

Pembrolizumab Improves Survival in Advanced Urothelial Cancer

Pembrolizumab (Keytruda, Merck) improved overall survival (OS) compared with chemotherapy in patients who had platinum-refractory advanced urothelial cancer, a new open-label phase 3 study found. This finding will be “practice-changing,” according to an accompanying editorial.

For KEYNOTE-045, which appeared online February 17 in the *New England Journal of Medicine*, Dr Joaquim Bellmunt and colleagues randomly assigned 542 patients with advanced urothelial cancer that had recurred or progressed after platinum-based chemotherapy to receive either pembrolizumab or the investigator’s choice of chemotherapy (vinflunine or a taxane).

After a median follow-up of 14.1 months, OS was significantly longer in the pembrolizumab group than in the chemotherapy group (10.3 vs 7.4 months; hazard ratio [HR], 0.73; $P=.002$). The difference in OS between the 2 groups was more pronounced among the patients with elevated expression of programmed death ligand 1 (PD-L1; 8.0 vs 5.2 months; HR, 0.57; $P=.005$), although these patients had inferior median OS. No significant difference in progression-free survival (PFS) was found between the pembrolizumab and chemotherapy groups, even among those with elevated expression of PD-L1. Patients in the pembrolizumab group were less likely than those in the chemotherapy group to experience treatment-related adverse events of any grade (60.9% vs 90.2%) or of grade 3 or higher (15.0% vs 49.4%).

In the editorial, Dr Guru Sonpavde wrote that although pembrolizumab represents a “major advance” for patients with advanced urothelial cancer, the majority of patients do not respond to immunotherapy.

Pravastatin Does Not Improve Survival in Small Cell Lung Cancer

The addition of pravastatin to standard chemotherapy for small cell lung cancer (SCLC) did not improve OS or PFS, according to the largest randomized trial of statin therapy in cancer. Preclinical studies had found that statins could inhibit tumor growth in SCLC and several other types of cancers, and numerous observational studies had supported an association between decreased mortality and statins among patients with cancer.

For LUNGSTAR, which appeared online February 27 in the *Journal of Clinical Oncology*, Dr Michael J. Seckl and colleagues recruited 846 patients (median age, 64 years) who had confirmed SCLC, a performance status of 0 to 3, and no history of statin use. Patients were randomly assigned to receive 40 mg of pravastatin

or placebo daily in addition to standard chemotherapy (every 3 weeks for up to 6 cycles) with etoposide and a platinum agent.

After a median follow-up of 39.6 months, 758 (89.6%) of the patients had died. Median OS was similar in the pravastatin group and the placebo group (10.6 vs 10.7 months, respectively; HR, 1.01; $P=.90$). Median PFS also was similar in the 2 groups (7.7 vs 7.3 months; HR, 0.98; $P=.81$).

The authors wrote that on the basis of the results of this trial, “Independent data monitoring committees of studies that are still recruiting or in follow-up should examine interim analyses of clinical endpoints and stop early if there is sufficient evidence for futility.”

Scalp Cooling Effective in Reducing Chemotherapy-Associated Alopecia

In 2 recent studies, the use of a scalp cooling device prevented significant hair loss in approximately half of women undergoing chemotherapy for early-stage breast cancer. The studies were published in the February 14 issue of the *Journal of the American Medical Association*.

In the first study, which used the Paxman Scalp Cooling System, Dr Julie Nangia and colleagues randomly assigned 182 women undergoing chemotherapy for stage 1 or 2 breast cancer to receive scalp cooling (119 patients) or no scalp cooling (63 patients). Chemotherapy was anthracycline-based in 36% of patients and taxane-based in 64% of patients. In an interim analysis of 142 participants, the rate of successful hair preservation—defined as less than 50% hair loss—was 50.5% in the scalp cooling group and 0% in the group without scalp cooling ($P<.001$). The study was terminated in response to this finding.

In the second study, which used the DigniCap system from Dignitana (cleared by the US Food and Drug Administration), Dr Hope S. Rugo and colleagues randomly assigned 122 patients with stage 1 or 2 breast cancer to receive scalp cooling (106 patients) or no scalp cooling (16 patients). None of the patients in the scalp cooling group received anthracyclines. The study found successful hair preservation in 66.3% of the patients who received scalp cooling vs 0% of those who did not receive scalp cooling ($P<.001$).

Scalp cooling devices are caps worn immediately before, during, and immediately after chemotherapy infusions. They are believed to reduce hair loss by inducing vasoconstriction, so that the uptake of chemotherapy agents in the scalp is reduced. Although no serious events occurred in either trial, there is a theoretical risk for cancer cells remaining in the scalp.