Data Presented at ASCO 2016 Builds upon Foundation of Abraxane® Plus Gemcitabine as a First-Line Treatment in Patients with Metastatic Pancreatic Cancer

Multiple presentations evaluate the treatment sequence with ABRAXANE plus gemcitabine in the first line setting and as a foundation for investigational combinations.

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) today announced that results from multiple sponsored and independent studies presented during the 52nd ASCO Annual Meeting evaluated the use of ABRAXANE® (paclitaxel protein-bound particles for injectable suspension)(albumin-bound) in combination with gemcitabine in first-line metastatic pancreatic cancer.

"This year's ASCO meeting continues to evaluate sequential therapy with ABRAXANE plus gemcitabine in the first-line and as a combination partner for investigational agents to treat metastatic pancreatic cancer," said Michael Pehl, President, Hematology and Oncology for Celgene. "The ABRAXANE plus gemcitabine combination is playing a key part in research designed to advance care for patients in this historically challenging disease."

Evaluating a Treatment Plan in Metastatic Pancreatic Cancer

For patients with metastatic pancreatic cancer, important considerations in defining a treatment plan include sequence, patient characteristics, comparative effectiveness and cost. At ASCO 2016 health outcomes analyses evaluating the treatment sequence with ABRAXANE plus gemcitabine as the first-line option are being presented.

An Italian multi-center real-life retrospective analysis highlighted outcomes of 122 patients who received first-line ABRAXANE plus gemcitabine followed by second-line treatment. (Abstract #4124 - Giordano). Second line treatments included FOLFOX/XELOX (45%), FOLFIRI (22%), FOLFIRINOX (18%), and other single agent therapies (15%). Median overall survival for patients receiving a second-line therapy following ABRAXANE plus gemcitabine was 13.5 months (95% CI 12.659-14.341), compared with 6.8 months for patients (99 patients) receiving BSC (95% CI 5.567-8.033), p < 0.0001. Also of note in the research presented at ASCO were two studies evaluating ABRAXANE plus gemcitabine in patients who exhibited elevated bilirubin levels, a common disease effect in metastatic pancreatic cancer. These studies provide insight into this patient population, which was excluded from the Phase III study of ABRAXANE plus gemcitabine.

In one observational interim analysis (Abstract #e15739 - zur Hausen), 20 (of 219) patients with a mean bilirubin level of 4.4 mg/dl (1.5-12.9) at baseline were followed for up to 4 cycles of ABRAXANE plus gemcitabine and methods of hyperbilirubinaemia were assessed. The mean bilirubin level of these patients dropped to 1.8 mg/dl (0.35-14.1; p=0.031) by the 2nd cycle. There were 14 (70%) patients that started treatment with a standard dosage and 6 (30%) that started with a reduced dose. Grade 3 or 4 toxicities were seen in 70 percent of patients with the most common being leukopenia, anemia and fever (each 20%).

An additional analysis of 29 patients (Abstract #e15717 - Pelzer) examined safety and survival with ABRAXANE/Gemcitabine in patients with elevated total bilirubin levels (≥ 1.2 to > 5 x ULN).

Administration of ABRAXANE in patients with hepatic impairment should be performed with caution. Patients with hepatic impairment may be at increased risk of toxicity, particularly from myelosuppression; such patients should be closely monitored for development of profound myelosuppression. According to the prescribing information, ABRAXANE is not recommended in patients who have total bilirubin > 5 x ULN or AST > 10 x ULN.

Multiple studies evaluated real-world comparative effectiveness and economic evaluations of first-line metastatic pancreatic treatments.

An independent, retrospective, Canadian comparative effectiveness analysis of ABRAXANE plus gemcitabine, FOLFIRINOX, and gemcitabine alone (Abstract #6561 - Wang) in five British Columbia cancer centers found the median overall survival of these treatments was 8.5 months for ABRAXANE plus gemcitabine (n=59), 7.8 months for FOLFIRINOX (n=59) and 3.1
months for gemcitabine alone. The analysis noted that patients receiving FOLFIRINOX were significantly younger (p < 0.001), had better performance status (p < 0.001) and had less disease burden at presentation (p=0.049), compared with ABRAXANE plus gemcitabine. Treatment discontinuation due to toxicities occurred in 36% of patients receiving FOLFIRINOX, 17% of patients receiving ABRAXANE plus gemcitabine and 23% of patients receiving gemcitabine alone.

A retrospective review of U.S. de-identified hospital data (Abstract #e15741 - Kim) evaluated the median time to treatment discontinuation and cost of ABRAXANE® plus gemcitabine and FOLFIRINOX in the first-line setting. In this analysis, patients treated with FOLFIRINOX had higher median total monthly treatment costs compared to ABRAXANE plus gemcitabine ($18,743 vs. $12,192; p < 0.05).

ABRAXANE plus gemcitabine as a foundation for investigational combinations in metastatic pancreatic cancer

Multiple studies presented at ASCO also evaluated ABRAXANE in combination with potential new agents in first-line metastatic pancreatic cancer. Agents being evaluated in combination with ABRAXANE plus gemcitabine in the first line include PEGPH20 (Abstract #4104 - Bullock), necuparanib (Abstract # 4117 - O'Reilly), indoximod (Abstract #3020 - Bahary) and napabucasin (Abstract #4128 - El-Rayes).

About ABRAXANE®

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 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 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 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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