and stool were analyzed at baseline (pre-FMT), before immunotherapy, and three weeks after it.

Results Patient 1 was diagnosed with recurrent melanoma of the lower limb with multiple in-transit lesions refractory to control with surgery and a single intralesional injection of IL-2. Patient received stool from Donor 1 and did not experience any adverse effects from FMT. At the time of treatment #4, a solitary large cutaneous lesion stabilized but the patient experienced grade 1 diarrhoea, grade 2 nausea, and grade 2 fatigue, and grade 2 depression (NCI-CTCAE v5.0). Patient 2 was diagnosed with recurrent melanoma of the parotid gland with metastatic lesions in the lungs. Patient 2 received stool from Donor 2 and experienced only grade 1 flatulence from FMT. At the time of treatment #3, the patient experienced grade 1 constipation. Both patients had a vigorous immune response to FMT measured by changes in the immune subpopulations in peripheral blood one week after FMT, including an increase in CD28+ CD8+ T cells and a decrease in PDL1 + CD3- cells. Following anti-PD1 therapy, both patients had an increase in CD39+ CD8+ T cell population. The PD1+ CD38+ CD8+ dysfunctional T cell levels decreased in both patients post-FMT and anti-PD1 therapy.

Conclusions FMT combined with anti-PD1 therapy in patients with advanced melanoma appears to be safe. A measurable immune response was observed one week after FMT in both patients. One patient experienced several grade 2 toxicities with stabilization of a large cutaneous lesion.

Acknowledgements This study is funded by a grant from The Lotte & John Hecht Memorial Foundation and a grant from The Medical Oncology Research Funds (MORF) from Western University.

Trial Registration NCT03772899

Ethics Approval The study was approved by Western University Institution's Ethics Board, approval number 113131, date of approval March 15, 2019.

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SAFETY & EFFICACY OF LIFILEUCEL (LN-144) TUMOR INFILTRATING LYMPHOCYTE THERAPY IN METASTATIC MELANOMA PATIENTS AFTER PROGRESSION ON MULTIPLE THERAPIES – INDEPENDENT REVIEW COMMITTEE DATA UPDATE

¹Amod Sarnaik, ¹Nikhil Khushalani, ²Jason Chesney, ³Harriet Kluger, ⁴Brendan Curti, ⁵Karl Lewis, ⁵Theresa Medina, ⁶Sajeve Thomas, ⁷Anna Pavlick, ⁸Eric Whitman, ⁹Salvador Algarra, ¹⁰Pippa Corrie, ¹¹Omid Hamid, ¹²Jose Lutzky, ¹³Judit Olah, ⁷Jeffrey Weber, ¹⁴James Larkin, ¹⁵Wen Shi, ¹⁵Kelly DiTrapani, ¹⁵Harry Qin, ¹⁵Mariam Mirgoli, ¹⁵Renee Wu, ¹⁵Toshimi Takamura, ¹⁵Maria Fardis, ¹⁶John Kirkwood*. ¹H. Lee Moffitt Cancer Center, Tampa, FL, USA; ²James Graham Brown Cancer Center, Louisville, KY, USA; ³Yale University School of Medicine, New Haven, CT, USA; ⁴Providence Cancer Institute, Portland, OR, USA; ⁵University of Colorado, Aurora, CO, USA; ⁶Univ. of Florida Health Cancer Center, Orlando, FL, USA; ⁷NYU Langone Medical Center, New York, NY, USA; ⁸Atlantic Health System Cancer Care, Morristown, NJ, USA; ⁹Clinica Universitaria de Navarra, Pamplona, Spain; ¹⁰Addenbrooke's Hospital, Cambridge, UK; ¹¹The Angeles Clinic and Research Institute, Los Angeles, CA, USA; ¹²Mount Sinai Comprehensive Cancer Center, Miami Beach, FL, USA; ¹³Szegedi Tudományegyetem Szent-Györgyi, Szeged, Hungary; ¹⁴The Royal Marsden NHS Foundation Trust, London, UK; ¹⁵Iovance Biotherapeutics, San Carlos, CA, USA; ¹⁶University of Pittsburgh Medical Center, Pittsburgh, PA, USA

10.1136/LBA2019.18

Background Treatment options are limited for patients with advanced melanoma who have progressed on checkpoint

inhibitors and targeted therapies such as BRAF/MEK inhibitors (if BRAF-V600E mutated). Adoptive cell therapy utilizing tumor-infiltrating lymphocytes (TIL) has shown antitumor efficacy with durable responses in heavily pretreated melanoma patients. Safety and efficacy of lifileucel, a centrally manufactured cryopreserved autologous TIL therapy assessed by both investigator and an independent review committee (IRC), are presented.

Methods C-144-01 is a global Phase 2 open-label, multicenter study of the safety and efficacy of lifileucel in patients with unresectable metastatic melanoma. We report on Cohort 2 (N = 66) patients with Stage IIIC/IV unresectable melanoma who received lifileucel. Tumors resected at local institutions were processed in central GMP facilities for TIL production in a 22-day process. Final TIL infusion product was cryopreserved and shipped to sites. Patients received one week of cyclophosphamide/fludarabine preconditioning lymphodepletion, a single lifileucel infusion, followed by up to 6 doses of IL-2. All responses were assessed by RECIST 1.1.

Results 66 patients had the following baseline characteristics: 3.3 mean prior therapies (anti-PD1 100%; anti-CTLA-4 80%; BRAF/MEK inhibitor 23%), relatively high tumor burden (106 mm mean target lesion sum of diameters), 44% with liver and/or brain lesions, median LDH 244 U/L. Objective Response Rate (ORR) by investigator was 36.4% (2 CR, 22 PR, 1 previously confirmed PR is now changed to SD) and Disease Control Rate (DCR) of 80.3%. At a median follow up of 9.7 months, median Duration of Response (DOR) has not been reached. The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens.

The ORR per IRC was 34.8% (2 CR, 21 PR) and DCR was 72.7%. At a median follow up of 6.9 months, the median IRC DOR has not been reached. Overall concordance rate of investigator and IRC read of response was 89.4%. The concordance compares favorably with literature reports in a metastatic disease.¹

Conclusions Lifileucel treatment resulted in a 36.4% ORR in heavily pretreated metastatic melanoma patients with high baseline disease burden who had received prior anti-PD1 and BRAF/MEK inhibitors, if tumor BRAF mutated. The high concordance of 89.4% between investigator and IRC confirms the original assessment of lifileucel efficacy in metastatic melanoma.²

Acknowledgements The authors would like to thank the patients and their families for participation in the study.

The authors would also like to acknowledge the support and dedication of all investigators and site team members from all participating clinical trial institutions.

Trial Registration ClinicalTrials.gov Identifier: NCT02360579

Ethics Approval Ethics Approval This trial was approved by Western Institutional Review Board - IRB Tracking Number: 20160198.

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