Fact Sheet

CABOSUN - Phase 2 Trial

of CABOMETYX® (cabozantinib) tablets versus Sunitinib in Previously Untreated Locally Advanced or Metastatic Renal Cell Carcinoma

PHASE 2, RANDOMIZED, OPEN LABEL, ACTIVE-CONTROLLED TRIAL[1]

- Trial was conducted at 488 sites in the U.S. and included 157 participants ages 18 and older[1,2]
- Patients had previously untreated RCC with a clear cell component that was locally advanced or had metastasized to nearby tissue, lymph nodes or other places in the body and measurable disease by Response Evaluation Criteria in Solid Tumors (RECIST) criteria[1,2]
- Patients were intermediate- or poor-risk per the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) criteria[1]
  - 80.9 percent of patients were intermediate-risk per IMDC criteria and 19.1 percent were poor-risk[2]
- Patients had ECOG Performance Status (PS) 0-2[2]
  - 46 percent of patients had ECOG PS 0, 41 percent had ECOG PS 1, and 13 percent had ECOG PS 2[2]
- Patients with brain metastases were eligible if metastases were adequately treated and stable for 3 months[2]

PATIENTS WERE RANDOMLY ASSIGNED TO RECEIVE EITHER:

- Oral cabozantinib: 60 mg once daily
- Oral sunitinib: 50 mg once daily, four weeks on followed by two weeks off

Primary endpoint

- **Progression-free survival**: time until either death or disease-worsening, per investigator review

Secondary endpoints

- **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
- **Safety**

CABOSUN was conducted by The Alliance for Clinical Trials in Oncology as part of Exelixis' collaboration with the National Cancer Institute's Cancer Therapy Evaluation Program.

For additional information on the study, visit https://clinicaltrials.gov

REFERENCES: **1.** ClinicalTrials.gov. Cabozantinib-s-malate or Sunitinib Malate in Treating Patients with Previously Untreated Locally Advanced or Metastatic Kidney Cancer. (https://clinicaltrials.gov/ct2/show/study/NCT01835158). Accessed February 2019. **2.** Choueiri T.K., Halabi, S., Sanford, Ben L., et al. Cabozantinib Versus Sunitinib As Initial Targeted Therapy for Patients With Metastatic Renal Cell Carcinoma of Poor or Intermediate Risk: The Alliance A031203 CABOSUN Trial. *Journal of Clinical Oncology.* 2017; 35:6, 591-597. Accessed February 2019. **3.** American Cancer Society. Cancer Facts & Figures 2019. (https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf). Accessed February 2019. **4.** Jonasch, E., Gao, J., Rathmell, W. Renal cell carcinoma. *BMJ.* 2014; 349:g4797. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4707715/) Accessed February 2019. **5.** National Cancer Institute. SEER Stat Fact Sheets: Kidney and Renal Pelvis Cancer. (http://seer.cancer.gov/statfacts/html/kidrp.html). Accessed February 2019. **6.** Decision Resources Report: Renal Cell Carcinoma. October 2014 (internal data on file).

WHAT IS RCC?

- Kidney cancer is among the top ten most commonly diagnosed forms of cancer among both men and women in the U.S.[3]
- Clear cell RCC is the most common type of kidney cancer in adults[4]
- In 2019, it is estimated that nearly 74,000 new cases will be diagnosed and 15,000 people will die from kidney cancer in the U.S.[3]
- If detected while the cancer resides only within the kidney, the five-year survival rate for RCC is 93 percent[5]
- The survival rate drops to only 12 percent once RCC has spread beyond the kidney to other parts of the body, also known as advanced or metastatic disease, for which there is no identified cure[5]
- An estimated 15,000 patients in the U.S. each year are in need of first-line treatment for advanced kidney cancer[6]

IMPORTANT SAFETY INFORMATION

The Prescribing Information for CABOMETYX includes Warnings and Precautions for hemorrhage, perforations and fistulas, thrombotic events, hypertension and hypertensive crisis, diarrhea, palmar-plantar erythrodysesthesia, proteinuria, osteonecrosis of the jaw, wound complications, reversible posterior leukoencephalopathy syndrome, and embryo-fetal toxicity.

