Background Immune-checkpoint inhibitors (ICIs) have revolutionized the treatment of advanced/metastatic non-small cell lung cancer patients (NSCLC), however, only a small subset of patients derives clinical benefit. To date, PD-L1 immunohistochemical evaluation is the gold-standard assay and the only approved biomarker, but associated with several limitations due to technical and biological factors such as spatial and temporal tumor heterogeneity. In this context, liquid biopsies emerge to serve to stratify the response to ICIs in NSCLC patients.

Methods This study enrolled advanced/metastatic NSCLC patients receiving ICI treatment. Plasma samples were obtained at baseline (T1) and at 8 weeks (T2) during the first response evaluation. Patients were classified as responders when showing progression-free survival (PFS) at baseline (T1) and at 8 weeks (T2) during the first response evaluation. Patients were classified as responders when showing an increase in NLR of 3 or more at 2 months of treatment and increasing risk of death with a high positive predictive value. NLR failure if validated in larger studies could be useful in treatment management.

Results Paired plasma samples from 21 patients were analyzed. PD-L1 tissue expression was not correlated with treatment response (p=0.394) nor matched the baseline EV PD-L1 levels (p=0.37) (Figure 1.A). However, the dynamics of EV PD-L1 (T1-T2) correlated with the treatment response, observing an increase of PD-L1 expression in non-responders and a decrease or stable levels in responders (p=0.043) (Figure 1.B). The predictive model reported an AUC of 0.85, 90% CI = 0.72–0.97, with 74.2% sensitivity and 73.5% specificity (Figure 1.C). Moreover, the increase of EV PD-L1 was associated with shorter overall survival (HR = 4.34, p = 0.037) and shorter progression-free survival (HR = 5.06, p = 0.025) (Figure 1 D & E).

Conclusions Our preliminary-study showed, for the first time, the predictive and prognostic value of EV PD-L1 dynamic changes in immunotherapy-treated NSCLC patients. Although larger studies are needed to validate these results, this promising biomarker could have important clinical implications, guiding treatment decisions in near real-time and improving the outcome of patients that could benefit from ICIs.

Acknowledgements We would like to extend our gratitude to all the patients that participated in the study.

Ethics Approval All patients consented to an Institutional Review Board–approved protocol (A.O. Papardo, Messina, Messina, Italy). Biological material was transfer to the University of Maryland, USA under signed MTA between both institutions (MTA/2020-13111).

REFERENCES
C-REACTIVE PROTEIN (CRP) AS A PROGNOSTIC DYNAMIC MONITORING OF RESPONSE TO IMMUNE CHECKPOINT INHIBITORS. RESULTS FROM A MULTI-CENTER INTERNATIONAL OBSERVATIONAL STUDY

Background CRP is an acute-phase protein produced primarily in response to interleukin-6 via transcriptional activation of the STAT3. Recent data have provided mechanistic insights in response to interleukin IL-6 via transcriptional activation of CRP is an acute-phase protein produced primarily

Results Baseline CRP value was available in 75.5% of patients, with 66% having CRP-H. The median CRP was 21.0 mg/l. Single-agent nivolumab (44%) and Chemo-ICI (33.3%) were the two most common therapies. Association of baseline CRP with median progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method and multivariate proportional hazards regression. Overall survival (OS) and baseline CRP were associated with survival (p=0.029). Compared to those with CRP-N (figure 1), patients with CRP-H had a significantly shorter median PFS [3.9 vs. 6.6 months, HR 1.41 95% CI: (1.07–1.86); p=0.013] and OS [8.6 vs. 14.8 months, HR 1.55 95% CI [1.13–2.14]; p=0.0060]. In Cox regression analysis, CRP-H was again found to be independent of association with shorter median PFS and OS.

Conclusions This is the largest international real-world dataset demonstrating significantly inferior outcomes associated with CRP > 10 mg/l in NSCLC patients treated with ICI based therapies. The potential influence of the immune suppressive effects of elevated CRP and IL-6 on the anti-tumor efficacy of ICIs needs prospective evaluation and could potentially be exploited as a therapeutic avenue in NSCLC.

Abstract 32 Figure 1 Kaplan-Meier Curves with 95% CI for PFS and OS Significantly inferior median PFS and OS were seen for patients with CRP-H vs. CRP-N.

Acknowledgements Susan Eubanks and Sue-Ann Joyner at the ECU IRB for their help and support.

Ethics Approval The primary IRB approval for this study was conducted under an ECU (P-MAIT-UMCIRB-15-001400). Individual approval was also obtained from the respective IRB of each participating institution.

REFERENCES

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0032

DYNAMIC MONITORING OF RESPONSE TO IMMUNE CHECKPOINT BLOCKADE THROUGH DEEP-LEARNING EMPOWERED ULTRA-SENSITIVE LIQUID BIOPSY IN MELANOMA

Background Clearance of circulating tumor DNA (ctDNA) following checkpoint blockade (CB) can precede radiographic response, 1 though current state of the art ctDNA detection via targeted panels faces limited sensitivity in low burden disease (figure 1). We previously showed that whole genome sequencing (WGS) of plasma can overcome low input of ctDNA to dynamically track low volume malignancy using matched tumor tissue. 2 We therefore sought to evaluate