOTERE in Combination Therapy for Chemotherapy-Naive NSCLC

Endpoint	TAXOTERE + Cisplatin	Vinorelbine + Cisplatin	p-value
Objective Response Rate (95% CI)[a]	31.6% (26.5%, 36.8%)	24.4% (19.8%, 29.2%)	Not Significant
Median Time to Progression[b] (95% CI)[a]	21.4 weeks (19.3, 24.6)	22.1 weeks (18.1, 25.6)	Not Significant

[a]Adjusted for multiple comparisons.
[b]Kaplan-Meier estimates.

14.4 Castration-Resistant Prostate Cancer

The safety and efficacy of TAXOTERE in combination with prednisone in patients with metastatic castration-resistant prostate cancer were evaluated in a randomized multicenter active control trial. A total of 1006 patients with Karnofsky Performance Status (KPS) ≥60 were randomized to the following treatment groups:

- TAXOTERE 75 mg/m^2 every 3 weeks for 10 cycles.
- TAXOTERE 30 mg/m^2 administered weekly for the first 5 weeks in a 6-week cycle for 5 cycles.
- Mitoxantrone 12 mg/m^2 every 3 weeks for 10 cycles.

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

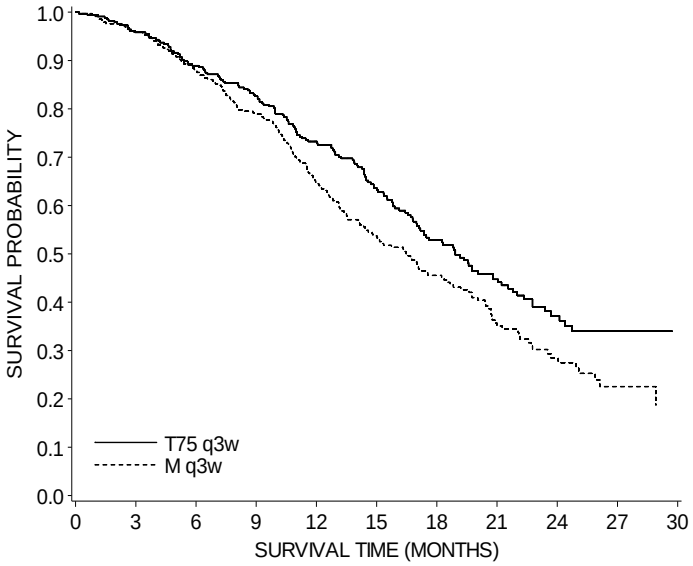
survival advantage was demonstrated compared to the mitoxantrone control arm. Efficacy results for the TAXOTERE every 3 week arm versus the control arm are summarized in Table 18 and Figure 5.

Table 18: Efficacy of TAXOTERE in the Treatment of Patients with Metastatic Castration-Resistant Prostate Cancer (Intent-to-Treat Analysis)

	TAXOTERE + Prednisone every 3 weeks	**Mitoxantrone + Prednisone 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 19 and Figures 6 and 7.

