**In the treatment of metastatic pancreatic cancer (MPAC)**

ABRAXANE® is indicated for the first-line treatment of patients with metastatic adenocarcinoma of the pancreas, in combination with gemcitabine.

Abraxane®
for Injectable Suspension
(paclitaxel protein-bound particles for injectable suspension)
(albumin-bound)

# ABRAXANE + GEMCITABINE: **A FIRST-LINE STANDARD OF CARE FOR PATIENTS ACROSS A BROAD RANGE OF PERFORMANCE STATUS (KPS 70-100)[1,2]**

## PREFERRED FIRST-LINE REGIMEN PER NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®) FOR MPAC[3]

| NCCN Category | PATIENTS WITH **GOOD PERFORMANCE STATUS PS 0 OR 1** | SOME PATIENTS WITH **PS 2 (KPS ≥70)†** |
|---|---|---|
| **1*** | | |

NCCN supports initiating ABRAXANE 125 mg/m$^2$ given QW3/4 and treating until disease progression or unacceptable toxicity

**ABRAXANE + gemcitabine as first-line therapy allows for a treatment plan with 5-FU–based second-line therapy[3]**

### STUDY DESIGN AND PRIMARY ENDPOINT

- Randomized phase III study of ABRAXANE + gemcitabine vs gemcitabine alone in first-line metastatic pancreatic cancer (N=861). Primary end point was OS. ABRAXANE (125 mg/m$^2$) + gemcitabine (1000 mg/m$^2$) was given Qw3/4. In the gemcitabine arm, gemcitabine (1000 mg/m$^2$) was given QW7/8 then QW3/4.[2]
- Median OS was 8.5 months (n=431) vs 6.7 months (n=430), respectively; HR: 0.72 (95% CI: 0.62-0.83); P<0.0001.[2]

*Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.[3]

†Good performance status for this regimen (AG) is defined as KPS ≥70, so some patients with an ECOG score of 2 may be eligible to receive this regimen (AG). The ABRAXANE phase III MPACT study enrolled patients with KPS ≥70.[3]

Good performance status is defined as ECOG 0-1 with patent biliary stent and adequate nutritional intake.

Please refer to the NCCN Guidelines® for pancreatic cancer for a complete list of recommended treatment options.

## IMPORTANT SAFETY INFORMATION

**WARNING - NEUTROPENIA**

- Do not administer ABRAXANE therapy to patients who have baseline neutrophil counts of less than 1500 cells/mm$^3$. In order to monitor the occurrence of bone marrow suppression, primarily neutropenia, which may be severe and result in infection, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving ABRAXANE
- Note: An albumin form of paclitaxel may substantially affect a drug's functional properties relative to those of drug in solution. DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS

### CONTRAINDICATIONS

**Neutrophil Counts**

- ABRAXANE should not be used in patients who have baseline neutrophil counts of <1500 cells/mm$^3$

**Hypersensitivity**

- Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be rechallenged with the drug

### WARNINGS AND PRECAUTIONS

**Hematologic Effects**

- Bone marrow suppression (primarily neutropenia) is dose-dependent and a dose-limiting toxicity of ABRAXANE. In a clinical study, Grade 3-4 neutropenia occurred in 38% of patients with pancreatic cancer
- Monitor for myelotoxicity by performing complete blood cell counts frequently, including prior to dosing on Days 1, 8, and 15 for pancreatic cancer
- Do not administer ABRAXANE to patients with baseline absolute neutrophil counts (ANC) of less than 1500 cells/mm$^3$
- In patients with adenocarcinoma of the pancreas, withhold ABRAXANE and gemcitabine if the ANC is less than 500 cells/mm$^3$ or platelets are less than 50,000 cells/mm$^3$ and delay initiation of the next cycle if the ANC is less than 1500 cells/mm$^3$ or platelet count is less than 100,000 cells/mm$^3$ on Day 1 of the cycle. Resume treatment with appropriate dose reduction if recommended

**Nervous System**

- Sensory neuropathy is dose- and schedule-dependent
- The occurrence of Grade 1 or 2 sensory neuropathy does not generally require dose modification
- If ≥ Grade 3 sensory neuropathy develops, withhold ABRAXANE treatment until resolution to ≤ Grade 1 followed by a dose reduction for all subsequent courses of ABRAXANE

