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319 Phase II trial of immunotherapy in primary glioblastoma: antigens from self-renewing autologous tumor cells presented by autologous dendritic cell vaccine

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with histologically/cytologically confirmed, previously treated, advanced solid tumors with HRRm and/or HRD per Lynparza HRR-HRD assay (Foundation Medicine, Inc., Cambridge, MA, USA), with an ECOG PS of 0-1. Patients will be grouped by biomarker status: subgroup 1: BRCAm; subgroup 2: HRRm without BRCAm; and subgroup 3: HRD positive without HRRm (loss of heterozygosity score ≥ 16 per Lynparza HRR-HRD assay). Patients will receive olaparib 300 mg twice daily + pembrolizumab 200 mg intravenously Q3W (35 cycles) until PD, unacceptable AEs, intercurrent illness, investigator decision, withdrawal of consent, or pregnancy. Tumor imaging assessment by blinded independent central review (BICR) per RECIST v1.1 or Prostate Cancer Working Group (PCWG)-modified RECIST v1.1 for prostate cancer will occur Q9W for 12 months, then Q12W until PD, start of new anticancer treatment, withdrawal of consent, pregnancy, or death. AEs will be monitored throughout the study and for 30 days after final dose (90 days for serious AEs). The primary endpoint is ORR (RECIST v1.1 or PCWG-modified RECIST version 1.1 by BICR). Secondary endpoints include duration of response (DOR) and PFS (RECIST v1.1 or PCWG-modified RECIST v1.1 by BICR), OS, and safety. Point estimate and exact Clopper-Pearson CI for ORR, and Kaplan-Meier estimates for DOR, PFS, and OS will be calculated. A total of 89 sites are currently enrolling in 20 countries.

Results N/A

Conclusions N/A

Trial Registration ClinicalTrials.gov identifier, NCT04123366

Ethics Approval An independent institutional review board or ethics committee approved the protocol at each study site, and the trial is being conducted in compliance with Good Clinical Practice guidelines and the Declaration of Helsinki.

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PHASE II TRIAL OF IMMUNOTHERAPY IN PRIMARY GLIOBLASTOMA: ANTIGENS FROM SELF-RENEWING AUTOLOGOUS TUMOR CELLS PRESENTED BY AUTOLOGOUS DENDRITIC CELL VACCINE

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Background Primary glioblastoma (GBM) is associated with poor survival. Adjunctive vaccines may improve survival by inducing or enhancing anti-GBM immune responses.

Methods A multi-institutional phase II clinical trial was conducted with a primary objective of 75% survival 15 months after intent-to-treat enrollment. Key eligibility criteria were: (1) primary GBM diagnosis, (2) age < 70 years at time of tumor resection, (3) successful GBM cell culture, (4) successful monocyte collection by leukapheresis, (5) Karnofsky Performance Status (KPS) > 70 after surgical recovery. Dendritic cells (DC) were differentiated from autologous monocytes, then incubated with autologous tumor antigens (ATA) from the GBM cell line-lysate to produce each patient-specific DC-ATA vaccine. Doses were suspended in 500 mcg granulocyte-macrophage colony-stimulating factor (GM-CSF)

at the time of subcutaneous injections at weeks 1, 2, 3, 8, 12, 16, 20 and 24. Patients were enrolled just prior to starting standard concurrent temozolomide (TMZ) and radiation therapy (RT) for the intent-to-treat after recovery from RT/TMZ.

Results Tumors were collected August 2018-January 2020. Cell line success rate was 71/73 (97%); monocyte collection success rate was 63/65 (97%), but 10 patients required a second leukapheresis. Patients were enrolled for in-to-treat October 2018-February 2020. The 60 patients included 42 men and 18 women with median age of 59 years (range of 27-70). Racial make-up was 43 White, 10 Hispanic, 2 Black, 1 Asian and 3 Other. KPS was 100 in 4, 90 in 25, 80 in 17 and 70 in 14 (mean 83.2). MGMT methylation was present in 13, absent in 31, and unknown in 16; IDH mutation was present in 7, absent in 50, and unknown in 3. 57 patients had received 380 doses with 9 still under treatment at time of abstract submission. 32 had completed all 8 doses; 16 had received fewer than 8 doses when they discontinued treatment. No patient discontinued treatment because of toxicity, but 28 have been hospitalized for 53 treatment-emergent central nervous system-related serious adverse events including seizures (15 episodes), falls and/or increased focal weakness (13 episodes), or severe headaches or visual changes (3 episodes).

Conclusions This patient-specific DC-ATA approach is feasible and may be increasing intratumor inflammation that is associated with on-target efficacy and/or toxicity. An interim survival analysis will be conducted in October 2020, 15 months after the median patient was enrolled; results will be available November 2020 as will immunologic data for 55 patients who received at least two injections.

Trial Registration ClinicalTrials.gov NCT03400917.

Ethics Approval The study was approved by UCI IRB, approval number 2018-4148.

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PHASE IIA STUDY OF ALPHA-DC1 VACCINE AGAINST HER2/HER3, CHEMOKINE MODULATION REGIMEN AND PEMBROLIZUMAB IN PATIENTS WITH ASYMPTOMATIC BRAIN METASTASIS FROM TRIPLE NEGATIVE OR HER2+ BREAST CANCER

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Background Brain metastases develop in up to 50% patients with metastatic triple negative breast cancer (TNBC) and HER2+ BC and are an increasing source of morbidity and mortality. HER3, overexpressed in triple negative and HER2 + brain metastatic breast cancer (BMBC), is a resistance factor to HER2-targeted therapies and a driver of CNS metastasis. Disease progression is associated with loss of anti-HER2/3 immunity. We have demonstrated that alphaDC1 loaded with glioma-specific peptides induce intratumoral production of chemokines (CXCL9, CXCL10, CXCL11, CCL5) which attract CXCR3- and CCR5- expressing cytotoxic T-lymphocytes (CTLs) and T-helper 1 (Th1) cells to brain tumors, inducing clinical responses and long-term disease stabilization