Table 19: 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

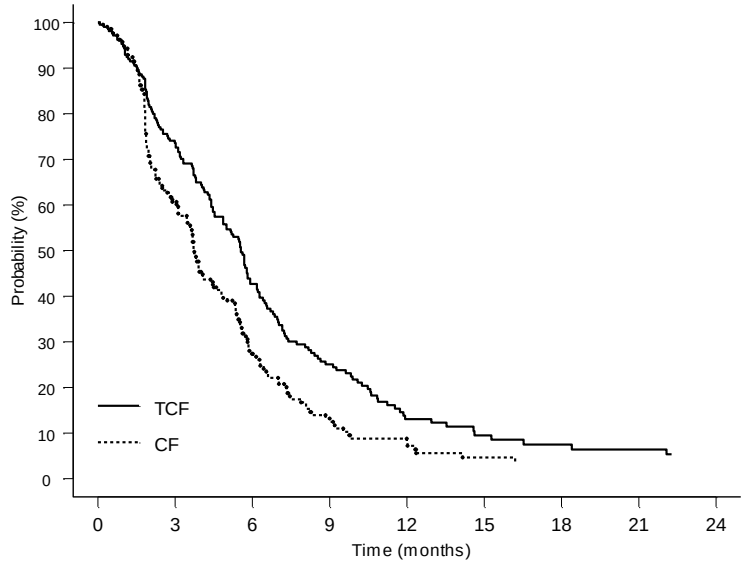
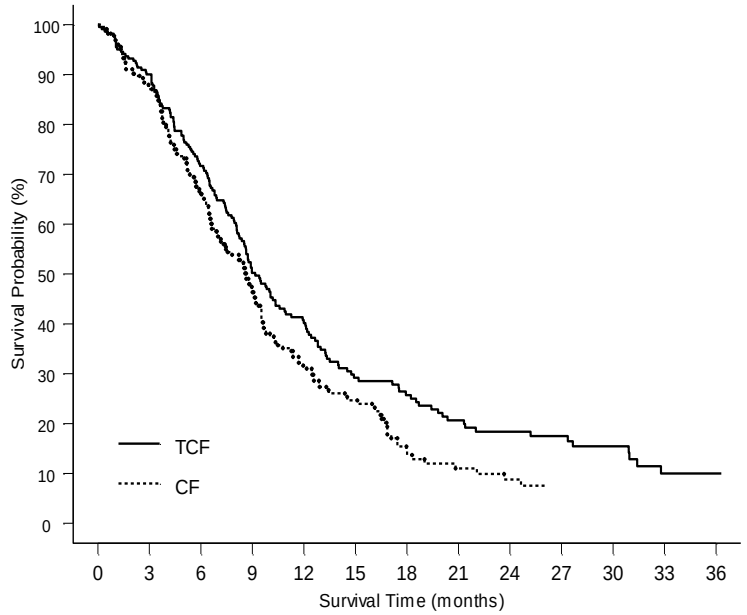


Figure 7: Gastric Cancer Study (TAX325) Survival K-M Curve



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 20 and Figures 8 and 9.

Table 20: 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

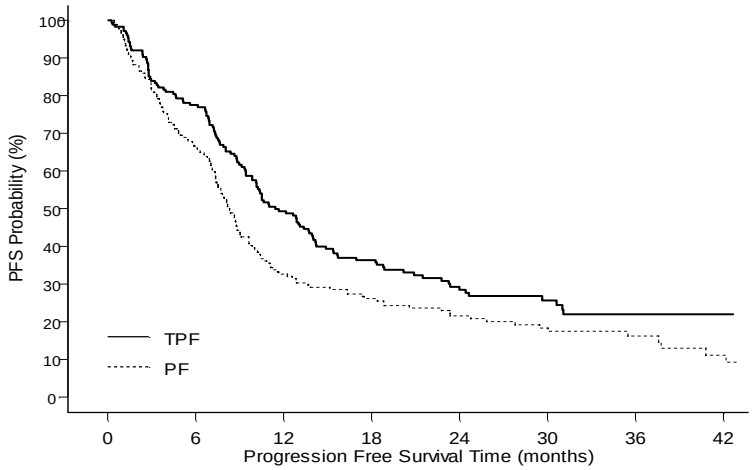
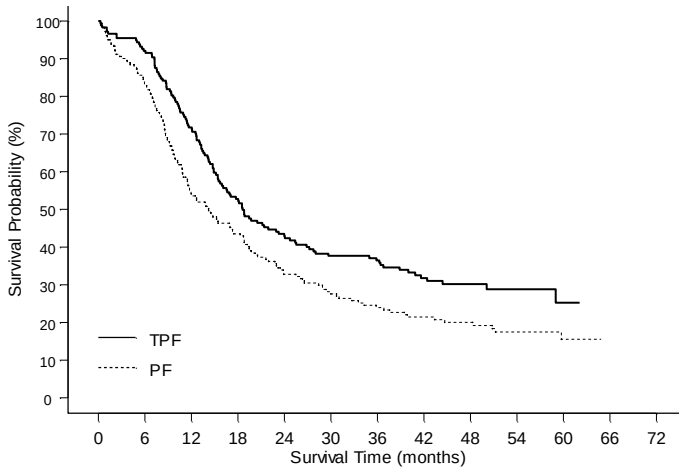


Figure 9: TAX323 Overall Survival K-M Curve



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/m^2 by intravenous infusion on day 1 followed by cisplatin (P) 100 mg/m^2 administered as a 30-minute to three-hour intravenous infusion, followed by the continuous intravenous infusion of fluorouracil (F) 1000 mg/m^2/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/m^2 as a 30-minute to three-hour intravenous infusion on day 1 followed by the continuous intravenous infusion of fluorouracil (F) 1000 mg/m^2/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 intravenous 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 any time following completion of CRT.

