TPS6121 Poster Session

A phase 2 clinical trial of preoperative pembrolizumab and chemotherapy followed by adjuvant pembrolizumab in resectable locoregionally recurrent head and neck squamous cell carcinoma.

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Background: Locoregional recurrence is a major cause of death in squamous cell carcinoma of head & neck (HNSCC) initially treated with curative intent approaches. While salvage surgery may still provide a chance for cure, disease-free survival (DFS) and overall survival (OS) rates remain low for this high-risk population. Neoadjuvant programmed death (PD)-1 inhibitor based approaches have shown promising clinical outcomes compared to upfront surgery in multiple cancer types, e.g. melanoma and non-small cell lung cancer. Recently, a randomized placebo-controlled phase III (KEYNOTE-689) trial evaluating peri-operative pembrolizumab in treatment-naïve locally advanced HNSCC met its primary endpoint of event-free survival. Since our trial is targeted at a higher risk patient (pt) population of locoregionally recurrent resectable HNSCC (already managed with curative intent once), we are evaluating the combination of pembrolizumab with chemotherapy in the neoadjuvant setting followed by adjuvant pembrolizumab therapy. **Methods:** This investigator-initiated non-randomized open-label phase 2 clinical trial is enrolling pts with resectable locoregionally recurrent HNSCC, with primary sites in oral cavity, oropharynx, larynx or hypopharynx. Pts must have documented duration of ≥6 months from completion of prior curative intent treatment for HNSCC (surgery and/or radiation therapy with/without platinum chemotherapy or cetuximab targeted therapy) to diagnosis of local or locoregional recurrence, and must have resectable disease. Study treatment plan consists of three phases: pre-operative phase, curative intent surgery, and adjuvant phase. In the pre-operative phase, pembrolizumab, cisplatin (or carboplatin) and docetaxel will be administered every 3 weeks for 2 treatment cycles. This will be followed by surgery within 6 weeks of cycle 2 day 1 in pre-operative phase. Adjuvant phase consists of pembrolizumab every 3 weeks until total of 15 cycles, disease recurrence, or intolerable adverse events. The primary endpoint of the trial is major pathological response (mPR) in surgical specimens after pre-operative treatment, defined as ≤ 10% residual invasive SCC within the resected primary tumor specimen and all sampled regional lymph nodes. Key secondary endpoints include safety, DFS, and OS. Correlative biomarker analyses are planned as exploratory endpoints. We hypothesize that treatment with pre-operative pembrolizumab and chemotherapy will lead to mPR rate of 15% compared to null hypothesis of 2%. If we find ≥2 pts with disease in mPR among 25 evaluable pts, the Simon two-stage design (14 pts in first stage) will have a power of 85.5% with a type I error rate of 7.4%. Safety rule is built in to monitor delays in surgery. 12 of planned 28 pts have been enrolled as of January 2025 (ClinicalTrials.gov NCT05726370). Clinical trial information: NCT05726370. Research Sponsor: Merck.