MD CONFERENCE EXPRESS

Trial Results Establish Clinical Benefit of RAD001 in Advanced Renal Cell Carcinoma

Late-breaking results from a phase 3, randomized, double-blind, multicenter study provide convincing evidence that RAD001 (everolimus) is a safe and effective treatment for patients with metastatic renal cell carcinoma (mRCC) and validate mTOR inhibition as a cancer treatment. Robert J. Motzer, MD, Memorial Sloan-Kettering Cancer Center, New York, NY, presented data from the study (NCT00410124), which compared RAD001 plus best supportive care (BSC) with BSC plus placebo in patients with mRCC. The trial was terminated after interim results demonstrated significantly better progression-free survival (PFS) for patients who received everolimus compared with those who received placebo.

According to Dr. Motzer, everolimus represents a new approach to cancer treatment by inhibiting the mTOR protein, a principal regulator of tumor cell division and blood cell vessel growth in cancer cells. "This is the first phase 3 trial that establishes clinical benefits and provides safety information for this new agent," he said.

The study randomly assigned 410 patients with metastatic clear cell carcinoma, whose disease had progressed while receiving vascular endothelial growth factor receptor tyrosine kinase inhibitor (VEGFr-TKI) therapy (sunitinib, sorafenib, or both), to receive everolimus plus BSC or placebo plus BSC. Patients were randomly assigned, in a 2:1 ratio, to receive either 10 mg of orally administered everolimus or the same daily dose of a placebo. Treatment was repeated in 28-day cycles, allowing for assessments of response and safety and was continued unless there was disease progression or intolerance of the treatment. Patients who showed signs of progression were unblinded and, if they were in the placebo arm, were given the opportunity to receive everolimus. When the study was terminated in October 2007, all patients were unblinded, and those who were in the placebo arm were offered open-label everolimus.

An analysis of data that followed early termination of the study showed a median PFS of 4.0 months for patients who received everolimus compared with 1.9 months for those in the placebo group ($p<0.001$; 95% CI; 0.22, 0.40). Twenty-six percent of patients in the everolimus group have experienced PFS of 6 months compared with 2% of patients in the placebo group. Secondary endpoints of safety and patient-reported outcomes were deemed acceptable. Median overall survival (OS) in the everolimus group is confounded by the built-in crossover and has not been reached. OS in the placebo group is 8.8 months. Additional data will be released when further analyses and follow-up are completed.

Dr. Motzer concluded that this trial establishes clinical benefit for everolimus following progression on tyrosine kinase inhibitor therapy with sunitinib or sorafenib. "Everolimus is the first and only agent that has an established clinical benefit for the treatment of patients with mRCC in this clinical setting and should become the standard of care," he said.

Highlights from the
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