TPS6122 Poster Session

A phase 3 randomized study of ASP-1929 photoimmunotherapy in combination with pembrolizumab versus standard of care in locoregional recurrent head and neck squamous cell carcinoma (HNSCC).

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Background: Recurrent (r) HNSCC carries a poor prognosis and a low survival rate. Locoregional (LR) progression significantly contributes to both morbidity and mortality in these patients, underscoring the importance of LR disease control. The approval of anti-PD-1 inhibitors (pembrolizumab, nivolumab) has expanded treatment options for rHNSCC, but response rates with monotherapy remain low. ASP-1929 photoimmunotherapy (PIT), a novel drug-device treatment, combines cetuximab with a light-activatable dye (IR700) to selectively target EGFR-expressing cancer cells and cause cell membrane destruction and rapid tumor necrosis after activation with local light illumination. Preclinical data have demonstrated that ASP-1929 PIT-mediated tumor necrosis and immunogenic cell death induces antitumor immunity and when combined with anti-PD-1 therapy, synergistically enhances anticancer activity. In an interim evaluation of a multicenter, phase 1/2a, open-label study of 19 patients with metastatic and/or rHNSCC, the combination of ASP-1929 PIT and pembrolizumab showed promising efficacy with a manageable safety profile.[1] The objective of this pivotal phase 3 study is to further evaluate the efficacy and safety of ASP-1929 PIT in combination with pembrolizumab in rHNSCC. **Methods:** The ASP-1929-381is a global phase 3, multi-center, randomized, open-label, controlled study of ASP-1929 PIT in combination with pembrolizumab vs pembrolizumab-based standard of care (SOC) in the first line treatment of LR rHNSCC with no distant metastases. Key inclusion criteria: rHNSCC patients without distant metastases who are candidates for SOC first-line treatment with pembrolizumab + chemotherapy; anti-PD-1 and anti-PD-L1-treatment naïve; at least one lesion accessible for PIT light treatment and RECIST 1.1 measurable; age ≥18 years; ECOG score 0 or 1. Key exclusion criteria: diagnosis and/or treatment of additional malignancy within 2 years of randomization; history of ≥ grade 3 cetuximab infusion reactions; prior allogeneic tissue/solid organ transplant; life expectancy <3 months. The study will enroll ~408 patients and begin with a 2:2:1 randomization into three arms (ASP-1929 PIT 320 mg/m^2 plus pembrolizumab vs ASP-1929 PIT 640 mg/m^2 plus pembrolizumab vs physicians' choice pembrolizumab-based SOC regimen). The SOC arm will include pembrolizumab monotherapy, or pembrolizumab in combination with platinum (cisplatin or carboplatin) + 5-fluorouracil or taxane (paclitaxel or docetaxel). The primary endpoint is overall survival (OS). Key secondary endpoints include complete response rate (CRR) and overall response rate (ORR). The study is currently enrolling in the US, with plans to expand to Taiwan, Japan, and other territories (NCT06699212). 1. Cognetti et al. J Clin Oncol 42, 2024 (suppl 16; abstr 6083). Clinical trial information: NCT06699212. Research Sponsor: Rakuten Medical, Inc.