TPS6117 Poster Session

Phase II trial of neoadjuvant chemotherapy (NAC) docetaxel-cisplatin alone (DC) or with anti-human papillomavirus (HPV) gene therapy PRGN-2009 (DCP) followed by surgery in patients (pts) with newly diagnosed HPV-associated oropharyngeal cancer (HPV-OPC).

Charalampos S. Floudas, Janet Valdez, Clint Allen, Melissa Wheatley, Ruchi Patel, Punam Thakkar, Arjun Joshi; Center for Immuno-Oncology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD; Surgical Oncology Program, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD; Division of Otolaryngology-Head and Neck Surgery, The George Washington University School of Medicine & Health Sciences, Washington, DC

Background: HPV-OPC is caused primarily by HPV16. Prognosis following standard-of-care (SOC) treatment, (surgery followed by adjuvant radiotherapy (RT), or concurrent chemoRT (CRT)) is favorable, with >80% 5-year recurrence-free survival (RFS). However, RT toxicity including tissue fibrosis results in long-term swallowing dysfunction and impacts quality of life (QOL). NAC treatment (DC) followed by surgery has resulted in clinical-to-pathologic down-staging or pathologic complete response (pCR) and avoidance of RT in most pts, with >90% 5-year survival, and induces HPV-specific T cell immunity. PRGN-2009 is a gorilla adenoviral vector based gene therapy harboring a DNA payload designed to induce HPV specific T-cell responses. This trial will evaluate the rate of pCR with NAC (DC) alone or combined with PRGN-2009 (DCP) in pts with newly diagnosed HPV-OPC. **Methods:** This is an investigator-initiated, single-center, randomized controlled phase II trial. Newly diagnosed HPV-positive OPC pts of stage I (cT1-2, N0-1) or II (T1-3, N0-2), M0 (AJCC Cancer Staging Manual, 8th ed.) planned for SOC surgery will be randomized to 2 treatment arms of 30 patients each, DC and DCP, to evaluate if PRGN-2009 may be associated with an increased rate of pathological CR (pCR) following neoadjuvant chemotherapy. DC consists of 3 cycles of intravenous cisplatin 75 mg/m^2 and docetaxel 75 mg/m^2 every 21 days (dose reductions allowed). DCP also includes PRGN-2009 induction dose pre-cycle 1, and one dose after each DC cycle (total 4 doses). Supportive measures include pre-infusion dexamethasone, antiemetics, neutropenia primary prophylaxis. Imaging (FDG PET, CT) will be performed at baseline. Research blood samples will be collected longitudinally. Mandatory research primary tumor biopsy will be performed at baseline and post-treatment tumor/tumor bed biopsy will be at the time of surgical resection. On-treatment tumor biopsies will be offered (optional). Study treatment and procedures will be performed at the NIH Clinical Center (Bethesda, MD). After treatment completion, pts will have surgery at their primary institution; adjuvant treatment determined per established risk factors. Primary endpoint is the rate of pCR in each arm. Secondary endpoints include safety and 2-year RFS in each arm. Exploratory objectives include assessment of changes in hearing (audiograms baseline/post-treatment), swallowing function (MD Anderson Dysphagia Inventory) and QOL (Functional Assessment of Cancer Therapy – Head & Neck); associations between changes in imaging, pathologic response, and circulating cell-free HPV DNA; changes in the tumor microenvironment and in HPV-specific T cell immunity. 8 of 60 pts planned have been enrolled. Clinical trial information: NCT06223568. Research Sponsor: NCI, NIH.