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AVEO Oncology Announces Publication of Long-Term Survival in Patients With Relapsed/Refractory Advanced Renal Cell Carcinoma Treated With Tivozanib: Analysis of the Phase III TIVO-3 Trial in The Oncologist

BOSTON, Feb. 06, 2024 (GLOBE NEWSWIRE) -- AVEO Oncology, an LG Chem company ("AVEO"), today announced *The Oncologist* has published a post-hoc analysis of long-term progression free survival, overall survival and safety data from the Phase 3 TIVO-3 trial evaluating FOTIVDA® (tivozanib) in patients with relapsed or refractory (R/R) advanced renal cell carcinoma (RCC). In the publication, FOTIVDA demonstrated a consistent safety profile and a long-term survival benefit in patients who were alive and progression-free at 12 months, suggesting a durable clinical benefit and safety across age groups regardless of prior treatment.

"The post-hoc analysis from TIVO-3 provides additional evidence supporting the clinical utility of tivozanib in the third- or fourth-line refractory setting in patients with advanced renal cell carcinoma," said lead author Kathryn E. Beckermann, MD, PhD, Assistant Professor of Medicine in the Division of Hematology Oncology at Vanderbilt-Ingram Cancer Center. "The results suggest there is a clinically meaningful population of patients who can experience a long-term survival benefit from tivozanib over sorafenib."

TIVO-3 compared the efficacy and safety of the vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors (TKIs) FOTIVDA and sorafenib (Nexavar®) in patients with R/R advanced RCC whose disease progressed with two or three prior systemic therapies. The trial included a predefined subgroup of patients (26%) who were previously treated with both an immuno-oncology (IO) therapy and a VEGFR TKI.

The post hoc analysis showed investigator-assessed landmark long-term progression-free survival (PFS) rates were higher with FOTIVDA compared to sorafenib (3 years: 12.3% vs. 2.4%; 4 years: 7.6% vs. 0%). After 22.8 months mean follow-up, the overall survival (OS) hazard ratio (HR) for FOTIVDA was 0.89 (95% confidence interval [CI]: 0.70-1.14); when conditioned on a clinically meaningful 12-month PFS time point, FOTIVDA showed significant improvement in OS compared to sorafenib (HR: 0.45; 95% CI: 0.22-0.91; 2-sided *P* = 0.0221). Mean time on treatment was 11.0 months with FOTIVDA and 6.3 months with sorafenib. There were fewer treatment-related adverse events (TRAEs) and lower dose modification rates with FOTIVDA than with sorafenib as well as fewer grade ≥3 TRAEs on FOTIVDA (46%) than sorafenib (55%). Dose modification rates were lower with FOTIVDA than with sorafenib across age and prior IO subgroups; and prior IO therapy did not impact dose reductions or discontinuations in either arm.

The advent of targeted therapies and IO therapies is considered a major advancement in the treatment of RCC, and IO-based combination therapy is the frontline standard of care for patients with advanced RCC who require systemic therapy.[4] However, despite the demonstrated benefits of

IO combination therapies, most patients with RCC ultimately experience disease progression and require subsequent treatments[5], underscoring the need for safe, tolerable and effective therapies in the refractory setting.

“For patients with relapsed or refractory advanced renal cell carcinoma, long-term progression-free survival is a vital measure of the value of anticancer therapy,” commented Michael Bailey, President and CEO of AVEO Oncology. “The long term PFS analysis combined with the post hoc conditional survival analysis is especially encouraging in this highly refractory population, as it builds upon the previously reported PFS advantage for FOTIVDA over sorafenib, a non-selective VEGFR TKI.”

Study Details

TIVO-3 was a Phase 3, global, open-label, parallel-arm study comparing the safety and efficacy of FOTIVDA versus sorafenib in patients with R/R advanced RCC whose disease progressed with two or three prior VEGFR TKI systemic regimens. The trial randomized 350 patients to receive FOTIVDA (1.5 mg once daily) or sorafenib (400 mg twice daily). The intent-to-treat (ITT) population included 175 patients in each arm; the safety population included 173 patients in the FOTIVDA arm and 170 in the sorafenib arm.

