2 new therapies show promise for cancer patients

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Clinical researchers at Scottsdale Healthcare and TGen today announced the results of two clinical trials that show promise for patients battling cancer.

The Phase I clinical trial findings, presented at the this weeks Annual Meeting of the American Association for Cancer Research by Daniel Von Hoff, MD, FACG, focused on basal cell carcinoma (BCC) and pancreatic cancer. The Arizona trials were conducted at TGen's Clinical Research Service (TCRS) at Scottsdale Healthcare, a strategic alliance between TGen and Scottsdale Healthcare's Clinical Research Institute.

Basal Cell Carcinoma

In the first trial, a novel molecule, GDC-0449, shrinks tumors in basal cell carcinoma (BCC) while having limited side effects, including a loss of sense of taste, and a small amount of hair loss and weight loss, suggesting a viable new treatment option. GDC-0449 works by blocking a pathway — a series of chemical reactions within a cell— known as Hedgehog, containing two genes (PTCH and SMO) that lead to a known tumor-promoting gene called GLI1. Alterations in any of these genes have been shown to lead to basal cell carcinoma and other diseases. GDC-0449 is a chemical synthetic designed to replicate the properties of cyclopamine, a chemical found in nature.

"Basal cell carcinoma affects about one million people a year and a

proportion of these patients have disease that is not curable with surgery. We currently do not have any treatments that can effectively slow tumor growth in these advanced patients. This finding has potential importance in this population," said Daniel D. Von Hoff, M.D., Physician in Chief at the Translational Genomics Research Institute (TGen) and Chief Medical Officer for the Scottsdale Clinical Research Institute at Scottsdale Healthcare.

Typically diagnosed with a simple biopsy, the risk of BCC increases for those individuals with a family history, or prolonged exposure to ultraviolet (or UV) rays from the sun. While BCC has an extremely low rate of metastasis, it can lead to scarring and disfigurement if left untreated.

The trial results showed durable clinical benefit —defined as tumor shrinkage visible on X-ray or other physical exam or improvement in symptoms without tumor growth— was observed in eight out of the nine patients evaluated.

The first patient treated in the trial has shown clinical improvement for approximately 450 days and is ongoing, Von Hoff says, with almost no side effects beyond minimal hair loss.

"He came to us short of breath and in pain, but he has had a very dramatic response with this drug," Von Hoff said.

Further evaluations of the study participants measured the presence of GLI1 in skin cells sampled from the participants. Among all patients tested to date, there was reduction in this marker, indicating that the drug was affecting the hedgehog pathway.

The trial, sponsored by Genentech, also included clinical sites at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

University, Baltimore, Maryland and Karmanos Cancer Institute, Detroit, Michigan.

Pancreatic Cancer

In the second trial, Von Hoff and colleagues showed that a novel combination of two drugs (nanoparticle albumin-bound paclitaxel, or "nab-pacilitaxel" and gemcitabine) showed a significant clinical benefit in more than 80 percent of pancreatic cancer patients.

"Unfortunately, most patients with pancreatic cancer have a very poor survival, and until now, the only option has been gemcitabine alone or in combination with erlotinib," said Von Hoff.

The researchers utilized the Target Now™ tumor profiling analysis, a cutting-edge oncology testing service performed by Caris Dx and Caris MPI, to better understand the characteristics expressed in patient's tumors. In this ongoing research program, Von Hoff and colleagues found the SPARC (Secreted Protein Acidic and Rich in Cysteine) protein to be commonly found in pancreatic cancer specimens. The SPARC protein is being investigated by Abraxis BioScience in this trial as a potential target for nab-paclitaxel. A test for SPARC, developed at Abraxis and Caris MPI and applied by Caris MPI under contract with Abraxis, was utilized to analyze SPARC in the pancreatic cancer patients in the trial.

The finding of SPARC protein in pancreatic cancer patients, also described by other investigators, was the basis for this phase I clinical trial that Von Hoff presented at AACR.

"Chemotherapy often means combining more than one drug, and we do not want to just take the next thing off the shelf. We want to know as much about a tumor as possible going in," Von Hoff said.

Researchers reported on the first 20 patients of what will eventually be a 42-patient trial.

“This was a phase I trial, and phase I trials are usually designed to test safety, hoping it will also determine efficacy. The fact that we saw this kind of activity in a phase I trial is dramatic,” Von Hoff said.

“The rationale behind the combination of Gemcitabine plus Abraxane was based on careful science and was designed and executed by some of the leading experts in pancreas cancer in the world. While the data is preliminary and longer follow-up will be important, the biochemical and radiographic responses look very encouraging”, says Dr. Laheru of Johns Hopkins Kimmel Cancer Center.

Source: The Translational Genomics Research Institute