

Novel targeted drug shows promise against advanced small cell lung cancer

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The experimental "smart-bomb" drug rovalpituzumab tesirine (Rova-T) appears safe and shows efficacy in treating patients with advanced small cell lung cancer (SCLC), according to results from a first-in-human clinical trial to be presented today by a Memorial Sloan Kettering Cancer Center (MSK) researcher at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago. (Abstract #LBA8505)

Further, the findings show that [patients](#) responded better to the drug when their tumors expressed high levels of delta-like protein 3 (DLL3), the protein Rova-T targets.

SCLC accounts for approximately 15 percent of all lung cancers and is particularly aggressive—about two-thirds of patients have extensive-stage disease when they are first diagnosed, and the median survival for these patients is less than a year. Substantial therapeutic advances for this disease have lagged far behind other cancers. Rova-T is the first molecularly targeted drug to show antitumor efficacy in SCLC.

"The goal is always to give the right patient the right drug at the right time, but patients with advanced small cell lung cancer have not benefited from any of the new targeted therapies available to patients with other types of cancer," said Charles M. Rudin, MD, PhD, Chief of the Thoracic Oncology Service at MSK, who will present the findings during a press briefing on impactful clinical research from the ASCO meeting. "They desperately need new treatment options, so the ability to predict whether a patient might respond to Rova-T by testing their tumor

for overexpression of the DLL3 protein is crucial because it may ultimately help us give this drug to the patients most likely to benefit from it, and avoid giving it to patients who won't."

The DLL3 protein is highly expressed in approximately two-thirds of SCLC tumors. Rova-T, an antibody-drug conjugate, binds to DLL3 on the surface of tumor cells and operates like a Trojan horse, bringing a toxic payload into the cell. The payload is too potent to give as a standalone drug but is relatively safe when attached to the antibody. Because the DLL3 protein is not expressed in healthy cells, damage to normal tissue while receiving Rova-T is limited.

Key Findings

The clinical trial included 74 patients with SCLC that had progressed after at least one course of therapy. Of the 60 evaluable patients treated with doses in the active range of 0.2-0.4 mg/kg, 68 percent experienced at least stabilization of disease, meaning their cancer did not get worse, and 18 percent had significant confirmed tumor reductions.

The study included 26 evaluable patients with tumors that overexpressed DLL3. Stable disease was achieved in 89 percent of these patients; 39 percent had significant confirmed tumor reductions.

Twelve of the patients whose tumors overexpressed DLL3 received Rova-T as third-line treatment, for which no approved therapy currently exists. Half of these patients had significant tumor reductions, and 92 percent experienced at least stabilization of disease. Four of these patients lived longer than six months, including two who lived for at least 18 months.

The side effects from Rova-T were manageable and included fluid accumulation, low platelet count, and rash.

What's Next

This was an early-phase clinical trial, so the results are considered preliminary until confirmed in larger trials with more patients.

"I encourage all oncology physicians and patients to seek out information about clinical trials, as they often give patients the opportunity to receive new drugs and other therapies years before they are more widely available," Dr. Rudin said. "It's increasingly important to remember that nearly every advance in cancer treatment available today was first evaluated in a clinical trial."

He added that future [clinical trials](#) investigating Rova-T's efficacy in treating SCLC will generally focus on the subset of patients whose tumors express the DLL3 target.

MSK currently has an open Rova-T clinical trial for patients with advanced SCLC who have received at least two prior therapies (NCT02674568). All patients enrolled in this pivotal trial will receive Rova-T, as there is no standard third-line treatment to test Rova-T against.

Dr. Rudin also noted there are other important lines of research to explore around Rova-T, including how the drug affects the tumor microenvironment; whether it prompts an immune response; and if there is a population of patients for whom this drug might not be safe.

Other institutions co-authoring the presentation at ASCO 2016 include the Sarah Cannon Research Institute and Tennessee Oncology, Nashville; Duke Cancer Institute, Durham; MD Anderson Cancer Center, Houston; Washington University, St. Louis; University of Alabama-Birmingham; and Stemcentrx, Inc, South San Francisco, who sponsored the trial.

Provided by Memorial Sloan Kettering Cancer Center

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