TPS4213 Poster Session

Total neoadjuvant therapy with induction immunochemotherapy and chemo-radiotherapy followed by surgery for locally advanced esophageal squamous cell carcinoma (TNT-ESCC).

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Background: Locally advanced esophageal squamous cell carcinoma (ESCC) is indicated for multi-modalities treatment strategies, including a neoadjuvant chemoradiotherapy (CRT) followed by surgery. While the CROSS trial established neoadjuvant CRT as a standard of care, distant metastasis remains a significant cause of treatment failure. Immune checkpoint inhibitors (ICIs) have demonstrated survival benefits in advanced or metastatic ESCC, and adjuvant nivolumab has shown efficacy following neoadjuvant CRT in locally advanced ESCC. Integrating ICI earlier in the treatment sequence through total neoadjuvant therapy may enhance the immune response against the primary tumor and the hidden metastases and potentially lead to improved survival outcomes. This phase II study evaluates induction immunochemotherapy followed by CRT before surgery in locally advanced ESCC. **Methods:** This is a single-center, single-arm, phase II study enrolling 50 patients with histologically confirmed ESCC (T3/4aN0M0 or T1-4aN1-3M0 according to the AJCC Cancer Staging System 8th ed). Eligible patients must have primary intrathoracic esophageal tumor ≤10 cm in length and ≤5 cm in radial diameter, an ECOG performance status of 0-1, and adequate organ function. Patients will receive induction immunochemotherapy consisting of tislelizumab (200 mg every 3 weeks), paclitaxel (175 mg/m^2 every 3 weeks), and cisplatin (75 mg/m^2 every 3 weeks) for two cycles. This is followed by CRT consisting of radiotherapy (45 Gy in 25 fractions, 1.8 Gy/day, 5 days/week) plus chemotherapy with weekly paclitaxel (50 mg/m^2) and cisplatin (30 mg/m^2) for 5 weeks. Esophagectomy will be performed 6 to 8 weeks after completing CRT. The primary endpoint is pathologic complete response (pCR) rate, defined as no residual tumor in the resected primary site and lymph nodes. We hypothesize that the pCR rate will increase from 35% (the historical control) to 55%. Based on a binomial precision design, the study is of 80% power and a unilateral α error of 0.05 to detect a statistically significant difference in pCR rate. Secondary endpoints include major pathological response rate, R0 resection rate, disease-free survival, event-free survival, distant metastasis-free survival, overall survival and safety. The study starts patient enrollment in March 2025 (registered at ClinicalTrials.gov as NCT06764355). Clinical trial information: NCT06764355. Research Sponsor: National Taiwan University Hospital; BeiGene.