Fact sheet

CABOMETYX

Learn about CABOMETYX™ (cabozantinib) tablets

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CABOMETYX is the first therapy to demonstrate in a large, randomized phase 3 trial improved overall survival, progression-free survival and objective response rate in patients with advanced kidney cancer.[1]

What is CABOMETYX?[1]

CABOMETYX is indicated for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.

Important Safety Information

The Prescribing Information for CABOMETYX includes Warnings and Precautions for Hemorrhage, Gastrointestinal Perforations and Fistulas, and Thrombotic Events. Please see Important Safety Information below and full U.S. prescribing information at https://cabometyx.com/downloads/cabometyxuspi.pdf

What is RCC?

- RCC is a type of cancer that forms in the tissues of the kidney that make urine[2]
- RCC accounts for 4% of all cancers in the United States[3]
- In the United States, approximately 62,700 new cases will be diagnosed and an estimated 14,240 people will die from RCC in 2016[4]

How does CABOMETYX work?[1]

CABOMETYX belongs to a class of drugs called tyrosine kinase inhibitors (TKIs). Tyrosine kinases are protein receptors on cells that are activated by the addition of a phosphate group. This addition leads to activation of many cellular processes through signaling cascades. TKIs inhibit this phosphate addition.

- CABOMETYX targets include MET, AXL and vascular endothelial growth factor receptors (VEGFR) -1, -2 and -3.
- In preclinical models, CABOMETYX has been shown to inhibit the activity of these receptors, which are associated with normal cellular function and tumor angiogenesis, invasiveness, metastasis and drug resistance.

What data is the CABOMETYX indication based on?[1]

The approval of CABOMETYX is based on findings from the METEOR phase 3 pivotal trial. METEOR compared CABOMETYX with everolimus in 658 patients with advanced RCC who experienced disease progression following treatment with a VEGFR-TKI.

- The METEOR trial demonstrated a statistically significant and clinically meaningful increase in overall survival for patients treated with CABOMETYX compared with everolimus, a current standard of care after first-line treatment.
    - CABOMETYX was associated with a significant 34 percent reduced risk of death compared with everolimus.
    - Median overall survival was 21.4 months for patients receiving CABOMETYX versus 16.5 months for those receiving everolimus (HR=0.66, 95% CI 0.53-0.83, P<0.0003).
- CABOMETYX was associated with a progression-free survival of 7.4 months versus 3.8 months for everolimus, corresponding to a 42 percent reduction in the rate of disease progression or death compared with everolimus (HR=0.58, 95% CI 0.45-0.74, P<0.0001).
- The objective response rate was 17 percent with CABOMETYX and 3 percent with everolimus (P<0.0001).

The most commonly reported (frequency ≥25 percent) side effects with CABOMETYX include diarrhea, fatigue, nausea, decreased appetite, palmar-plantar erythrodysesthesia syndrome, hypertension, vomiting, decreased weight and constipation.

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1. CABOMETYX™ (cabozantinib) Prescribing Information. Available at https://cabometyx.com/downloads/cabometyxuspi.pdf. 2. National Cancer Institute. Kidney Cancer- Patient Version. (http://www.cancer.gov/types/kidney.) Accessed March 25, 2016. 3. National Cancer Institute. Genetics of Kidney Cancer. (http://www.cancer.gov/types/kidney/hp/kidney-genetics-pdq). Accessed March 25, 2016. 4. National Cancer Institute. SEER Stat Fact Sheets: Kidney and Renal Pelvis Cancer. (http://seer.cancer.gov/statfacts/html/kidrp.html). Accessed April 24, 2016.

Important Safety Information

Hemorrhage: Severe hemorrhage occurred with CABOMETYX. The incidence of Grade ≥3 hemorrhagic events was 2.1% in CABOMETYX-treated patients and 1.6% in everolimus-treated patients. Fatal hemorrhages also occurred in the cabozantinib clinical program. Do not administer CABOMETYX to patients that have or are at risk for severe hemorrhage.

