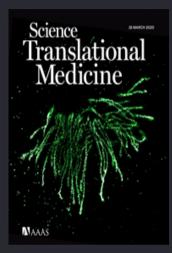
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ARTICLE

Strong vaccine responses during chemotherapy are associated with prolonged cancer survival

View article page

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Human papiliomavirus type 16 (HP v 16) is a major HP v type several chemotherapeutics and demonstrated synergistic effects with HPV16 synthetic long peptide (SLP) vaccination in two mouse models causing anogenital cancers and the predominant HPV type causing oropharyngeal cancers. Studies in healthy individuals and of HPV-induced cancer (16, 17). Careful analysis of the immunopatients have assigned a major role for HPV16 E6/E7 oncoproteinmodulatory effects of chemotherapy revealed that the combination specific type 1 T cell immunity in the protection against progressive of carboplatin and paclitaxel elicited a systemic and local reduction premalignant disease and a better response to standard therapy at in the cancer-driven abnormal numbers of immunosuppressive myeloid cells (18). A pilot experiment in patients with late-stage the stage of cancer (7, 8). Despite all patients with progressive disease being infected with HPV16, such an immune response is usually cervical cancer showed the optimal time point to start vaccination not demonstrable or insufficient to have clinical impact (7-10). with the therapeutic HPV16-SLP vaccine ISA101 to be 2 weeks after Raising the numbers of HPV-specific T cells by therapeutic vaccine the second cycle of carboplatin/paclitaxel. At that time point, the

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systemic abnormally high numbers of immunosuppressive myeloid vaccination (n = 72), there were 63 (87.5%) patients with TEAEs, cells had declined to the numbers seen in healthy donors. This co-16 (22.2%) patients with treatment-emergent serious AEs (SAEs), 20 incided with decreased immunosuppression and a stronger T cell (27.8%) patients with National Cancer Institute Common Terminology response to a single timed ISA101 vaccine injection (18). Criteria for Adverse Events (NCI-CTCAE) grade 3 or 4 TEAEs, and These findings led to the design of the current study, in which 4 (5.7%) patients with TEAEs that led to withdrawal (table S4). From patients with late-stage HPV16-positive cervical cancer were vaccinated a comparison of tables S3 and S4, it follows that most of the serious with ISA101 in a timed manner during chemotherapy. Successive TEAEs in the current study were expected toxicities related to chemopatient cohorts were vaccinated with increasing ISA101 doses, and therapy or to complications associated with progression of cervical half of the patients in each cohort also received pegylated type 1 cancer. Previous trials documented treatment-emergent injection interferon (IFN) (PegIntron). This was tried because IFN α is a site reactions (TEISRs, defined as vaccination site or ISRs) and strong promoter of cross-presentation of proteins by dendritic cells treatment-emergent systemic allergic reactions (TESARs, defined (DCs) (19) and is responsible for the up-regulation of costimulatory as drug hypersensitivity, hypersensitivity, injection-related reacmolecule expression and costimulatory cytokine production by DCs tion, systemic inflammatory response syndrome, vaccination com-(20) and also promotes more efficient processing and presentation of plication or cytokine release syndrome) as TEAEs that are likely

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