Pfizer Logo

Pfizer Reports Results From Phase 3 Study Of Torisel (temsirolimus) In Combination With Bevacizumab In Advanced Renal Cell Carcinoma (RCC)

Thursday, August 09, 2012 - 10:30pm

"Additional analyses will be performed to help us understand this result. The study outcome, involving combination therapy, does not change the safety and efficacy relationship of single-agent TORISEL for advanced RCC patients with a poor prognostic risk profile."

(BUSINESS WIRE)--Pfizer Inc. announced today that the Phase 3 INTORACT trial (B1771006), evaluating the combination of bevacizumab plus TORISEL® (temsirolimus) compared with bevacizumab plus interferon-alfa-2a (IFN-?-2a) in the first-line treatment of patients with advanced renal cell carcinoma (RCC) across risk groups, did not meet its primary endpoint of superiority in extending progression free survival (PFS) in the study population. Additional efficacy endpoints and safety data for the combination treatments in both arms are being analyzed and will be presented at an upcoming major medical congress.

“This trial advances our knowledge about the role and limitations of combining targeted therapies in the treatment of advanced RCC,” said Dr. Mace Rothenberg, senior vice president of clinical development and medical affairs for Pfizer’s Oncology Business Unit. “Additional analyses will be performed to help us understand this result. The study outcome, involving combination therapy, does not change the safety and efficacy relationship of single-agent TORISEL for advanced RCC patients with a poor prognostic risk profile.”

Approximately 270,000 new cases of this tumor are diagnosed worldwide annually, and about 20 percent of cases present with advanced disease at the time of diagnosis.[1] Approximately 13,000 individuals die of this tumor in the U.S. each year.

The combination of bevacizumab and IFN-?-2a is approved as first-line treatment for advanced RCC and clinical supplies of both of these drugs in this trial were provided through an agreement with Roche.

About TORISEL® (temsirolimus)

TORISEL is approved in the U.S. and other countries for the treatment of advanced RCC. TORISEL is approved in the European Union for the first-line treatment of patients with advanced renal cell carcinoma (RCC) who have at least three of six prognostic risk factors.

TORISEL is the only intravenous mammalian target of rapamycin (mTOR) inhibitor approved for the treatment of advanced RCC. TORISEL is the only treatment to show a significant improvement in overall survival (OS) in treatment-naïve, poor risk patients with advanced RCC in a Phase 3 pivotal trial.

Based on preclinical studies, TORISEL inhibits the activity of mTOR, an intracellular protein implicated in multiple growth-related cellular functions including proliferation, growth and survival. The inhibition of mTOR also reduces levels of certain growth factors, such as vascular endothelial growth factor (VEGF), which are overexpressed in solid tumors like kidney cancer and are thought to play a crucial role in angiogenesis, the process by which tumors acquire blood vessels, nutrients and oxygen needed for growth.

Important TORISEL® (temsirolimus) Safety Information

TORISEL is contraindicated in patients with bilirubin >1.5 x ULN and should be used with caution when treating patients with mild hepatic impairment (bilirubin >1 – 1.5 x ULN or AST > ULN but bilirubin ? ULN). If TORISEL must be given to patients with mild hepatic impairment, reduce the dose of TORISEL to 15 mg/week. In a phase 1 study, the overall frequency of ? grade 3 adverse reactions and deaths, including deaths due to progressive disease, was greater in patients with baseline bilirubin > 1.5 x ULN.

Hypersensitivity/infusion reactions, including flushing, chest pain, dyspnea, hypotension, apnea, loss of consciousness, hypersensitivity and anaphylaxis, may occur very early in the first infusion or with subsequent infusions. Pretreat with an H1 antihistamine. TORISEL infusion should be interrupted in patients with infusion reactions and appropriate therapy given.

Serum glucose, serum cholesterol, and triglycerides should be tested before and during TORISEL treatment. TORISEL is likely to result in hyperglycemia and hyperlipemia. This may result in the need for an increase in the dose of, or initiation of, insulin and/or oral hypoglycemic agent therapy and/or lipid-lowering agents, respectively.

