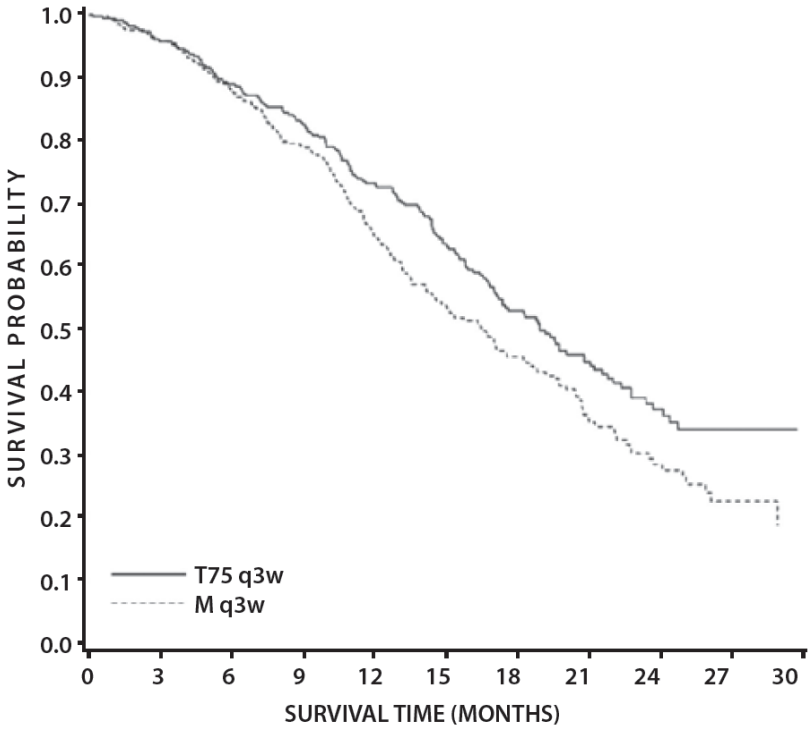
Figure 5 - TAX327 Survival K-M Curves



14.5 Gastric Adenocarcinoma

A multicenter, open-label, randomized trial was conducted to evaluate the safety and efficacy of Docetaxel Injection 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 Docetaxel Injection (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 Docetaxel Injection in the Treatment of Patients with Gastric Adenocarcinoma

Endpoint	**TCF n=221**	**CF n=224**
Median TTP (months) (95% CI)	5.6 (4.86-5.91)	3.7 (3.45-4.47)
Hazard ratio† (95% CI) *p-value	0.68 (0.55-0.84) 0.0004	
Median survival (months) (95% CI)	9.2 (8.38-10.58)	8.6 (7.16-9.46)
Hazard ratio† (95% CI) *p-value	0.77 (0.62-0.96) 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 Docetaxel Injection 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

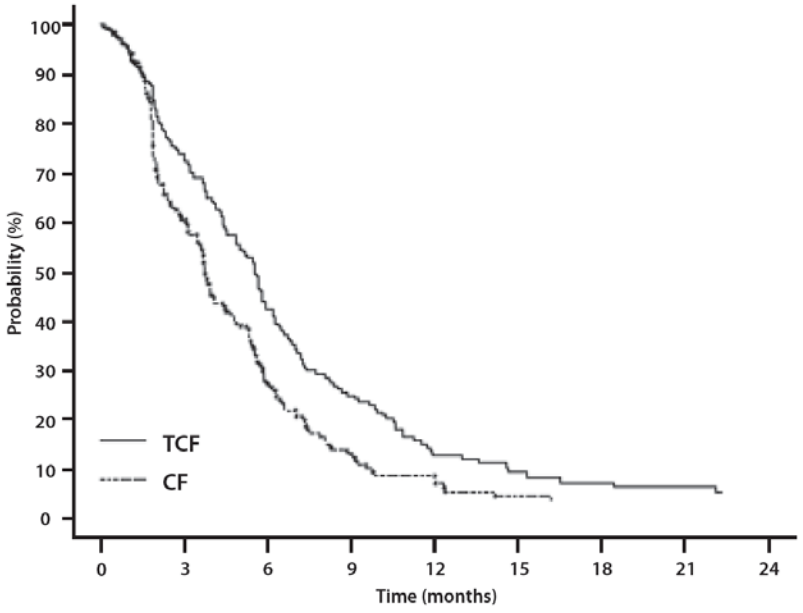
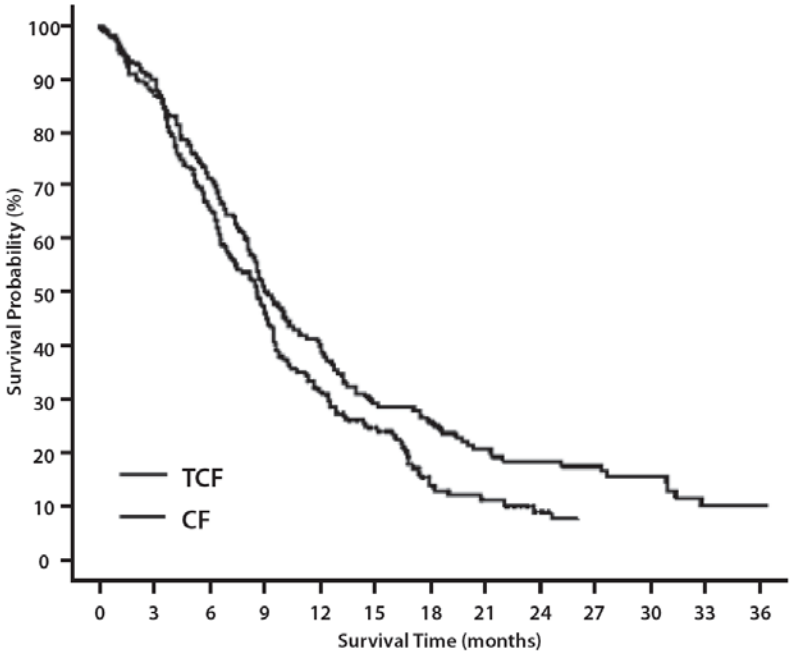


