Ethics Approval This study was approved by the following Ethics Committees: COMITE DE PROTECTION DES PERSONNES, Sud-Méditerranée V (Gustave Roussy, IPC), Comité d'Ethique Institut Jules Bordet, COMITÉ DE ÉTICA DE INVESTIGACIÓN CLÍNICA CON MEDICAMENTOS del Hospital Universitari Vall d'Hebron, Ethikkommission an der TU Dresden, HRA London-Surrey Borders Research Ethics Committee.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0316

317 A PHASE 1/1B STUDY OF SBT6050, A HER2-DIRECTED MONOCLONAL ANTIBODY CONJUGATED TO A TOLL-LIKE RECEPTOR 8 AGONIST, IN SUBJECTS WITH ADVANCED HER2-EXPRESSING SOLID TUMORS

[1]Leisha Emens*, [2]Muralidhar Beeram, [3]Erika Hamilton, [4]Sarina Piha-Paul, [5]Valerie Odegard, [5]Sue Hamke, [5]Naomi Hunder, [6]Samuel Klempner. *[1]University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [2]The Start Center for Cancer Care, San Antonio, TX, USA; [3]Sarah Cannon Research Institute, Nashville, TN, USA; [4]MD Anderson Cancer Center, Houston, TX, USA; [5]Silverback Therapeutics, Inc., Seattle, WA, USA; [6]Massachusetts General Hospital, Boston, MA, USA*

Background New strategies are needed to improve outcomes in human epidermal growth factor receptor 2 (HER2)-expressing cancers. SBT6050 is a novel therapeutic comprising a specific small molecule toll-like receptor (TLR) 8 agonist conjugated to a HER2-directed monoclonal antibody. TLR8 is highly expressed in myeloid cells that are prevalent in human tumors, including dendritic cells (DCs) and macrophages, and modulates their pro-inflammatory activity. SBT6050 is designed to activate human myeloid cells only in the presence of moderate-to-high HER2 expression (immunohistochemistry [IHC] 2+ or 3+) and binds to the same epitope as pertuzumab. In preclinical studies, SBT6050 potently induces a broad spectrum of antitumor immune mechanisms, including proinflammatory cytokine and chemokine production, inflammasome activation, and indirect activation of T and natural killer (NK) cells. TLR8 agonism has emerged as a promising approach to overcome resistance to immune checkpoint inhibitors in tumors lacking T-cell infiltrates, as these cancers are often replete with myeloid cells. Using an SBT6050 mouse surrogate in vivo, curative single-agent efficacy was observed in multiple murine tumor models, including a model deficient in T, B, and NK cells. In preclinical toxicology studies in nonhuman primates, SBT6050 was well tolerated, supporting a first-in-human starting dose that is predicted to be pharmacologically active, with a short escalation to projected clinically active doses. Preclinical studies also support combinations with checkpoint inhibitors and with trastuzumab to further enhance antitumor activity.

Methods SBT6050-101 is an ongoing phase 1/1b, first-in-human, open-label, multicenter study. Eligible subjects are adults with histologically confirmed, HER2-expressing (IHC 2+ or 3+), locally advanced (unresectable) and/or metastatic cancer. Subjects must have measurable disease per the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 and have previously received all therapies known to confer clinical benefit. SBT6050 is given subcutaneously every 2 weeks and treatment may continue for up to 2 years or until disease progression, unacceptable toxicity, or other reason for discontinuation. The trial objectives are to evaluate the safety and tolerability of SBT6050 and to identify the maximum tolerated dose and recommended phase 2 dose (RP2D). The study has 2 parts: Part 1, consisting of a dose escalation using a standard 3+3 design, and Part 2, consisting of 5 parallel expansion cohorts based on tumor type and HER2 expression level and treated with SBT6050 at the RP2D. Pharmacokinetics, immunogenicity, and antitumor activity will be evaluated and pharmacodynamic markers of myeloid cell activation will be assessed in peripheral blood and on-treatment tumor biopsies.

