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Perioperative pembrolizumab for locally advanced thymic epithelial tumors

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Background

Locally advanced thymic epithelial tumors (TETs) are considered potentially resectable, but perioperative treatment yields limited long-term efficacy. We hypothesized that adding perioperative pembrolizumab to standard therapy may improve response, resectability, and disease-free survival (DFS).

Methods

In this single-arm prospective phase 2 trial (MK3475-971 study), patients with potentially resectable TETs (Masaoka-Koga stage III–IV) received neoadjuvant paclitaxel (175 mg/m^2), cisplatin (75 mg/m^2), and pembrolizumab (200 mg) every 3 weeks for three cycles followed by surgery and maintenance pembrolizumab for 2 years. Tumor response was assessed using CT and PET/CT, followed by surgery. R1/R2-resected patients received adjuvant radiotherapy concomitant with pembrolizumab. The primary endpoint was a major pathological response (MPR). Secondary endpoints included pathologic complete response (pCR), R0 resection rate, objective response rate (ORR), 1-year DFS rate, and safety.

Results

From March 2020 to January 2025, forty patients were, including 7 (17.5%) WHO B3, 29 (72.5%) TC, and 31 stage IV (77.5%). The median follow-up duration was 23.3 months (95% CI 17.8–35.0). Baseline PD-L1 tumor proportion score (TPS) was ≥50% in 18 (45%), 1–49% in 10 (25%), <1% in 11 (27.5%), and unevaluable in one patient. The ORR to neoadjuvant therapy was 69.7%, and 28 patients received surgery (70.0%). Among the patients who received surgery, R0 resection rate was 71.4%. MPR and pCR were observed in 13 (46.4%) and 5 (17.9%) patients, respectively. MPR was significantly more frequent in TC than in thymoma (44.8% vs. 0.0%, P=0.020), while no significant difference was found according to PD-L1 TPS. Among the patients who received surgery, The 1-year DFS rate was 89.6% (95% CI 77.0-100.0), and the median DFS was 49.3 months (95% CI 25.3–NR) from the timepoint of surgery. Most of the AEs were grade 1 or 2 (n=21, 52.5%), with 9 (22.5%) being grade 3 and 5 (12.5%) being grade 4. Two thymoma patients died from myocarditis.

Conclusions

Perioperative pembrolizumab showed promising MPR and R0 resection rates as well as promising long-term DFS in stage III–IV TETs.

Clinical trial identification

NCT03858582 (MK3475-971).

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Legal entity responsible for the study

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Disclosure

H.A. Jung: Financial Interests, Personal, Advisory Board: Yuhan, Gaurdant, AIMEDBIO; Financial Interests, Personal and Institutional, Funding: Yuhan. S. Lee: Financial Interests, Personal, Advisory Role: AstraZeneca/MedImmune; Financial Interests, Personal, Advisory Board: Roche, Merck, Pfizer, Lilly, BMS/Ono, Takeda, Janssen, IMBdx; Financial Interests, Personal and Institutional, Funding: Merck, AstraZeneca, Lunit. J.S. Ahn: Financial Interests, Advisory Role: Bayer, Yooyoung Pharmaceutical Co, Ltd, Pharmbio Korea, Guardant Health, Yuhan, ImmuneOncia, Therapex, Daiichi Sankyo Korea, Roche. M. Ahn: Financial Interests, Personal, Advisory Role: AstraZeneca, Lilly, MSD, Takeda, Alpha pharmaceutical, Amgen, Merck Serono, Pfizer, Yuhan, Arcus Ventures; Financial Interests, Personal and Institutional, Funding: Yuhan. All other authors have declared no conflicts of interest.