Figure 7 -Gastric Cancer Study (TAX325) Survival K-M Curve



14.6 Head and Neck Cancer

Induction Chemotherapy Followed by Radiotherapy (TAX323)

The safety and efficacy of Docetaxel Injection 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 Docetaxel Injection arm received Docetaxel Injection (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.

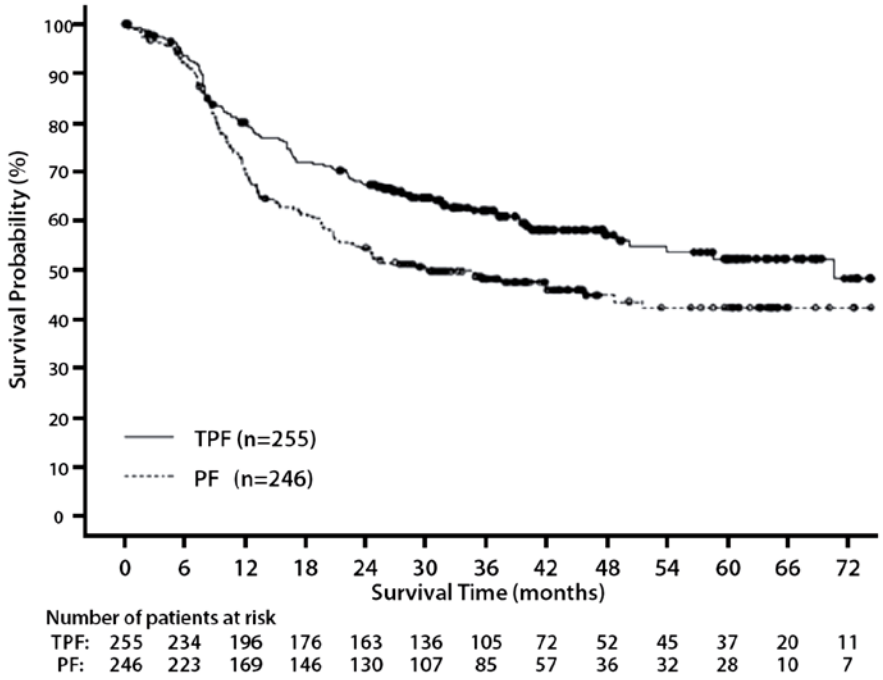
The primary endpoint in this study, progression-free survival (PFS), was significantly longer in the TPF arm compared to the PF arm, p=0.0077 (median PFS: 11.4 vs. 8.3 months, respectively) with an overall median follow-up time of 33.7 months. Median overall survival with a median follow-up of 51.2 months 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 21: Efficacy of Docetaxel Injection in the Induction Treatment of Patients with Locally Advanced SCCHN (Intent-to-Treat Analysis)

Endpoint	Docetaxel Injection + 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 Docetaxel Injection+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

Docetaxel Injection, USP is supplied in single-dose or multiple-dose vials as a sterile, pyrogen-free, non-aqueous pale-yellow to brownish yellow solution. Discard unused portion of the single-dose vial.

