EXPLORING REAL-WORLD CONCORDANCE OF TUMOR MUTATION BURDEN (TMB) FROM BLOOD AND TISSUE IN PATIENTS WITH SOLID TUMORS

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Background Tumor mutational burden (TMB) is an approved biomarker for immunotherapy in metastatic cancer patients. While initially measured from tissue (tTMB), TMB derived from circulating tumor DNA (ctDNA) – also known as blood TMB (bTMB) – is increasingly being used in the clinic. Currently, real-world concordance between tTMB and bTMB is not well understood.

Methods From October 2020 to July 2022, cancer patients who had both tTMB and bTMB results were selected. Commercial next generation sequencing (NGS) testing for both tissue and blood, i.e. by Tempus xT (Tempus; Chicago, IL) and Guardant360 (Guardant Health; Redwood City, CA) were utilized. Patients were classified according to clinical variables and tumor burden, and correlation analyses or tests of independence were performed. To explore the significance of concordant and discordant bTMB:tTMB ratio, patients were divided into tertiles based on their bTMB:tTMB ratio as ‘low’, ‘mid’, and ‘high’. ‘Low’ and ‘high’ subgroups were considered to be discordant while ‘mid’ was considered to be concordant.

Results From a total of 95 patients included in the study, 69 patients (72.6%) had lung carcinoma and 26 (27.4%) had other cancers, including but not limited to thyroid, brain, and cervical cancer. Median bTMB was 9.6 mut/Mb and median tTMB was 4.0 mut/Mb. The distributions of bTMB and tTMB differed significantly (Wilcoxon signed-rank V=268.5, n=95, p<0.001). bTMB was moderately correlated with tTMB (Spearman $\rho=0.49$, p < 0.001) (figure 1). Twelve patients had tTMB > 10 mut/Mb while 45 patients had bTMB > 10 mut/Mb. When patients were divided according to cancer type, moderate correlation between bTMB and tTMB remained statistically significant for both lung adenocarcinoma, lung squamous cell carcinoma, and other lung cancer types. The regression lines for lung cancer subtypes displayed marked differences in slope. Dividing patients by site of tissue biopsy revealed that the degree of correlation was pronounced for tissue samples from primary and metastatic sites, not from the lymph nodes. Correlation appeared equivalent between smoker and never smokers. However, dividing patients by concordant and discordant bTMB:tTMB ratio did not reveal any significant differences in clinical variables or tumor burden (table 1).

Conclusions Cancer type and site of tissue biopsy may influence concordance between tTMB and bTMB. Future studies with more patients may help define the optimal bTMB threshold for receiving immunotherapy, which may be different from the tTMB threshold.

REFERENCES


Ethics Approval The study was approved by Northwestern University’s Institutional Review Board, study number STU00207117.