2501 **Oral Abstract Session**

Phase II evaluation of the triple combination of PDS0101, M9241, and bintrafusp alfa in patients with HPV 16 positive malignancies.

Julius Strauss, Charalampos S. Floudas, Houssein Abdul Sater, Michell Manu, Elizabeth Lamping, Deneise C Francis, Lisa M. Cordes, Jenn Marte, Renee Nicole Donahue, Caroline Jochems, Jason Redman, Ravi Amrit Madan, Marijo Bilusic, Fatima Karzai, Scott Norberg, Christian S. Hinrichs, Lauren V Wood, Frank K Bedu-Addo, Jeffrey Schlom, James L. Gulley; Laboratory of Tumor Immunology and Biology, NCI, NIH, Bethesda, MD; Genitourinary Malignancies Branch, NCI, NIH, Bethesda, MD; NIH, Bethesda, MD; Genitourinary Malignancies Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD; Laboratory of Tumor Immunology and Biology, National Cancer Institute, Bethesda, MD; National Cancer Institute-National Institute of Health, Bethesda, MD; National Cancer Institute at the National Institutes of Health, Bethesda, MD; PDS Biotechnology, Princeton, NJ; Genitourinary Malignancies Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD

Background: There are more than 630,000 cases of HPV associated malignancies including cervical, oropharyngeal and anal cancer worldwide annually. HPV 16 is responsible for the majority of these cases. About 15-20% of HPV associated malignancies respond to PD-(L)1 inhibitors, but for the overwhelming majority of patients who progress on these immunotherapies there is no effective standard of care therapy. Preclinical studies have shown that the triple combination of PDS0101 (Versamune-HPV), a liposomal multipeptide therapeutic vaccine targeting HPV 16 E6/E7, M9241, a tumor-targeting immunocytokine composed of IL-12 heterodimers fused to a monoclonal antibody targeting free DNA in necrotic tumor regions, and bintrafusp alfa, a bifunctional fusion protein targeting TGF-β and PD-L1, resulted in maximum HPV-specific T cell responses, T cell tumor infiltration and tumor reduction as compared to any one or two of these agents alone. **Methods:** Fourteen pts with HPV 16+ relapsed or refractory advanced cancer were enrolled to the triple combination of PDS0101, M9241 and bintrafusp alfa (NCT04287868). Pts received bintrafusp alfa at 1200 mg flat dose i.v. every 2 weeks, M9241 at 16.8 mcg/kg s.c. every 4 weeks and PDS0101 given as two separate 0.5 ml s.c. injections every 4 weeks. Dose reductions of M9241 to 8 mcg/kg were allowed as well as skipped doses of any agent for ongoing toxicities. **Results:** Fourteen pts with advanced HPV 16+ cancers (5 cervical, 2 vaginal/vulvar, 4 anal, 3 oropharyngeal) were treated. 4/14 (28.6%) pts had a grade 3 treatment related toxicity including grade 3 hematuria in 2 pts with cervical ca and prior pelvic radiation and grade 3 AST/ALT elevation in 2 pts, one with anal ca and one with vaginal ca. For one patient with grade 3 AST/ALT elevation dose reduction of M9241 from 16.8 to 8 mcg/kg allowed for continued treatment with AST/ALT remaining at grade 1 or less. One additional patient had transient asymptomatic grade 4 neutropenia. No other treatment related grade 3 or greater toxicities were noted. 10/14 (71%) pts have had objective responses: 1 CR (anal ca) and 9 PRs (3 cervical, 2 vulvar/vaginal, 2 anal, 2 oropharyngeal) with 9/10 of these responses ongoing after a median 5 month of follow up. Of the 14 pts, 6 pts have checkpoint nave disease and 8 pts have checkpoint refractory disease. 5/6 (83%) pts with checkpoint nave disease and 5/8 (63%) pts with checkpoint refractory disease have had objective responses. Analyses of immune responses and other immune correlates are ongoing. **Conclusions:** Triple combination of PDS0101, M9241 and bintrafusp alfa appears to have a manageable safety profile along with early evidence of notable clinical activity for pts with both checkpoint nave as well as checkpoint refractory HPV 16+ advanced malignancies. Clinical trial information: NCT04287868. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

© 2021 by American Society of Clinical Oncology. Visit abstracts.asco.org and search by abstract for disclosure information.