was long lasting. Further, 40 percent of patients who received varying concurrent dosages had an objective response — meaning at least a 50 percent reduction in tumor size. Side effects from the drug combination were manageable and often reversible.

“We are very excited about the response rates these patients have experienced. This kind of deep and rapid tumor regression has never been seen in melanoma using immunotherapy, and suggests that these two drugs could be better used in combination than alone,” said Jedd D. Wolchok, MD, PhD. Dr. Wolchok, a medical oncologist at the Ludwig Center for Cancer Immunotherapy at Memorial Sloan Kettering Cancer Center, is lead author on *The New England Journal of Medicine* paper and also presented the findings at ASCO.

Dr. Wolchok and his team combined ipilimumab and nivolumab because promising results in preclinical testing suggested the drugs impact the immune system in a complementary way. By blocking the inhibitory marker CTLA-4, ipilimumab, which the FDA approved for advanced melanoma in 2011, activates the immune system, prompting T cells to start attacking the tumor. Blocking PD-1 further activates T cells in a different manner, allowing them to continue the attack.

“Previous studies had shown that ipilimumab alone could prolong overall survival in advanced melanoma patients, and nivolumab alone could produce durable tumor responses in melanoma and other cancers, so the combination of the two drugs was quite logical and well supported by preclinical and clinical trial data,” he said.

However, Dr. Wolchok notes that not all patients respond to immunotherapy and determining why some patients do not is becoming an extremely important part of advancing this field.

Because of the strong Phase I findings, researchers will begin testing the combination this June as a therapy for patients newly diagnosed with advanced melanoma in a randomized Phase III trial led by Memorial Sloan Kettering and taking place at more than 150 institutions worldwide.

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