592 UPDATED RECURRENCE FREE SURVIVAL FOR NEOADJUVANT BINTRAFUSP ALFA (BA) FOR HPV UNRELATED HNSCC AND RESULTS FROM BA PLUS A MULTITARGETED RECOMBINANT ADENOVIRUS 5 VACCINE FOR HPV UNRELATED HNSCC

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Background Individuals with head and neck squamous cell carcinoma (HNSCC) not associated with human papillomavirus (HPV) experience high rates of recurrence and poor survival. Clinical studies suggest that neoadjuvant immune checkpoint blockade can improve recurrence free survival (RFS) in newly diagnosed, advanced stage HNSCC. We conducted a clinical trial (NCT04247282) where patients received neoadjuvant immunotherapy prior to surgical resection, with bintrafusp alfa (BA), a bifunctional fusion protein composed of the transforming growth factor (TGF)-βRII receptor (a TGF-β 'trap') fused to a human IgG1 anti-PDL1 antibody (Arm A) or BA + an adenovirus-based vaccine (TriAdeno) targeting three human tumor-associated antigens-CEA, MUC1, and brachyury (Arm B). We recently reported results from Arm A (BA alone).

Methods Participants received BA 1,200 mg IV on days 1 and 15 alone (Arm A) or with TriAdeno 5×10^{11} viral particles per vector on day 1 (Arm B) before returning to the community for surgery followed by adjuvant treatments as indicated per standard of care. The primary outcome measure was percentage of individuals with pathologic complete response (pCR) or clinical-to-pathological downstaging (CTPD). Secondary outcome measures included 1- and 2-year recurrence free survival, objective response per RECISTv1.1, incidence of surgery delay beyond 4 weeks from planned surgery, and safety.

Results A total of 14 patients received BA on Arm A and 6 patients received BA + TriAdeno on Arm B. Safety and efficacy data (excluding 2-year RFS) from Arm A were reported previously. Two-year RFS data for Arm A are now mature and are 85.6% (12/14 patients). For Arm B, 3/6 (50%) patients had CTPD and 1- and 2-year RFS were 83.3% (5/6 patients). No Arm B patients had a pCR or an objective response per RECISTv1.1. There were no treatment-related surgical delays. Among 6 treated patients on Arm B, one patient experienced a $\geq$3 treatment-related adverse event (grade 4 pneumonitis).

Conclusions In this small study, neoadjuvant PD-L1 and TGF-beta blockade +/- TriAdeno vaccine produces 2-year RFS outcomes that exceed historical values in HNSCC not associated with HPV infection. Consistent with other studies of neoadjuvant checkpoint blockade, the toxicity profile is similar to experience in the metastatic population and does not result in surgical delays.

Ethics Approval This study involved human participants and was approved by the National Institutes of Health Institutional Review Board (RB00012078). Participants gave informed consent to participate in the study.

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