43

HIGHLY MULTIPLEXED DIGITAL SPATIAL PROFILING OF THE TUMOR MICROENVIRONMENT OF NON-SMALL-CELL LUNG CANCER (NSCLC)

¹Arutha Kulasinghe*, ²Connor O'Leary, ³Rahul Ladwa, ³Majid Warkiani, ¹Kenneth O'byrne. ¹Queensland University of Technology, Kelvin Grove, Australia; ²Princess Alexandra Hospital, Woolloongabba, Australia; ³University of Technology Sydney, Sydney, Australia

Background Profiling the tumour microenvironment (TME) has been informative in understanding the underlying tumour-immune interactions. Multiplex immunohistochemistry(mIHC) coupled with molecular barcoding technologies have revealed greater insights into the TME.

Methods In this study, we utilised the Nanostring GeoMX Digital Spatial Profiler (DSP) platform to profile a NSCLC tissue microarray for protein markers across immune cell profiling, immuno-oncology(IO) drug target, immune activation status, immune cell typing, and pan-tumour protein modules. Regions of interest (ROIs) were selected that described tumour, TME and normal adjacent tissue (NAT) compartments.

Results Our data revealed that paired analysis (n=18) of patient matched compartments indicated that the TME was significantly enriched in CD27, CD3, CD4, CD44, CD45, CD45RO, CD68, CD163, and VISTA relative to tumour. Unmatched analysis indicated that the NAT(n=19) was significantly enriched in CD34, fibronectin, IDO1, LAG3, ARG1 and PTEN when compared to the TM E(n=32). Univariate Cox proportional hazards indicated that the presence of cells expressing CD3 (HR:0.5, p=0.018), CD34(HR:0.53, p=0.004) and ICOS (HR:0.6, p=0.047) in tumour compartments were significantly associated with improved overall survival (OS).

Conclusions We implemented both high-plex and high-throughput methodologies to the discovery of protein biomarkers and molecular phenotypes within biopsy samples and demonstrate the power of such tools for a new generation of pathology research.

Acknowledgements This study was funded by the Princess Alexandra Hospital Foundation grant for KOB. AK is supported by an NHMRC ECF Fellowship (APP1157741) and Cure Cancer (APP1182179).

Ethics Approval The study was approved by the QUT Human Research Ethics Board

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0043>

44

BODY COMPOSITION MAY BE PROGNOSTIC AND PREDICTIVE OF CLINICAL OUTCOMES IN METASTATIC RENAL CELL CARCINOMA (MRCC) PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS (ICI)

¹Dylan Martini*, ¹T Anders Olsen, ²Subir Goyal, ²Yuan Liu, ¹Sean Evans, ¹Benjamin Magod, ¹Jacqueline Brown, ³Lauren Yantorni, ³Greta Russler, ¹Sarah Caulfield, ¹Jamie Goldman, ¹Bassel Nazha, ¹Wayne Harris, ¹Omer Kucuk, ¹Bradley Carthon, ¹Viraj Master, ¹Mehmet Bilen. ¹Emory University School of Medicine, Atlanta, GA, USA; ²Emory University, Atlanta, GA, USA; ³Winship Cancer Institute, Atlanta, GA, USA

Background Immune checkpoint inhibitors (ICI) have revolutionized the treatment of metastatic renal cell carcinoma (mRCC). Biomarkers for mRCC patients treated with ICI are limited, and body composition is underutilized in mRCC. We investigated the association between body composition and clinical outcomes in ICI-treated mRCC patients.

Methods We performed a retrospective analysis of 79 ICI-treated mRCC patients at Winship Cancer Institute from

2015–2020. Patients with CT scans within 2 months of ICI-initiation were included. Baseline CT images were collected at mid-L3 and segmented using SliceOMatic v5.0 (TomoVision). Density of skeletal muscle (SM), subcutaneous fat, inter-muscular fat, and visceral fat were measured and converted to indices by dividing by height(m)² (SMI, SFI, IFI, and VFI, respectively). Total fat index (TFI) was defined as the sum of SFI, IFI, and VFI. Patients were characterized as high versus low for each variable at gender-specific optimal cuts using overall survival (OS) as the primary outcome. A prognostic risk score was created based on the beta coefficient from the multivariable Cox model (MVA) after best subset variable selection. Body composition risk score was calculated as IFI + 2*SM mean + SFI, and patients were classified as high (0–1), intermediate (2), or low-risk (3–4). Kaplan-Meier method and Log-rank test were used to estimate OS and PFS and compare the risk groups. Concordance statistics (C-statistics) were used to measure the discriminatory magnitude of the model.

Results Most were male (73%), and median age was 61 years. Patients were primarily intermediate (54%) or poor-risk (30%) per IMDC criteria and most received ICI as first (35%) or second-line (51%) therapy. The body composition high-risk patients had significantly shorter OS (HR: 6.37, p<0.001), PFS (HR: 4.19, p<0.001), and lower chance of CB (OR: 0.23, p=0.044) compared to low-risk patients in MVA (table 1). Patients with low TFI had significantly shorter OS (HR: 2.72, p=0.002), PFS (HR: 1.91, p=0.025), and lower chance of CB (OR: 0.25, p=0.008) compared to high TFI patients in MVA. The C-statistics were higher for body composition risk groups and TFI compared to IMDC and BMI (table 2). The median OS and PFS were shorter for high-risk versus intermediate and low-risk patients (figures 1–2).

Abstract 44 Table 1 MVA* of association between body composition risk groups and TFI with clinical outcomes

	OS		PFS		CB	
	HR (CI)	p-value	HR (CI)	p-value	OR (CI)	p-value
Body Composition Risk Group Analysis						
High Risk: Risk Score=0-1 n=20	6.37 (2.40-16.92)	<0.001**	4.19 (1.87-9.42)	<0.001**	0.23 (0.05-0.96)	0.044**
	Median Survival: 6.3 months		Median Survival: 2.5 months			
	24-Month Survival: 29.2%		12-Month Survival: 15.0%			
Intermediate Risk: Risk Score=2 n=42	1.56 (0.61-3.95)	0.350	2.05 (0.98-4.29)	0.057	0.49 (0.15-1.59)	0.238
	Median Survival: 24.6 months		Median Survival: 4.8 months			
	24-Month Survival: 53.1%		12-Month Survival: 26.6%			
Low Risk: Risk Score=3-4 n=18	1		1		1	
	Median Survival: 44.5 months		Median Survival: 12.4 months			
	24-Month Survival: 82.1%		12-Month Survival: 54.3%			
Categorical Total Fat Index (TFI) Analysis***						
Low n=34	2.72 (1.43-5.17)	0.002**	1.91 (1.09-3.35)	0.025**	0.25 (0.09-0.70)	0.008**
High n=45	1		1		1	

* MVA controlled for race, gender, clear cell RCC, Baseline BMI, Age, anti-PD-1 monotherapy, IMDC risk groups and number of prior lines of therapy.

**Statistically significant at the level of p<0.05

***High vs low TFI determined by optimal cut analysis