2023 ASCO® ANNUAL MEETING

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TPS5119: Prime-boost Immunotherapeutic Trial in Men with Biochemical Recurrence After Definitive Local Therapy for Prostate Cancer

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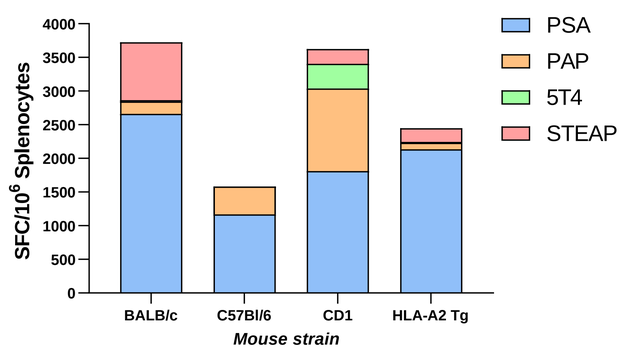
BACKGROUND

VTP-850

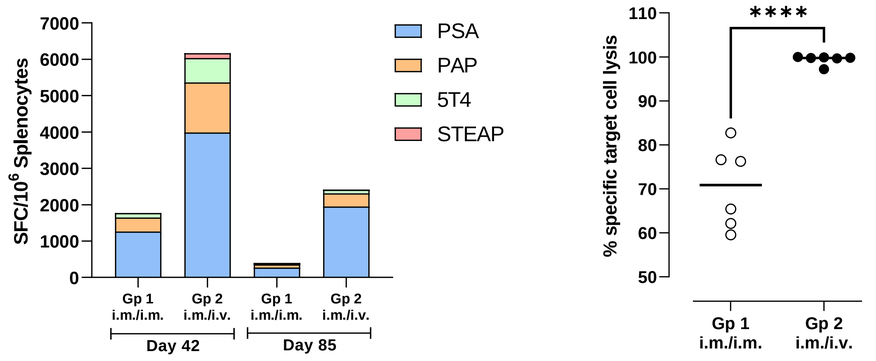
VTP-850 is a novel, antigen-specific immunotherapeutic encoding multiple antigens, designed to induce a polyclonal T cell response to kill tumor cells and prevent advancement to metastatic disease. VTP-850 consists of 2 nonreplicating viral-vectored components administered sequentially: ChAdOx1-PCAQ, based on an adenoviral vector, and MVA-PCAQ, based on a modified vaccinia virus Ankara (MVA) vector. Both components encode the same 4 prostate cancer antigens: prostate-specific antigen (PSA), prostatic acid phosphatase (PAP), six transmembrane epithelial antigen of prostate 1 (STEAP1), and 5T4, an oncofetal antigen.

PRE-CLINICAL IMMUNE RESPONSE



Preclinical studies in inbred, outbred, and HLA-A2 transgenic mice show that VTP-850 is highly immunogenic. The results indicate that VTP-850 can elicit T cell responses (measured by IFNγ ELISpot) to each of the 4 encoded antigens, with the responses to PSA of greatest magnitude in all mouse strains studied.

INTRAVENOUS ADMINISTRATION



In these mouse studies, the intravenous administration of the MVA-PCAQ resulted in up to a 6-fold increase in the magnitude of induced antigen-specific T cells (left, measured by IFNγ ELISpot) and increased functional activity (right, measured by a targeted *in vivo* killing assay), relative to the intramuscular route.

METHODS

PCA001 is a Phase 1/2 first-in-human multicenter trial to evaluate safety, PSA response rate and duration, and immunogenicity of VTP-850 in men with biochemical recurrence of prostate cancer after definitive local therapy.

INCLUSION/EXCLUSION CRITERIA

Patients who have undergone primary therapy for prostate cancer and have biochemical recurrence are eligible.

Participants must have nonmetastatic (M0) disease; serum PSA of >0.3 ng/mL for participants with prior radical prostatectomy or serum PSA of 2 ng/mL above nadir for participants with prior external beam radiation or brachytherapy; PSA doubling time ≤12 months; and testosterone >75 ng/dL.

Participants cannot have received ADT within 6 months prior to Day 1 and cannot have received prior chemotherapy, immunotherapy or experimental agent for prostate cancer.

OBJECTIVES/ENDPOINTS

Primary Endpoint
- Safety: incidence of AEs and SAEs

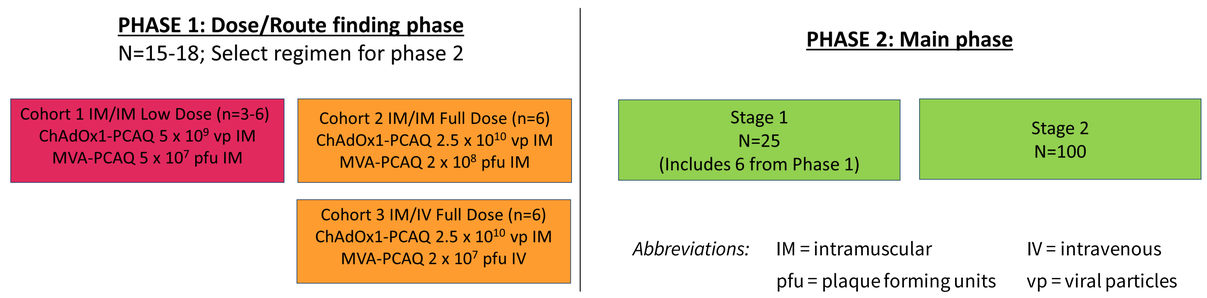
Secondary Endpoints
- PSA response, durable PSA response, duration of PSA response, metastasis-free survival, time to metastasis, time to start of androgen deprivation therapy (ADT)

Exploratory Endpoints
- Immune response to the VTP-850 antigens

STUDY DESIGN

Phase 1 (15-18 participants) will follow a 3+3 design to determine the recommended phase 2 regimen: dose level of both ChAdOx1-PCAQ and MVA-PCAQ, and route of administration of MVA-PCAQ (IM or IV).

Phase 2 will consist of 2 stages. In Stage 1, 19 additional participants will be enrolled at the chosen Phase 2 regimen. If 4 or more of the 25 participants (including the 6 Phase 1 participants who received the same regimen) have a PSA response (defined as ≥50% reduction in serum PSA compared to baseline at any time, measured twice consecutively, at least 2 weeks apart), Stage 2 will enroll 100 additional participants.



Dosing:

Participants will be followed for 6 months or until start of new therapy (e.g. ADT) or until development of metastatic disease. Participants who have a PSA response during the 6 months follow up will be followed for up to an additional 18 months

Participant screening visits have begun in the USA, with sites in Spain and Italy planned to open later in 2023. Active sites are listed on ClinicalTrials.gov

References:
1 *Vardeu A, Davis C, McDonald I, Stahlberg G, Thapa B, Piotrowska K et al. Intravenous administration of viral vectors expressing prostate cancer antigens enhances the magnitude and functionality of CD8+ T cell responses. Journal for immunotherapy of cancer 2022. 10. 10.1136/jitc-2022-005398.*

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