About FOTIVDA® (tivozanib)

FOTIVDA® (tivozanib) is an oral, next-generation vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitor (TKI). It is a potent, selective inhibitor of VEGFRs 1, 2, and 3 with a long half-life designed to improve efficacy and tolerability. AVEO received U.S. Food and Drug Administration (FDA) approval for FOTIVDA on March 10, 2021, for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies, based on data from the TIVO-3 trial comparing FOTIVDA to sorafenib. FOTIVDA was approved in August 2017 in the European Union and other countries in the territory of its partner EUSA Pharma (UK) Limited for the treatment of adult patients with advanced RCC. FOTIVDA has been shown to significantly reduce regulatory T-cell production in preclinical models.[6] FOTIVDA was discovered by Kyowa Kirin.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTION

Hypertension and Hypertensive Crisis: Control blood pressure prior to initiating FOTIVDA. Monitor for hypertension and treat as needed. For persistent hypertension despite use of anti-hypertensive medications, reduce the FOTIVDA dose.

Cardiac Failure: Monitor for signs or symptoms of cardiac failure throughout treatment with FOTIVDA.

Cardiac Ischemia and Arterial Thromboembolic Events: Closely monitor patients who are at increased risk for these events. Permanently discontinue FOTIVDA for severe arterial thromboembolic events, such as myocardial infarction and stroke.

Venous Thromboembolic Events: Closely monitor patients who are at increased risk for these events. Permanently discontinue FOTIVDA for severe venous thromboembolic events.

Hemorrhagic Events: Closely monitor patients who are at risk for or who have a history of bleeding.

Proteinuria: Monitor throughout treatment with FOTIVDA. For moderate to severe proteinuria, reduce the dose or temporarily interrupt treatment with FOTIVDA.

Thyroid Dysfunction: Monitor before initiation and throughout treatment with FOTIVDA.

Risk of Impaired Wound Healing: Withhold FOTIVDA for at least 24 days before elective surgery. Do not administer for at least 2 weeks following major surgery and adequate wound healing. The safety of resumption of FOTIVDA after resolution of wound healing complications has not been established.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): Discontinue FOTIVDA if signs or symptoms of RPLS occur.

Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.

Allergic Reactions to Tartrazine: The 0.89 mg capsule of FOTIVDA contains FD&C Yellow No.5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible patients.

ADVERSE REACTIONS

The most common (≥20%) adverse reactions were fatigue, hypertension, diarrhea, decreased appetite, nausea, dysphonia, hypothyroidism, cough, and stomatitis, and the most common Grade 3 or 4 laboratory abnormalities (≥5%) were sodium decreased, lipase increased, and phosphate decreased.

DRUG INTERACTIONS

Strong CYP3A4 Inducers: Avoid coadministration of FOTIVDA with strong CYP3A4 inducers.

USE IN SPECIFIC POPULATIONS

Lactation: Advise not to breastfeed.
Females and Males of Reproductive Potential: Can impair fertility.
Hepatic Impairment: Adjust dosage in patients with moderate hepatic impairment. Avoid use in patients with severe hepatic impairment.

To report SUSPECTED ADVERSE REACTIONS, contact AVEO Pharmaceuticals, Inc. at 1-833-FOTIVDA (1-833-368-4832) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see FOTIVDA Full Prescribing Information which is available at www.AVEOoncology.com.

About AVEO Pharmaceuticals, Inc.
AVEO is an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for patients with cancer. AVEO currently markets FOTIVDA® (tivozanib) in the U.S. for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies. AVEO continues to develop FOTIVDA in immuno-oncology and other novel targeted combinations in RCC and other indications, and has other investigational programs in clinical development. AVEO became a wholly owned subsidiary of LG Chem Life Sciences USA, Inc. on January 19, 2023. AVEO continues to operate under the AVEO Oncology, an LG Chem company, name.

About LG Chem, Ltd. and LG Chem Life Sciences
LG Chem, Ltd. (LG Chem) is a leading global chemical company with a diversified business portfolio in the key areas of petrochemicals, advanced materials, and life sciences. The company manufactures a wide range of products from high-value added petrochemicals to renewable plastics, specializing in cutting-edge electronic and battery materials, as well as drugs and vaccines to deliver differentiated solutions for its customers. LG Chem Life Sciences develops, manufactures, and globally commercializes pharmaceutical products, with a focus on Oncology, Immunology, and Metabolic diseases. Our mission is to transform people's lives through inspiring science and leading innovation. For more information, please visit www.lgchem.com

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