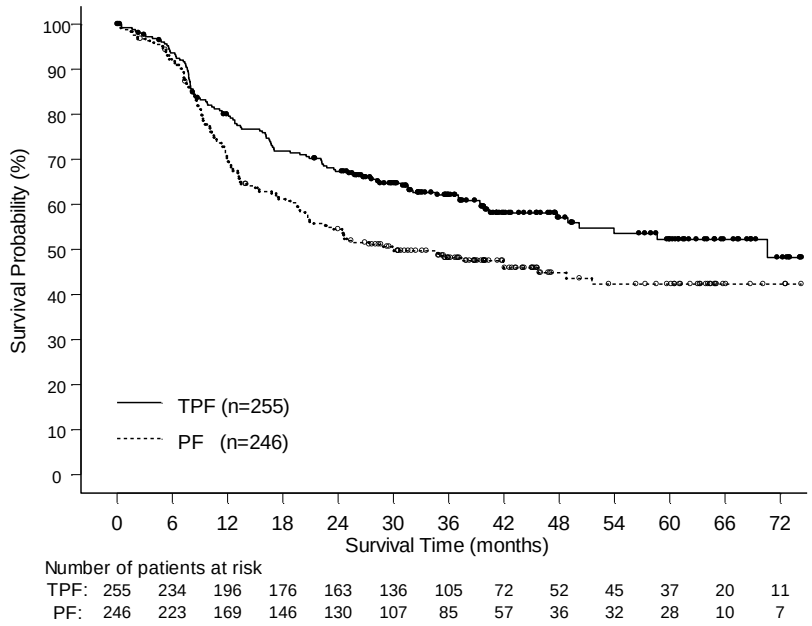
The primary efficacy endpoint, overall survival (OS), was significantly longer (log-rank test, p=0.0058) with the TAXOTERE-containing regimen compared to PF (median OS: 70.6 vs 30.1 months, respectively, hazard ratio [HR]=0.70, 95% confidence interval [CI]=0.54-0.90). Overall survival results are presented in Table 21 and Figure 10.

Table 21: Efficacy of TAXOTERE in the Induction Treatment of Patients with Locally Advanced SCCHN (Intent-to-Treat Analysis)

Endpoint	**TAXOTERE + Cisplatin + Fluorouracil n=255**	**Cisplatin + Fluorouracil n=246**
Median overall survival (months) (95% CI)	70.6 (49.0-NE)	30.1 (20.9-51.5)
Hazard ratio: (95% CI) *p-value	0.70 (0.54-0.90) 0.0058	

A Hazard ratio of less than 1 favors TAXOTERE+cisplatin+fluorouracil
*unadjusted log-rank test
NE - not estimable

Figure 10: TAX324 Overall Survival K-M Curve



15 REFERENCES

1. "OSHA Hazardous Drugs." http://www.osha.gov/SLTC/hazardousdrugs/index.html

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

One-vial TAXOTERE (Injection)

TAXOTERE Injection is supplied in a single-dose vial as a sterile, pyrogen-free, non-aqueous solution. Discard unused portion.

TAXOTERE 20 mg/mL (NDC 0075-8003-01)

TAXOTERE (docetaxel) Injection 20 mg/1 mL: 20 mg docetaxel in 1 mL 50/50 (v/v) ratio polysorbate 80/dehydrated alcohol.

The vial is in a blister pack in one carton.

TAXOTERE 80 mg/4 mL (NDC 0075-8004-04)

TAXOTERE (docetaxel) Injection 80 mg/4 mL: 80 mg docetaxel in 4 mL 50/50 (v/v) ratio polysorbate 80/dehydrated alcohol.

The vial is in a blister pack in one carton.

16.2 Storage

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

16.3 Handling and Disposal

TAXOTERE is a hazardous drug. Follow applicable special handling and disposal procedures.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Bone Marrow Suppression

Advise patients that periodic assessment of their blood count will be performed to detect neutropenia, thrombocytopenia, and/ or anemia *[see Contraindications (4), Warnings and Precautions (5.3)]*. Instruct patients to monitor their temperature frequently and immediately report any occurrence of fever.

Enterocolitis and Neutropenic Colitis

Advise patients of the symptoms of colitis, such as abdominal pain or tenderness, and/or diarrhea, with or without fever, and instruct patients to promptly contact their healthcare provider if they experience these symptoms *[see Dosage and Administration (2.7) and Warnings and Precautions (5.4)]*.

