PEOPLE

CU Cancer Center

Dan Theodorescu, MD, PhD, started his position as director of the Samuel Oschin Comprehensive Cancer Institute at Cedars-Sinai Medical Center in Los Angeles, CA, on July 1. He previously served as director of the University of Colorado Cancer Center in Aurora, where he was also a professor of surgery and pharmacology. Theodorescu is the founding co-editor-in-chief of *Bladder Cancer* and is a member of the editorial board of *Cancer Research*. In addition, he serves on the National Cancer Policy Forum of the National Academies. Theodorescu has studied the molecular mechanisms underlying bladder cancer, discovering genes that regulate tumor growth and metastasis.

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With Theodorescu's departure, **Richard Schulick, MD, MBA,** became director of the University of Colorado Cancer Center on July 1. He will continue to serve as the chair of the department of surgery at the University of Colorado School of Medicine. Previously, he was chief of the division of surgical oncology; a professor of surgery, oncology, and obstetrics and gynecology; and director of the pancreas cancer program at Johns Hopkins University in Baltimore, MD. Schulick has authored more than 300 publications and is the principal investigator on several clinical trials.

Pembrolizumab OK'd for Cervical Cancer

In June, the FDA approved the PD-1 inhibitor pembrolizumab (Keytruda; Merck) as a second-line treatment for patients with recurrent or metastatic cervical cancer whose tumors express PD-L1. It's the first such drug approved for a gynecologic cancer.

The FDA concurrently approved the PD-L1 IHC 22C3 pharmDx Kit (Dako) as a companion diagnostic.

Currently, patients with advanced cervical cancer receive chemotherapy, often in combination with bevacizumab (Avastin; Genentech), says Charles Drescher, MD, of Fred Hutchinson Cancer Research Center in Seattle, WA. However, few patients are cured by first-line treatment, and second-line options have been a "potpourri of dealer's choice of modestly active drugs," he says.

"Fortunately, in the U.S., cervical cancer is not a particularly common disease, and metastatic disease is even less common," he says, but a better second-line treatment option "is an urgent need for the population—there really are no [effective] alternatives."

Pembrolizumab was approved based on results of the ongoing phase II KEYNOTE-158 trial, a basket trial testing its activity in 11 types of advanced solid tumors. In the cervical cancer arm, 77 of 98 patients expressed PD-L1 with a combined positive score of at least 1 (the ratio of the number of PD-L1–expressing tumor and infiltrating immune cells to the total number of tumor cells). Patients were treated with the drug after chemotherapy and had an objective response rate (ORR) of 14.3%, with 11.7% partial responses and 2.6% complete responses. Of the patients who responded, 10 of 11 responded for at least 6 months.

"It's a whole new option that we just didn't have [before]," Drescher says, adding that because pembrolizumab is already approved for so many other indications, "its toxicity profile is well known, it's not hard to deliver, and it's available most anywhere, so I think that it'll be very rapid clinical uptake."

For Krishnansu Tewari, MD, of the University of California, Irvine, in Orange, who, on behalf of the NCI-sponsored Gynecologic Oncology Group, ran the trial that led to bevacizumab's approval in 2014, any option for patients at high risk for progression and death "is a good thing."

However, he notes that he is not overly impressed with the ORR and points out that although most women with squamous cervical cancer express PD-L1, that isn't necessarily true for patients with other histologies, such as adenocarcinoma.

"To an extent, it will change practice because we have nothing else, but we need to do better," he says, adding that researchers are exploring other options.

For example, the AIM2CERV study is evaluating the use of maintenance axalimogene filolisbac (ADXS11-001; Advaxis), a *Listeria*-based immunotherapy, following first-line therapy, and Iovance Biotherapeutics is conducting a phase II trial of LN-145, an adoptive T-cell therapy with autologous tumor-infiltrating lymphocytes. Additionally, Genentech is running clinical trials on its PD-L1 inhibitor atezolizumab (Tecentriq).

Other clinical trials are investigating combination therapy for cervical cancer, including pembrolizumab plus chemotherapy and radiation, and AstraZeneca's durvalumab (Imfinzi) plus tremelimumab and radiation.

"When the Gynecologic Oncology Group did the [bevacizumab] study, no one was doing any work in the cervix cancer field, and now there's probably 10 different studies going on," Tewari says. "Hopefully one of these new treatments will be even more effective." –*Catherine Caruso* ■

LOXO-292 Reins In RET-Driven Tumors

A selective and potent RET inhibitor, LOXO-292 (Loxo Oncology), is showing early signs of efficacy, yielding responses across a range of *RET* alterations and tumor types, and a favorable safety profile, according to interim phase I data presented on June 2 at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL (J Clin Oncol 36, 2018 [suppl; abstr 102]).

"It's very exciting to see a drug like this that's not only active but also highly tolerable," said lead trial investigator Alexander Drilon, MD, of Memorial Sloan Kettering Cancer Center in New York, NY, who made the presentation. "It really lends itself to prolonged dosing, especially considering that these patients can have long-term benefit with this treatment."

Gene fusions involving *RET* occur in approximately 10% of papillary thyroid cancers (PTC), 2% of non–small