**Sepsis**

- Sepsis occurred in 5% of patients with or without neutropenia who received ABRAXANE in combination with gemcitabine
- Biliary obstruction or presence of biliary stent were risk factors for severe or fatal sepsis
- If a patient becomes febrile (regardless of ANC), initiate treatment with broad-spectrum antibiotics
- For febrile neutropenia, interrupt ABRAXANE and gemcitabine until fever resolves and ANC ≥1500 cells/mm$^3$, then resume treatment at reduced dose levels

**Please see additional Important Safety Information on reverse side, and full Prescribing Information, including Boxed WARNING, inside pocket.**

## IMPORTANT SAFETY INFORMATION (CONT'D)

**Pneumonitis**

- Pneumonitis, including some cases that were fatal, occurred in 4% of patients receiving ABRAXANE in combination with gemcitabine
- Monitor patients for signs and symptoms and interrupt ABRAXANE and gemcitabine during evaluation of suspected pneumonitis
- Permanently discontinue treatment with ABRAXANE and gemcitabine upon making a diagnosis of pneumonitis

**Hypersensitivity**

- Severe and sometimes fatal hypersensitivity reactions, including anaphylactic reactions, have been reported
- Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be rechallenged with this drug
- Cross-hypersensitivity between ABRAXANE and other taxane products has been reported and may include severe reactions such as anaphylaxis. Patients with a previous history of hypersensitivity to other taxanes should be closely monitored during initiation of ABRAXANE therapy

**Hepatic Impairment**

- Because the exposure and toxicity of paclitaxel can be increased with hepatic impairment, administration of ABRAXANE in patients with hepatic impairment should be performed with caution
- Patients with hepatic impairment may be at an increased risk of toxicity, particularly from myelosuppression, and should be monitored for development of profound myelosuppression
- For pancreatic adenocarcinoma, ABRAXANE is not recommended for patients with moderate to severe hepatic impairment (total bilirubin >1.5 x ULN and AST ≤10 x ULN)

**Albumin (Human)**

- ABRAXANE contains albumin (human), a derivative of human blood

**Embryo Fetal Toxicity**

- Based on mechanism of action and findings in animals, ABRAXANE can cause fetal harm when administered to a pregnant woman
- Advise females of reproductive potential of the potential risk to a fetus.
- Advise females of reproductive potential to use effective contraception and avoid becoming pregnant during treatment with ABRAXANE and for at least six months after the last dose of ABRAXANE
- Advise male patients with female partners of reproductive potential to use effective contraception and avoid fathering a child during treatment with ABRAXANE and for at least three months after the last dose of ABRAXANE

### ADVERSE REACTIONS

- Among the most common (≥20%) adverse reactions in the phase III study, those with a ≥5% higher incidence in the ABRAXANE/gemcitabine group compared with the gemcitabine group are neutropenia (73%, 58%), fatigue (59%, 46%), peripheral neuropathy (54%, 13%), nausea (54%, 48%), alopecia (50%, 5%), peripheral edema (46%, 30%), diarrhea (44%, 24%), pyrexia (41%, 28%), vomiting (36%, 28%), decreased appetite (36%, 26%), rash (30%, 11%), and dehydration (21%, 11%)
- Of these most common adverse reactions, those with a ≥2% higher incidence of Grade 3-4 toxicity in the ABRAXANE/gemcitabine group compared with the gemcitabine group, respectively, are neutropenia (38%, 27%), fatigue (18%, 9%), peripheral neuropathy (17%, 1%), nausea (6%, 3%), diarrhea (6%, 1%), pyrexia (3%, 1%), vomiting (6%, 4%), decreased appetite (5%, 2%), and dehydration (7%, 2%)
- Thrombocytopenia (all grades) was reported in 74% of patients in the ABRAXANE/gemcitabine group vs 70% of patients in the gemcitabine group
- The most common serious adverse reactions of ABRAXANE (with a ≥1% higher incidence) are pyrexia (6%), dehydration (5%), pneumonia (4%), and vomiting (4%)
- The most common adverse reactions resulting in permanent discontinuation of ABRAXANE were peripheral neuropathy (8%), fatigue (4%), and thrombocytopenia (2%)
- The most common adverse reactions resulting in dose reduction of ABRAXANE are neutropenia (10%) and peripheral neuropathy (6%)
- The most common adverse reactions leading to withholding or delay in ABRAXANE dosing are neutropenia (16%), thrombocytopenia (12%), fatigue (8%), peripheral neuropathy (15%), anemia (5%), and diarrhea (5%)
- Other selected adverse reactions with a ≥5% higher incidence for all-grade toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group, respectively, are asthenia (19%, 13%), mucositis (10%, 4%), dysgeusia (16%, 8%), headache (14%, 9%), hypokalemia (12%, 7%), cough (17%, 7%), epistaxis (15%, 3%), urinary tract infection (11%, 5%), pain in extremity (11%, 6%), arthralgia (11%, 3%), myalgia (10%, 4%), and depression (12%, 6%)
- Other selected adverse reactions with a ≥2% higher incidence for Grade 3-4 toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group are thrombocytopenia (13%, 9%), asthenia (7%, 4%), and hypokalemia (4%, 1%)

