TPS3633 **Poster Session**

A phase II study of pembrolizumab, carboplatin, paclitaxel, and radiation for the treatment of early-stage anal cancer: Big Ten Cancer Research Consortium GI22-588.

Anita Turk, Salma K. Jabbour, Yixing Jiang, Dustin A. Deming; Indiana University Melvin and Bren Simon Comprehensive Cancer Center, Indianapolis, IN; Rutgers Cancer Institute, New Brunswick, NJ; University of Maryland Greenebaum Comprehensive Cancer Center, Baltimore, MD; University of Wisconsin Carbone Cancer Center, Madison, WI

Background: Anal squamous cell carcinoma (SCC) is an evolving public health challenge, with increasing incidence and mortality rates, particularly in older women with long-standing HPV infections. Standard-of-care treatment for early-stage anal SCC—5-fluorouracil (5FU) and mitomycin-C (MMC) with radiation—achieves high cure rates but poses significant toxicity risks, with grade 3-5 adverse events occurring in up to 70% of patients. Recent clinical trials, such as DECREASE and ACT4, have explored radiation de-escalation strategies, but limited progress has been made in expanding systemic treatment options for locally advanced disease. Building on pilot data demonstrating favorable clinical complete responses (cCR) with carboplatin and paclitaxel combined with radiation in patients ineligible for SOC regimens, this phase II trial evaluates the addition of pembrolizumab to this combination to enhance efficacy while reducing toxicity. **Methods:** This is a single-arm, phase II trial evaluating concurrent chemoradiation with weekly carboplatin (AUC 2), paclitaxel (50 mg/m^2), and pembrolizumab (200 mg every three weeks during chemoradiation and 400 mg every six weeks during maintenance) for early-stage anal SCC in patients ineligible for 5FU and MMC. The chemoradiation phase consists of up to six weeks of therapy with 50.4 Gy delivered over 28 fractions. Maintenance pembrolizumab is administered for up to eight cycles. The primary endpoint is the cCR rate at six months post-chemoradiation. Secondary endpoints include safety, tolerability, tumor downstaging, and disease-free survival. Exploratory objectives include the evaluation of genomic alterations and biomarkers such as versican and keratin 17 as predictors of therapeutic response. Major eligibility criteria include histologically confirmed stage I-IIIA anal SCC, measurable disease per RECIST v1.1, and treatment-naïve status. Key exclusions include active autoimmune disease requiring immunosuppression within two years and prior checkpoint inhibitor therapy. The target enrollment is 23 patients, with an accrual period of 12 months and an anticipated study duration of two years. The study is currently enrolling participants through the Big Ten Cancer Research Consortium. Clinical trial information: NCT06493019. Research Sponsor: Merck.