TORISEL may result in immunosuppression. Patients should be carefully observed for the occurrence of infections, including opportunistic infections.

Cases of interstitial lung disease, some resulting in death, have occurred. Some patients were asymptomatic or had minimal symptoms. Patients should undergo baseline radiography prior to TORISEL therapy and periodically thereafter, even in the absence of clinical respiratory symptoms. Follow patients closely and, if clinically significant respiratory symptoms develop, consider withholding TORISEL until recovery of symptoms and radiographic improvement of pneumonitis findings. Some patients required TORISEL discontinuation and/or treatment with corticosteroids and/or antibiotics.

Cases of fatal bowel perforation occurred with TORISEL. These patients presented with fever, abdominal pain, metabolic acidosis, bloody stools, diarrhea, and/or acute abdomen.

Cases of rapidly progressive and sometimes fatal acute renal failure not clearly related to disease progression occurred in patients who received TORISEL.

Due to abnormal wound healing, use TORISEL with caution in the perioperative period.

Patients with central nervous system tumors (primary CNS tumor or metastases) and/or receiving anticoagulation therapy may be at an increased risk of developing intracerebral bleeding (including fatal outcomes) while receiving TORISEL.

Live vaccinations and close contact with those who received live vaccines should be avoided.

TORISEL may cause fetal harm. Patients and their partners should be advised to avoid pregnancy throughout treatment and for 3 months after TORISEL therapy has stopped.

Elderly patients may be more likely to experience certain adverse reactions including diarrhea, edema and pneumonia.

The most common (incidence ?30%) adverse reactions observed with TORISEL are: rash (47%), asthenia (51%), mucositis (41%), nausea (37%), edema (35%), and anorexia (32%). The most common laboratory abnormalities (incidence ?30%) are anemia (94%), hyperglycemia (89%), hyperlipemia (87%), hypertriglyceridemia (83%), elevated alkaline phosphatase (68%), elevated serum creatinine (57%), lymphopenia (53%), hypophosphatemia (49%), thrombocytopenia (40%), elevated AST (38%), and leukopenia (32%).

Most common grades 3/4 adverse events and laboratory abnormalities included asthenia (11%), dyspnea (9%), hemoglobin decreased (20%), lymphocytes decreased (16%), glucose increased (16%), phosphorus decreased (18%), and triglycerides increased (44%).

Pleural effusion, hemodynamically significant pericardial effusions requiring intervention, convulsions, rhabdomyolysis, Stevens-Johnson Syndrome, complex regional pain syndrome and extravasations have been reported during postmarketing use.

Strong inducers of CYP3A4/5 (eg, dexamethasone, rifampin) and strong inhibitors of CYP3A4 (eg, ketoconazole, atazanavir) may decrease and increase concentrations of the major metabolite of TORISEL, respectively. If alternatives cannot be used, dose modifications of TORISEL are recommended.

Avoid St. John’s Wort which may decrease TORISEL plasma concentrations, and grapefruit juice which may increase plasma concentrations of the major metabolite of TORISEL.

The combination of TORISEL and sunitinib resulted in dose-limiting toxicity (Grade 3/4 erythematous maculopapular rash, and gout/cellulitis requiring hospitalization).

For more information on TORISEL, including full prescribing information for TORISEL (temsirolimus), please visit www.pfizer.com.

About Pfizer Oncology

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options to improve the outlook for cancer patients worldwide.

As a leader in the treatment of advanced RCC, Pfizer Oncology is dedicated to offering multiple treatments and investigating new agents in different populations and stages of disease. Pfizer Oncology has helped transform treatment expectations for advanced kidney cancer, providing confidence and options to physicians, allowing them to better tailor treatment for different patient populations.

For more information please visit www.Pfizer.com.

[1] Lam JS, Breda A, Belldegrun AS and Figlin RA. Evolving principles of surgical management and prognostic factors for outcome in renal cell carcinoma. *J Clin Oncol.* 2008;24:5565-5575.

Pfizer Inc. Media: Jenifer Antonacci, 610-427-0369 or Investor: Jennifer Davis, 212-733-0717