molecular signatures unveiled in this study, and extending their analysis to encompass more cancers.

“There are certainly cancers in which biological sex is a prognostic factor, so this is a very intriguing study,” says Michael Davies, MD, PhD, deputy chair of melanoma at MD Anderson, who wasn’t involved in the research. “These candidates [sex-biased signatures] will need to be explored in greater detail, including in the context of systemic therapies. Additional confirmation may lead to the development of sex-specific therapeutic approaches.” –Alissa Poh

Nods for Atezolizumab and Nivolumab from FDA

The FDA has greenlighted atezolizumab (Tecentriq; Genentech) and nivolumab (Opdivo; Bristol-Myers Squibb) under its accelerated approval program for advanced urothelial carcinoma and relapsed or refractory classical Hodgkin lymphoma (cHL), respectively. Both drugs target the same immune checkpoint. Atezolizumab prevents the PD-L1 ligand from interacting with its receptor, PD-1; nivolumab blocks the receptor itself.

Atezolizumab is the first PD-L1 inhibitor to receive the FDA’s nod, and also the first approved drug for urothelial carcinoma in more than 20 years. “Essentially, it’s been a desert for therapeutic advancement since the early 1990s,” says Jonathan Rosenberg, MD, a medical oncologist at Memorial Sloan Kettering Cancer Center in New York, NY.

The FDA’s decision on atezolizumab was based on data from a phase II study, led by Rosenberg, involving 310 patients with locally advanced or metastatic urothelial carcinoma. The objective response rate (ORR) for all patients was 15%, and considerably higher (26%) for those with PD-L1 expression in 5% or more of their tumor-infiltrating immune cells. The agency has also approved a companion diagnostic, the Ventana PD-L1 (SP142) assay, to evaluate PD-L1 status in patients prior to treatment with atezolizumab.

According to Rosenberg, the response durability is key—after a year of treatment, 84% of responders showed no sign of tumor progression, and 15 of these patients no longer had detectable tumors. “That’s almost unheard of in platinum chemotherapy-resistant bladder cancer,” he says.

Nivolumab is already approved for melanoma, non–small cell lung cancer, and renal cell carcinoma. With cHL added to the list, it’s now the first PD-1 inhibitor approved for a hematologic malignancy. The PD-L1 and PD-L2 genes on chromosome 9p24 are frequently amplified in cHL, resulting in overexpression of these ligands.

“It’s thought that this is a genetically hardwired mechanism that cHL cells use to limit an effective immune response against the tumor,” says Margaret Shipp, MD, a medical oncologist at Dana-Farber Cancer Institute in Boston, MA, and an investigator on two phase II studies of nivolumab in cHL, upon which the FDA based its decision.

The two trials enrolled a total of 95 patients with cHL whose disease was refractory to or had relapsed after autologous stem cell transplantation and post-transplantation treatment with the CD30-targeting antibody–drug conjugate brentuximab vedotin (Adcetris; Seattle Genetics). Treatment with nivolumab induced an ORR of 65%, including seven complete remissions. The median duration of response was 8.7 months.

At the American Society of Clinical Oncology’s annual meeting in Chicago, IL, June 3–7, updated data from 80 patients in one of the studies (CheckMate-205) were presented. The ORR with nivolumab was 66%—including 31 of 43 patients who didn’t respond to brentuximab vedotin—and the median duration of response was 7.8 months. The median progression-free survival was 10 months.

Full approval for atezolizumab and nivolumab is contingent upon randomized phase III studies assessing additional end points, including median overall survival. –Kim Smuga-Otto

For more news on cancer research, visit Cancer Discovery online at http://cancerdiscovery.aacrjournals.org/content/early/by/section.
Correction: Nods for Atezolizumab and Nivolumab from FDA

In this article (Cancer Discov 2016;6:811), which was published in the August 2016 issue of Cancer Discovery (1), the Ventana PD-L1 (SP142) assay, a complementary diagnostic, was incorrectly referred to as a companion diagnostic. The online version of the article has been corrected. The publisher regrets the error.

REFERENCE

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