Please see additional Important Safety Information below and the full Prescribing Information for CABOMETYX at https://cabometyx.com/ downloads/CABOMETYXUSPI.pdf.

MEDIA CONTACT

Lindsay Treadway
Public Affairs and Advocacy Relations
Exelixis, Inc.

(650) 837-7522
ltreadway@exelixis.com

EXELIXIS®

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage: Severe and fatal hemorrhages occurred with CABOMETYX. The incidence of Grade 3 to 5 hemorrhagic events was 5% in CABOMETYX patients. Discontinue CABOMETYX for Grade 3 or 4 hemorrhage. Do not administer CABOMETYX to patients who have a recent history of hemorrhage, including hemoptysis, hematemesis, or melena.

Perforations and Fistulas: Gastrointestinal (GI) perforations, including fatal cases, occurred in 1% of CABOMETYX patients. Fistulas, including fatal cases, occurred in 1% of CABOMETYX patients. Monitor patients for signs and symptoms of perforations and fistulas, including abscess and sepsis. Discontinue CABOMETYX in patients who experience a fistula that cannot be appropriately managed or a GI perforation.

Thrombotic Events: CABOMETYX increased the risk of thrombotic events. Venous thromboembolism occurred in 7% (including 4% pulmonary embolism) and arterial thromboembolism in 2% of CABOMETYX patients. Fatal thrombotic events occurred in CABOMETYX patients. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or serious arterial or venous thromboembolic event requiring medical intervention.

Hypertension and Hypertensive Crisis: CABOMETYX can cause hypertension, including hypertensive crisis. Hypertension occurred in 36% (17% Grade 3 and <1% Grade 4) of CABOMETYX patients. Do not initiate CABOMETYX in patients with uncontrolled hypertension. Monitor blood pressure regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume at a reduced dose. Discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

Diarrhea: Diarrhea occurred in 63% of CABOMETYX patients. Grade 3 diarrhea occurred in 11% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 diarrhea, Grade 3 diarrhea that cannot be managed with standard antidiarrheal treatments, or Grade 4 diarrhea.

Palmar-Plantar Erythrodysesthesia (PPE): PPE occurred in 44% of CABOMETYX patients. Grade 3 PPE occurred in 13% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 PPE or Grade 3 PPE.

Proteinuria: Proteinuria occurred in 7% of CABOMETYX patients. Monitor urine protein regularly during CABOMETYX treatment. Discontinue CABOMETYX in patients who develop nephrotic syndrome.

Osteonecrosis of the Jaw (ONJ): ONJ occurred in <1% of CABOMETYX patients. ONJ can manifest as jaw pain, osteomyelitis, osteitis, bone erosion, tooth or periodontal infection, toothache, gingival ulceration or erosion, persistent jaw pain, or slow healing of the mouth or jaw after dental surgery. Perform an oral examination prior to CABOMETYX initiation and periodically during treatment. Advise patients regarding good oral hygiene practices. Withhold CABOMETYX for at least 28 days prior to scheduled dental surgery or invasive dental procedures. Withhold CABOMETYX for development of ONJ until complete resolution.

Wound Complications: Wound complications were reported with CABOMETYX. Stop CABOMETYX at least 28 days prior to scheduled surgery. Resume CABOMETYX after surgery based on clinical judgment of adequate wound healing. Withhold CABOMETYX in patients with dehiscence or wound healing complications requiring medical intervention.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic finding on MRI, can occur with CABOMETYX. 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 and females of reproductive potential of the potential risk to a fetus. Verify the pregnancy status of females of reproductive potential prior to initiating CABOMETYX and advise them to use effective contraception during treatment and for 4 months after the last dose.

ADVERSE REACTIONS

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

DRUG INTERACTIONS

Strong CYP3A4 Inhibitors: If coadministration with strong CYP3A4 inhibitors cannot be avoided, reduce the CABOMETYX dosage. Avoid grapefruit or grapefruit juice.

Strong CYP3A4 Inducers: If coadministration with strong CYP3A4 inducers cannot be avoided, increase the CABOMETYX dosage. Avoid St. John's wort.

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.

EXELIXIS®