after transfer. Dendritic cells (DC) are professional antigen presenting cells and have the ability to optimally activate T lymphocytes.[3] We hypothesized that the combination of autologous TIL containing a population of HLA-A0201 restricted MART-1 reactive CD8+ TIL with autologous MART-1 antigen-pulsed DCs will result in enhanced proliferation and prolonged survival of the transferred antigen-specific T cells in vivo, thus leading to improved clinical responses.

Methods This is a randomized phase II trial of lymphodepleting chemotherapy followed by autologous TILs ± DC vaccine and high dose Interleukin-2 (IL-2) for patients with metastatic melanoma. Patients were randomized to receive TIL alone or TIL + DCs pulsed with MART-1 peptide. The primary objective was to determine whether patients receiving TIL + DCs have sustained persistence of infused T cells compared to patients treated with TIL alone. Secondary endpoints included evaluation of tumor response and survival.

Results A total of 18 patients with stage IV melanoma were treated; 89% with stage M1c, including 56% with brain metastasis; 17% had high LDH level. All but one patient were checkpoint naïve prior to TIL. Ten patients received TIL alone and eight received TIL + DC. Treatments were well tolerated with no grade 5 adverse events. There were no toxicities conferred by the DC vaccination. The ORR was 63% (5/8) in TIL + DC arm (1 CR, 4 PR) and 40% (4/10) in TIL arm alone (1 CR, 3 PR) (P=0.64). There was no statistically significant difference in survival between the arms. The median progression-free survival (PFS) was 3.6 months in the TIL arm and 7.2 months in the TIL+DC arm, while the median overall survival (OS) was 4.1 years in the TIL arm and 2 years in the TIL+DC arm. Tracking of the infused MART-1 reactive CD8+ T cells in the blood over time by flow cytometry showed no difference in persistence between the two arms.

Conclusions ACT with TILs has robust response in checkpoint naïve advanced melanoma patients. Despite numerically higher response rate in the TIL+DC arm, due to small patient number there was no statistically significant difference between the arms. Further testing of this approach in a prospective trial post-ICI is warranted.

Trial Registration All metastatic melanoma TIL lines were derived from tumor tissue obtained from patients enrolled on the TIL ACT clinical trial [institutional review board (IRB)-approved protocol# 2004-0069, NCT00338377] at The University of Texas MD Anderson Cancer Center.

Ethics Approval The United States Food and Drug Administration and the Institutional Review Board at MD Anderson Cancer Center approved the study. This study was conducted according to the principles from the Declaration of Helsinki.

Consent All study participants granted a written informed consent prior to treatment initiation.

REFERENCES

1. Rosenberg SA, Restifo NP. Adoptive cell transfer as personalized immunotherapy for human cancer. *Science* 2015;**348**(6230):62–8.
2. Forget MA, Haymaker C, Hess KR, Meng YJ, Creasy C, Karpinets T, *et al*. Prospective Analysis of Adoptive TIL Therapy in Patients with Metastatic Melanoma: Response, Impact of Anti-CTLA4, and Biomarkers to Predict Clinical Outcome. *Clin Cancer Res*. 2018;**24**(18):4416–28.
3. Banchereau J, Steinman RM. Dendritic cells and the control of immunity. *Nature*. 1998;**392**(6673):245–52.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0311

312 FEMALE SEX INDEPENDENTLY PREDICTS ADJUVANT IMMUNOTHERAPEUTIC BENEFIT FROM CTLA4 IMMUNE CHECKPOINT INHIBITION

[1]Ahmad Tarhini*, [2]Ni Kang, [3]Sandra Lee, [4]F Stephen Hodi, [5]Gary Cohen, [6]Omid Hamid, [7]Laura Hutchins, [8]Jeffrey Sosman, [9]Harriett Kluger, [10]Zeynep Eroglu, [11]Henry Koon, [12]Donald Lawrence, [13]Kari Kendra, [14]David Minor, [15]Carrie Lee, [16]Mark Albertini, [17]Lawrence Flaherty, [18]Teresa Petrella, [19]Howard Striecher, [10]Vernon Sondak, [20]John Kirkwood. *[1]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [2]Dana Farber Cancer Institute – ECOG-ACRI, Boston, MA, USA; [3]Dana Farber Cancer Institute ECOG-ACRIN, Boston, MA, USA; [4]Dana Farber Cancer Institute, Boston, MA, USA; [5]Greater Baltimore Medical Center, Baltimore, MD, USA; [6]Angeles Clinic and Research Institute, Los Angeles, CA, USA; [7]University of Arkansas, Little Rock, AR, USA; [8]Northwestern University, Chicago, IL, USA; [9]Yale University, New Haven, CT, USA; [10]H. Lee Moffitt Cancer Center, Tampa, FL, USA; [11]Bristol Myers Squibb, Cleveland, OH, USA; [12]Massachusetts General Hospital, Boston, MA, USA; [13]Ohio State University, Columbus, OH, USA; [14]Sutter-California Pacific Medical Center, San Francisco, CA, USA; [15]University of North Carolina at Chapel H, Chapel Hill, NC, USA; [16]University of Wisconsin, Madison, WI, USA; [17]Wayne State University/Karmanos Cancer I, Detroit, MI, USA; [18]Odette Cancer Center, Toronto, ON, Canada; [19]National Cancer Institute, Rockville, MD, USA; [20]University of Pittsburgh, Pittsburgh, PA, USA*

Background Sex differences in tumor immunity and response to immunotherapy were shown in murine models and descriptive analyses from recent clinical trials. Female sex hormones have been implicated in melanoma development and response to systemic therapy. We hypothesized a gender difference in response to adjuvant immunotherapy with ipilimumab (3 or 10 mg/kg; ipi3 or ipi10) versus high dose IFNα (HDI) as tested in the E1609 trial.

