(AEs). Correlative studies will evaluate pre- and post-treatment characteristics of T cells in the tumor microenvironment and blood.

Results N/A

Conclusions N/A

Ethics Approval The study was approved by the University of Miami Sylvester Cancer Center PRMC #20200847

Consent N/A

REFERENCES

- Woo SR, Tunis ME, Goldberg MV, *et al.* Immune inhibitory molecules LAG-3 and PD-1 synergistically regulate T-cell function to promote tumoral immune escape. *Cancer Res* 2012. **72**(4): p. 917–27.
- Durante MA, Rodriguez DA, Kurtenbach S, *et al.* Single-cell analysis reveals new evolutionary complexity in uveal melanoma. *Nat Commun* 2020;11(1):496. Published 2020 Jan 24. doi:10.1038/s41467-019-14256-1
- Karlsson J, Nilsson LM, Mitra S, *et al.* Molecular profiling of driver events in metastatic uveal melanoma. *Nat Commun* 2020;11(1):1894. Published 2020 Apr 20. doi:10.1038/s41467-020-15606-0

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0430>

431

PROSPECTIVE, RANDOMIZED TRIAL OF THE TUMOR LYSATE, PARTICLE ONLY VACCINE COMPARED TO THE TUMOR LYSATE, PARTICLE-LOADED, DENDRITIC CELL VACCINE TO PREVENT RECURRENCE FOR RESECTED STAGE III/IV MELANOMA

¹Patrick McCarthy*, ¹Lexy Adams, ¹Robert Chick, ¹Guy Clifton, ¹Timothy Vreeland, ¹Anne O'Shea, ¹Phillip Kemp Bohan, ¹Annelies Hickerson, ¹Jessica Campf, ¹John Myers, ¹Tommy Brown, ¹Diane Hale, ²Mark Faries, ³John Hyngstrom, ⁴Adam Berger, ⁵James Jakub, ⁶Jeffrey Sussman, ⁷Montaser Shaheen, ⁸Thomas Wagner, ⁹George Peoples. ¹Brooke Army Medical Center, San Antonio, TX, USA; ²The Los Angeles Angeles Clinic, CA, USA; ³University of Utah, Salt Lake City, UT, USA; ⁴Thomas Jefferson University, Philadelphia, PA, USA; ⁵Mayo Clinic, Rochester, MN, USA; ⁶University of Cincinnati, Cincinnati, OH, USA; ⁷University of Arizona, Phoenix, AZ, USA; ⁸Orbis Health Solutions, Greenville, SC, USA; ⁹Cancer Vaccine Development Group, San Antonio, TX, USA

Background The autologous tumor lysate, particle-loaded, dendritic cell (TLPLDC) vaccine is safe and effective in improving 24 and 36-month disease-free survival (DFS) in patients (pts) with resected stage III/IV melanoma who completed the primary vaccine series. The tumor lysate, particle only (TLPO) vaccine has been developed to accelerate production by omitting DC isolation and ex vivo loading in favor of in vivo phagocytosis of the TL-loaded particles. We are currently conducting a randomized and double-blind trial of the TLPO vs TLPLDC to improve DFS and overall survival (OS) in patients with resected late stage melanoma.

Methods Patients with stage III/IV melanoma who were clinically disease-free after standard of care therapies were randomized to receive TLPO vs TLPLDC (2:1) as a continuation of the phase IIb trial comparing TLPLDC vs placebo (2:1). For the TLPLDC vaccine, autologous TL was loaded into yeast cell wall particles (YCWP) which were then phagocytized by isolated autologous DC ex vivo. For the placebo DC were loaded with empty YCWP. For TLPO, the autologous TL-loaded YCWP were coated with a chemoattractant and injected intradermally for in vivo phagocytosis. Some patients in the TLPLDC arm received G-CSF prior to DC harvest to minimize blood draw (60 mL instead of 120 mL without G-CSF). For all arms, six vaccine/placebo doses were administered intradermally at 0, 1, 2, 6, 12, and 18 mos. Data was analyzed by an intention-to-treat (ITT) analysis for DFS and OS by the Kaplan-Meier method and compared by log-rank test.

