January 22, 2016

Data Presented at ASCO GI Highlight the Feasibility of Second-Line Treatment in Patients with Metastatic Pancreatic Cancer Who Have Received First-Line Abraxane Plus Gemcitabine

Multiple analyses examined ABRAXANE (paclitaxel protein-bound particles for injectable suspension)(albumin-bound) and gemcitabine followed by 5-FU-based regimens

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ: CELG) today announced that results from multiple analyses presented during the 2016 ASCO Gastrointestinal Cancers Symposium (ASCO GI) evaluated the outcomes of second-line treatments following ABRAXANE® (paclitaxel protein-bound particles for injectable suspension)(albumin-bound) and gemcitabine (AG) in first-line metastatic pancreatic cancer patients.

In particular, a post-hoc analysis of MPACT, the pivotal phase III study of AG compared with gemcitabine alone in first-line metastatic pancreatic cancer evaluated the outcomes of patients who received a second-line treatment during an observational extension of the study.

A total of 347 (40%) patients received second-line therapy in the extension, and of those patients, the majority (77%, including 132 who had received AG in the first line and 135 who had received gemcitabine alone) received 5-FU-based therapies or capecitabine combinations.

A post hoc analysis of overall survival (OS) was conducted and demonstrated that patients (n=170) who received AG, followed by second-line therapy had a median OS of 12.8 months, compared with 9.9 months for patients (n= 177) who received gemcitabine alone, followed by second-line therapy. Of patients receiving second-line therapies, the majority (n=132) received 5FU or capecitabine-containing regimens and had a median OS of 13.5 months. Patients receiving FOLFIRINOX (FFX) following AG (n=18) had the longest median overall survival at 15.7 months. OS was calculated using the Kaplan-Meier method.

The analysis provided data demonstrating the feasibility of second-line treatment in patients with MPC after first-line AG.

"As the body of research and approved options increase in pancreatic cancer, there is now evidence that second-line treatment is feasible and beneficial for certain patients with metastatic disease," said Dr. David Goldstein, medical oncologist at Prince of Wales Hospital in Sydney, Australia and the lead investigator of the analysis. "We are seeing an exciting evolution in the treatment of this disease and for patients and physicians, it is now time to consider a total treatment plan when choosing an initial therapy."

A retrospective cohort study performed using data U.S. community data from Navigating Cancer, an electronic medical record platform, sought to compare the time to treatment discontinuation and database persistence, used as a proxy for OS, between AG and FFX in the first-line setting.

The analysis showed that time to treatment discontinuation and database persistence for patients with first-line metastatic pancreatic cancer (n=202) were numerically similar (8.6 in each arm) between AG (n=122) and FFX (n=80). With the exception of the age of patients, which favored FFX (median age 67 for AG years vs. 61.4 years for FFX), baseline characteristics were generally similar between the groups.

There was a higher incidence of adverse events (all grades) with FFX compared with AG (95% vs. 84%). Most common AE's that led to discontinuation were anemia (8% for FFX and 2% for AG), neutropenia (6% for each), and dehydration (5% and 3%, respectively).

The analysis also evaluated various treatment plans including first-line AG, followed by second-line 5-FU-based therapies and first-line FFX, followed by second-line gemcitabine-based therapies. The duration of treatment for the AG arm was a median 8.7 months, compared with 8.4 months for the FFX arm (p=0.52). Further, the database persistence (proxy for OS) for patients receiving AG followed by 5-FU-based therapies (n=25) was a median 12.7 months, compared with 9.3 months for patients receiving FFX followed by gemcitabine-based therapies (n=41) (p=0.48).
There were four additional studies evaluating the sequence of AG followed by 5-FU-based therapies at the meeting:

- Outcome of second-line treatment (2L Tx) following nab-paclitaxel (nab-P) + gemcitabine (G) or G alone for metastatic pancreatic cancer (MPC). (Goldstein #333)
- Comparative effectiveness and resource utilization of nab-paclitaxel plus gemcitabine (nab-P+G) versus FOLFIRINOX (FFX) in first-line treatment of advanced pancreatic adenocarcinoma (PDAC) in a U.S. community oncology setting (Braiteh #433)
- Can the sequence of chemotherapy regimens influence outcome in patients with metastatic pancreatic adenocarcinoma (MPAC)? (Schmidt #428)
- Irinotecan and infusional 5-fluorouracil (mFOLFIRI) in patients with refractory advanced pancreas cancer (APC): A single institution experience. (Bupathi #215)

Indications

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

Important Safety Information

**WARNING - NEUTROPENIA**

- Do not administer ABRAXANE therapy to patients who have baseline neutrophil counts of less than 1500 cells/mm³. 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/mm³

**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 Å cells/mm³
- In patients with adenocarcinoma of the pancreas, withhold ABRAXANE and gemcitabine if the ANC is less than 500 cells/mm³ or platelets are less than 50,000 Å cells/mm³ and delay initiation of the next cycle if the ANC is less than 1500 cells/mm³ or platelet count is less than 100,000 Å cells/mm³ 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/mm³, then resume treatment at reduced dose levels.

**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.

**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.

**Use in Pregnancy: Pregnancy Category D**

- ABRAXANE can cause fetal harm when administered to a pregnant woman.
- If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus.
- Women of childbearing potential should be advised to avoid becoming pregnant while receiving ABRAXANE.

**Use in Men**

- Men should be advised not to father a child while receiving 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

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

Nursing Mothers

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

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.

**About Celgene**

Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global biopharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through next-generation solutions in protein homeostasis, immuno-oncology, epigenetics, immunology and neuro-inflammation. For more information, please visit www.celgene.com. Follow Celgene on Social Media: @Celgene, Pinterest, LinkedIn, Facebook and YouTube.

**Forward-Looking Statements**

This press release contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, many of which are discussed in more detail in our Annual Report on Form 10-K and our other reports filed with the Securities and Exchange Commission.


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