Clinical trial finds new class of cancer drugs safe and effective

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The safety and preliminary efficacy of a new class of tumor fighting drugs were reported today by Scottsdale Healthcare's Virginia G. Piper Cancer Center Clinical Trials and the Translational Genomics Research Institute (TGen).

Early results from the phase I, first in-human study of an RNA interface (RNAi) drug were announced during the American Association for Cancer Research (AACR) Annual Meeting 2013, April 6-10, in Washington, D.C. The drug, TKM-080301 (also known as TKM-PLK1) is being developed by Tekmira Pharmaceuticals Corporation.

The study was conducted at Virginia G. Piper Cancer Center Clinical Trials at Scottsdale Healthcare, a partnership with TGen. It found that the RNAi drug acts by silencing the PLK1 gene involved in tumor growth and can be safely administered in humans. Most patients tolerated the drug well; some showed therapeutic benefit.

"RNAi therapies are a unique approach to cancer treatment as they have the potential to 'turn off' the genes' coding for proteins involved in cancer cell division," said Dr. Ramesh K. Ramanathan, Medical Director of Virginia G. Piper Cancer Center Clinical Trials at Scottsdale Healthcare and deputy director of the Clinical Translational Research Division of TGen. "Using a lipid nanoparticle, the RNAi drug can be delivered to a cancer cell to block the expression of specific proteins involved in tumor growth."

TKM-080301 targets a specific gene called polo-like kinase 1 (PLK1), which codes for a protein involved in tumor cell growth. Prior research has shown that high levels of PLK1 are present in many types of cancer, including many of the more aggressive forms.

"Our preclinical results have shown that by decreasing PLK1 levels in cancer cells, we can stop tumor growth and kill the cancer cells," Dr. Ramanathan said.

He and his colleagues have been enrolling patients with advanced solid tumors or lymphoma into the ongoing multicenter, open-label, dose-escalation study. Sequential cohorts of three to six patients have been assigned to escalating doses of TKM-080301 as a 30-minute intravenous infusion. To date, the researchers have assigned 23 patients to the drug at doses ranging from 0.15 mg/kg per week to 0.9 mg/kg per week.

The most common drug-related adverse events have been mild to moderate and include fever, chills, nausea, vomiting and fatigue. Dose-limiting toxicities were observed at the 0.9 mg/kg per-week dose. One patient with a history of asthma experienced shortness of breath and hypoxia; another patient had thrombocytopenia. The researchers subsequently reduced the maximum dose to 0.75 mg/kg per week.

Two patients have been assigned to TKM-080301 for more than six months and have shown no evidence of cumulative toxicity. One of these patients has stable disease and the other has a durable confirmed partial response.

"RNAi therapies, such as the one used in our study, have the potential to make a significant and broad impact on how we treat cancer because we have the ability to target virtually any protein involved in the disease," Ramanathan said. "This approach has the potential to augment the currently available cancer treatments to improve outcomes for the

patient."

Provided by The Translational Genomics Research Institute