Hypersensitivity Reactions

Ask patients whether they have previously received paclitaxel therapy, and if they have experienced a hypersensitivity reaction to paclitaxel. Instruct patients to immediately report to

their healthcare provider signs of a hypersensitivity reaction *[see Contraindications (4), Warnings and Precautions (5.5)]*.

Fluid Retention

Advise patients to report signs of fluid retention such as peripheral edema in the lower extremities, weight gain, and dyspnea immediately to their healthcare provider *[see Warnings and Precautions (5.6)]*.

Second Primary Malignancies

Advise patients on the risk of second primary malignancies during treatment with TAXOTERE *[see Warnings and Precautions (5.7)]*.

Cutaneous Reactions

Advise patients that localized erythema of the extremities and severe skin toxicities may occur. Instruct patients to immediately report severe cutaneous reactions to their healthcare provider *[see Dosage and Administration (2.7) and Warnings and Precautions (5.8)]*.

Neurologic Reactions

Advise patients that neurosensory symptoms or peripheral neuropathy may occur. Instruct patients to immediately report neurologic reactions to their healthcare provider *[see Dosage and Administration (2.7) and Warnings and Precautions (5.9)]*.

Eye Disorders

Advise patients that vision disturbances and excessive tearing are associated with TAXOTERE administration. Instruct patients to immediately report any vision changes to their healthcare provider *[see Warnings and Precautions (5.10)]*.

Gastrointestinal Reactions

Explain to patients that nausea, vomiting, diarrhea, and constipation are associated with TAXOTERE administration. Instruct patients to report any severe events to their healthcare provider *[see Adverse Reactions (6)]*.

Cardiac Disorders

Advise patients to report any irregular and/or rapid heartbeat, severe shortness of breath, dizziness, and/or fainting immediately to their healthcare provider *[see Adverse Reactions (6)]*.

Other Common Adverse Reactions

Advise patients that other common adverse reactions associated with TAXOTERE may include alopecia (cases of permanent hair loss have been reported), asthenia, anorexia, dysgeusia, mucositis, myalgia, nail disorders, or pain. Instruct patients to report these reactions to their healthcare provider if serious events occur *[see Adverse Reactions (6)]*.

Importance of Corticosteroids

Explain the significance of oral corticosteroids such as dexamethasone administration to the patient to help facilitate compliance. Instruct patients to report to their healthcare provider if they were not compliant with the oral corticosteroid regimen *[see Dosage and Administration (2.6)]*.

Embryo-Fetal Toxicity

TAXOTERE can cause fetal harm. Advise patients to inform their healthcare provider of a known or suspected pregnancy. Advise patients to avoid becoming pregnant while receiving this drug. Advise female patients of reproductive potential to use effective contraceptives during treatment and for 2 months after the last dose of TAXOTERE. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of TAXOTERE *[see Warnings and Precautions (5.12), and Use in Specific Populations (8.1, 8.3)]*.

Lactation

Advise women not to breastfeed during TAXOTERE treatment and for 1 week after the last dose *[see Use in Specific Populations (8.2)]*.

Infertility

Advise males of reproductive potential that TAXOTERE may impair fertility *[see Nonclinical Toxicology (13.1)]*.

Alcohol Content in TAXOTERE

Explain to patients the possible effects of the alcohol content in TAXOTERE, including possible effects on the central nervous system *[see Warnings and Precautions (5.13)]*.

Tumor Lysis Syndrome

Advise patients of the potential risk of tumor lysis syndrome and to immediately report any signs or symptoms associated with this event (nausea, vomiting, confusion, shortness of breath, seizure, irregular heartbeat, dark or cloudy urine, reduced amount of urine, unusual tiredness, muscle cramps) to their healthcare provider. Advise patients of the importance of keeping scheduled appointment for blood work or other laboratory tests and of drinking adequate fluids to avoid dehydration. *[see Warnings and Precautions (5.14)]*.

Ability to Drive or Operate Machines

Explain to patients that TAXOTERE may impair their ability to drive or operate machines due to its side effects *[see Adverse Reactions (6)]* or due to the alcohol content of TAXOTERE *[see Warnings and Precautions (5.13)]*. Advise them not to drive or use machines if they experience these side effects during treatment.

Drug Interactions

Inform patients about the risk of drug interactions and the importance of providing a list of prescription and non-prescription drugs to their healthcare provider *[see Drug Interactions (7)]*.

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Bridgewater, NJ 08807
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Patient Information
TAXOTERE (TAX-O-TEER)
(docetaxel) injection
for intravenous use

What is the most important information I should know about TAXOTERE?
TAXOTERE can cause serious side effects, including death.

