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Rigosertib Phase 1 results lead to disease-focused Phase 2 development

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Results of a phase 1 clinical trial reported at the American Association for Cancer Research (AACR) annual conference show that orally administered Rigosertib is well tolerated in patients with advanced solid tumors. This is the first trial in which orally administered Rigosertib, a dual kinase inhibitor, was studied in solid tumors. Intravenously rigosertib is already in phase 3 clinical trials for myelodysplastic syndrome and pancreatic cancer and oral rigosertib is being studied in a pair of Phase II trials in lower-risk transfusion dependent MDS patients. The drug candidate is being developed by Onconova Therapeutics, Inc., of Pennington, NJ.

Overall, 48 patients were included in the Phase I trial with oral rigosertib, and 7 remained on study for at least six months. Six head and neck cancer patients included in this study had failed platinum-based therapies, and 2 of these patients showed a response to Rigosertib – one with the disappearance of lung metastasis and another with greater than 50 percent decrease of liver metastasis. These 2 patients have received oral rigosertib treatment for 98 and 48 weeks.

"The results from the head and neck cancer patients are interesting, revealing that the drug worked in a subset of patients," says Antonio Jimeno, MD, PhD, investigator at the University of Colorado Cancer Center and director of the university's Head and Neck Cancer Medical Oncology Program. "To learn more about the relationship between response and genetic make-up of the tumor, we've been investigating molecular correlates in a surrogate Phase 2 trial in patient-derived

animal models of head and neck cancer."

As highlighted in the AACR presentation, genetic analysis of tumor samples from the Phase 1 trial and continuing genetic analysis of animal models, performed at both the Colorado Molecular Correlates Laboratory (CMOCO) and Dr. Jimeno's research laboratory, detected several potential biomarkers, including the genes PIK3CA and PTEN, which are both members of the signaling pathway targeted by the drug. Whole-exome sequencing of patient samples also revealed what Jimeno calls, "a short list of core alterations in genes for further exploration as predictive biomarkers."

"These promising results from human trial combined with relevant animal models established in our laboratories are helping us learn more about this drug and its mechanism of action. Based on these studies, we are initiating an 80-patient, multi-institutional Phase 2 trial," says Jimeno. In this trial, tissue samples from patients will be analyzed by sequencing and using other genomic tools to fully explore the predictive capability of these candidate biomarkers.

"We have seen meaningful activity in a subset of patients in the Phase I trial and we confirmed this in the surrogate animal model," Jimeno says. "The hope is that broad genetic analysis will help identify biomarkers for accurately matching the drug with the right patients in the future."

"It's an exciting time for an exciting drug," Jimeno says.

Provided by University of Colorado Denver