**Postmarketing Experience With ABRAXANE and Other Paclitaxel Formulations**

- Severe and sometimes fatal hypersensitivity reactions have been reported with ABRAXANE. The use of ABRAXANE in patients previously exhibiting hypersensitivity to paclitaxel injection or human albumin has not been studied. In postmarketing experience cross-hypersensitivity between ABRAXANE and other taxanes has been reported.
- There have been reports of congestive heart failure, left ventricular dysfunction, and atrioventricular block with ABRAXANE, primarily among individuals with underlying cardiac history or prior exposure to cardiotoxic drugs
- There have been reports of extravasation of ABRAXANE. Given the possibility of extravasation, it is advisable to monitor closely the ABRAXANE infusion site for possible infiltration during drug administration

### DRUG INTERACTIONS

- Caution should be exercised when administering ABRAXANE concomitantly with medicines known to inhibit or induce either CYP2C8 or CYP3A4

### USE IN SPECIFIC POPULATIONS

**Pregnancy**

- Based on the mechanism of action and findings in animals, ABRAXANE can cause fetal harm when administered to a pregnant woman. Advise females of the potential risk to a fetus and to avoid becoming pregnant while receiving ABRAXANE.

**Lactation**

- Paclitaxel and/or its metabolites were excreted into the milk of lactating rats. Nursing must be discontinued when receiving treatment with ABRAXANE and for two weeks after the last dose

**Females and Males of Reproductive Potential**

- Females of reproductive potential should have a pregnancy test prior to starting treatment with ABRAXANE
- Advise females of reproductive potential to use effective contraception and avoid becoming pregnant during treatment with and for at least six months after the last dose of ABRAXANE *[see Warnings and Precautions]*
- Advise males with female partners of reproductive potential to use effective contraception and avoid fathering a child during treatment with ABRAXANE and for at least three months after the last dose of ABRAXANE *[see Warnings and Precautions]*
- Based on findings in animals, ABRAXANE may impair fertility in females and males of reproductive potential

**Pediatric**

- The safety and effectiveness of ABRAXANE in pediatric patients have not been evaluated

**Geriatric**

- Diarrhea, decreased appetite, dehydration, and epistaxis were more frequent in patients 65 years or older compared with patients younger than 65 years old who received ABRAXANE and gemcitabine in adenocarcinoma of the pancreas

**Renal Impairment**

- There are insufficient data to permit dosage recommendations in patients with severe renal impairment or end stage renal disease (estimated creatinine clearance <30 mL/min)

### DOSAGE AND ADMINISTRATION

- Do not administer ABRAXANE to patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment
- Do not administer ABRAXANE to any patient with total bilirubin greater than 5 x ULN or AST greater than 10 x ULN
- Dose reductions or discontinuation may be needed based on severe hematologic, neurologic, cutaneous, or gastrointestinal toxicity
- Monitor patients closely

**Please see full Prescribing Information, including Boxed WARNING, inside pocket.**

**References: 1.** Data on file. IntrinsiQ Monthly Market Share Report. Ending Jun 2016. **2.** Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med*. 2013;369:1691-1703. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma V1.2016. © National Comprehensive Cancer Network, Inc 2016. All rights reserved. Accessed June 28, 2016. To view the most recent and complete version of the guidelines, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN content are trademarks owned by the National Comprehensive Cancer Network, Inc.

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(paclitaxel protein-bound particles for injectable suspension) (albumin-bound)