Pembrolizumab Improves OS in Treatment of Advanced Urothelial Cancer

By Dave Levitan

The programmed death 1 (PD-1) inhibitor pembrolizumab yielded significantly improved overall survival (OS) compared with investigator’s choice chemotherapy as second-line therapy in advanced urothelial cancer, according to a new study. This is the first second-line option to offer improved outcomes in this setting.

There is no standard therapy in the second-line setting for this malignancy; paclitaxel, docetaxel, and vinflunine are commonly used but have not been shown to offer substantial clinical benefit. The new KEYNOTE-045 study included 542 patients randomized to either pembrolizumab (270 patients) or investigator’s choice of those three chemotherapy agents (272 patients); the results were presented by Andrea Necchi, MD, of the Fondazione IRCCS Istituto Nazionale dei Tumori in Milan, Italy, at the European Cancer Congress 2017 in Amsterdam.

Most patients in the study had visceral disease (87.3%), and 34.3% had liver metastases. The median follow-up period was 9.0 months, and pembrolizumab significantly improved OS compared with chemotherapy. The median OS was 10.3 months with pembrolizumab compared with 7.4 months with chemotherapy, for a hazard ratio (HR) of 0.73 (95% CI, 0.59–0.91; \( P = .0022 \)).

There was no difference with regard to progression-free survival, with a median of 2.1 months with pembrolizumab and 3.3 months with chemotherapy, for an HR of 0.98 (95% CI, 0.81–1.19; \( P = .42 \)).

The objective response rate was better with the immunotherapy agent, at 21.1% compared with 11.4% with chemotherapy, for a treatment difference of 9.6% (\( P = .0011 \)).

There were fewer adverse events of any grade with pembrolizumab (60.9% vs 90.2%), as well as fewer grade 3-5 treatment-related adverse events (15.0% vs 49.4%); four patients in each study arm died due to treatment-related adverse events.

Necchi noted that the better toxicity profile is important “because this patient population tends to be mostly elderly patients who have many other illnesses and health conditions as well,” according to a press release.

Necchi also noted that the median duration of response was not reached with pembrolizumab, while it was only 4.3 months with investigator’s choice chemotherapy.

“KEYNOTE-045 is a landmark study,” Necchi said. “It represents a real advance in the second-line treatment of advanced bladder cancer. ...These results support the use of pembrolizumab as the new standard of care for advanced bladder cancer.”