IMMUNOTHERAPY — THE WAY FORWARD IN CANCER MEDICINE

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Immunotherapy, specifically immune checkpoint inhibitors targeting the PD-1/PD-L1 pathway, took center stage at the recent American Society of Clinical Oncology (ASCO) meeting in Chicago, Illinois. The Arie Crown Theatre was the site of the Clinical Science Symposium in relation to these paradigm-shifting therapies where nearly 1,500 physicians, nurses and collaborators were packed to hear about the therapies that would help not only melanoma patients but also those with lung, renal, ovarian and a host of other carcinomas. The data presented, build on a deeper understanding of the biological interplay between tumor cells and the immune system; specifically, immune checkpoint inhibition targeting the PD-1/PD-L1 pathway.

Dr. Omid Hamid, MD, Director of the Melanoma Program and Chief of Clinical Research at The Angeles Clinic and Research Institute, presented groundbreaking new trial data on “Clinical activity, safety, and biomarkers of MPDL3280A, an engineered PD-L1 antibody in patients with locally advanced or metastatic melanoma,” to a large audience at the ASCO meeting.

The programmed death ligand1 (PD-L1) protein is frequently over expressed on the surface of many cancer cells such as melanoma, lung cancer, colon cancer, renal cell cancer and other solid tumors. The protein functions as a disguise, allowing cancer cells to evade recognition by the immune system, thus promoting tumor growth. The agent MPDL3280A attaches to the PD-L1 protein, exposing the cancer cell to the patient’s immune system, thereby restoring the body’s anti-tumor T cell activity. In the study presented, MPDL3280A was administered intravenously every three weeks for 16 cycles. A response (CR/PR) or stable

ABOUT US

The Angeles Clinic and Research Institute was established by a group of physicians who came from academic backgrounds and sought to establish an environment where world-class patient care was the top priority. The Clinic’s physicians include widely recognized oncologists and leaders in cancer medicine who, together with expert radiology services, radiation oncology, specialized oncologic nurses, and a dedicated support staff, have created a state-of-the-art center for oncology in the Los Angeles area. In addition to superb clinical care, our physicians are known for their world-class clinical research. The Institute has earned an international reputation for developing new cancer therapies, providing the best in traditional and experimental treatments, and expertly guiding and training the next generation of clinicians and researchers.

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disease (SD) was demonstrated in 34% of the melanoma patients. A striking 87% response rate (CR/PR and SD) was noted in those with PD-L1 positive tumors; however, 20% of PD-L1 negative tumors also responded suggesting some activity in this group as well. The toxicity profile of this agent was favorable, with no dose-limiting toxicity identified up to a dose of 20 mg/kg. Notably, no episodes of pneumonitis or colitis were observed. As with other agents in this class, responses appear to be durable. Based on this level of anti-tumor activity and the favorable toxicity profile observed, trials combining MPDL3280A with other agents are ongoing and available at The Angeles Clinic and Research Institute (www.theangelesclinic.org).

Results of patients with other solid tumors including lung and kidney cancer, who were also treated with MPDL3280A, were also reported at the ASCO meeting.

“The Angeles Clinic and Research Institute has been involved with PD-1/PD-L1 antibodies since their inception. We were the first to have lambrolizumab (MK-3475), a drug deemed by the FDA to be a breakthrough therapy, available for our patients,” states Dr. Hamid. Important data with this agent were also updated at ASCO. In 135 patients with advanced melanoma, including those who had experienced disease progression after CTLA-4 antibody monotherapy (ipilimumab), a 38% response rate was noted. With a median follow-up of 11 months, median duration of response has not been reached; again demonstrating that responses to this class of agents are durable and clinically meaningful. The primary objective of the study was to evaluate toxicity with varying doses. Most noted toxicities were grade 1 or 2 and consisted of generalized symptoms, including fatigue, fever, chills, myalgia and headache. Grade 3 or 4 drug-related adverse events were reported by 13% of patients. Results from this body of work were simultaneously published in The New England Journal of Medicine (Hamid et al).

Dr. Jedd Wolchok of Memorial Sloan Kettering Cancer Center presented data at ASCO on the combination of the anti-PD-1 antibody nivolumab with ipilimumab. These data were also simultaneously published in The New England Journal of Medicine (Wolchok et al). Much has been made of the data presented, which also demonstrated high response rates with PD-1 directed therapy. The Angeles Clinic and Research Institute is proud to be the first site in the United States with the ability to offer this therapy (nivolumab and ipilimumab combination) to our patients through a major phase III collaborative effort.

The field of immunotherapy has had considerable impact in the treatment of melanoma. More importantly, we believe the lessons learned to date have broad application for all cancers. The future of oncology remains rooted in the development of new therapeutic strategies. The Angeles Clinic and Research Institute remains committed to providing all of our patients with the latest in innovative and paradigm-shifting therapies.

References
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