Results in Phase I trial of OMP-54F28, a Wnt inhibitor targeting cancer stem cells

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At the 50th Annual Meeting of the American Society for Clinical Oncology (ASCO), University of Colorado Cancer Center researchers reported results of a Phase I trial of OMP-54F28 (FZD8-Fc), an investigational drug candidate discovered by OncoMed Pharmaceuticals targeting cancer stem cells (CSCs). The drug was generally well tolerated, and several of the 26 patients with advanced solid tumors experienced stable disease for greater than six months. Three trials are now open for OMP-54F28 (FZD8-Fc) in combinations with standard therapy for pancreatic, ovarian and liver cancers, being offered at the CU Cancer Center and elsewhere.

"These are optimistic results for one of the first targeted therapies for cancer stem cells," says Antonio Jimeno, MD, PhD, investigator at the CU Cancer Center, director of the university's Cancer Stem Cell-Directed Clinical Trials Program, and principal investigator of the clinical trial at the CU Cancer Center site. "And it is great to work with such a science-focused sponsor, whose vision aligns with ours: bringing to the clinic cutting-edge drugs and ideas that are focused on targeting CSCs. In the context of the collaboration between the Gates Center for Stem Cell Biology and the CU Cancer Center this was the second clinical trial we offered to our patients with the specific intent to eliminate the CSCs in their tumors."

OMP-54F28 (FZD8-Fc) is an antagonist of the Wnt pathway, a key CSC signaling pathway that regulates the fate of these cells. The Wnt pathway is known to be inappropriately activated in many major tumor types,

including colon, breast, liver, lung and pancreatic cancers, and is critical for the function of CSCs. Because of this extensive validation, in the Jimeno lab and elsewhere, the Wnt pathway has been a major focus of anti-cancer drug discovery efforts. OMP-54F28 (FZD8-Fc) and a sister compound also developed by OncoMed, vantictumab (OMP-18R5), are two of the first therapeutic agents targeting this key pathway to enter clinical testing. In multiple preclinical models, OMP-54F28 (FZD8-Fc) has shown its effectiveness in reducing CSC populations, leading to associated anti-tumor activity, either as a single agent or when combined with chemotherapy.

"The ongoing line of work with this drug is an excellent example of the bench getting even closer to the bedside – our lab work with the drug in patient-derived xenograft models of disease makes possible the clinical trials taking place at the University of Colorado Hospital next door," Jimeno says.

The Phase I clinical trial of OMP-54F28 (FZD8-Fc) is an open-label dose escalation study in patients with advanced solid tumors for which there was no remaining standard curative therapy. Patients are assessed for safety, immunogenicity, pharmacokinetics, biomarkers, and initial signals of efficacy. The trial is conducted at Pinnacle Oncology Hematology in Scottsdale, Arizona, the University of Michigan Comprehensive Cancer Center, Ann Arbor, Michigan, and the CU Cancer Center under the direction of Principal Investigators Dr. Michael S. Gordon, Dr. David Smith and Dr. Antonio Jimeno, respectively.

The most common adverse events, mild to moderate and manageable, included dysgeusia (altered taste), fatigue, muscle spasms, decreased appetite, alopecia and nausea. One related Grade 3 or greater adverse event of Grade 3 increased blood phosphorus was reported. One moderate sacral insufficiency fracture occurred in one patient at the highest tested dose of 20 mg/kg every three weeks after 6 cycles.

"The drug is now being developed in combination with standard of care in three Phase 1b clinical trials, with the CU Cancer Center being one of the active sites," Jimeno says. "In pancreatic, ovarian and liver cancers, we hope that by adding anti-cancer stem cell drugs to standard of care, we can control proliferating cells within the tumor that could otherwise help the tumor regenerate in the face of existing chemotherapies."

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