In the nonsquamous population, Paz-Ares and colleagues demonstrated that nivolumab benefit appeared greater in patients with PD-L1 expression at all cutoffs — which included 1%, 5% and 10% expression levels in tumor cells. Among patients with PD-L1 expression in 1% or more of tumor cells, those who received nivolumab demonstrated a median OS that exceeded 17 months, whereas patients who received docetaxel demonstrated a median OS of 9 months. Patients with 10% or greater PD-L1 expression demonstrated the greatest OS benefit with nivolumab (HR = 0.4; 95% CI, 0.27-0.59). Higher PD-L1 expression also appeared associated with a greater response rate with pembrolizumab in the study by Garon and colleagues (≥ 50% PD-L1 expression, 45% vs. < 1% PD-L1 expression, 10.7%), as well as prolonged median PFS in the atezolozumab study by Spira and colleagues (9.7 months vs. 3.9 months; HR = 0.57; 95% CI, 0.28-1.11).

However, patients in the squamous population of the CheckMate 017 trial derived benefit from nivolumab regardless of PD-L1 expression. PD-L1 overexpression potentially will be one biomarker in the treatment of NSCLC, although its use is a work in progress, Herbst said.

“Ultimately, I believe PD-L1 is going to be a biomarker,” Herbst said. “Right now, it’s not a good enough biomarker for me to exclude someone from immune checkpoint therapy, because even the group that was negative for the biomarker still seemed to have at least equal benefit to docetaxel with a potential tail on the curve. There are also major issues with tissue heterogeneity. There could even be some long-term benefit for PD-L1-negative patients.”

However, the data have showed that anyone with at least 1% positivity of PD-L1 expression — a very low threshold — may benefit, rendering the biomarker relatively ineffective, Spira told HemOnc Today.

“The only section where there is not a significant benefit is the low-expression group or the negative group and, in that scenario, the therapy is no different than docetaxel,” Spira said. “Given the side-effect profile, there is probably not a patient in the world who would not want to receive atezolozumab compared with docetaxel.”

The biggest problem is inconsistency in the biomarker assays, Spira added.

“Given what we’ve seen and what we know, PD-L1 status is going to become irrelevant,” Spira said. “Part of the issue is, it’s really difficult to get across common language because of the way these drugs are being approved. All the assays are being done for one particular drug. This is unique compared with everything else in oncology, and it is going to be hard to compare biomarkers.”

There has been some headway in the development of a biomarker for all the anti-PD-L1/PD-1 drugs, but researchers await data to determine each biomarker’s practical importance as the drugs reach FDA approval, Spira added.

The ways in which researched tested and defined “high” PD-L1 expression differs in each of these studies, Matthew D. Cover Story continues on page 12.