Methods E1609 demonstrated significant overall survival (OS) benefit with ipi3 versus HDI.[1] We investigated treatment efficacy between ipi and HDI in the subgroups by sex (female, male), age (< 55 or ≥55), stage at study entry (IIIB, IIIC, M1a/1b), ECOG performance status (PS 0, 1), ulceration (yes, no), primary tumor (known, unknown), number of lymph nodes involved (0, 1, 2–3, 4+). Forest plots were created to compare OS and RFS with ipi3 vs. HDI and ipi10 vs. HDI using the concurrently randomized ITT populations. For the estimated HRs, 95% confidence intervals were created for all subgroups.

Results The subgroups of female, stage IIIC, PS=1, ulcerated, in-transit without lymph node involvement demonstrated significant improvement in overall survival (OS) and/or relapse free survival (RFS) with ipi3 versus HDI as summarized in table 1. Female sex was significant for both OS and RFS and was further explored. In investigating RFS with ipi3 versus HDI, a multivariate Cox regression model including sex, treatment and interaction term of sex*treatment, indicated a significant interaction between sex and treatment (P = 0.026). Including sex, PS (0 vs. 1), age (<55 vs. 55+), ulceration (yes vs. no), stage (IIIB, IIIC, M1a, M1b), treatment and interaction term of sex*treatment, indicated a significant interaction between sex and treatment (P = 0.024). While similar trends were seen, no significant interactions between sex and treatment effect were found in the OS multivariate analysis or in the comparison of ipi10 versus HDI. When exploring age, in the univariate analyses in the ipi3 versus HDI comparison older women appeared to drive most of the difference (age ≥55: OS, P=0.02 and RFS, P=0.08; differences non-significant for women <55). Table 1.

Conclusions Female sex was independently associated with RFS adjuvant immunotherapeutic benefit from ipi3, supporting a potentially important role for female related factors in the immune response against melanoma, and these warrant further investigation.

Abstract 312 Table 1 Treatment efficacy between ipi3 and HDI by subgroup

Group	HR, 95% CI	
	OS	RFS
Female sex	0.60 (0.40, 0.92)	0.66 (0.49, 0.89)
In-transit, LN-ve	0.55 (0.29, 1.02)	0.58 (0.38, 0.88)
Ulceration	0.70 (0.50, 0.98)	0.83 (0.65, 1.07)
Stage IIIC	0.67 (0.48, 0.95)	0.78 (0.61, 1.01)
PS = 1	0.55 (0.32, 0.95)	0.74 (0.49, 1.12)

Trial Registration NCT01274338
Ethics Approval The study protocol was approved by the institutional review board (IRB) of each participating institution and conducted in accordance with Good Clinical Practice guidelines as defined by the International Conference on Harmonisation. This study was monitored by the ECOG-ACRIN DataSafety Monitoring Committee and the NCI.
Consent All patients provided IRB-approved written informed consent.

REFERENCE

1. Tarhini AA, Lee SJ, Hodi FS, Rao UNM, Cohen GI, Hamid O, Hutchins LF, Sosman JA, Kluger HM, Eroglu Z, Koon HB, Lawrence DP, Kendra KL, Minor DR, Lee CB, Albertini MR, Flaherty LE, Petrella TM, Streicher H, Sondak VK, Kirkwood JM. Phase III Study of Adjuvant Ipilimumab (3 or 10 mg/kg) Versus High-Dose Interferon Alfa-2b for Resected High-Risk Melanoma: North American Intergroup E1609. *J Clin Oncol*. 2020 Feb 20;**38**(6):567–575. PMID: 31880964.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0312

Clinical trials in progress

313 A PHASE 1 EVALUATION OF TEBOTELIMAB, A BISPECIFIC PD-1 X LAG-3 DART® MOLECULE, IN COMBINATION WITH MARGETUXIMAB IN PATIENTS WITH ADVANCED HER2+ NEOPLASMS

