Fact Sheet

METEOR - Phase 3 Pivotal Trial

of CABOMETYX® (cabozantinib) tablets in Advanced Renal Cell Carcinoma

What is RCC?

- RCC is the most common type of kidney cancer[3]
- RCC accounts for nearly 4% of all cancers in the United States[4]
- In the United States, approximately 65,000 new cases will be diagnosed and an estimated 15,000 people will die from RCC annually[5]

CABOMETYX is a kinase inhibitor indicated for the treatment of patients with advanced RCC.

The Prescribing Information for CABOMETYX includes Warnings and Precautions for hemorrhage, GI perforations and fistulas, thrombotic events, hypertension and hypertensive crisis, diarrhea, palmar-plantar erythrodysesthesia syndrome, reversible posterior leukoencephalopathy syndrome, and embryofetal toxicity. Please see additional Important Safety Information on reverse, and full Prescribing Information at https://www.cabometyx.com/downloads/CABOMETYXUSPI.pdf.

METEOR is a phase 3 pivotal trial evaluating the effect of CABOMETYX® (cabozantinib) tablets compared with everolimus in patients with advanced renal cell carcinoma (RCC) whose disease has progressed after at least one prior anti-angiogenic therapy. The trial was conducted at 173 sites in 26 countries, and enrollment was weighted toward Western Europe, North America and Australia.

Trial Design[1]

Phase 3, open-label, randomized, event-driven, international trial

- The study included 658 patients who were 18 years of age or older with advanced or metastatic RCC with clear cell component
- Patients must have received prior treatment with at least one vascular endothelial growth factor receptor-tyrosine kinase inhibitor (VEGFR-TKI) and must have had radiographic progression during treatment or within 6 months after the most recent dose of the VEGFR inhibitor

Patients were randomly assigned to:

- CABOMETYX 60 mg once daily (n=330)
- Everolimus 10 mg once daily (n=328)

Patients were stratified based on prognostic risk criteria and number of prior VEGFR-TKIs.[2] No cross-over was allowed between the study arms.

Primary study endpoint	Secondary study endpoints
• **Progression-free survival:** time until either death or disease-worsening, per independent radiology review, in the first 375 patients randomized	• **Overall survival:** time from randomization until death from any cause in the intent-to-treat study population • **Objective response rate:** proportion of patients with tumor size reduction of a predefined amount and for a minimum time period

For additional information on the study, refer to ClinicalTrials.gov Identifier: NCT01865747.

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1. Choueiri et. Al., Cabozantinib versus Everolimus in Advanced Renal-Cell Carcinoma. *N Engl J Med* 2015; 373:1814-1823. **2.** Motzer, R.J. et. al. Prognostic Factors for Survival in Previously Treated Patients With Metastatic Renal Cell Carcinoma. *J Clin Oncol* 2004; 22(3):454-63. **3.** American Cancer Society. What is Kidney Cancer? (https://www.cancer.org/cancer/kidney-cancer/about/what-is-kidney-cancer.html.) Accessed August 2018. **4.** National Cancer Institute. SEER. Cancer Stat Facts: Kidney and Renal Pelvis Cancer. (https://seer.cancer.gov/statfacts/html/kidrp.html.) Accessed August 2018. **5.** American Cancer Society. Cancer Facts & Figures 2018. (https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf.) Accessed August 2018.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage: Severe and fatal hemorrhages have occurred with CABOMETYX. In RCC trials, the incidence of Grade ≥3 hemorrhagic events was 3% in CABOMETYX patients. Do not administer CABOMETYX to patients that have or are at risk for severe hemorrhage.

Gastrointestinal (GI) Perforations and Fistulas: In RCC trials, GI perforations were reported in 1% of CABOMETYX patients. Fatal perforations occurred in patients treated with CABOMETYX. In RCC studies, fistulas were reported in 1% of CABOMETYX patients. Monitor patients for symptoms of perforations and fistulas, including abscess and sepsis. Discontinue CABOMETYX in patients who experience a GI perforation or a fistula that cannot be appropriately managed.

Thrombotic Events: Thrombotic events increased with CABOMETYX. In RCC trials, venous thromboembolism occurred in 9% (including 5% pulmonary embolism) and arterial thromboembolism occurred in 1% of CABOMETYX 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: Treatment-emergent hypertension, including hypertensive crisis, increased with CABOMETYX. In RCC trials, hypertension was reported in 44% (18% Grade ≥3) of CABOMETYX 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 if there is evidence of hypertensive crisis or for severe hypertension that cannot be controlled with antihypertensive therapy or medical management.

Diarrhea: In RCC trials, diarrhea occurred in 74% of CABOMETYX patients. Grade 3 diarrhea occurred in 11% of CABOMETYX 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.

Palmar-Plantar Erythrodysesthesia (PPE): In RCC trials, PPE occurred in 42% of CABOMETYX patients. Grade 3 PPE occurred in 8% of CABOMETYX patients. Withhold CABOMETYX in patients who develop intolerable Grade 2 PPE or Grade 3 PPE until improvement to Grade 1; resume CABOMETYX at a reduced dose.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic finding on MRI, occurred in the cabozantinib clinical program. Evaluate for RPLS in patients 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. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during CABOMETYX treatment and for 4 months after the last dose.

ADVERSE REACTIONS

The most commonly reported (≥25%) adverse reactions were: diarrhea, fatigue, nausea, decreased appetite, hypertension, PPE, weight decreased, vomiting, dysgeusia, and stomatitis.

DRUG INTERACTIONS

Strong CYP3A4 Inhibitors: If concomitant use with strong CYP3A4 inhibitors cannot be avoided, reduce the CABOMETYX dosage.

Strong CYP3A4 Inducers: If concomitant use with strong CYP3A4 inducers cannot be avoided, increase the CABOMETYX dosage.

USE IN SPECIFIC POPULATIONS

Lactation: Advise women not to breastfeed while taking CABOMETYX and for 4 months after the final dose.

Hepatic Impairment: In patients with mild to moderate hepatic impairment, reduce the CABOMETYX dosage. CABOMETYX is not recommended for use in patients with severe hepatic impairment.

Please see accompanying full Prescribing Information at https://cabometyx.com/downloads/CABOMETYXUSPI.pdf.

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