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

Alcohol Content in Docetaxel Injection
Explain to patients the possible effects of the alcohol content in Docetaxel Injection, 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 Docetaxel Injection 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 Docetaxel Injection [*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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Patient Information
Docetaxel (doe-se-TAKS-el) Injection
for intravenous use

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

- **The chance of death in people who receive Docetaxel Injection is higher if you:**
  - have liver problems
  - receive high doses of Docetaxel Injection
  - have non-small cell lung cancer and have been treated with chemotherapy medicines that contain platinum
- **Docetaxel Injection can affect your blood cells.** Your healthcare provider should do routine blood tests during treatment with Docetaxel Injection. 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 Docetaxel Injection 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 Docetaxel Injection. 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 Docetaxel Injection and can lead to death. You may be at higher risk of developing a severe allergic reaction to Docetaxel Injection if you are allergic to paclitaxel. Your healthcare provider will monitor you closely for allergic reactions during your Docetaxel Injection 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 Docetaxel Injection. This can be life threatening. To decrease the chance of this happening, you must take another medicine, a corticosteroid, before each Docetaxel Injection treatment. You must take the corticosteroid exactly as your healthcare provider tells you. Tell your healthcare provider or nurse before your Docetaxel Injection 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 Docetaxel Injection 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 Docetaxel Injection.

  Your healthcare provider will check you for new cancers during and after your treatment with Docetaxel Injection.
- **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 Docetaxel Injection?

Docetaxel Injection 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 Docetaxel Injection is effective in children.

Do not receive Docetaxel Injection if you:

- have a low white blood cell count.
- have had a severe allergic reaction to:
  - docetaxel, the active ingredient in Docetaxel Injection, **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 Docetaxel Injection?**" 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 Docetaxel Injection.

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

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

  Females who are able to become pregnant:
  - Your healthcare provider will check to see if you are pregnant before you start treatment with Docetaxel Injection.
  - You should use effective birth control (contraception) during treatment with Docetaxel Injection and for 6 months after the last dose.

  Males with female partners who are able to become pregnant should use effective birth control during treatment with Docetaxel Injection and for 3 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 Docetaxel Injection passes into your breast milk. Do not breastfeed during treatment with Docetaxel Injection 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. Docetaxel Injection may affect the way other medicines work, and other medicines may affect the way Docetaxel Injection 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 Docetaxel Injection?

- Docetaxel Injection will be given to you as an intravenous (IV) injection into your vein, usually over 1 hour.
- Docetaxel Injection is usually given every 3 weeks.
- Your healthcare provider will decide how long you will receive treatment with Docetaxel Injection.
- Your healthcare provider will check your blood cell counts and other blood tests during your treatment with Docetaxel Injection to check for side effects of Docetaxel Injection.
- 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 Docetaxel Injection.

What are the possible side effects of Docetaxel Injection?

Docetaxel Injection may cause serious side effects including death.

- **See "What is the most important information I should know about Docetaxel Injection?"**
- **Neurologic problems.** Neurologic symptoms are common in people who receive Docetaxel Injection 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.
- **Docetaxel Injection contains alcohol.** The alcohol content in Docetaxel Injection may impair your ability to drive or use machinery right after receiving Docetaxel Injection. Consider whether you should drive, operate machinery or do other dangerous activities right after you receive Docetaxel Injection 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 Docetaxel Injection. Tell your healthcare provider right away if you have any symptoms of TLS during treatment with Docetaxel Injection, including:

- o nausea
- o vomiting
- o confusion
- o shortness of breath
- o irregular heartbeat
- o dark or cloudy urine
- o reduced amount of urine
- o unusual tiredness
- o muscle cramps

- You may experience side effects of Docetaxel Injection 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 Docetaxel Injection 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 Docetaxel Injection?"**)
- 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 Docetaxel Injection administration such as increased skin pigmentation, redness, tenderness, swelling, warmth or dryness of the skin
- tissue damage if Docetaxel Injection 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.
Docetaxel Injection may affect fertility in males. Talk to your healthcare provider if this is a concern for you.
These are not all the possible side effects of Docetaxel Injection. 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 Docetaxel Injection.
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 Docetaxel Injection that is written for health professionals.

What are the ingredients in Docetaxel Injection?
Active ingredient: docetaxel
Inactive ingredients: (20 mg injection): polysorbate 80, citric acid monohydrate, and dehydrated alcohol.

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This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: November 2020

Every three-week injection of Docetaxel Injection 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

(Docetaxel Injection Treatment Day)
Day 3 Date: _____ Time: _____ AM _____ PM

Every three-week injection of Docetaxel Injection for prostate cancer
Take your oral corticosteroid medicine as your healthcare provider tells you.

Oral corticosteroid dosing:
Date: _____ Time: _____
Date: _____ Time: _____

(Docetaxel Injection Treatment Day)
Time: _____