expansion, give rise to differentiated subsets, and mediate long-term tumor control and T cell persistence, in line with recent murine ICB studies mediated by TCF⁺ progenitor T cells.⁴⁻⁵ Our data also suggest that TIL subsets mediating ACT-response (stem-like CD39⁻) might be distinct from TIL subsets enriched for anti-tumor-reactivity (terminally differentiated CD39⁺) in human TIL.⁶⁻⁷

Acknowledgements We thank Don White for curating the melanoma patient cohort, and J. Panopoulos (Flowjo) for helpful discussions on high-dimensional analysis, and NCI Surgery Branch members for helpful insights and suggestions. S. Krishna acknowledges funding support from NCI Director's Innovation Award from the National Cancer Institute.

Trial Registration NA

Ethics Approval The study was approved by NCI's IRB ethics board.

REFERENCES

- Goff SL, et al. Randomized, prospective evaluation comparing intensity of lymphodepletion before adoptive transfer of tumor-infiltrating lymphocytes for patients with metastatic melanoma. *J Clin Oncol* 2016;**34**:2389–2397.
- Snyder A, et al. Genetic basis for clinical response to CTLA-4 blockade in melanoma. *N Engl J Med* 2014;**371**:2189–2199.
- McGranahan N, et al. Clonal neoantigens elicit T cell immunoreactivity and sensitivity to immune checkpoint blockade. *Science* 2016;**351**:1463–1469.
- Sade-Feldman M, et al. Defining T cell states associated with response to checkpoint immunotherapy in melanoma. *Cell* 2019;**176**:404.
- Miller BC, et al. Subsets of exhausted CD8 T cells differentially mediate tumor control and respond to checkpoint blockade. *Nat. Immunol* 2019;**20**:326–336.
- Simoni Y, et al. Bystander CD8 T cells are abundant and phenotypically distinct in human tumour infiltrates. *Nature* 2018;**557**:575–579.
- Gros A, et al. PD-1 identifies the patient-specific CD8⁺ tumor-reactive repertoire infiltrating human tumors. *J Clin Invest* 2014;**124**:2246–2259.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0773>

Checkpoint blockade therapy

774

ANTIBIOTIC ADMINISTRATION PRIOR TO IMMUNOTHERAPY LEADS TO POOR OVERALL SURVIVAL ACROSS MULTIPLE MALIGNANCIES

¹Eric Vick*, ¹Inas Abuali, ²Sarah Ludvigsen, ²Andrew Kelleher, ²Nathanael Moore, ³Nicholas Arias, ¹Shuchi Gulati, ¹Trisha Wise-Draper. ¹University of Cincinnati Cancer Center, Cincinnati, OH, USA; ²University of Cincinnati Medical Center, Cincinnati, OH, USA; ³University of Cincinnati, Cincinnati, OH, USA

Background The use of immune checkpoint inhibitors (ICI) has increased significantly in the past five years, along with the number of available drugs and regimens. ICIs have dramatically increased survival in cancer patients, however, there has been data to show that they have reduced efficacy in the presence of antibiotics.¹ Antibiotic use prior and during ICI therapy was associated with worsening clinical outcomes in patients with renal cell carcinoma,² melanoma,³ and non-small-cell-lung-cancer.⁴ Specifically, exposure within 60 days of initiation of ICIs in NSCLC seemed most detrimental, however, some studies have suggested that antibiotics disrupt intestinal microflora for up to six months.⁵⁻⁶ Therefore, we hypothesized that the duration of the antibiotic effect on ICI efficacy may be present for a longer duration.

Methods The electronic medical record was queried at the University of Cincinnati Medical Center for the administration of ICIs and antibiotics. Data was collected on the use, type, and duration of antibiotics before ICI use after administration with relevant demographic and clinicopathologic variables

including treatment type, cancer type, staging information, and clinical course including subsequent antibiotic use. Univariate (Fischer's Exact) and multivariate analysis (multiple logistic regression) were conducted and survival analysis was determined according to log-rank testing.

Results 217 patients were examined. The median age was 64 (range 22-93), 38% were female, 73% had ECOG 0-1, and 77% were white. Cancer types included melanoma 24%, non-small cell lung cancer (NSCLC) 34%, small cell lung cancer 2%, renal cancer 11%, urothelial cancer 10%, head and neck cancers 11%, and 16% other primaries. 20% remained on ICI at the time of data entry. The most

Abstract 774 Figure 1 Antibiotics up to six months before ICI reduce OS

Figure 1: Antibiotics Prior to Checkpoint Inhibitor Therapy Lead to Inferior Overall Survival: Analysis of patients treated with any type of antibiotic lead to worsened overall survival compared to those who did not receive antibiotics or who received a one time dose of cefazolin. Statistical analysis showed by both Log Rank and Wilcoxon testing p-values were <0.0001 with median survival 6.5y vs. 2.3y for those who received antibiotics prior to ICI treatment (HR 3.4, 95% CI 2.2 to 5.3).