Abstract 431 Figure 1 TLPO vs TLPLDC (n=20) DFS. Disease-free survival of TLPO patients compared to similar TLPLDC patients (n=20)

Abstract 431 Figure 2 TLPO vs TLPLDC (n=20) OS. Overall survival of TLPO patients compared to similar TLPLDC patients (n=20)

Abstract 431 Figure 3 TLPO vs TLPLDC subsets vs Placebo DFS. Disease-free survival of TLPO patients compared to placebo and all TLPLDC patients (n=103) stratified by use of G-CSF

Abstract 431 Figure 4 TLPO vs TLPLDC subsets vs Placebo OS. Disease-free survival of TLPO patients compared to placebo and all TLPLDC patients (n=103) stratified by use of G-CSF

Results 63 pts were randomized to TLPO (n=43) vs TLPLDC (n=20). The TLPO cohort contained more females and received less chemotherapy (0% vs 10%), but otherwise were comparable. There were no differences in DFS (p=0.948) or OS (p=0.779) between the two vaccines (figures 1&2). Comparing the TLPO pts to all other pts in the phase IIB trial [TLPLDC+G-CSF (n=57), TLPLDC-G-CSF (n=46), and placebo (n=41)] the TLPO arm had improved DFS compared to placebo (p=0.019) and TLPLDC+G-CSF (p=0.001), but roughly equivalent to the TLPLDC-G-CSF arm (p=0.276) (figure 3). A similar trend was seen in OS analysis, though differences were not statistically significant (figure 4).

Conclusions TLPO and TLPLDC vaccines (without the use of G-CSF) improve DFS in patients with resected stage III/IV melanoma compared to placebo. The TLPO vaccine may offer advantages via reduced cost and vaccine production time. TLPO should be closely considered for further clinical trials.

Trial Registration NCT02301611: Phase IIB TL + YWCP + DC in Melanoma TLPLDC IND#16101 TLPO IND#17274

Ethics Approval This study was approved by WIRB; protocol #20141932

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0431>

432

3-YEAR RESULTS OF THE PHASE 2 RANDOMIZED TRIAL FOR TALIMOGENE LAHERPAREPVEC (T-VEC) NEOADJUVANT TREATMENT PLUS SURGERY VS SURGERY IN PATIENTS WITH RESECTABLE STAGE IIIB-IVM1A MELANOMA

¹Reinhard Dummer*, ²David Gyorki, ³John Hyngstrom, ⁴Adam Berger, ⁵Robert Conry, ⁶Lev Demidov, ⁷Edward Chan, ⁸Hoi-Shen Radcliffe, ⁹Mark Faries, ⁹Merrick Ross. ¹University Hospital of Zurich, Zurich, SC, Switzerland; ²Peter MacCallum Cancer Centre, Melbourne, Australia; ³University of Utah Huntsman Cancer Insti, Salt Lake City, UT, USA; ⁴Cancer Institute of New Jersey, New Brunswick, NJ, USA; ⁵University of Alabama School of Medicine, Birmingham, AL, USA; ⁶N.N. Blokhin Russian Cancer Research Cen, Moscow, Russian Federation; ⁷Amgen Inc., Thousand Oaks, CA, USA; ⁸The Angeles Clinic and Research Institu, Los Angeles, CA, USA; ⁹University of Texas MD Anderson Cancer C, Houston, TX, USA

Background Neoadjuvant immunotherapies and targeted therapies for advanced melanoma are an active area of investigation. This is the first clinical trial of an approved oncolytic viral immunotherapy as a neoadjuvant treatment in advanced melanoma and the largest randomized controlled neoadjuvant trial including all types of resectable regional metastases to date. Previously published 2-year primary analysis results reported improved recurrence-free survival (RFS, HR 0.66, P=0.038) and overall survival (OS, HR 0.49, P=0.050) for neoadjuvant T-VEC plus surgery vs immediate surgery in resectable stage IIIB-IVM1a melanoma patients.¹ Here, we report the 3-year interim analysis results.

Methods Patients with resectable stage IIIB-IVM1a melanoma and ≥ 1 injectable cutaneous, subcutaneous, or nodal lesions were randomized 1:1 to receive 6 doses/12 weeks of neoadjuvant T-VEC then surgery (Arm 1) vs immediate surgical resection (Arm 2). T-VEC was administered until surgery, no remaining injectable tumors, or intolerance. RFS was defined as time from randomization to the first of local, regional, or distant recurrence, or death, where patients who did not receive surgery were imputed as events at baseline. Key secondary and exploratory endpoints include

safety, an RFS sensitivity analysis that censored events at the start of subsequent anticancer therapy, OS, and event-free survival (EFS), defined as time from randomization to disease progression that precludes surgery, or local, regional or distant recurrence post-surgery, or death from any cause, whichever occurs first. All P values are descriptive. NCT02211131.