[1]Manish Patel*, [2]Jason Luke, [3]Erika Hamilton, [4]Bartosz Chmielowski, [5]George Blumenschein, [6]Hedy Kindler, [7]Shakeela Bahadur, [8]Cesar Santa-Maria, [9]Janine Koucheki, [9]Jichao Sun, [10]Sanjeev Kaul, [9]Francine Chen, [9]Xiaoyu Zhang, [9]John Muth, [9]Patrick Kaminker, [9]Paul Moore, [9]Bradley Sumrow, [11]Susanna Ulahannan. *[1]Florida Cancer Specialists/Sarah Cann, Sarasota, FL, USA; [2]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [3]Sarah Cannon Research Institute, Nashville, TN, USA; [4]University of California Los Angeles, Los Angeles, CA, USA; [5]MD Anderson Cancer Center, Houston, TX, USA; [6]University of Chicago, Chicago, IL, USA; [7]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [8]Sidney Kimmel Comprehensive Cancer Ctr, Baltimore, MD, USA; [9]MacroGenics, Inc., Rockville, MD, USA; [10]Bio-ClinPharm Consulting, LLC, Cranbury, NJ, USA; [11]SCRI Nashville/OUHSC, OKC, OK, USA*

Background Tebotelimab, also known as MGD013, is an investigational, Fc bearing bispecific tetravalent DART molecule designed to bind PD-1 and LAG-3 and sustain/restore the function of exhausted T cells.[1] Margetuximab, an investigational Fc-engineered anti-HER2 monoclonal antibody, has similar HER2 binding and antiproliferative properties to trastuzumab, but with enhanced Fc-mediated effector function. In vitro studies have demonstrated upregulation of LAG-3/PD-L1 expression on immune cells after margetuximab exposure, along with enhanced lytic activity of immune cells primed by margetuximab in the presence of tebotelimab.

Methods This study characterizes safety, PK/PD, and preliminary antitumor activity of tebotelimab plus margetuximab in patients with advanced HER2+ malignancies. A one-step 3+3 dose escalation phase of tebotelimab (300 and 600 mg) combined with margetuximab 15 mg/kg, both every 3 weeks, was followed by cohort expansion of patients with breast, gastric or gastroesophageal, and other HER2+ tumors.
Results At data-cutoff, 31 patients (2.0 median lines of prior therapy; 64.5% with prior HER2-directed therapy) were treated. Median duration of treatment is 10.3 weeks with 17 patients remaining on treatment. No maximum tolerated dose was defined. Treatment-related adverse events (TRAEs) occurred in 23/31 (74.2%) patients, most commonly diarrhea (n=6), nausea, ALT increased (n=5, each), AST increased, and myalgia (n=4, each). The rate of Grade 3 TRAEs was 19.4%, with no Grade 4–5 TRAEs observed. Immune-related AEs were consistent with events observed with anti-PD-1 antibodies and were manageable with supportive treatment. Among 20 response-evaluable patients (i.e., received on-treatment scan), 8 objective responses (6 confirmed) per RECIST v1.1 have been observed, including a confirmed complete response (cholangiocarcinoma) and 7 partial responses (breast [2], microsatellite stable colorectal cancer [2], esophageal adenocarcinoma [1], ovarian cancer [1], and microsatellite stable gastroesophageal junction carcinoma).[1] Immunohistochemistry (IHC) of available baseline tumor specimens (n=17) demonstrated low PD-L1 expression with combined positive scores of either 0 (n=16) or 1 (n=1, colorectal cancer). Investigations into other potential correlative biomarkers, including LAG-3 and PD-1 by IHC and gene expression profiling by NanoString, remain ongoing.
Conclusions Tebotelimab in combination with margetuximab has demonstrated an acceptable safety profile and encouraging early evidence of anti-tumor activity, with a preliminary overall response rate (ORR) of 40% (8/20) [including unconfirmed responses] among late-line patients with various advanced HER2+ malignancies.
Trial Registration NCT03219268
Ethics Approval This study was approved by each Institution's Ethics Board prior to enrollment of subjects.

REFERENCE

1. Luke J, *et al*. A phase I, first-in-human, open-label, dose-escalation study of MGD013, a bispecific DART molecule binding PD–1 and LAG–3, in patients with unresectable or metastatic neoplasms. *J Clin Oncol* **38**:2020 (suppl; abstr 3004).

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0313

315 W0180 NOVEL ANTI-VISTA ANTIBODY: RATIONALE FOR TARGET PATIENT POPULATION AND FIRST-IN-HUMAN TRIAL DESIGN IN MONOTHERAPY AND IN COMBINATION WITH ANTI-PD1 ANTIBODY

[1]Ignacio Melero, [2]Carlos Gomez-Roca, [3]Pierre Ferre, [3]Pierre Ferre, [3]Eric Chetaille, [3]Aurelie Petain, [3]Celine Thuilliez, [3]Isabelle Vandenberghe, [3]Francisco Cruzalegui, [3]Asmaa Boudribila, [3]Mariya Pavlyuk, [4]Aurelien Marabelle*. *[1]Centro de Investigacion de Medica Applic, Pamplona, Spain; [2]Institut Universitaire du Cancer, Toulouse, France; [3]Pierre Fabre Research Institute, Toulouse, France; [4]Institut Gustave Roussy, Villejuif, France*

Background V-domain Ig suppressor of T cell Activation (VISTA) is a negative checkpoint regulator of T cell response.[1] VISTA is expressed within the tumor microenvironment, where its blockade can enhance antitumor immune responses.[2] Furthermore, an increase in VISTA expression has been reported after treatment by anti-PD1/L1 and anti-CTLA4.[3,4]