Abstract 774 Figure 2 Antibiotics up to six months before ICI reduce PFS

Figure 2: Antibiotics Prior to Checkpoint Inhibitor Therapy Lead to Inferior Progression-Free Survival: Analysis of patients treated with any type of antibiotic lead to worsened progression-free survival as well compared to those who did not receive antibiotics or who received a one time dose of cefazolin. Statistical analysis showed by both Log Rank and Wilcoxon testing p-values were 0.0027 and 0.0011 respectively. Median PFS from initiation of immunotherapy was 1.1y vs. 0.46y for those who received antibiotics prior to ICI treatment (HR 1.7, 95% CI 1.2 to 2.5).

common ICIs were pembrolizumab, nivolumab, followed by ipilimumab-nivolumab, ipilimumab, and durvalumab. 81 patients of 218 received antibiotics within 6 months of receiving checkpoint inhibitors. Of antibiotics administered, the most common classes were cephalosporins (86%), fluoroquinolones (28%), and glycopeptides (23%) with substantial overlap. Overall survival and progression-free survival was improved for those who did not receive antibiotics prior to ICI therapy (median OS 6.5 vs. 2.3 years, HR 0.36, $p < 0.0001$; median PFS 1.1 vs 0.5 years, HR 0.6, $p = 0.0027$) (figure 1 and 2 respectively). Linear regression showed no significant association between antibiotic use prior to ICI use and age, sex, race, ICI type, or ECOG status.

Conclusions This data adds to the growing body of knowledge that the use of antibiotics prior to ICI treatment leads to inferior overall and progression-free survival.

Acknowledgements We would like to thank the Roman Jandarov, UC Cancer Center, the University of Cincinnati Division of Hematology and Oncology, Department of Internal Medicine of the University of Cincinnati, and the University of Cincinnati Medical Center for their continued support.

Ethics Approval IRB 2019-0610

REFERENCES

- Pinato DJ, Gramenitskaya D, Altmann DM, Boyton RJ, Mullish BH, Marchesi JR, et al. Antibiotic therapy and outcome from immune-checkpoint inhibitors. *J Immunother Cancer* 2019;7:287.
- Ueda K, Yonekura S, Ogasawara N, Matsunaga Y, Hoshino R, Kurose H, et al. The impact of antibiotics on prognosis of metastatic renal cell carcinoma in Japanese patients treated with immune checkpoint inhibitors. *Anticancer Res* 2019;39:6265–71.
- Elkrief A, El Raichani L, Richard C, Messaoudene M, Belkaid W, Malo J, et al. Antibiotics are associated with decreased progression-free survival of advanced melanoma patients treated with immune checkpoint inhibitors. *Oncoimmunology* 2019;8:e1568812.
- Ruiz-Patiño A, Barrón F, Cardona AF, Corrales L, Mas L, Martín C, et al. Antibiotics impair immune checkpoint inhibitor effectiveness in Hispanic patients with non-small cell lung cancer (AB-CLICaP). *Thorac Cancer* 2020;(9):2552–2560.
- Pinato DJ, Howlett S, Ottaviani D, Urus H, Patel A, Mineo T, et al. Association of prior antibiotic treatment with survival and response to immune checkpoint inhibitor therapy in patients with cancer. *JAMA Oncol* 2019;5(12):1774–1778.
- Panda S, Khader IE, Casellas F, Vivancos JL, Cors MG, Santiago A, et al. Short-term effect of antibiotics on human gut microbiota. *PLoS ONE* 2014;9.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0774>

775

RARE CASE REPORTS ON THYMIC CARCINOMA PATIENTS TREATED WITH PEMBROLIZUMAB

¹Evelyn Paszkan*, ¹Erna Ganofsky, ²Zolt Megyesi, ²Aron Ghimesy, ²Balazs Dome, ²Laszlo Agocs, ¹Erika Toth, ²Ferenc Renyi-Vamos, ¹Gabor Rubovszky. ¹National Institute of Oncology, Budapest, Hungary; ²Semmelweis University and National Institute of Oncology, Budapest, Hungary

Background Thymomas and thymic carcinomas (TC) are intrathoracic malignancies that, although rare, represent the most common anterior mediastinal tumors in adults (comprising approximately 0.2–1.5% of all malignancies).¹ Recent accumulating evidence on immune checkpoint pathways suggests that immunotherapy might be a promising therapeutic option for refractory TCs.² We herein report two cases of a pembrolizumab-treated TC patient.

