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Author/s:

Dummer, R;Gyorki, D;Hyingstrom, J;Berger, A;Conry, R;Demidov, L;Chan, E;Radcliffe, H-S;Faries, M;Ross, M

Title:

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

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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

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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 neoadjuvant 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.

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Trial Registration NCT02211131

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

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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