ABSTRACT #415556

HB-300, a Novel Arenavirus-based Cancer Immunotherapy in Patients With Metastatic Castration-resistant Prostate Cancer

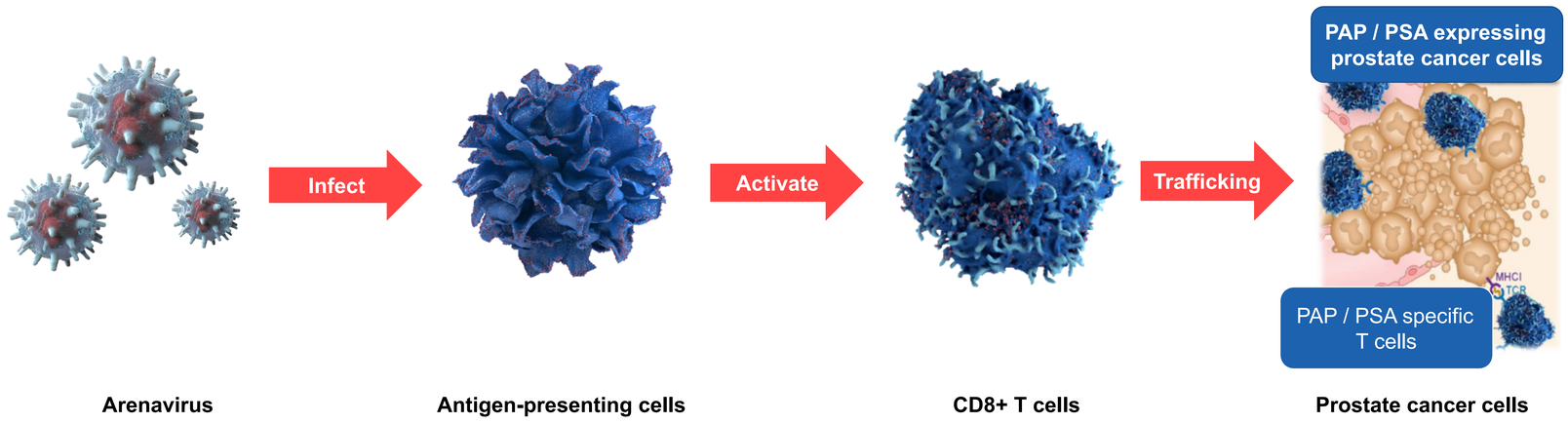
David Chism[1], Biren Saraiya[2], Tanya Dorff[3], Brendan Curti[4], Edwin Posadas[5], Carlisle Saint-Paul[6], Subhendu Mukhopadhyay[7], Leena Desai[7], Henning Lauterbach[7], Rounak Nassirpour[7], Alexander Grill[7], Ali Manouchehri[7], Kia Katchar[7], Kevin Hibbert[7], Katia Schlienger[7], Susan F. Slovin[8]

[1]Thompson Cancer Survival Center, Knoxville, TN; [2]The Cancer Institute of New Jersey, New Brunswick, NJ; [3]City of Hope, Los Angeles, CA; [4]Providence Cancer Center Oncology and Hematology Care Clinic, Portland, OR; [5]Cedars-Sinai Medical Center, Los Angeles, CA; [6]Syneos Health, Morrisville, NC; [7]Hookipa Pharma Inc., New York, NY; [8]Memorial Sloan Kettering Cancer Center, New York, NY