- **The chance of death in people who receive TAXOTERE is higher if you:**
  - have liver problems
  - receive high doses of TAXOTERE
  - have non-small cell lung cancer and have been treated with chemotherapy medicines that contain platinum
- **TAXOTERE can affect your blood cells.** Your healthcare provider should do routine blood tests during treatment with TAXOTERE. This will include regular checks of your white blood cell counts. If your white blood cells are too low, your healthcare provider may not treat you with TAXOTERE until you have enough white blood cells. People with low white blood cell counts can develop life-threatening infections. The earliest sign of infection may be fever. Follow your healthcare provider's instructions for how often to take your temperature during treatment with TAXOTERE. Call your healthcare provider right away if you have a fever.
- **Swelling (inflammation) of the small intestine and colon.** This can happen at any time during treatment and could lead to death as early as the first day you get symptoms. Tell your healthcare provider right away if you develop new or worse symptoms of intestinal problems, including stomach (abdominal) pain or tenderness or diarrhea, with or without fever.
- **Severe allergic reactions** are medical emergencies that can happen in people who receive TAXOTERE and can lead to death. You may be at higher risk of developing a severe allergic reaction to TAXOTERE if you are allergic to paclitaxel. Your healthcare provider will monitor you closely for allergic reactions during your TAXOTERE infusion.

  Tell your healthcare provider right away if you have any of these signs of a severe allergic reaction:
  - trouble breathing
  - sudden swelling of your face, lips, tongue, throat, or trouble swallowing
  - hives (raised bumps), rash, or redness all over your body
- **Your body may hold too much fluid (severe fluid retention)** during treatment with TAXOTERE. This can be life threatening. To decrease the chance of this happening, you must take another medicine, a corticosteroid, before each TAXOTERE treatment. You must take the corticosteroid exactly as your healthcare provider tells you. Tell your healthcare provider or nurse before your TAXOTERE treatment if you forgot to take your corticosteroid dose or do not take it as your healthcare provider tells you. Tell your healthcare provider right away if you have swelling in your legs or feet, weight gain or shortness of breath.
- **Risk of new cancers.** An increase in new (second) cancers has happened in people treated with TAXOTERE together with certain other anticancer treatments. This includes certain blood cancers, such as acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), non-Hodgkin's Lymphoma (NHL), and kidney cancer.
  - Changes in blood counts due to leukemia and other blood disorders may occur years after treatment with TAXOTERE.

  Your healthcare provider will check you for new cancers during and after your treatment with TAXOTERE.
- **Severe skin problems.**

  Tell your healthcare provider right away if you have any of these signs of a severe skin reaction:
  - redness and swelling of your arms and legs.
  - blistering, peeling, or bleeding on any part of your skin (including your lips, eyes, mouth, nose, genitals, hands or feet) with or without a rash. You may also have flu-like symptoms such as fever, chills, or muscle aches.
  - red, scaly rash all over your body with blisters, small red or white bumps under the skin that contain pus (pustules), and fever.

What is TAXOTERE?

TAXOTERE is a prescription anticancer medicine used to treat certain people with:

- breast cancer
- non-small cell lung cancer
- prostate cancer
- stomach cancer
- head and neck cancer

It is not known if TAXOTERE is effective in children.

Do not receive TAXOTERE if you:

- have a low white blood cell count.
- have had a severe allergic reaction to:
  - docetaxel, the active ingredient in TAXOTERE, or
  - any other medicines that contain polysorbate 80. Ask your healthcare provider or pharmacist if you are not sure.

See "**What is the most important information I should know about TAXOTERE?**" for the signs and symptoms of a severe allergic reaction.

See the end of this Patient Information for a complete list of the ingredients in TAXOTERE.

Before you receive TAXOTERE, tell your healthcare provider about all of your medical conditions, including if you:

- are allergic to any medicines, including paclitaxel. See "**Do not receive TAXOTERE if you**".
- have liver problems
- have kidney problems
- are pregnant or plan to become pregnant. TAXOTERE can harm your unborn baby. You should not become pregnant during treatment with TAXOTERE. Tell your healthcare provider if you become pregnant or you think you may be pregnant during treatment with TAXOTERE.

  Females who are able to become pregnant:
  - Your healthcare provider will check to see if you are pregnant before you start treatment with TAXOTERE.
  - You should use effective birth control (contraception) during treatment with TAXOTERE and for 2 months after the last dose.

