KIDNEY CANCER NEWS

Cabozantinib Approved for First-Line Treatment of Advanced Renal Cell Carcinoma

Cabozantinib (Cabometyx, Exelixis) received an expanded indication from the US Food and Drug Administration (FDA) on December 19 as a first-line treatment in patients with advanced renal cell carcinoma (RCC). The agent was previously approved in April 2016 for use in patients with advanced RCC who had received prior antiangiogenic therapy. The recommended daily dose is 60 mg by mouth.

Cabozantinib is an oral small-molecule tyrosine kinase inhibitor. In vitro biochemical and/or cellular assays have shown that cabozantinib inhibits the tyrosine kinase activity of MET, vascular endothelial growth factor receptor 1 (VEGFR1), VEGFR2, VEGFR3, AXL, RET, ROS1, TYRO3, MER, KIT, TRKB, FLT3, and TIE2.

Approval was based on data from CABOSUN (Cabozantinib Versus Sunitinib As Initial Targeted Therapy for Patients With Metastatic Renal Cell Carcinoma of Poor or Intermediate Risk), a phase 2 open-label multicenter study of 157 patients with intermediate- or poor-risk previously untreated RCC. Risk groups were defined by the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) categories.

Most participants were male (78%), and the median age was 63 years. Most patients—81%—fell into the intermediate-risk group (1-2 risk factors), and 19% fell into the poor-risk group (≥3 risk factors). More than one-third (36%) had metastasis to bone. The Eastern Cooperative Oncology Group performance status was 0 in 46% of patients, 1 in 41%, and 2 in 13%.

Patients were randomly assigned to receive 60 mg of cabozantinib daily (n=79) or 50 mg of sunitinib (Sutent, Pfizer) daily (n=78) until disease progression or unacceptable toxicity; the patients assigned to sunitinib received treatment for 4 weeks followed by 2 weeks without treatment. The median duration of treatment was 6.5 months (range, 0.2-28.7) in the patients receiving cabozantinib and 3.1 months (range, 0.2-25.5) in the patients receiving sunitinib.

Within 30 days of treatment, 4 deaths occurred in the cabozantinib group and 6 deaths in the sunitinib group. The causes of death in the cabozantinib group were gastrointestinal perforation in 2 patients, acute renal failure in 1 patient, and clinical deterioration in 1 patient.

A blinded independent radiology review committee estimated the median progression-free survival, which was 8.6 months (95% CI, 6.8-14.0) for patients taking cabozantinib vs 5.3 months (95% CI, 3.0-8.2) for patients taking sunitinib (hazard ratio [HR], 0.48; 95% CI, 0.31-0.74; *P*=.0008). The difference between overall survival in the cabozantinib and sunitinib groups was not statistically significant; the difference between the partial response rates in the 2 groups also was not statistically significant.

The most commonly reported adverse reactions to cabozantinib, which occurred in at least 1 in 4 patients in METEOR (A Study of Cabozantinib vs Everolimus in Subjects With Metastatic Renal Cell Carcinoma), the study that served as the basis for initial approval of the drug, were diarrhea, fatigue, nausea, decreased appetite, hypertension, palmar-plantar erythrodysesthesia, weight loss, vomiting, dysgeusia, and stomatitis. The most common grade 3/4 adverse reactions to cabozantinib in CABOSUN, affecting 5% or more of patients treated with the agent, were hypertension, diarrhea, hyponatremia, hypophosphatemia, palmar-plantar erythrodysesthesia, fatigue, increased alanine aminotransferase, decreased appetite, stomatitis, pain, hypotension, and syncope. A total of 21% of patients receiving cabozantinib and 22% of patients receiving sunitinib experienced an adverse reaction that led to drug discontinuation.

The median average daily dose was 50.3 mg for cabozantinib and 44.7 mg for sunitinib (excluding the scheduled nondosing days for sunitinib). Overall, 46% of patients in the cabozantinib group and 35% of those in the sunitinib group received reduced dosing.

The expanded indication for cabozantinib was granted through priority review. The agent is also approved for the treatment of medullary thyroid cancer, in which case it is marketed as Cometriq. Cometriq and Cabometyx have different formulations and are not interchangeable.

Patients should not eat for at least 2 hours before and at least 1 hour after taking cabozantinib; the tablets should be swallowed whole with a full glass of water (they should not be crushed). In addition, patients taking cabozantinib should not consume grapefruit or grapefruit juice.