BACKGROUND

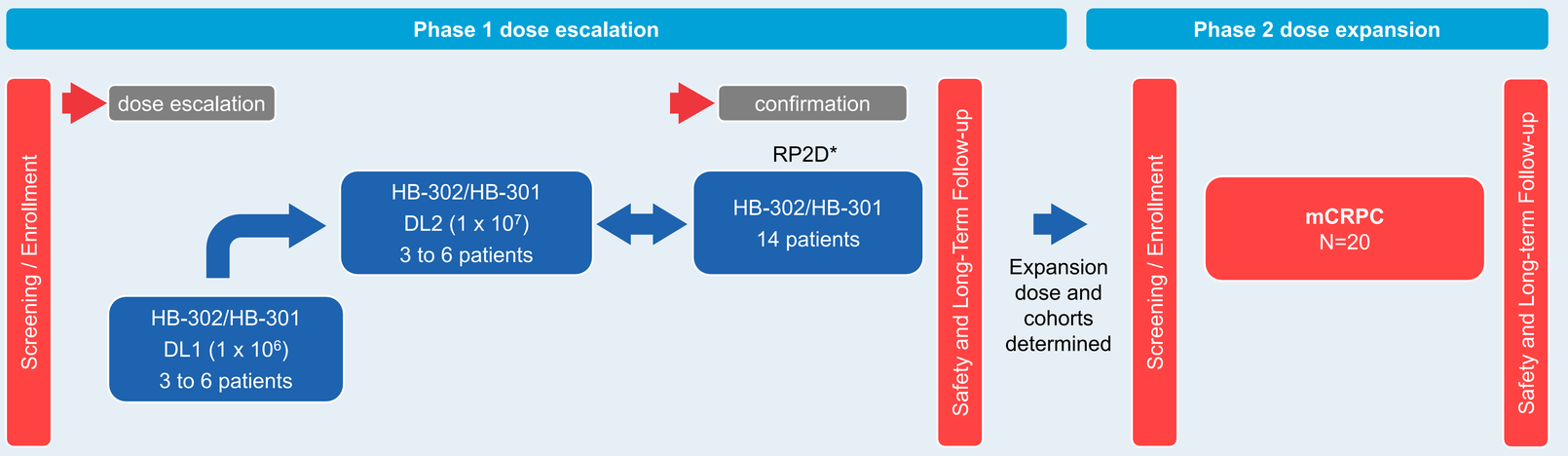
- Prostate cancer is the most frequent malignant neoplasm in men.
- Approved treatments for mCRPC, despite notable advancements, are noncurative and can cause significant toxicity. Thus, there is an unmet need for novel therapies that enhance survival and minimize adverse effects.
- Immunotherapy targeting self-antigens in prostate cancer is evolving and requires overcoming multiple mechanisms that mediate immune tolerance.
- HB-301 (LCMV) and HB-302 (PICV) are genetically engineered viral vectors that deliver human prostate cancer-associated antigens PAP and PSA, and have been developed to control tumor development/progression in patients with mCRPC.
- These nonlytic viral vectors are designed to overcome immune tolerance mechanisms by targeting antigen-presenting cells and delivering antigens for efficient cytotoxic T lymphocyte (CTL) induction, which induces specific CD8+ T cell responses against the antigens, ultimately aimed at CTL-mediated elimination of tumor cells.
- Nonclinical studies in mice showed that the vectors were well tolerated and induced CD8+ T cell responses irrespective of the viral backbone, and sequential alternating administration of HB-302/HB-301 induced the highest CD8+ T cell responses.
- The tissue tropism, biodistribution, and sustained activity profile of these vectors have already been investigated within the previously initiated and currently ongoing HB-200 program (which uses similar viral backbones encoding E6/E7 in HPV16+ cancers), with encouraging initial clinical activity and manageable safety and tolerability.
- The sequential alternating administration of HB-302 and HB-301 has the potential to provide therapeutic benefits to participants with mCRPC.

Mechanism of Action: The Replicating Arenaviral Vector Technology Drives CD8+ T Cell Activation and Anti-tumor Activity

