

Title

Phase 1 Trial of Personalized Neoantigen DNA Vaccines in Combination with Nivolumab, Ipilimumab, and PROSTVAC in Metastatic Androgen Pathway Modulator Sensitive Prostate Cancer

Authors

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Background:

Immune checkpoint blockade (ICB) monotherapy has shown limited efficacy in prostate cancer. We conducted a phase 1 trial testing whether a personalized neoantigen DNA vaccine could be manufactured from metastatic tissue and safely combined with PROSTVAC and dual ICB in metastatic androgen pathway modulator sensitive (mAPMS), a setting not previously studied. Our data, combined with the recent announcement from Merck and Moderna of significantly improved DFS in the Phase 3 INTERpath-001 trial of Intismeran Autogene plus pembrolizumab support a similar approach in prostate cancer patients.

Patients and Methods:

Patients with high-risk/high-volume mAPMS who completed chemohormonal therapy (ADT plus docetaxel) were enrolled (NCT03532217). Treatment consisted of PROSTVAC-VF with nivolumab and ipilimumab (Phase A), followed by personalized neoantigen DNA vaccine with nivolumab (Phase B). Primary endpoints were feasibility and safety; secondary endpoints included failure-free survival (FFS), overall survival (OS), and PSA response.

Results:

Nineteen patients were enrolled (median age, 63 years). Fifteen (79%) received the neoantigen vaccine and 12 (63%) completed the full protocol, establishing feasibility. Treatment was well tolerated: no grade 4 treatment-related adverse events (TRAEs) occurred, and grade 3 TRAEs occurred in 4 patients (colitis, anorexia, hypophysitis, hyponatremia, hypophosphatemia), all during Phase A. At a median follow-up of 61.3 months, median FFS and OS were each 81 months (5-year FFS, 57.4%; 5-year OS, 57.9%). PSA decline $\geq$ 50% occurred in 6 of 19 patients (31.6%). Vaccine recipients had significantly longer FFS (log-rank $P = .0085$) and OS (log-rank $P = .0121$) than non-recipients in exploratory analysis.

Conclusion:

A personalized neoantigen DNA vaccine combined with PROSTVAC and dual ICB after chemohormonal therapy in mAPMS is feasible and safe, with encouraging long-term survival that supports evaluation in a randomized trial.

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