e20506 Publication Only

TP53 mutation as a prognostic factor in metastatic non-small cell lung cancer (NSCLC): A retrospective review.

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Background: TP53 is one of the most commonly mutated genes found in all cancers including NSCLC. We assessed prevalence of TP53 mutation in patients with metastatic NSCLC at our institution and correlated with clinical characteristics and prognosis. **Methods:** We analyzed next-generation sequencing (NGS) results of the metastatic NSCLC patients diagnosed at our institution for which complete clinical characteristics were available between 2008-2022. Patients were divided into those with TP53 mutations and wild types. Clinical characteristics, treatment history and outcomes were evaluated for each group. **Results:** A total of 107 patients were selected for final analysis based on availability of data. 40 patients (37%) were noted to have presence of TP53 mutation. There was no difference in ethnicity, median age (63.5 years in mutated vs 66 years in the wild type, p = 0.137) and gender (62.5% of mutated p53 being men vs wild type having 47.8% men, p= 0.129). The most common histology was adenocarcinoma (80%) followed by squamous cell carcinoma (14%). There was no difference in histology between the groups. TP53 was noted to be the most common mutation (37%) followed by KRAS (23%) and EGFR (19%). Patients with TP53 mutation were more likely to have concurrent EGFR (20.5% vs 13.4%, p= 0.037) and PI3KCA (10% vs 1.5%, p= 0.044) mutations. Patients with TP53 mutation were also noted to have a higher tumor mutational burden (p=0.002) but there was no difference in PDL-1 expression between the groups. The most common site of metastasis at diagnosis was brain and bones with no difference between the groups. Patients with TP53 mutation were more likely to receive immune checkpoint inhibitors (p = 0.017) however no difference was noted in other treatment modalities used in the two groups. The median progression free survival (10.6 vs 19 months, p $<$0.001) and overall survival (19.1 months vs 30.2, p = 0.019) for patients with mutated TP53 was significantly worse than wild type TP53. Patients with mutated TP53 had a significantly higher unadjusted hazard of mortality (HR = 1.70, 95% CI: 1.10 – 2.61) compared to those with wild type TP53. In adjusted analysis, patients with mutated TP53 had 2.39 (95% CI: 1.31 – 4.37) higher hazard of mortality after controlling for all other factors. **Conclusions:** TP53 is one of the most commonly found mutations in metastatic NSCLC. Although there was no difference in metastasis to brain and bones and despite being more likely to have received immune checkpoint inhibitors, patients with TP53 mutations had significantly worse prognosis as compared to patients with wild type TP53. In clinical trials presence of TP53 mutation should be reported as it may influence outcomes irrespective of the treatment. Research Sponsor: None.