## PEOPLE


University of Michigan Rogel Cancer Center

In June, **Lori L. Pierce, MD,** began a 1-year term as president of the American Society of Clinical Oncology (ASCO) at the ASCO20 Virtual Scientific Program, succeeding Howard "Skip" Burris III, MD. Pierce is a professor of radiation oncology and vice provost for Academic and Faculty Affairs at the University of Michigan in Ann Arbor. Her research focuses on improving treatment for breast cancer with radiotherapy and radiosensitizing agents. She also studies how women with *BRCA1/2*-positive breast cancer fare when treated with radiotherapy.


Dana-Farber Cancer Institute

**George D. Demetri, MD,** professor of medicine at Harvard Medical School in Boston, MA, received the David A. Karnofsky Memorial Award at the ASCO virtual meeting for his contributions to translational research in cancer. Demetri, who is also senior vice president for experimental therapeutics and director of the Sarcoma Center at Dana-Farber Cancer Institute in Boston, studies targeted therapies for sarcomas. His research led to the approval of imatinib mesylate (Gleevec; Novartis) for the treatment of gastrointestinal stromal tumors.


Dana-Farber Cancer Institute

Also at the ASCO meeting, **Pasi A. Jänne, MD, PhD,** professor of medicine at Harvard Medical School and director of the Belfer Center for Applied Cancer Science and the Lowe Center for Thoracic Oncology, both at Dana-Farber, received the Science of Oncology Award for his contributions to basic cancer research. Jänne studies genomic alterations in lung cancer. He has been involved in the preclinical and clinical development of therapies that target ALK, EGFR, and MET, among others.

## COM701 Shows Antitumor Activity, +/– Nivolumab

A novel immune checkpoint inhibitor has shown early signs of efficacy, both on its own and combined with the PD-1 inhibitor nivolumab (Opdivo; Bristol-Myers Squibb), in patients with a variety of advanced solid tumors. Findings from this ongoing phase I trial were presented by Ryan Sullivan, MD, of Massachusetts General Hospital in Boston, during the American Association for Cancer Research (AACR) Virtual Annual Meeting I: April 27–28, 2020.

The investigational agent, COM701 (Compugen), targets the DNAM–TIGIT signaling pathway in T cells. Specifically, COM701 prevents the coinhibitory receptor PVRIG from binding to its ligand, PVRL2, which would otherwise—alongside interactions between the related receptor TIGIT and a different ligand, PVR—drive immunosuppression in the tumor microenvironment. "Pharmacologic inhibition frees PVRL2 and PVR to interact instead with [the costimulatory receptor] DNAM, resulting in enhanced T-cell effector function," Sullivan explained.

COM701's monotherapy potential was first highlighted at the 2019 Society for Immunotherapy of Cancer Annual Meeting. During the AACR meeting, Sullivan reported updated data from this cohort of patients, as well as preliminary findings from the combination arm with nivolumab. "Coinhibition of PD-1 is a logical approach," he noted, "given that the PD-1 pathway is a known negative regulator of DNAM signaling."

A wide variety of tumor types were represented in this trial, Sullivan added, including melanoma, mesothelioma, and adenoid cystic carcinoma; all patients had advanced or metastatic disease and had had a median of four to six prior therapies. Of 28 evaluable patients, 16 were given COM701 alone, and 12 received nivolumab as well. The majority saw their disease stabilize, several durably (more than 6 months). Taken together with one partial response in each study arm, the clinical benefit rate was 69% in the COM701 cohort and 75% in the combination group. COM701 was largely well tolerated, Sullivan said, with fatigue and nausea being the main side effects.

The two partial responses were seen in a patient with primary peritoneal carcinoma who received single-agent COM701, and another with microsatellite-stable colorectal cancer (MSS-CRC) in the combination arm. Sullivan observed that the former's "pelvic metastases have regressed notably," and both patients remain responsive to treatment after many months—almost a year now for the patient with MSS-CRC. "These are tumor types that aren't predicted to respond to immune checkpoint inhibition," he pointed out.

"The MSS-CRC case is especially interesting," agreed study discussant Ignacio Melero, MD, PhD, of Clínica Universidad de Navarra in Pamplona, Spain. "Nivolumab's activity in this patient population is extremely limited, yet here there was clear radiologic evidence of response, followed by a decrease in circulating levels of CEA," a prognostic marker for colorectal cancer.

For Sullivan, COM701 is another step toward fulfilling the "critical unmet need of finding better options for patients who are primarily refractory to, develop resistance on, or relapse following current checkpoint blockade."

Melero, too, believes that "PVRIG is a promising target to advance in immunotherapy." He would like to see translational data emerge from this trial, noting that with COM701, "the quest for a useful biomarker for patient selection is very much pending."

Meanwhile, based on preclinical evidence supporting parallel inhibition of not only PVRIG and PD-1 but also TIGIT, the triple combination of COM701 with nivolumab and BMS-986207, an experimental anti-TIGIT agent, will soon be evaluated, Sullivan said. A phase I/II trial is expected to launch later this year. Given that there are multiple companies jostling in the TIGIT space—including Roche (tiragolumab) and Merck (MK-7684)—this avenue looks set to be closely watched for its therapeutic potential. –*Alissa Poh* ■