Results N/A

Conclusions N/A

Trial Registration NCT04460456

Ethics Approval The study was approved by MD Anderson Cancer Center Institutional Review Board, approval number 2020-0326 MOD001.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0317

318 OLAPARIB PLUS PEMBROLIZUMAB IN PATIENTS WITH PREVIOUSLY TREATED ADVANCED SOLID TUMORS WITH HOMOLOGOUS RECOMBINATION REPAIR MUTATION AND/OR HOMOLOGOUS RECOMBINATION REPAIR DEFICIENCY: KEYLYNK-007

[1]Timothy A Yap*, [2]Mallika Dhawan, [3]Andrew E Hendifar, [4]Michele Maio, [5]Taofeek K Owonikoko, [6]Miguel Quintela-Fandino, [7]Ronnie Shapira-Frommer, [8]Sanatan Saraf, [8]Ping Qiu, [8]Fan Jin, [8]Alexander Gozman, [9]Douglas A Levine. *[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA; [3]Samuel Oschin Cancer Center, Cedars-Sinai Medical Center, Los Angeles, CA, USA; [4]Center for Immuno-Oncology, University Hospital of Siena, Siena, Italy; [5]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [6]Centro Nacional de Investigaciones Oncológicas, Madrid, Spain; [7]Chaim Sheba Medical Center, Tel HaShomer, Israel; [8]Merck and Co., Inc., Kenilworth, NJ, USA; [9]Laura and Isaac Perlmutter Cancer Center, New York, NY, USA*

Background Treatment with the anti–PD-1 antibody pembrolizumab has improved clinical outcomes in multiple previously treated advanced solid tumors. The poly (ADP-ribose) polymerase (PARP) inhibitor olaparib has shown antitumor activity as monotherapy in patients with previously treated advanced ovarian, breast, pancreatic, and prostate cancers with BRCA1/BRCA2 mutations (BRCAm). Activity was also seen in patients with previously treated advanced solid tumors with other homologous recombination repair mutation (HRRm) and in those with ovarian cancer with homologous recombination repair deficiency (HRD) phenotype. PARP inhibitors have been found to increase interferon signaling and tumor infiltrating lymphocytes, enhancing tumor susceptibility to immune checkpoint blockade. Antitumor activity of PD-(L)1 plus PARP inhibition was found to be higher than expected with either agent alone in patients with recurrent ovarian cancer regardless of BRCAm or HRD status and in patients with BRCAm breast cancer. KEYLYNK-007 (NCT04123366) evaluates the antitumor activity and safety of olaparib in combination with pembrolizumab in patients with previously treated advanced solid tumors with HRRm and/or HRD.

Methods This phase 2, nonrandomized, multicenter, open-label study will enroll approximately 300 patients aged ≥18 years

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.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0318

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

[1]Daniela Bota*, [3]David Piccioni, [4]Christopher Duma, [5]Renato LaRocca, [6]Santosh Kesari, [6]Jose Carrillo, [7]Robert O'Donnell, [8]Robert Aiken, [2]Frank Hsu, [2]Xiao-Tang Kong, [2]Thomas Taylor, [9]Gabriel Nistor, [10]Robert Dillman. *[1]Unviersity of California, Irvine, Orange, USA; [2]UCI, Orange, USA; [3]UCSD, San Diego, CA, USA; [4]Hoag Hospital, Newport Beach, CA, USA; [5]Norton Cancer Center, Louisville, KY, USA; [6]John Wayne Cancer Institute, Santa Monica, California, USA; [7]UCDavis, Davis, USA; [8]Rutgers, New Brunswick, NJ, USA; [9]Aivita Biomadical, Irvine, CA, USA; [10]Aivita Biomedical, Irvine, California, USA*

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.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0319

320 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

[1]Shipra Gandhi*, [2]Peter Forsyth, [3]Mateusz Opyrchal, [2]Kamran Ahmed, [2]Hung Khong, [1]Kristopher Attwood, [1]Ellis Levine, [1]Tracey O'Connor, [1]Amy Early, [1]Robert Fenstermaker, [1]Dheerendra Prasad, [1]Kazuaki Takabe, [2]Brian Czerniecki, [1]Pawel Kalinski. *[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [2]Moffitt Cancer Center, Tampa, FL, USA; [3]Washington University, St. Louis, MO, USA*

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