140 ASSESSMENT OF DIFFERENCES IN TUMOR MUTATIONAL BURDEN IDENTIFIED ON LIQUID BIOPSY IN 16,870 PATIENTS NEWLY DIAGNOSED WITH METASTATIC CANCER

[1]Eugene Kwon, [1]Daniel Childs, [1]Bradley Stish, [1]Stephen Boorjian, [1]Matthew Tollefson, [1]Cameron Britton, [1]Ahmed Mahmoud, [2]Angela Thompson, [2]Reagan Barnett, [2]Leylah Drusbosky, [2]Leslie Bucheit*. *[1]Mayo Clinic, Rochester, MN, USA; [2]Guardant Health, Redwood City, CA, USA*

Background Tumor mutational burden (TMB) has emerged as a biomarker of response to immune checkpoint inhibition (ICI), with pembrolizumab approved for patients with a TMB of >10 mut/Mb regardless of solid tumor type. Predictive TMB cutoffs have not been optimized to account for differences in results based on genetic platform, manner of collection (tissue versus blood-based), or tumor type, though some data suggest disease-specific cut-offs may better identify patients who are likely to benefit from ICI. While described in tissue-based assays, blood-based TMB (bTMB) values and histology-specific differences are not well characterized for those newly diagnosed metastatic solid tumors. Here, we present results of bTMB assessment in nearly 17,000 newly diagnosed patients.

Methods Genomic results were queried for patients with newly diagnosed metastatic non-small cell lung cancer (NSCLC), colorectal, breast, prostate, gastric, melanoma or bladder cancer (as designated by ordering clinicians on requisition forms), who had Guardant360 (Guardant Health) testing between October 1, 2020, and June 1, 2022. Three factors were assessed across cancer types: 1) rate of evaluable bTMB, 2) median bTMB at diagnosis, and 3) percentage of patients whose initial bTMB value was above disease-specific cut-offs generated from prior Guardant cohorts[1] (≥80th percentile bTMB values in mut/Mb – NSCLC: 20.2, CRC: 20.1, breast: 15.3, prostate: 13.4, gastric: 13.8, melanoma: 23.8, bladder: 20.2).

Results 16,870 patients were included, most diagnosed with NSCLC (table 1). Newly diagnosed patients with prostate cancer had the lowest rate of evaluable bTMB (<75%); all other cancer types were near or above 80% evaluable. Newly diagnosed patients with bladder cancer and melanoma had the highest median bTMB, while the lowest values were observed for breast and prostate cancers. Less than 20% of newly diagnosed patients with prostate or colorectal cancers had bTMB values above the cancer-type specific cut-off; all other cancer types had >20% of patients with bTMB values above cut-offs.

Conclusions bTMB is evaluable in most patients with newly diagnosed metastatic disease, supporting the feasibility of using circulating tumor DNA to determine TMB. Approximately 20% had a bTMB value above the cancer-specific cut-offs, suggesting potential responsiveness to ICI. Notably, prostate cancer was low across all factors assessed which may reflect its 'cold' biology; assessment of bTMB over time, rather than only at diagnosis, may better inform bTMB utility for patients with certain cancers. Further studies are needed to explore the utility of serial TMB assessment and correlate bTMB values with clinical treatment and outcomes.

Abstract 140 Table 1 bTMB values in patients newly diagnosed with metast

Cancer type	bTMB evaluable	Median bTMB (mut/Mb)	Number of patients who had bTMB greater than cancer type cut-off
NSCLC	8509/10,333 (82%)	12.44	1825 (21%)
Colorectal	1978/2281 (87%)	9.57	95 (13%)
Breast	1621/1984 (82%)	7.89	298 (21%)
Prostate	856/1155 (74%)	7.99	149 (17%)
Gastric	433/525 (82%)	8.61	95 (22%)
Melanoma	274/347 (79%)	14.94	99 (26%)
Bladder	208/245 (85%)	19.36	61 (29%)

http://dx.doi.org/10.1136/jitc-2022-SITC2022.0140

REFERENCE

1. Drusbosky L, *et al. Journal of Clinical Oncology* 39, no. 15_suppl. 2021; 3040–3040. DOI: 10.1200/JCO.2021.39.15_suppl.3040