Gastrointestinal (GI) Perforations and Fistulas: Fistulas were reported in 1.2% (including 0.6% anal fistula) of CABOMETYX-treated patients and 0% of everolimus-treated patients. GI perforations were reported in 0.9% of CABOMETYX-treated patients and 0.6% of everolimus-treated patients. Fatal perforations occurred in the cabozantinib clinical program. Monitor patients for symptoms of fistulas and perforations. Discontinue CABOMETYX in patients who experience a fistula that cannot be appropriately managed or a GI perforation.

Thrombotic Events: CABOMETYX treatment results in an increased incidence of thrombotic events. Venous thromboembolism was reported in 7.3% of CABOMETYX-treated patients and 2.5% of everolimus-treated patients. Pulmonary embolism occurred in 3.9% of CABOMETYX-treated patients and 0.3% of everolimus-treated patients. Events of arterial thromboembolism were reported in 0.9% of CABOMETYX-treated patients and 0.3% of everolimus-treated patients. Fatal thrombotic events occurred in the cabozantinib clinical program. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or any other arterial thromboembolic complication.

Hypertension and Hypertensive Crisis: CABOMETYX treatment results in an increased incidence of treatment-emergent hypertension. Hypertension was reported in 37% (15% Grade ≥3) of CABOMETYX-treated patients and 7.1% (3.1% Grade ≥3) of everolimus-treated patients. Monitor blood pressure prior to initiation and regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume CABOMETYX at a reduced dose. Discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy. Discontinue CABOMETYX if there is evidence of hypertensive crisis or severe hypertension despite optimal medical management.

Diarrhea: Diarrhea occurred in 74% of patients treated with CABOMETYX and in 28% of patients treated with everolimus. Grade 3 diarrhea occurred in 11% of CABOMETYX-treated patients and in 2% of everolimus-treated patients. Withhold CABOMETYX in patients who develop intolerable Grade 2 diarrhea or Grade 3-4 diarrhea that cannot be managed with standard antidiarrheal treatments until improvement to Grade 1; resume CABOMETYX at a reduced dose. Dose modification due to diarrhea occurred in 26% of patients.

Palmar-Plantar Erythrodysesthesia Syndrome (PPES): Palmar-plantar erythrodysesthesia syndrome (PPES) occurred in 42% of patients treated with CABOMETYX and in 6% of patients treated with everolimus. Grade 3 PPES occurred in 8.2% of CABOMETYX-treated patients and in <1% of everolimus-treated patients. Withhold CABOMETYX in patients who develop intolerable Grade 2 PPES or Grade 3 PPES until improvement to Grade 1; resume CABOMETYX at a reduced dose. Dose modification due to PPES occurred in 16% of patients.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic finding on MRI, occurred in the cabozantinib clinical program. Perform an evaluation for RPLS in any patient presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.

Embryo-fetal Toxicity: CABOMETYX can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with CABOMETYX and for 4 months after the last dose.

Adverse Reactions: The most commonly reported (≥25%) adverse reactions are: diarrhea, fatigue, nausea, decreased appetite, PPES, hypertension, vomiting, weight decreased, and constipation.

Drug Interactions: Strong CYP3A4 inhibitors and inducers: Reduce the dosage of CABOMETYX if concomitant use with strong CYP3A4 inhibitors cannot be avoided. Increase the dosage of CABOMETYX if concomitant use with strong CYP3A4 inducers cannot be avoided.

Lactation: Advise a lactating woman not to breastfeed during treatment with CABOMETYX and for 4 months after the final dose.

Reproductive Potential: Contraception—Advise females of reproductive potential to use effective contraception during treatment with CABOMETYX and for 4 months after the final dose. **Infertility —**CABOMETYX may impair fertility in females and males of reproductive potential.

Hepatic Impairment: Reduce the CABOMETYX dose in patients with mild (Child-Pugh score [C-P] A) or moderate (C-P B) hepatic impairment. CABOMETYX is not recommended for use in patients with severe hepatic impairment.

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