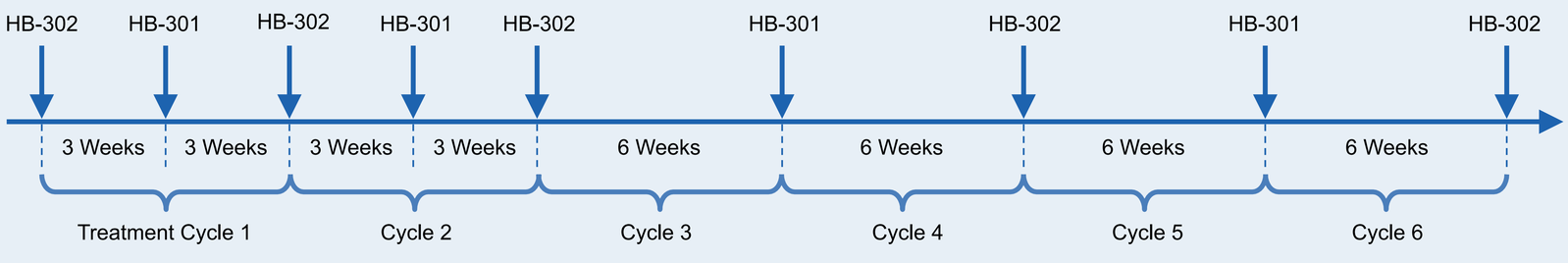


STUDY DESIGN

- H-300-001 is a multinational, multicenter, open-label, first-in-human Phase 1/2 study of HB-302/HB-301 alternating 2-vector therapy in participants with mCRPC comprising 2 parts:
  - Phase 1 dose escalation and RP2D confirmation
  - Phase 2 dose expansion
- In total, approximately 70 participants aged 18 years and older will be enrolled to receive HB-302/HB-301 alternating 2-vector therapy, with approximately 50 participants in Phase 1 and 20 participants in Phase 2
- HB-302/HB-301 alternating 2-vector therapy will be administered via short IV infusion Q3W for the first 5 doses and Q6W from the fifth dose onward
  - HB-302 is to be administered first followed 3 or 6 weeks later by HB-301



* At least 1 cohort for RP2D confirmation.



STUDY DESIGN (continued)

Cohort / Dose Level	HB-302 Dose RCV FFU†	HB-301 Dose RCV FFU†
Cohort 1 (starting dose; DL1)	1 x 10^6	1 x 10^6
Cohort 2 (DL2)	1 x 10^7	1 x 10^7

†Note: The dose level for HB-302 and HB-301 is provisional. It is possible for modified dose levels to be added during the course of the study.

OBJECTIVES AND ENDPOINTS

OBJECTIVES FOR PHASE 1

Primary	• RP2D • Safety and tolerability
Secondary	• Preliminary efficacy (ORR, DOR, DCR, PFS [radiological and biochemical], OS, and duration of stable disease)
Exploratory	• Immunogenicity; pharmacodynamic biomarkers

OBJECTIVES FOR PHASE 2

Primary	• Preliminary antitumor activity (ORR)
Secondary	• Duration of preliminary antitumor activity (DOR, DCR, PFS [radiological and biochemical], OS, and duration of stable disease) • Safety and tolerability
Exploratory	• Immunogenicity; pharmacodynamic biomarkers

KEY INCLUSION CRITERIA

- Patients ≥18 years old
- Adenocarcinoma of the prostate
- Evidence of metastatic disease
- Documented castration-resistant disease (serum testosterone <50 ng/dL or 1.7 nmol/L)
- ≥1 prior standard of care therapy (ARSI; androgen-metabolism inhibitor; 1st generation anti-androgen)
- ECOG PS 0 or 1
- Acceptable organ function and QTc at baseline
- Optional pretreatment and on-treatment tumor biopsy

KEY EXCLUSION CRITERIA

- Prior chemotherapy in the metastatic castration-resistant setting (docetaxel; cabazitaxel)
- Active brain metastasis
- Presence of liver metastasis
- Systemic anticancer therapy <28 days prior to study start
- Anti-androgen/ARSI <2 weeks prior to study start
- Therapeutic or palliative radiation therapy <2 weeks prior to study start
- Active auto-immune disease, immunosuppressive agents <6 months prior study start, or transplant
- Uncontrolled pain or symptoms related to mCRPC

ASSESSMENTS

- Efficacy will be assessed as follows:
  - Visceral/soft tissue response according to RECIST v1.1 / iRECIST
  - Bone response according to PCWG3[1]
  - PSA response according to PCWG3[1]

STATUS

- This study is currently open to enrollment in the United States

CLINICALTRIALS.GOV IDENTIFIER

NCT05553639

ABBREVIATIONS

ARSI = androgen-receptor signaling inhibitor; DCR = disease control rate; DL1 = dose level 1; DL2 = dose level 2; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; HPV16+ = human papillomavirus 16–positive; iRECIST = immune-modified Response Evaluation Criteria in Solid Tumors; IV = intravenous; LCMV = lymphocytic choriomeningitis virus; mCRPC = metastatic castration-resistant prostate cancer; ORR = objective response rate; OS = overall survival; PAP = prostatic acid phosphatase; PCWG3 = Prostate Cancer Working Group 3; PFS = progression-free survival; PICV = Pichinde virus; PS = performance status; PSA = prostate-specific antigen; Q3W = every 3 weeks; Q6W = every 6 weeks; RCV FFU = replication-competent virus focus-forming units; RECIST = Response Evaluation Criteria in Solid Tumors; RP2D = recommended Phase 2 dose.

REFERENCE

1. Scher HI, et al; Prostate Cancer Clinical Trials Working Group 3. *J Clin Oncol*. 2016;34(12):1402-1418.

CONTACT

- For additional information please contact XXXX