Methods Immunotherapy is accessible through individual permission for the treatment of TC in Hungary. We retrospectively collected data of two TC patients treated with pembrolizumab in one institute.

Results The first patient was a 66-year-old woman. Squamous cell TC was diagnosed in her left parasternal region. She was

a former smoker, had no history of autoimmune disorders, and had no associated symptoms at the time of diagnosis. She underwent open thymectomy. The histology proved type C (WHO classification) TC with a pathological TNM of T1aN0 and microscopic-positive margins. Consequently, the patient received 60 Gy of postoperative radiotherapy. Nine months after the surgery local recurrence and multiple hepatic metastases appeared. Six cycles of chemotherapy (ADOC regimen) were introduced as first-line systemic therapy which resulted in stable disease (SD) for 8 months. Pembrolizumab was administered as second-line treatment (200 mg every 3 weeks) for 6 cycles. The best result was SD. Due to progression, third-line docetaxel treatment was initiated. Shortly after, ptosis and diplopia developed. Myasthenia gravis was diagnosed, and third-line chemotherapy was judged ineffective. The second patient was a 63-year-old man. He was diagnosed with unresectable TC and treated with chemotherapy (ADOC regimen) up-front. After six cycles the tumor regressed, and surgery was performed with R2 result. Postoperatively, the patient was given six cycles of chemotherapy (cisplatin/etoposide) and radiotherapy. Six months later local progression was detected and pembrolizumab was commenced. Eight cycles of pembrolizumab produced SD as best response. No immune-related adverse effects (irAEs) were detected. After progression Sunitinib therapy was started. In both cases, additional immunohistochemistry investigations were performed.

Conclusions In the literature, there is no phase 3 trial on immune-checkpoint inhibitor (ICI) therapy of TC. Phase 2 trials reported promising results with pembrolizumab.^{3–4} However, there are conflicting results with other ICIs.⁵ Before starting, it is important to rule out autoimmune disorders to evade serious, even life-threatening immune-complications. The high likelihood of irAEs in TC also underpin the importance of predictive biomarkers. Further studies are required to evaluate the efficacy and safety of immunotherapy in TC.

Acknowledgements The authors thank the multidisciplinary clinical teams involved in the treatment and management of the patient.

REFERENCES

- Bushan K, Sharma S, Verma H. A review of thymic tumors. *Indian Journal of Surgical Oncology* 2013;4(2):112–116. <https://doi.org/10.1007/s13193-013-0214-2>
- Isshiki T, Isobe K, Tochigi N, et al. Successful use of pembrolizumab to treat refractory thymic carcinoma with high PD-L1 expression. *Case Rep Oncol* 2018;11(3):688–692. Published 2018 Oct 31. doi:10.1159/000493187
- Giaccone G, Kim C, Thompson J, McGuire C, Kallakury B, Chahine JJ, et al. Pembrolizumab in patients with thymic carcinoma: a single-arm, single-centre, phase 2 study. *Lancet Oncol* 2018;19:247–255.
- Cho J, Kim HS, Ku BM, Choi YL, Cristescu R, Han J, et al. Pembrolizumab for patients with refractory or relapsed thymic epithelial tumor: an open-label phase II trial. *J Clin Oncol* 2019;37(JCO201773184):2162–2170.
- Katsuya Y, Horinouchi H, Seto T, Umemura S, Hosomi Y, Satouchi M, et al. Single-arm, multicentre, phase II trial of nivolumab for unresectable or recurrent thymic carcinoma: PRIMER study. *Eur J Cancer* 2019;113:78e86.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0775>

776

A ROLE FOR IMMUNE CHECKPOINT BLOCKADE TO ENHANCE T CELL-MEDIATED RESPONSES IN COMBINATION WITH CHEMOTHERAPY IN OESOPHAGEAL ADENOCARCINOMA

Maria Davern*, Joanne Lysaght, Andrew Sheppard, Stephen Maher, Noel Donlon, John Reynolds, Fiona Connell, Conall Hayes, Ross King, Anshul Bhardwaj. Trinity College Dublin, Dublin, Ireland

Background Combining immune checkpoint inhibitors (ICIs) with immunogenic chemotherapies is a promising approach in