Results As of April 30, 2020, median follow-up for all patients was 41.3 months. For Arm 1 vs. Arm 2, the 3-year KM estimates of RFS were 46.5% vs. 31.0% (HR 0.67, P=0.043). In the RFS sensitivity analysis that removed the potential effect of subsequent anticancer therapy on RFS, the 3-year Kaplan-Meier (KM) estimates of RFS were 49.1% for Arm 1 and 22.9% for Arm 2 (HR 0.60, P=0.022). The 3-year KM estimates of EFS were 50.3% for Arm 1 and 32.7% for Arm 2 (HR 0.58, P=0.015). For OS, the 3-year KM estimates were 83.2% for Arm 1 and 71.6% for Arm 2 (HR 0.54, P=0.061). No new safety signals were detected.

Conclusions At 3-year follow up, we continued to observe improved RFS and OS and observed improved EFS with neo-adjuvant T-VEC plus surgery compared with surgery alone. These results build upon the prior 2-year results to support the treatment effect of neoadjuvant T-VEC on advanced resectable melanoma. The final analysis will occur at 5 years.

Acknowledgements • The authors thank the investigators, patients, and study staff who are contributing to this study. • The study was sponsored and funded by Amgen Inc. • Medical writing support was provided by Christopher Nosala (Amgen Inc.).

Trial Registration NCT02211131

Ethics Approval The study was approved by all institutional ethics boards.

REFERENCE

1. Dummer R, Gyorki DE, Hyngstrom J, et al. Primary 2-year (yr) results of a phase II, multicenter, randomized, open-label trial of efficacy and safety for talimogene laherparepvec (T-VEC) neoadjuvant (neo) treatment (tx) plus surgery (surg) vs surg in patients (pts) with resectable stage IIIB-IVM1a melanoma. *Ann Oncol* 2019;30: V903.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0432>

433

TALIMOGENE LAHERPAREPVEC (T-VEC) IN COMBINATION WITH IPILIMUMAB (IPI) VERSUS IPI ALONE FOR ADVANCED MELANOMA: 4-YEAR INTERIM ANALYSIS OF A RANDOMIZED, OPEN-LABEL, PHASE 2 TRIAL

¹Igor Puzanov*, ²Jason Chesney, ³Frances Collichio, ⁴Parminder Singh, ⁵Mohammed Milhem, ⁶John Glaspy, ⁷Omid Hamid, ⁸Merrick Ross, ⁹Philip Friedlander, ¹⁰Claus Garbe, ¹¹Theodore Logan, ¹²Axel Hauschild, ¹³Celeste Lebbe, ¹⁴Min Yi, ¹⁴Wendy Snyder, ¹⁵Janice Mehnert. ¹Roswell Park Comprehensive Cancer Insti, Buffalo, NY, USA; ²J. Graham Brown Cancer Center, Louisville, KY, USA; ³The University of North Carolina at Chapel Hill, NC, USA; ⁴Mayo Clinic Scottsdale School of Medicine, Tucson, AZ, USA; ⁵University of Iowa Hospitals and Clinics, Iowa City, IA, USA; ⁶University of California Los Angeles Sch, Porter Ranch, CA, USA; ⁷The Angeles Clinic and Research Institute, Los Angeles, CA, USA; ⁸MD Anderson Cancer Center, Houston, TX, USA; ⁹Mt Sinai School of Medicine, New York, NY, USA; ¹⁰University Hospital Tuebingen, Tuebingen, Germany; ¹¹Indiana University Simon Cancer Center, Indianapolis, IN, USA; ¹²University of Kiel, Kiel, Germany; ¹³Ap-hp Dermatology Cic Departments, Paris, France; ¹⁴Amgen Inc., Thousand Oaks, CA, USA; ¹⁵Rutgers Cancer Institute of New Jersey, New York, NY, USA

Background This is the first randomized trial evaluating an oncolytic virus with an immune checkpoint inhibitor in