  Males with female partners who are able to become pregnant should use effective birth control during treatment with TAXOTERE and for 4 months after the last dose.

  Talk to your healthcare provider if you have questions about birth control options that are right for you.
- are breastfeeding or plan to breastfeed. It is not known if TAXOTERE passes into your breast milk. Do not breastfeed during treatment with TAXOTERE and for 1 week after the last dose.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. TAXOTERE may affect the way other medicines work, and other medicines may affect the way TAXOTERE works.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How will I receive TAXOTERE?

- TAXOTERE will be given to you as an intravenous (IV) injection into your vein, usually over 1 hour.
- TAXOTERE is usually given every 3 weeks.
- Your healthcare provider will decide how long you will receive treatment with TAXOTERE.
- Your healthcare provider will check your blood cell counts and other blood tests during your treatment with TAXOTERE to check for side effects of TAXOTERE.
- Your healthcare provider may stop your treatment, change the timing of your treatment, or change the dose of your treatment if you have certain side effects while receiving TAXOTERE.

What are the possible side effects of TAXOTERE?

TAXOTERE may cause serious side effects including death.

- See **"What is the most important information I should know about TAXOTERE?"**
- **Neurologic problems.** Neurologic symptoms are common in people who receive TAXOTERE but can be severe. Tell your healthcare provider right away if you have numbness, tingling, or burning in your hands or feet (peripheral neuropathy) or weakness of your legs, feet, arms, or hands (motor weakness).
- **Vision problems** including blurred vision or loss of vision. Tell your healthcare provider right away if you have any vision changes.
- **TAXOTERE injection contains alcohol.** The alcohol content in TAXOTERE may impair your ability to drive or use machinery right after receiving TAXOTERE. Consider whether you should drive, operate machinery or do other dangerous activities right after you receive TAXOTERE treatment.
- **Tumor lysis syndrome (TLS).** TLS is caused by the fast breakdown of cancer cells. TLS can cause kidney failure, the need for dialysis treatment, or heart problems, and may lead to death. Your healthcare provider will do blood tests to check for TLS when you first start treatment and during treatment with TAXOTERE. Tell your healthcare provider right away if you have any symptoms of TLS during treatment with TAXOTERE, including:
  - nausea
  - vomiting
  - confusion
  - shortness of breath
  - irregular heartbeat
  - dark or cloudy urine
  - reduced amount of urine
  - unusual tiredness
  - muscle cramps
- You may experience side effects of this medicine that may impair your ability to drive, use tools, or operate machines. If this happens, do not drive or use any tools or machines before discussing with your healthcare provider.

The most common side effects of TAXOTERE include:

- infections
- low white blood cells (help fight infections), low red blood cells (anemia) and low platelets (help blood to clot)
- allergic reactions (See **"What is the most important information I should know about TAXOTERE?"**)
- changes in your sense of taste
- shortness of breath
- constipation
- decreased appetite
- changes in your fingernails or toenails
- swelling of your hands, face or feet
- feeling weak or tired
- joint and muscle pain
- nausea and vomiting
- diarrhea
- mouth or lip sores
- hair loss: in some people, permanent hair loss has been reported
- redness of the eye, excess tearing
- skin reactions at the site of TAXOTERE administration such as increased skin pigmentation, redness, tenderness, swelling, warmth or dryness of the skin
- tissue damage if TAXOTERE leaks out of the vein into the tissues

Tell your healthcare provider if you have a fast or irregular heartbeat, severe shortness of breath, dizziness or fainting during your infusion. If any of these events occurs after your infusion, get medical help right away.

TAXOTERE may affect fertility in males. Talk to your healthcare provider if this is a concern for you.

These are not all of the possible side effects of TAXOTERE. For more information, ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of TAXOTERE.

Medicines are sometimes prescribed for purposes other than those listed in this Patient Information. You can ask your pharmacist or healthcare provider for information about TAXOTERE that is written for health professionals.

What are the ingredients in TAXOTERE?

Active ingredient: docetaxel
Inactive ingredients: polysorbate 80 and dehydrated alcohol solution, with citric acid for pH adjustment.

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For more information, call 1-800-633-1610 or go to www.sanofi-aventis.com.

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: January 2023

Every three-week injection of TAXOTERE for breast, non-small cell lung and stomach, and head and neck cancers
Take your oral corticosteroid medicine as your healthcare provider tells you.

Oral corticosteroid 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 your oral corticosteroid medicine as your healthcare provider tells you.

Oral corticosteroid dosing:

Date: _____ Time:_____

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