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ECOG-ACRIN EA6174: STAMP: Surgically treated adjuvant merkel cell carcinoma with pembrolizumab, a phase III trial

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Background

Merkel cell carcinoma (MCC) is a rare, aggressive form of neuroendocrine skin cancer with high rates of recurrence after resection. While immune checkpoint inhibitors show efficacy in metastatic MCC, their role in the adjuvant setting remains investigational. EA6174 evaluates the role of adjuvant pembrolizumab (pembro) in patients (pts) with resected MCC.

Methods

This phase III trial randomized pts with resected MCC (stage II-IV, stage I pts without sentinel lymph node biopsy) 1:1 to Arm A (adjuvant pembro 200 mg q 3 weeks X 17 doses, n=147) or Arm B (observation, n=146), stratified by disease stage and intention to treat with radiation (RT). Co-primary endpoints were relapse free survival (RFS) and overall survival (OS). 280 pts provided 80% power with one-sided type 1 error rate of 0.05 to evaluate the hazard ratio (HR) of 0.56 hierarchically (RFS before OS). One-sided p-values from the log-rank test are reported.

Results

From 10/1/2018-4/7/2023 293 pts enrolled (median age 69 years, 199 [67.9%] male, 247 [84.3%] stage III). Stratification factors (stage, intended RT) were balanced across arms. At final analysis (90 RFS events), RFS in Arm A (42 recurrence events) was numerically higher than Arm B (48 recurrence events), but not statistically significant (p=0.105). The HR for RFS was 0.80, 95% CI (0.53, 1.22). With median follow up of 40 months, 1- and 2-year RFS rates are 83% [90% CI 78, 89] and 73% [90% CI 67, 79] in Arm A and 71% (90% CI 65, 78) and 66% (90% CI 59, 73) in Arm B. Distant metastasis-free survival (DMFS) was significantly higher in Arm A (HR:0.58 [90%CI 0.35, 0.94]; p-value=0.032). For pts who did not receive adjuvant RT (n=79 Arm A, n=80 Arm B), RFS was numerically higher in arm A (HR: 0.62 [90%CI 0.37,1.02]; p-value=0.056). Safety events were consistent with known pembro and RT toxicities. ≥ Grade 3 treatment-related events (related to pembro and to RT when administered) occurred in 31% of Arm A and 4% of Arm B pts. One pt in Arm A had treatment-related grade 5 pneumonitis. Mature OS data are not yet available (data lock 8/20/25).

Conclusions

In EA6174, the first phase III report of adjuvant immunotherapy in MCC, pembro resulted in a trend toward improved RFS and significantly prolonged DMFS. Final OS data will further inform clinical practice.

Clinical trial identification

NCT03712605, Release date: 10/19/2018.

Legal entity responsible for the study

ECOG-ACRIN Cancer Research Group.

Funding

NCI/CTEP.

Disclosure

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